NCCPC The National Collaborating Centre for Primary Care

Medicines Adherence: involving patients in decisions about prescribed medicines and supporting adherence

Full Guideline

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National Collaborating Centre for Primary Care

RCGP Royal College of General Practitioners

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Nunes V, Neilson J, O'Flynn N, Calvert N, Kuntze S, Smithson H, Benson J, Blair J, Bowser A, Clyne W, Crome P, Haddad P, Hemingway S, Horne R, Johnson S, Kelly S, Packham B, Patel M, Steel J (2009). Clinical Guidelines and Evidence Review for Medicines Adherence: involving patients in decisions about prescribed medicines and supporting adherence. London: National Collaborating Centre for Primary Care and Royal College of General Practitioners.

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Preface

The prescription of medicines is a core element of the delivery of modern health care. Medicines are widely used not only to relieve symptoms and cure conditions but to prevent ill health in the future. Medical advances, combined with an ageing population, have resulted in many patients taking multiple medicines in complex regimes. There is an increasing number and diversity of healthcare professionals involving in prescribing, dispensing or reviewing medicines. Prescribing was once the preserve of the medical profession but prescribing rights are now available to other health professionals either as independent or supplementary prescribers.

Medicine-taking is a complex human behaviour and patients evaluate medicines, and the risks and benefits of medicines using the resources available to them. Unwanted and unused medicines reflect inadequate communication between professionals and patients - about health problems and how they might be treated, and about patients' ongoing assessment and experience of treatments. This guideline will be of help to all healthcare professionals by providing guidance on how to involve patients in the decision to prescribe medicines and on how to support patients in their subsequent use of medicines. The recommendations include advice to healthcare professionals to ensure there are robust mechanisms to ensure communication between the many professionals who may be involved in each patient's care.

The guideline has been developed using standard NICE methodology. Patient involvement and adherence are central to medicine –taking yet these areas are less well researched than medicines themselves. The guideline development process has highlighted the areas in which evidence is lacking and the Guideline Development Group has indicated those areas they consider high priority for research at the end of the guideline. Developing recommendations from the evidence might have been difficult if not for the commitment and expertise of the Guideline Development Group. I am

extremely grateful to them for the good humour and skill they brought to their task.

Norma O' Flynn
Clinical Director,
National Collaborating Centre for Primary Care

Introduction

The prescription of medicines is central to medical care and drug costs amount to around 10% of NHS expenditure. In 2006-2007, the NHS in England spent £10.6billion on drugs, around three quarters of which was in primary care. It is thought that between a half and third of all medicines prescribed for long term conditions are not taken as recommended [1]. The estimated drug cost of unused or unwanted medicines in the NHS is around £100million annually [2].

A Cochrane review "Interventions for enhancing medication adherence" [3] concluded that improving medicines taking may have a far greater impact on clinical outcomes than an improvement in treatments.

If the prescription was appropriate then this may represent a loss not just for patients but also for the healthcare system and society. The costs are both personal and economic. Non adherence may limit the benefits of medicines resulting in lack of improvement or deterioration in health. The economic costs are not limited to wasted medicines but also include the knock-costs arising from increased demands for healthcare if health deteriorates.

Adherence is defined as 'the extent to which the patient's behaviour matches agreed recommendations from the prescriber'. Adherence shifts the balance between professional and patient to suggest there should be agreement between professional and patient about the prescriber's recommendation.

Nonadherence is a large problem but it should not be seen as the patient's problem. Rather, it represents a limitation in the delivery of healthcare, often due to a failure to fully agree the prescription in the first place or to identify and provide the support that patients need later on.

Addressing nonadherence is not about getting patients to take more medicines per se. It starts with an understanding of patients' perspectives of medicines and the reasons why they may not want or are unable to use them [4 5]. Practitioners have a duty to help patients make informed decisions about treatment and use appropriately prescribed medicines to best effect.

There are many causes of nonadherence but they fall into two overlapping categories: intentional and unintentional. Unintentional nonadherence occurs when the patient wants to follow the agreed treatment but is prevented from doing so by barriers that are beyond their control. Examples include poor recall or comprehension of instructions, difficulties in administering the treatment, inability to pay for the treatment or simply forgetting to take it. Unintentional nonadherence is related to limitations in the persons' capacity and resources affecting their ability to implement their intention to adhere. Intentional nonadherence occurs when the person decides not to follow the treatment recommendations.

This guideline provides recommendations on the process of involving patients in decisions about medicines and on supporting the patient in their adherence to medicine. We have not made separate recommendations for carers and families. The principal relationship is between patient and healthcare professional and the patient has a right to decide who should be involved in their care. With patient consent, carers should have access to appropriate levels of information and support.

There are an increasing number of healthcare professionals now involved in prescribing of medicines, dispensing and reviewing of medicines. It is not within the remit of a guideline to recommend which healthcare professional carries out these roles. Healthcare professionals need to be aware of and work within legal and professional codes.

Patient-Centered Care

This guideline offers best practice advice on how to involve patients in decisions about prescribed medicines and how to support adherence.

All NICE clinical guidelines state that treatment and care should take into account patients' needs and preferences and patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. Good communication between healthcare professionals and patients is essential. It should be supported by evidence-based written information tailored to each patient's needs.

If the patient agrees, families and carers should also have the opportunity to be involved in decisions about treatment and care. Families and carers should be given the information and support they need.

If patients do not have the capacity to make decisions, healthcare professionals should follow the Department of Health guidelines – 'Reference guide to consent for examination or treatment' (2001) (available from www.dh.gov.uk). Healthcare professionals should also follow the code of practice that accompanies the Mental Capacity Act (summary available from www.publicguardian.gov.uk).

Key principles

- Healthcare professionals should adapt their consultation style to the needs of individual patients so that all patients have the opportunity to be involved in decisions about their medicines at the level they wish.
- Establish the most effective way of communicating with each patient and, if necessary, consider ways of making information accessible and understandable (for example, using pictures, symbols, large print, different languages, an interpreter or a patient advocate).
- Offer all patients the opportunity to be involved in making decisions about prescribed medicines. Establish what level of involvement in decision-making the patient would like.
- Be aware that increasing patient involvement may mean that the patient decides not to take or to stop taking a medicine. If in the healthcare professional's view this could have an adverse effect, then the information provided to the patient on risks and benefits and the patient's decision should be recorded.
- Accept that the patient has the right to decide not to take a medicine, even if you do not agree with the decision, as long as the patient has the capacity to make an informed decision and has been provided with the information needed to make such a decision.
- Be aware that patients' concerns about medicines, and whether they believe they need them, affect how and whether they take their prescribed medicines.
- Offer patients information that is relevant to their condition, possible treatments and personal circumstances, and that is easy to understand and free from jargon.
- Recognise that non-adherence is common and that most patients are non-adherent sometimes. Routinely assess adherence in a non-judgemental way whenever you prescribe, dispense and review medicines.

- Be aware that although adherence can be improved, no specific intervention can be recommended for all patients. Tailor any intervention to increase adherence to the specific difficulties with adherence the patient is experiencing.
- Review patient knowledge, understanding and concerns about medicines, and a patient's view of their need for medicine at intervals agreed with the patient, because these may change over time. Offer repeat information and review to patients, especially when treating long-term conditions with multiple medicines.

1 Guidance

The following guidance is based on the best available evidence. These recommendations apply to all healthcare professionals who prescribe or dispense medicines or who have a role in making decisions about medicines with patients. Healthcare professionals are reminded of their duty under the Disability Discrimination Act (2005) to make reasonable adjustments to ensure that all people have the same opportunity for health.

1.1 Recommendations

Patient involvement in decisions about medicines

Communication

Good communication between healthcare professionals and patients is needed for involvement of patients in decisions about medicines and for supporting adherence. Some patients may find it easier to communicate with their healthcare professional than others.

1.1.1 Healthcare professionals should adapt their consultation style to the needs of individual patients so that all patients have the opportunity to be involved in decisions about their medicines at the level they wish.

1.1.2 Consider any factors such as physical or learning disabilities, sight or hearing problems and difficulties with reading or speaking English, which may affect the patient's involvement in the consultation.

1.1.3 Establish the most effective way of communicating with each patient and, if necessary, consider ways of making information accessible and understandable (for example, using pictures, symbols, large print, different languages, an interpreter or a patient advocate).

1.1.4 Encourage patients to ask about their condition and treatment.

1.1.5 Ask patients open ended questions because these are more likely to uncover patients' concerns.

1.1.6 Be aware that the consultation skills needed for increasing patient involvement can be improved.

Increasing patient involvement

Patient involvement in the decision making process requires that healthcare professionals acknowledge patients' views about their condition and its treatment, and that both healthcare professional and patient have a role in making decisions about treatment. Simple interventions to increase patient involvement do not necessarily increase the overall length of consultation and may be justified by benefits, particularly over the course of a long term condition.

1.1.7 Offer all patients the opportunity to be involved in making decisions about prescribed medicines. Establish what level of involvement in decision making the patient would like.

1.1.8 Discuss with the patient why they might benefit from the treatment. Clearly explain the disease or condition and how the medicine will influence this.

1.1.9 Explain the medical aims of the treatment to patients and openly discuss the pros and cons of proposed medicines. The discussion should be at the level preferred by the patient.

1.1.10 Clarify what the patient hopes the treatment will achieve.

1.1.11 Avoid making assumptions about patient preferences about treatment. Talk to the patient to find out their preferences, and note any non verbal cues that may indicate you need to explore the patient’s perspective further.

1.1.12 Healthcare professionals have a duty to help patients to make decisions about their treatment based on an understanding of the likely benefits and risks rather than on misconceptions.

1.1.13 Accept that patients may have different views from healthcare professionals about the balance of risks, benefits and side effects of medicines.

1.1.14 Be aware that increasing patient involvement may mean that the patient decides not to take or to stop taking a medicine. If in the healthcare professional’s view this could have an adverse effect, then the information provided to the patient on risks and benefits and the patient's decision should be recorded.

1.1.15 Accept that the patient has the right to decide not to take a medicine, even if you do not agree with the decision, as long as the patient has the capacity to make an informed decision and has been provided with the information needed to make such a decision.

1.1.16 Assess the patient's capacity to make each decision using the principles in the Mental Capacity Act (2005) (www.opsi.gov.uk/ACTS/acts2005/ukpga_20050009_en_1). To lack capacity patients must: (a) have an impairment of or disturbance or malfunction of brain and mind, and (b) demonstrate lack of capacity to:

- understand the information relevant to the decision
- retain information for long enough to use it in the decision
- use or weigh information as part of the process of making the decision
- communicate the decision (whether by talking, using sign language or any other means).

1.1.17 If the patient has specific concerns, record a summary of the discussion, because this may be helpful in future consultations.

1.1.18 Encourage and support patients, families and carers to keep an up to date list of all medicines the patient is taking. The list should include the names and dosages of prescription and non prescription medicines and herbal and nutritional supplements. If the patient has any allergic or adverse reactions to medicines, these should be noted.

Understanding the patient's knowledge, beliefs and concerns about medicines

There is evidence that patients make decisions about medicines based on their understanding of their condition and the possible treatments, their view of their own need for the medicine and their concerns about the medicine.

1.1.19 Be aware that patients' concerns about medicines, and whether they believe they need them, affect how and whether they take their prescribed medicines.

1.1.20 Ask patients what they know, believe and understand about medicines before prescribing new treatments and when reviewing medicines.

1.1.21 Ask if the patient has any specific concerns about their medicines, whenever you prescribe, dispense or review medicines. These may include concerns about becoming dependent on medicines and concerns about adverse effects. Address these concerns.

1.1.22 Be aware that patients may wish to minimise how much medicine they take.

1.1.23 Be aware that patients may wish to discuss:

- what will happen if they do not take the medicine suggested by their healthcare professional
- non pharmacological alternatives to medicines
- how to reduce and stop medicines they may have been taking for a long time, particularly those known to be associated with withdrawal symptoms
- how to fit taking the medicine into their daily routine
- how to make a choice between medicines if they believe they are taking too many medicines.

Providing information

Patients need information about their condition and possible treatments if

they are to be involved in making informed decisions about medicines. The format and content of the information provided should meet the needs of individual patients.

1.1.24 Offer patients information about medicines before the medicines are prescribed.

1.1.25 Offer patients information that is relevant to their condition, possible treatments and personal circumstances, and that is easy to understand and free from jargon.

1.1.26 Check that patients have any information they wish about medicines when the medicines are dispensed.

1.1.27 Discuss information on medicines with the patient rather than just presenting it. The discussion should take into account what the patient understands and believes about the condition and treatment.

1.1.28 Do not assume that the patient information leaflets (PILs) that patients receive with their medicines will meet each patient's needs. Address concerns that patients may have after reading the standard PILs.

1.1.29 Patients differ in the type and amount of information they need and want. Therefore the provision of information should be individualised and is likely to include, but not be limited to:

- what the medicine is
- how the medicine is likely to affect their condition (that is, its benefits)
- likely or significant adverse effects and what to do if they think they are experiencing them
- how to use the medicine

- what to do if they miss a dose
- whether further courses of the medicine will be needed after the first prescription
- how to get further supplies of medicines.

1.1.30 Be careful not to make assumptions about a patient's ability to understand the information provided. Check with the patient that they have understood the information. Information for patients should be clear and logical and, if possible, tailored to the needs of the individual patient.

1.1.31 Suggest where patients might find reliable information and support after the consultation: for example, by providing written information or directing them to other resources (for example, NHS Choices [www.nhs.uk]).

1.1.32 Provide inpatients with the same information as patients in other settings. Information should include:

- what the medicine is
- how the medicine is likely to affect their condition (that is, its benefits)
- likely or significant adverse effects and what to do if they think they are experiencing them
- how to use the medicine
- what to do if they miss a dose
- whether further courses of the medicine will be needed after the first prescription
- how to get further supply after discharge.

Supporting adherence

Assessing adherence

Patients do not always take their medicines exactly as prescribed, and healthcare professionals are often unaware of how patients take their medicines. The purpose of assessing adherence is not to monitor patients but rather to find out whether patients need more information and support.

1.2.1 Recognise that non adherence is common and that most patients are non adherent sometimes. Routinely assess adherence in a non judgemental way whenever you prescribe, dispense and review medicines.

1.2.2 Consider assessing non adherence by asking the patient if they have missed any doses of medicine recently. Make it easier for them to report non adherence by:

- asking the question in a way that does not apportion blame
- explaining why you are asking the question
- mentioning a specific time period such as ‘in the past week’
- asking about medicine-taking behaviours such as reducing the dose, stopping and starting medicines.

1.2.3 Consider using records of prescription re ordering, pharmacy patient medication records and return of unused medicines to identify potential non adherence and patients needing additional support.

Interventions to increase adherence

Patients may need support to help them make the most effective use of their medicines. This support may take the form of further information and discussion, or involve practical changes to the type of medicine or the regimen. Any interventions to support adherence should be considered on a

case by case basis and should address the concerns and needs of individual patients.

1.2.4 If a patient is not taking their medicines, discuss with them whether this is because of beliefs and concerns or problems about the medicines (intentional non adherence) or because of practical problems (unintentional non adherence).

1.2.5 Be aware that although adherence can be improved, no specific intervention can be recommended for all patients. Tailor any intervention to increase adherence to the specific difficulties with adherence the patient is experiencing.

1.2.6 Find out what form of support the patient would prefer to increase their adherence to medicines. Together, you and your patient should consider options for support.

1.2.7 Address any beliefs and concerns that patients have that result in reduced adherence.

1.2.8 Because evidence supporting interventions to increase adherence is inconclusive, only use interventions to overcome practical problems associated with non adherence if a specific need is identified. Target the intervention to the need. Interventions might include:

- suggesting that patients record their medicine taking
- encouraging patients to monitor their condition
- simplifying the dosing regimen
- using alternative packaging for the medicine
- using a multi compartment medicines system.

1.2.9 Side effects can be a problem for some patients. If this is the case you should:

- discuss how the patient would like to deal with side effects

- discuss the benefits, side effects and long term effects with the patient to allow them to make an informed choice
- consider adjusting the dosage
- consider switching to another medicine with a different risk of side effects
- consider what other strategies might be used (for example, timing of medicines).

1.2.10 Ask patients if prescriptions charges are a problem for them. If they are, consider possible options to reduce costs.

Reviewing medicines

Patients may use medicines long term. The initial decision to prescribe medicines, the patient's experience of using the medicines and the patient's needs for adherence support should be reviewed regularly. The patient's own list of medicines may be a useful aid in a medicines review.

1.3.1 Review patient knowledge, understanding and concerns about medicines, and a patient's view of their need for medicine at intervals agreed with the patient, because these may change over time. Offer repeat information and review to patients, especially when treating long term conditions with multiple medicines.

1.3.2 Review at regular intervals the decision to prescribe medicines, according to patient choice and need.

1.3.3 Enquire about adherence when reviewing medicines. If non adherence is identified, clarify possible causes and agree any action with the patient. Any plan should include a date for a follow up review.

1.3.4 Be aware that patients sometimes evaluate prescribed medicines using their own criteria such as their understanding of their condition or the symptoms most troubling to them. They may, for example, stop and start the

medicine or alter the dose and check how this affects their symptoms. Ask the patient whether they have done this.

Communication between healthcare professionals

Patients may be under the care of healthcare professionals from different disciplines and specialties at the same time; responsibility for patients' care may be transferred between healthcare professionals, and medicines reviews may be carried out by healthcare professionals other than the prescriber. Therefore good communication between healthcare professionals is required to ensure that fragmentation of care does not occur.

1.4.1 Healthcare professionals involved in prescribing, dispensing or reviewing medicines should ensure that there are robust processes for communicating with other healthcare professionals involved in the patient's care.

1.4.2 On transfer between services (for example, between hospitals and care homes or on discharge from hospital), give all patients and subsequent healthcare or other providers a written report containing:

- the patient's diagnosis
- a list of all medicines the patient should be taking
- clear identification of any new medicines that were started
- clear identification of any medicines that were stopped, with reasons
- clear information on which medicines should be continued after transfer from that service and for how long
- any known adverse reactions and allergies the patient has experienced
- any potential difficulties with adherence and any actions taken (for example, provision of a multi compartment medicines system).

1.4.3 Healthcare professionals involved in reviewing medicines should inform the prescriber of the review and its outcome. This is particularly important if

the review involves discussion of difficulties with adherence and further review is necessary.

1.2 Aim of the guideline

Clinical guidelines are defined as 'systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances.'

This guideline gives recommendations to clinicians and others on how to involve adults and carers in decisions about prescribed medicine.

1.3 How the guideline is set out

Both the evidence statements and narratives of the research studies on which our recommendations are based are found within each topic section. The evidence statements precede the narrative for each topic. Also included in each chapter is a brief explanation of why the GDG made the specific recommendations. The evidence tables with details of the research studies that describe the studies reviewed are found in Appendix C.

1.4 Scope

The guideline was developed in accordance with a scope given by the National Institute for Health and Clinical Excellence (NICE, 'the Institute'). The scope set the remit of the guideline and specified those aspects of the identification and management of medicines adherence to be included and excluded. The scope was published in April 2007 and is reproduced here in Appendix A.

During development the guideline title was Medicines Concordance. Stakeholder comment during consultation indicated that retaining the term concordance in the title was potentially misleading and unhelpful to healthcare professionals. NICE Guidance Executive agreed to the title Medicines Adherence: involving patients in decisions about prescribed medicines and supporting adherence as this more clearly explains the content of the guideline.

Whom the guideline is intended for

This guideline is of relevance to those who work in or use the National Health Service (NHS) in England and Wales:

Population

Groups that will be covered

a) Adults, including those with co morbidities, learning disabilities or language and/or cultural differences.

Groups that will not be covered

Children and young people. However, the guideline recommendations may be considered for a child or young person who is deemed competent to express a view on their prescription.

Healthcare setting

All consultations with healthcare professionals in any NHS setting that relate to the initiation or review of prescribed medicine.

Areas that will be covered

a) Shared decision-making about medicines and medicine-taking as reported by the patient or carer. The guideline will focus on the barriers (such as communication difficulties, cultural issues, low health literacy and physical limitations), facilitators (including structural or procedural factors), beliefs and health behaviours that influence decision-making and adherence.

b) Shared decision-making about medicines and medicine-taking as reported by the healthcare professional. The guideline will focus on the barriers (such as communication difficulties, cultural issues and time), facilitators (including structural or procedural factors), beliefs and health behaviours that influence decision-making and adherence.

c) The effectiveness and cost-effectiveness of interventions to facilitate the process of shared decision-making about medicines (looking at time of intervention – before, during, or after the consultation with the healthcare

professional; and mode of delivery). The target of the intervention may be the patient, the carer, the prescriber, any healthcare professional providing ongoing support or a combination of these.

d) The effectiveness and cost-effectiveness of interventions to promote adherence in medicine-taking (looking at time of intervention – before, during, or after the consultation with the healthcare professional; and mode of delivery). The target of the intervention may be the patient, the carer, the prescriber, the dispenser or any other healthcare professional providing ongoing support or a combination of these.

e) The evidence on single or multiple medicines as it relates to issues around decision-making and adherence.

f) The skills and competencies required by prescribers to involve patient in decisions regarding prescribed medicines.

Areas outside the remit of the guideline

The administration of medicines will not be covered. Administration is defined as giving a medicine by introduction into the body (for example, orally or by injection), or by external application (for example application of an impregnated dressing).

1.5 Guideline Limitations

Guideline limitations are as follows:

- NICE clinical guidelines usually do not cover issues of service delivery, organisation or provision (unless specified in the remit from the Department of Health).
- NICE is primarily concerned with health services and so recommendations are not provided for social services and the voluntary sector. However, the guideline may address important issues in how NHS clinicians interface with these sectors.

- Generally, the guideline does not cover rare, complex, complicated or unusual conditions.
- It is not possible in the development of a clinical guideline to complete extensive systematic literature reviews of all pharmacological toxicity. NICE expects the guidelines to be read alongside the summaries of product characteristics.

1.6 Responsibility and support for guideline development

1.6.1 The National Collaborating Centre for Primary Care (NCC-PC)

The NCC-PC is a partnership of primary care professional associations and was formed as a collaborating centre to develop guidelines under contract to NICE. It is entirely funded by NICE. The NCC-PC is contracted to develop four guidelines at any one time, although there is some overlap at start and finish. Unlike many of the other centres which focus on a particular clinical area, the NCC-PC has a broad range of topics relevant to primary care. However, it does not develop guidelines exclusively for primary care. Each guideline may, depending on the scope, provide guidance to other health sectors in addition to primary care.

The Royal College of General Practitioners (RCGP) acts as the host organisation. The Royal Pharmaceutical Society and the Community Practitioners and Health Visitors' Association are partner members with representation from other professional and lay bodies on the Board. The RCGP holds the contract with the Institute for the NCC-PC.

1.6.2 The development team

The development team had the responsibility for this guideline throughout its development. They were responsible for preparing information for the Guideline Development Group (GDG), for drafting the guideline and for responding to consultation comments. The development team working on this guideline consisted of the:

- **Guideline lead**
  who is a senior member of the NCC-PC team who has overall responsibility for the guideline
- **Information scientist**
  who searched the bibliographic databases for evidence to answer the questions posed by the GDG
- **Reviewer (Health Services Research Fellow**)
  with knowledge of the field, who appraised the literature and abstracted and distilled the relevant evidence for the GDG
- **Health economist**
  who reviewed the economic evidence and assisted the GDG in considering cost-effectiveness
- **Project manager**
  who was responsible for organising and planning the development, for meetings and minutes and for liaising with the Institute and external bodies
- **Chair**
  who was responsible for chairing and facilitating the working of the GDG meetings

The members of the development team attended the GDG meetings and participated in them. The development team also met regularly with the Chair of the GDG during the development of the guideline to review progress and plan work.

Other guidelines normally have a Clinical Advisor who is someone with an academic understanding of the research in the area and its practical implications to the service, who advises the development team on searches and the interpretation of the literature. Due to the conceptual nature of the guideline topic and the different academic stances on explaining such behaviour, the development team chose not to have a formal Clinical Advisor.

1.6.3 The Guideline Development Group (GDG)

A Chair was chosen for the group and his primary role was to facilitate and chair the GDG meetings.

The GDG consisted of a diverse multidisciplinary group with an interest and/or expertise in medicines adherence. The Chair, a general practitioner with special interest in epilepsy identified by the NCC-PC, oversaw the work of the group.

Nominations for group members were invited from various stakeholder organisations, selected to ensure appropriate combination of members including healthcare professionals and patient representatives.

Each GDG member was expected to act as an individual expert in their own right and not as a representative of their parent organisation, although they were encouraged to keep their nominating organisation informed of the process.

Nominees who were not selected for the GDG were invited to act as Expert Peer Reviewers and were sent drafts of the guideline by the Institute during the consultation periods and invited to submit comments using the same process as stakeholders.

In accordance with guidance from NICE, all GDG members' interests were recorded on a standard declaration form that covered consultancies, fee-paid work, share-holdings, fellowships, and support from the healthcare industry. Details of these can be seen in Appendix E.

The names of GDG members appear listed below.

Full GDG members

Dr Henry Smithson (Chair)
General Practitioner; Senior Clinical University Teacher, Academic Unit of Primary Medical Care, Sheffield

Professor Rob Horne
Professor of Behavioural Medicine, Head of Department of Practice and Policy, The School of Pharmacy, University of London

Dr John Benson
Senior Lecturer in General Practice, General Practice and Primary Care Research Unit, Department of Public Health and Primary Care, University of Cambridge

Mr Shaun Johnson
Patient representative; Mind Link National Advisory Panel; Trustee, LAMP (the Leicestershire Action for Mental Health Project)

Mrs Alison Bowser
Patient representative; independent patient advocate; patient representative for Medicines and Healthcare products Regulatory Authority, Cornwall and Isles of Scilly Primary Care Trust and Royal College of General Practitioners

Dr Mahendra Patel
Lecturer/Research Fellow, Institute of Pharmaceutical Innovation, University of Bradford

Mr Stephen Hemingway
Senior Lecturer in Mental Health, University of Huddersfield

Mrs Bunis Packham
Nurse Consultant – Thrombosis and Anticoagulation, Barnet and Chase Farm Hospitals NHS Trust

Mr Jim Blair
Senior Lecturer in Learning Disabilities, Kingston University/St George's University of London; Interim Consultant Nurse (Learning Disabilities) St George's Healthcare NHS Trust

Professor Peter Crome
Professor of Geriatric Medicine, Keele University; Honorary Consultant Geriatrician, North Staffordshire Combined Healthcare NHS Trust

Dr Peter Haddad
Consultant Psychiatrist, Greater Manchester West Mental Health NHS Foundation Trust; Honorary Senior Lecturer in Psychiatry, University of Manchester

Dr Jonathan Steel
General Practitioner, Gloucestershire; Chairman, GP Network, Royal College of Physicians

Dr Sean Kelly
Consultant Physician and Gastroenterologist, York Hospital; Honorary Senior Lecturer, Hull York Medical School

Dr Wendy Clyne
Assistant Director, Medicines Partnership Programme, NPC Plus, Keele University

National Collaborating Centre for Primary Care

Dr Norma O'Flynn
Guideline Lead and Clinical Director

Ms Elizabeth Shaw
Guideline Lead (until February 2007) and Deputy Chief Executive (until February 2008)

Ms Vanessa Nunes
Senior Health Services Research Fellow/Project Manager

Ms Julie Neilson
Health Services Research Fellow

Ms Stefanie Kuntze
Health Economist (until October 2008)

Dr Neil Calvert
Senior Health Economist

1.6.4 Guideline Development Group meetings

The GDG met on 12 occasions (with one two day GDG meeting), at approximately 2 monthly intervals over a period of 11 months and 6 weekly intervals over a period of 6 months to review the evidence identified by the project team, to comment on its quality and completeness and to develop recommendations for clinical practice based on the available evidence. The final recommendations were agreed by the full GDG.

1.7 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future.

The GDG noted the generally poor quality of research in the area of medicines adherence and the potential clinical and economic gains that would accrue from the development of cost-effective, equitable and patient-centred interventions to support adherence to appropriate prescriptions The GDG believe that there is an urgent need to provide specific adherence funding streams to support structured programmes of research particularly where the health gains from medicines adherence are likely to be high.

The central theme underpinning this guideline is that adherence to medicines taking is a variable behaviour that should be based on informed choice and shared decision making, principally between the patient and the practitioner. Medicines carry the potential for harm as well as benefit and there are questions about what constitutes good prescribing and good medicine-taking. The key research agenda therefore relates to behaviour change for practitioners and patients to support the best use of medicines.
The research recommendations from this guideline are for research programmes which are described below under the themes of A): Developing effective, equitable interventions to support adherence to appropriately prescribed medicines B) Informed choice and shared decision making, C)

Support processes: prescribing-related consultations and medicines usage review and D) Groups for special consideration- vulnerable groups.

A): Developing effective, equitable interventions to support adherence to appropriately prescribed medicines.

Research Questions

1. What are the most clinically effective and cost-effective methods for identifying and addressing the perceptual barriers (such as beliefs and concerns about medicines) which influence motivation to start and continue with treatment and the practical barriers (such as limitations in personal capacity and resources), which limit an individuals' ability to implement intentions to adhere to medicines?

Why this is important

Systematic reviews of adherence interventions show that although adherence can be improved, the effects were generally modest and there is considerable room for improvement. Few previous interventions have been systematically developed, using appropriate theoretical models, nor have they have been modelled and piloted with assessment of process variables as well as outcomes. We now know why previous interventions have failed, but also how we can improve the content, development and testing of new approaches. The challenges for research in medicines adherence are similar to those for other health-related behaviours such as smoking cessation, exercise and diet: how to influence and change behaviour. Interventions should be developed using an appropriate theoretical framework with a phased approach to testing that includes assessment of process (i.e. the things that are targeted for change) as well as outcomes and a need for an individual approach, as recommended in the Medical Research Council Framework. There are particular questions relating to vulnerable groups (see Section C). Interventions may need to address adherence when initiating treatment (for newly prescribed medicine), but also over the course of treatment through maintenance of appropriate adherence patterns, preventing sub-optimal adherence and changing sub-optimal adherence, once patterns have developed. Interventions targeted at the individual patient level are likely to be

more effective if they address both motivational factors and capacity limitations).

A systematic programme of adherence research across long-term conditions is essential to guide the delivery of recommendations for medicines use within NHS NSFs and address a fundamental inefficiency in healthcare delivery. The potential benefits are likely to include: better care tailored to patient needs, higher rates of adherence to appropriate medicines, fewer unwanted and unused prescriptions, more effective management of long-term conditions, increased patient safety and satisfaction and fewer emergency admissions.

B) Informed choice and shared decision making

Research questions:

1. What are the most clinically effective and cost-effective ways of communicating the potential benefits and risks of medicines to promote informed choice?
2. What are the strengths, weaknesses and consequences of different approaches to joint decision-making, seen from the vantage point of various stakeholders (e.g. prescribers, patients, funders)?

Why is this important?

The principles of informed choice and shared decision-making have largely been developed from theoretical and conceptual models. The competencies listed for shared decision- making consist of a number of different skills and patients have shown that they may be valued differently by different people. While the right of patients to be involved in treatment decisions is accepted, the practice of shared decision making may result in practitioners and patients playing different roles than they have to date in health care consultations. This may have implications for responsibility and accountability. Information asymmetries also need to be addressed and this may require structural changes to health services and their delivery. Patient related outcomes need to be included.

C) Support processes: prescribing-related consultations and medicines usage review

Research Questions

1. How can we enable new and existing prescribers to identify individuals at risk of nonadherence or those who are a priority for medicines review and adherence support. How can we best provide it?
2. How can practitioners and patients be supported to improve the quality of prescribing-related consultations and medicine use reviews so that they facilitate informed choice and optimal adherence to medicine?
3. How can we facilitate the open disclosure of medicine-taking behaviours within consultations relating to medicines prescribing and review? How can we equip health practitioners to respond appropriately and effectively?
4. What are the effects of non-prescriber medicine reviews (e.g. by pharmacists) on patients, prescribers and outcomes? How can the process of medicine review be enhanced or improved to address issues of informed choice and adherence?

Why this is important?

Nonadherence is often a hidden problem. Many patients are reluctant to express doubts and concerns about medicines because they fear that it will displease the practitioner. We need better methods for overcoming this problem and promoting open discussions about medicines and adherence.

There is a new and growing agenda relating to non-medical prescribers (pharmacists, nurses etc.) This is a key context issue and there are a range of questions relating to patient perspectives on new prescribers and to new and existing prescribers' perceptions and skills. The effects of new prescribers on patient adherence to medicines should be included in any research agendas designed to evaluate new prescribers. The inclusion of formal procedures for medicine review within the pharmacy contract in England provides an opportunity for improved medicine support for patients. We need a better understanding of the effects of non-prescriber medicine review on medicines

usage and outcomes and of how reviews might be improved to benefit patients and society.

D. Overarching issues Groups for special consideration, vulnerable groups

Consideration of vulnerable groups cuts across the above themes and is relevant for all research questions. Work in this area requires systematic reviews of the available literature followed by empirical studies. Specific questions are:

1. What are the effects of social disadvantage and ethnicity on informed choice, shared decision making and adherence to prescribed medicines?
2. How do the perceptions and life circumstances of different age groups (children, young adults, elderly people) influence informed choice, shared decision making and adherence. What are the implications for interventions to support these?
3. What are the particular barriers to medicines use for people with multiple pathologies (and their informal carers) and what interventions are required?

Why this is important

Perceptions of medicines and the value an individual places on sharing decisions with their practitioner have been found to differ by groups such as the elderly and severity of condition. Research into the factors and impact on adherence could inform clinicians and shape clinical care.

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1.9 Glossary

Adherence	Adherence – 'the extent to which the patient's behaviour matches agreed recommendations from the prescriber'. Adherence emphasises the need for agreement and that the patient is free to decide whether or not to adhere to the prescriber's recommendation.
Compliance	Compliance – 'the extent to which the patient's behaviour matches the prescribers' recommendations'.
Concordance	Concordance – this is a recent term whose meaning has changed. It was initially applied to the consultation process in which prescriber and patient agree therapeutic decisions that incorporate their respective views, but now includes patient support in medicine-taking as well as prescribing communication. Concordance reflects social values but does not address medicine-taking and may not lead to improved adherence
Cost-benefit analysis	A type of economic evaluation where both costs and benefits of healthcare treatment are measured in the same monetary units. If benefits exceed costs, the evaluation would recommend providing the treatment.
Cost-consequences analysis	A type of economic evaluation where various health outcomes are reported in addition to cost for each intervention, but there is no overall measure of health gain.

Cost-effectiveness analysis	An economic study design in which consequences of different interventions are measured using a single outcome, usually in 'natural' units (for example, life-years gained, deaths avoided, heart attacks avoided, cases detected). Alternative interventions are then compared in terms of additional cost per additional unit of effectiveness.
Cost-effectiveness model	An explicit mathematical framework, which is used to represent clinical decision problems and incorporate evidence from a variety of sources in order to estimate the costs and health outcomes. See also Markov model.
Cost-minimisation analysis	An economic evaluation that finds the least costly alternative therapy after the proposed interventions has been demonstrated to be no worse than its main comparator(s) in terms of effectiveness and toxicity.
Cost-utility analysis	A form of cost-effectiveness analysis in which the units of effectiveness are quality-adjusted life-years (QALYs).
Decision analysis	A systematic way of reaching decisions, based on evidence from research. This evidence is translated into probabilities, and then into diagrams or decision trees which direct the clinician through a succession of possible scenarios, actions and outcomes.
Decision problem	A clear specification of the interventions, patient populations and outcome measures and perspective adopted in an evaluation, with an explicit justification, relating these to the decision which the analysis is to inform.

Discounting	Costs and benefits incurred today have a higher value than costs and benefits occurring in the future. Discounting health benefits reflects individual preference for benefits to be experienced in the present rather than the future. Discounting costs reflects individual preference for costs to be experienced in the future rather than the present. For NICE economic evaluations, health outcomes will be discounted at 3.5% and costs at 3.5% per annum, following the recommendations of the UK Treasury.
Dispensing professional	Professional trained in dispensing medicine, generally a pharmacist or a general practitioner in a dispensing practice
Dominance	An intervention is said to be dominated if there is an alternative intervention that is both less costly and more effective. See also extended dominance.
Dosette box	A type of compliance aid. Other terms used are NOMAD, MANRAX and monitored dose system.
Economic evaluation	Comparative analysis of alternative health strategies (interventions or programmes) in terms of both their costs and consequences.
Extended dominance	An intervention is extendedly dominated when it can be dominated by a combination of two alternative interventions (i.e. if x% of the population are treated with intervention A, and y% are treated with intervention C where x + y = 100%, the overall result will be an intervention strategy that is both cheaper and more effective than intervention B). See also dominance.

Extrapolation	In data analysis, predicting the value of a parameter outside the range of observed values.
Forgiveness	The ability of a drug to sustain its pharmacological action after a dose has been missed
GDG	Guideline development group who developed the guideline
Health care professional (HCP)	Any health care professional- specialists, general practitioner, pharmacists, nurse prescribers who are involved in the prescribing of medicines, dispensing of medicines or have designated roles e.g. specialist nurses, in the discussion with patients about those medicines.
Health economics	The study of the allocation of scarce resources among alternative healthcare treatments. Health economists are concerned with both increasing the average level of health in the population and improving the distribution of healthcare resources.
Health-related quality of life	A combination of an individual's physical, mental and social well-being; not merely the absence of disease.
Informed adherence	Informed adherence refers to an outcome of informed choice in decision to take medicines and supported adherence

Incremental Cost Effectiveness Ratio (ICER)	The difference in costs between two interventions being compared divided by the difference in effects of the two interventions. For instance, if A and B are being compared, then the ICER would be calculated as Costs of B – costs of A divided by effects of B – effects of A
Life-year	A measure of health outcome that shows the number of years of remaining life expectancy.
Life-years gained	Average years of life gained per person as a result of an intervention.
Markov model	A modelling technique used when a greater number of health states needs to be considered. They are particularly useful for disease in which events can occur repeatedly over time.
Medicines	The term medicines is used in the guideline to apply to drug treatments that patients may take orally or self-administer such as creams to the skin and drops.
Medicine review	A face to face meeting between a professional and a patient to discuss the patients medicines and medicine-taking behaviour
Opportunity cost	The opportunity cost of investing in a healthcare intervention is the value of other healthcare programmes that are foregone or displaced by its introduction. This may be best measured by the health benefits that could have been achieved had the money been spent on the next best alternative healthcare intervention.
Persistence	The length of time from initiation to discontinuation of therapy. Persistence is measured in units of time.

Perspective	(or viewpoint): This determines which costs to include. For NICE evaluations the perspective is from the NHS and includes costs to the NHS and Personal Social Services. Costs to other public bodies and to patients and carers may be considered as an additional factor.
Probabilistic sensitivity analysis	Probability distributions are assigned to the uncertain parameters and are incorporated into evaluation models based on decision analytical techniques (for example, Monte Carlo simulation).
Quality adjusted life-years (QALYS)	An index of survival that is adjusted to account for the person's quality of life during this time. QALYs have the advantage of incorporating changes in both quantity (longevity/mortality) and quality (morbidity, psychological, functional, social and other factors) of life. Used to measure benefits in cost-utility analysis, QALYS are calculated by estimating the number of years of life gained from a treatment and weighting each year with a quality-of-life score between zero and one.
Shared Decision Making (SDM)	Shared-decision making (SDM) is described as a model of decision making where information exchange is a two way process in the consultation and both deliberation and decision are made by both health care professional and patient.
Specialist	One who has expertise in a particular field of medicine by virtue of additional training and experience.
Time horizon	The time span used in the NICE appraisal that reflects the period over which the main differences between interventions in health effects and use of healthcare resources are expected to be experienced, and taking into account the limitations of supportive evidence.

Unit-dose packaging	Unit-dose packaging is the packaging of a single dose in a non-reusable container.
Utility	This concept is applied in health care to mean the individual's valuation of their state of well-being deriving from the use of health care interventions. In brief, utility is a measure of the preference for, or desirability of, a specific level of health status or specific health outcome.
Willingness to pay (WTP)	WTP refers to the amount that a decision maker is willing to pay for an additional unit of outcome (e.g. an additional QALY). If the WTP is higher than the ICER, the intervention is cost effective. If not, the intervention is not cost effective.

2 Methods

2.1 Introduction

This chapter sets out in detail the methods used to generate the recommendations for clinical practice that are presented in the subsequent chapters of this guideline. The methods are in accordance with those set out by the Institute in 'The guidelines manual'. April 2007. London: National Institute for Health and Clinical Excellence. Available from: www.nice.org.uk/guidelinesmanual. *The Guideline Development Process – an overview for stakeholders, the public and the NHS* describes how organisations can become involved in the development of a guideline.

2.2 Developing key clinical questions (KCQs)

A series of key questions created from the scope was the first step in the development of the guideline. The key questions formed the starting point for the subsequent evidence reviews and facilitated the development of recommendations by the GDG.

The key questions were developed by the project team with the guidance from the GDG. Where possible, the questions were refined into specific research questions by the project teams to aid literature searching, appraisal and synthesis. However, due to the generic nature of the guideline, full PICO parameters were not applicable to the developed research questions. The full list of key questions is shown in appendix B.

Reviews of the evidence using systematic methods relating to searching and appraisal were conducted to answer the clinical questions in line with The guidelines manual. The GDG and development teams agreed appropriate inclusion and exclusion criteria for each topic area in accordance with the scope.

2.3 Literature search strategy

2.3.1 Scoping search

An initial scoping search for published guidelines, systematic reviews, economic evaluations and ongoing research was carried out on the following databases or websites: National Library for Health (NLH) Guidelines Finder, National Guidelines Clearinghouse, Scottish Intercollegiate Guidelines Network (SIGN), Guidelines International Network (GIN), Canadian Medical Association (CMA) Infobase (Canadian guidelines), National Health and Medical Research Council (NHMRC) Clinical Practice Guidelines (Australian Guidelines), New Zealand Guidelines Group, BMJ Clinical Evidence, Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE) and Heath Technology Assessment Database (HTA), NHS Economic Evaluations Database (NHSEED) National Research Register and Current Controlled Trials.

2.3.2 Evidence review for guideline development

The aim of the evidence review was to identify the most relevant, published evidence in relation to the key clinical questions generated by the GDG. Reviews of the evidence using systematic methods relating to searching and appraisal of the evidence were conducted.

The following bibliographic databases were searched from their inception to the latest date available: Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE), Health Technology Database (HTA), MEDLINE, EMBASE, CINAHL, AMED (Allied and Complementary Medicine Database), CENTRAL (Cochrane Controlled Trials Register). When appropriate to the question PsycINFO was also searched.

The search strategies were developed in MEDLINE and then adapted for searching in other bibliographic databases. Systematic reviews and randomised controlled trials were searched for using methodological search filters designed to limit searches to these study designs. These were devised

by the Centre for Reviews and Dissemination and the Cochrane Collaboration. The economic literature was identified by conducting searches in NHS Economic Evaluations Database (NHSEED) and in MEDLINE and EMBASE using an economics search strategy developed by ScHARR at the University of Sheffield.

Databases of the results of the searches for each question or topic area were created using the bibliographic management software Reference Manager.

The search strategies for all questions or topic areas developed for the Medline database are detailed in appendix B. Details of all literature searches for the evidence reviews are available from the NCC-PC. Further references were also suggested by the GDG.

2.3.3 How the evidence reviews were conducted

The research literature relating to shared decision-making and adherence is complex and overlapping. It was decided that individual literature searches for each clinical question would result in a duplication of work as the retrieved evidence would potentially overlap from question to question. Very focused searches would also be likely to miss relevant literature as terminology is not standardised. Broad searches were therefore undertaken to produce evidence reviews on each of the following key topics:

- Shared decision-making in the context of prescribed medicine.
- Barriers to shared decision-making and adherence in the context of prescribed medicine.
- Interventions to enhance adherence in the context of prescribed medicine.

The retrieved evidence was then sifted and allocated to the relevant clinical question.

Additional focused literature searches were undertaken for some of the key clinical questions. The GDG viewed the questions as important in clinical practice and wished to ensure that no important study had been missed out. These were:

- What tools are available to help elicit patients' information needs about medicines?
- What tools are available to help elicit patients' beliefs about medicines?
- How can a practitioner detect whether a patient agrees/disagrees with recommendation to take medicines?
- How can practitioners elicit patient's preferences for involvement in decisions about medicines?
- Do interventions to increase patient involvement increase length of the consultation?
- Does change in dosing regime affect adherence?
- Does medicine formulation/packaging affect adherence?
- What is the effect of prescription charges/costs on adherence to prescribed medicine?
- How can practitioners assess adherence?
- Do medicine reviews increase adherence to prescribed medicine?
- Does the use of multi-compartment medicine systems increase adherence to prescribed medicine? [see chapter 8 for more detail on this question]*

*This review was originally titled 'does the use of dosette boxes increase adherence to prescribed medicine'. The evidence search using a variety of terms returned no studies. After consultation it was brought to our attention that devices like dosette boxes may be classified under different headings and that some researchers label them as 'reminders' or as 'packaging'. We therefore re-examined the papers included in the packaging review and reminder reviews and extracted those relevant to dosette-type devices. The review by Heneghan (2006) and some RCTs/systematic reviews which had been incorrectly placed with the packaging and reminder questions are now relocated to the question. These we have termed multi-compartment medicine systems although there is no agreed term in the published literature. The original search terms matched the terms needed for this restructured

multi-compartment medicine system question. For example the search terminology included ‘dosette’, ‘nomad’ or ‘manrax’ ‘monitored dosage system’ and ‘compliance aid’.

The specific search strategy for each topic area varied and was agreed with the development team (with input from the GDG as necessary). The review parameters were agreed with the GDG and aimed to provide the best available evidence. For further details on the methodology and inclusion/exclusion criteria please see individual evidence reviews.
The literature on barriers to shared decision-making and medicine taking, shared decision-making and adherence to medicine is not well indexed, therefore, despite the comprehensive and detailed searches, some trials that met our criteria may have been missed.

In line with NICE Equality scheme additional searches of the literature were undertaken to ensure that general searches had located all evidence relevant to vulnerable groups in the United Kingdom[1].

2.4 Identifying the evidence

After the search of titles and abstracts was undertaken, full papers were obtained if they appeared to address the key clinical question. The highest level of evidence was sought. However, other types of quantitative evidence, qualitative evidence and expert formal consensus results were used when randomised controlled trials were not available. Only English language papers were reviewed. Following a critical review of the full text paper, articles not relevant to the subject in question were excluded. Studies that did not report on relevant outcomes were also excluded.

2.5 Critical appraisal of the evidence

From the papers retrieved, the Senior Health Services Research Fellow (SHSRF) and the Health Service Research Fellow (HSRF) synthesized the evidence for each question or questions into a narrative summary. These form the basis of this guideline. Each study was critically appraised using the

[1] www.nice.org.uk/aboutnice/howwework/NICEEqualityScheme.jsp

Institute's criteria for quality assessment and the information extracted for included studies is given in Appendix C. The content and delivery of interventions was poorly defined in many studies and it was difficult to decide which studies should be included or excluded. The GDG advised on which studies to include and exclude in these circumstances. Background papers, for example those used to describe the concepts used in the guideline, were referenced but not extracted.

2.5.1 Choice of outcomes

When agreeing key clinical questions the GDG discussed the choice of outcomes for each search. A variety of outcomes are currently found in studies on shared decision-making but the outcomes primarily looked at were patient preferences, identification of beliefs and patient agreement to the decision. Any additional information on factors which may have influenced the study results and had an impact on the wider implementation of an intervention, such as participants' age, ethnicity or social status; dropout rates and payments or rewards given to participants, were recorded in the evidence tables considered by the GDG. The primary outcome measure for all the evidence reviews on interventions to increase adherence was adherence. Adherence levels were the outcome also for studies examining medicine review.

2.6 Health Economics methods

Economic evaluation provides a formal comparison of benefits and harms as well as the costs of alternative health programmes. It helps to identify, measure, value and compare costs and consequences of alternative treatment options. These outcomes are usually synthesised in cost-effectiveness (CEA) or cost utility analysis (CUA), which reflect the principle of opportunity costs. For example, if a particular treatment strategy were found to yield little health gain relative to the resources used, then it could be advantageous to re-deploy resources to other activities that yield greater health gain.

To assess the cost-effectiveness of interventions to increase adherence (interventions to increase adherence), we conducted a comprehensive systematic review of the economic literature relating to medicines and nonadherence.

In accordance with the NICE social value judgement the primary criteria applied for an intervention to be considered cost effective were either:

a) The intervention dominated other relevant strategies (that is it is both less costly in terms of resource use and more clinically effective compared with the other relevant alternative strategies); or

b) The intervention cost less than £ 20,000 per quality-adjusted life-year (QALY) gained compared with the next best strategy (or usual care).

2.6.1 Health Economic evidence review methodology

The following information sources were searched:

- Medline (Ovid) (1966-June 2006)
- Embase (1980-June 2006)
- NHS Economic Evaluations Database (NHS EED)
- PsycINFO
- Cumulative Index to Nursing and Allied Health Literature (CINAHL)

The electronic search strategies were developed in Medline and adapted for use with the other information databases. The clinical search strategy was supplemented with economic search terms. Titles and abstracts retrieved were subjected to an inclusion/exclusion criterion and relevant papers were ordered. No criteria for study design were imposed a priori. In this way the searches were not constrained to randomised controlled trials (RCTs) containing formal economic evaluations. Papers included were:

- Full/partial economic evaluations

- Considered patients over 16 years of age
- Written in English, and reported health economic information that could be generalised to UK.

The full papers were critically appraised by a health economist using a standard validated checklist. A general descriptive overview of the studies, their quality, and conclusions was presented and summarised in the form of a narrative review.

Each study was categorised as one of the following types of full economic evaluation: cost-effectiveness analysis, cost-utility analysis (i.e. cost-effectiveness analysis with effectiveness measured in terms of QALYs gained) or cost-minimisation analysis. Other studies which did not provide an overall measure of health gain or attempt to synthesise costs and benefits were categorised as 'cost-consequence analysis.' Such studies were considered partial economic evaluations.

2.6.2 Cost-effectiveness modelling methods

De novo modelling was considered for aspects of medicine taking. However, due to heterogeneity in the population covered by this guideline this was not possible. This is discussed in more detail in Chapter 10.

2.7 Forming recommendations

In preparation for each meeting, the narrative and extractions for the questions being discussed were made available to the GDG one week before the scheduled GDG meeting. These documents were available on a closed intranet site and sent by post to those members who requested it.

GDG members were expected to have read the narratives and extractions before attending each meeting. The GDG discussed the evidence at the meeting and agreed evidence statements and recommendations. Any changes were made to the electronic version of the text on a laptop and projected onto a screen until the GDG were satisfied with these.

All work from the meetings was posted on the closed intranet site following the meeting as a matter of record and for referral by the GDG members.

2.8 Areas without evidence and consensus methodology

The table of clinical questions in Appendix B indicates which questions were searched.

In cases where evidence was sparse, the GDG derived the recommendations via informal consensus methods, using extrapolated evidence where appropriate. All details of how the recommendations were derived can be seen in the 'Evidence to recommendations' section of each of the chapters.

2.9 Update

Literature searches were repeated for the initial evidence-based questions at the end of the GDG development process allowing any relevant papers published up until June 2008 to be considered. Only those studies where recommendations needed substantial revisions were added in detail. Future guideline updates will consider evidence published after this cut-off date.

Two years after publication of the guideline, NICE will ask the National Collaborating Centre to determine whether the evidence base has progressed significantly to alter the guideline recommendations and warrant an early update. If not, the guideline will be considered for update approximately four years after publication

2.10 Consultation

The guideline has been developed in accordance with the Institute's guideline development process. This has included allowing registered stakeholders the opportunity to comment on the scope of the guideline and the draft of the full and short form guideline. In addition, the draft was reviewed by an independent Guideline Review Panel (GRP) established by the Institute.

The comments made by the stakeholders, peer reviewers and the GRP were collated and presented for consideration by the GDG. All comments were

considered systematically by the GDG and the development team recorded the agreed responses.

2.11 Relationships between the guideline and other national guidance

2.11.1 National Service Frameworks

The National Service Framework for Older People (2001) makes specific recommendations for medicine review in older people.

2.11.2 Related NICE Guidance

This guideline differs from most NICE guidelines in that it is not condition specific but makes recommendations on how to involve patients in decisions about medicines. This guidance should be used in conjunction with condition specific NICE guidance which makes recommendations on what treatments are clinically and cost effective.

NICE and the National Patient Safety Agency (NPSA) have recently produced joint guidance on medicines reconciliation when adult patients are admitted to hospital (www.NICE.org.uk/PSG001).

2.11.3 Other national guidance

In formulating recommendations consideration was given to

- *Report of the Committee on Safety of Medicines Working Group on Patient Information' (2005)*
- General Medical Council document, Consent: doctors and patients making decision together. http://www.gmc-uk.org/news/articles/Consent_guidance.pdf
- Mental Capacity Act 2005 http://www.opsi.gov.uk/ACTS/acts2005/pdf/ukpga_20050009_en.pdf
- Disability Discrimination Act 1995 http://www.opsi.gov.uk/acts/acts1995/plain/ukpga_19950050_en_1

Through review of published guidance, personal contact and commenting on guideline scope, endeavours were made to ensure that boundaries between guidance were clear and advice was consistent.

2.12 Disclaimer

Healthcare providers need to use clinical judgement, knowledge and expertise when deciding whether it is appropriate to apply guidelines. The recommendations cited here are a guide and may not be appropriate for use in all situations. The decision to adopt any of the recommendations cited here must be made by the practitioner in light of individual patient circumstances, the wishes of the patient, clinical expertise and resources.

The NCC-PC disclaims any responsibility for damages arising out of the use or non-use of these guidelines and the literature used in support of these guidelines.

2.13 Funding

The National Collaborating Centre for Primary Care was commissioned by the National Institute for Health and Clinical Excellence to undertake the work on this guideline.

3 Principles and concepts used in the development of the guideline

Clinical guidelines generally provide guidance on the management of clinical conditions. To inform the recommendations evidence is sought regarding the benefits and harms, as well as cost of treatments. This guideline seeks to inform patient involvement in decisions about medicines across clinical areas and as such is more interested in patient and health care professional behaviour than evidence for individual treatments. The development of the guideline required the Guideline Development Group (GDG) to engage with topics more usually found in psychological and sociological literature as well as philosophical and legal issues such as rights and duties of patients and professionals. The GDG discussed these issues at length to develop a working consensus which then allowed them to examine the literature and develop recommendations. These discussions are included in the relevant sections of the guideline where they informed recommendations. The GDG also wished to see the principles they used to develop the guideline brought together in one chapter. This chapter brings together those discussions from different parts of the guideline. Some of this content is therefore relevant to individual chapters and rather than repeat the sections we have inserted hyperlinks to this chapter where appropriate.

3.1 Patients' rights to be involved in decisions about medicines

The prescribing of medicines to patients has become a central part of the delivery of modern medical care. Studies and commentaries on medicine-taking by patients have often emphasised the objective health and cost impacts incurred when patients do not take medicine as prescribed [6]. There is an often unstated and perhaps unrecognised assumption that patients should take medicines as suggested by health professionals [7]. While objective health and cost impacts of patients' behaviour in relation to medicines is important, the right of patients to make decisions in regard to their own health is

accepted in modern practice. The approach taken by this guideline is that patients have a right to be involved in decisions about medicines to the extent that they wish and it is the role of health professionals to facilitate and support patients in their involvement in decision-making and to support patients in taking medicine if the decision has been to prescribe.

It is particularly important for people who are known to frequently experience inequalities in health to have their right recognised to be effectively engaged in decision-making e.g. those with learning disabilities, mental health problems and people of black and ethnic minority origin. These individuals must be afforded equal opportunities for healthier outcomes through the effective provision of appropriate access and support. Practitioners must be aware of their legal duties and responsibilities to make *'reasonable adjustments'* in line with the Disability Discrimination Act (2005).

3.2 What is meant by involving patients in decisions about medicines?

Early analysis of consultations between healthcare professionals and patients indicated that consultations were primarily led by the health care professional. Bain (1976) [8] a general practitioner, tape-recorded his own consultations to examine what actually happened in consultations and found that he talked at least as much as the patients did. Tuckett and colleagues (1985) [9] found that doctors frequently inhibited patients from asking questions and did little to encourage patients to present their own view. Historically healthcare professionals have had the dominant role in making treatment decisions and these professionals have primarily been medical professionals. Charles and colleagues (1999) [10] outline a number of assumptions on which this dominant role was based: a single best treatment existed and physicians would be well versed in current clinical thinking; physicians would apply this knowledge consistently to all patients and were in best position to evaluate treatment decisions and tradeoffs; and because of their professional concern for the welfare of their patients, physicians had a legitimate interest in each treatment decision. Significant asymmetry between professionals and patients also

existed in terms of education, income and status. The assumptions underlying the dominant role of the professional have been increasingly challenged as both medicine and society changed [11]. More treatments for conditions have become available with complex risk – benefit analyses required. It was recognised that it is the patient who has to live with the consequences of these decisions and might be in a better position than the professional to evaluate and weigh these. Medical practice has also shifted away from acute care towards both chronic long term care and preventative care which requires a long-term commitment to medicines taking and may require frequent monitoring of medicines and illness. The principles of informed consent and informed choice in relation to treatment decisions are now enshrined in law and there is an inherent implication in these that the patient is making a decision in relation to their own healthcare. Previous asymmetries between health professionals and patients in terms of education and access to information have also lessened. Parallel to these developments has been sociological and psychological studies that examined patients' medicine-taking behaviour which provided evidence that patients' decisions were rational and logical when using patients' own understanding (see chapter 5).

The concepts of shared-decision making and patient-centredness are part of the response to the need to recognise the role of the patient in medical encounters and decisions. In the literature shared decision-making (SDM) is described as one model of decision-making. In this model information exchange is a two way process in the consultation and both deliberation and decision are made by both health care professional and patient. This is in contrast to a 'paternalistic' model where information is given to the patient and deliberation and decision are made by the health care professional or an 'informed' model where information is given to the patient and the patient makes the deliberation and decision [10]. Intermediate models are also recognised where decision may be led by the professional or handed to the professional following full sharing of information between both parties. Patient-centredness is an approach to the patient which encompasses the sharing of power and responsibility. Mead and Bower (2000) [12] have described patient-centredness as having 5 dimensions (1) adopting the bio-psychosocial

perspective (this means using biological, psychological and social understandings of disease and illness experience); (2) understanding the patient as person; (3) sharing power and responsibility between the doctor and patient; (4) building a therapeutic alliance and (5) understanding them as a person. Despite the interest in these concepts and an agreement that there is a moral value inherent in them, it is accepted by many working in the area that the operationalisation of these concepts is still evolving [13], [11], [14]. The difficulties relating to how to enact shared decision making include overcoming asymmetry in knowledge and experience between patients and health care professional, the difficulty in recognising a shared decision and what this concept means in terms of responsibility of the clinician.

Current evidence exploring health care professionals' views indicate that they perceive difficulties in implementing SDM. A recent systematic review which examined qualitative and quantitative research on health care professionals' views about implementing SDM identified several perceived barriers (Gravel 2006) [15]. The studies included in the systematic review were primarily qualitative and the vast majority of the practitioners were medical practitioners. The three most commonly perceived barriers were time constraints, lack of applicability to patient characteristics and lack of applicability to the clinical situation.

Thompson (2007) [16] describes the current literature as being primarily derived from the perspective of professionals – policy makers, academics or medical professionals and not from the perspective of patients. Using interviews and focus groups he describes patients' wish for involvement to be dynamic with demand varying according to the need for health care, personal characteristics of the patient and the patient-professional relationship. Wish for involvement is higher in this model when illness is chronic, trust in the professional is low and the patient is active. Demand is lower when illness is acute and serious, the patient passive and trust in the professional is high.

Surveys of patients indicate that when asked patients as a group do ask for increased involvement in healthcare decisions. The Picker Institute (2007) [17] published a report examining patient experience of the NHS between 2002

and 2006. Using the results of 26 national patient surveys they report patients' information needs not being met and patients wanting more involvement in health care decisions. In regard to medicines, patients reported wanting more involvement in medicine choices than they currently receive. The surveys indicate that professionals were giving less information about side effects over the time of the surveys and patients felt that fewer decisions were shared decisions in 2006 than in 2004 and 2005.

The literature on decision-making first evolved in the context of life-threatening diseases such as cancer [11] and included decisions for example as to whether or not to have surgery [18].These were often one-off decisions with major consequences. In the case of medicines the initial involvement in the decision to prescribe a medicine is necessarily followed by ongoing, often daily decisions by patients to continue taking the medicine prescribed. Involving patients in decisions to take medicines concerns not just the decisions made within a consultation but also attention to the ongoing decisions that patients make about their medicines following the consultation with a health care professional.

3.3 What are we trying to achieve in involving patients in decisions about medicines?

The outcome that we wish to see from patient involvement is an informed choice by the patient in regard to their use of medicines. The term informed adherence has been used to describe an outcome of informed choice and supported adherence [19]. In this understanding achieving a shared agreement is limited if the patient is then not supported to implement their intentions to take the medicine as recommended. Similarly, stipulating unconditional and unquestioning adherence to prescribers' instructions as our goal is, in most cases, not justified if the patient has not made an informed choice about taking the medicine.

In most cases the patient is free to decide whether to take the treatment or not. However, the healthcare practitioner has a responsibility to help ensure that the choice is an informed one. Informed patient choice, rather than

'compliance' is the desired outcome of the discussion. If the patient decides to accept the prescription, then the aim is to facilitate appropriate adherence to the agreed recommendations for how it should be taken to maximise its efficacy and safety for the individual and optimise benefits and reduce risk.

Facilitating informed choice involves more than the provision of information. Informing should be an active process, which involves more than simply presenting the evidence. It also entails eliciting the patient's beliefs and identifying whether pre-existing beliefs might act as a barrier to an accurate interpretation of the evidence. If the interpretation of information is influenced by misconceptions about the illness and treatment, then the patient's choice may not be 'informed'.

3.4 Roles and responsibilities of patients and health care professionals

Concern has been expressed by practitioners that sharing decisions with patients may conflict with their duty of care to patients or their legal or ethical obligations [20]. While the UK General Medical Council (GMC) (2001)[2] considered one of the key duties of a doctor to 'respect the rights of patients to be fully involved in decisions about their care' for many clinicians there is a legitimate area of concern or indeed of conflict between respect for autonomy of the patient and the duty of beneficence when a clinician feels uncomfortable about a patient's wishes. The GMC (2008)[3] has recently updated guidance for doctors about patient consent which makes explicit the right of competent patients to make decisions about their own healthcare. The guidance emphasises the need for doctors to maximise opportunities and patients abilities to make decisions for themselves and that doctors must respect competent patients' decisions even if they do not agree with them. Doctors do not have to provide a treatment to patients which they believe is not in the patients' interest but must under such circumstances explain their reasons and other options, including a second opinion to the patient. It

[2] http://www.gmc-uk.org/publications/annual_reports/review_archive/report2002.pdf
[3] http://www.gmc-uk.org/publications/business_plans/Business_Plan_2008.pdf

remains important however for health care professionals to do their utmost to ensure that patients' choices are informed choices as outlined above.

The Mental Capacity Act (2005) [4] governs the making of decisions for people who lack capacity in England and Wales. Under the Act healthcare professionals are advised that they must work on the presumption that every adult patient has the capacity to make decisions about their care, and to decide whether to agree to, or refuse, an examination, investigation or treatment. A patient is regarded as lacking capacity once it is clear that, having been given all appropriate help and support, they cannot understand, retain, use or weigh-up the information needed to make that decision, or communicate their wishes[5].

Healthcare professionals are advised that assumptions must not be made that a patient lacks capacity to make a decision solely because of their age, disability, appearance, behaviour, medical condition (including mental illness), their beliefs, their apparent inability to communicate, or the fact that they make a decision that health professionals disagree with[6].

Healthcare practitioners need also to consider their obligations to the wider society and cost constraints of the healthcare system in which they work when prescribing.

3.5 Understanding the influences on medicine-taking by patients

If health care professionals are to facilitate patient involvement in decisions about medicines it is helpful and necessary to understand how patients approach the taking of medicines, in particular the ongoing appraisal of medicines that continues after a consultation. Investigation into why patients do not take medicines as prescribed indicates that the decision to take medicines and the continuing taking of medicines should be considered as a complex behaviour. Fig 1 indicates a diagrammatic representation of current

[4] http://www.opsi.gov.uk/ACTS/acts2005/pdf/ukpga_20050009_en.pdf
[5] http://www.gmc-uk.org/publications/business_plans/Business_Plan_2008.pdf
[6] http://www.gmc-uk.org/publications/business_plans/Business_Plan_2008.pdf

evidence regarding factors and influences on medicine-taking by patients. As the figure shows there are a number of influences on patients. Many of these factors interact and the arrows indicate the dynamic nature of the process.

Internal factors represent the beliefs and experiences of the patient. These include the patient's beliefs about their symptoms or disease, their beliefs about medicines in general and their own reaction to medicines. These will influence their intention to take a medicine as suggested by a health care professional. Even when patients intend to take a medicine they can experience difficulty in doing so because of practical problems such as packaging or complexity of regime or they may forget to take medicines. Patients conduct their own appraisal of the medicine they are taking and evaluate its effects against their own expectations of what the medicine will achieve. This feeds into their beliefs about their medicines which in turn influences their intention to take or not to take the prescribed medicines.

External factors are those that feed into the patient's internal appraisal process. These include communication with family and friends and the communication they have with their health care professionals. Information about medicines will be available from multiple sources including documentation patients get with their medicines, from the pharmacist or dispenser or from any other health care professional the patients comes into contact with. Patients may get information from other patients who have taken the same medicine. Patients may be influenced by the attitude in society to a particular medicine or medicines in general and information may be received from media sources.

The research evidence indicates that patients' decisions about medicines are made within the patients' own frames of reference and make sense within the patients' understanding. Patients however often do not disclose to the health professional any reluctance to take medicines or disagreement with the prescribers recommendation of a prescription or their non-taking of medicines. The onus is on the health professional to elicit and explore patients' beliefs and experiences and facilitate the patient making an informed choice about whether or not to take a prescribed medicine.

When patients do not take medicine as prescribed they may therefore be doing this on an intentional basis i.e. they have made their own appraisal and have decided to take the medicine in their own way or even not at all. This may be done with full information about medicines, illness and consequences of taking or not taking recommended medicine.

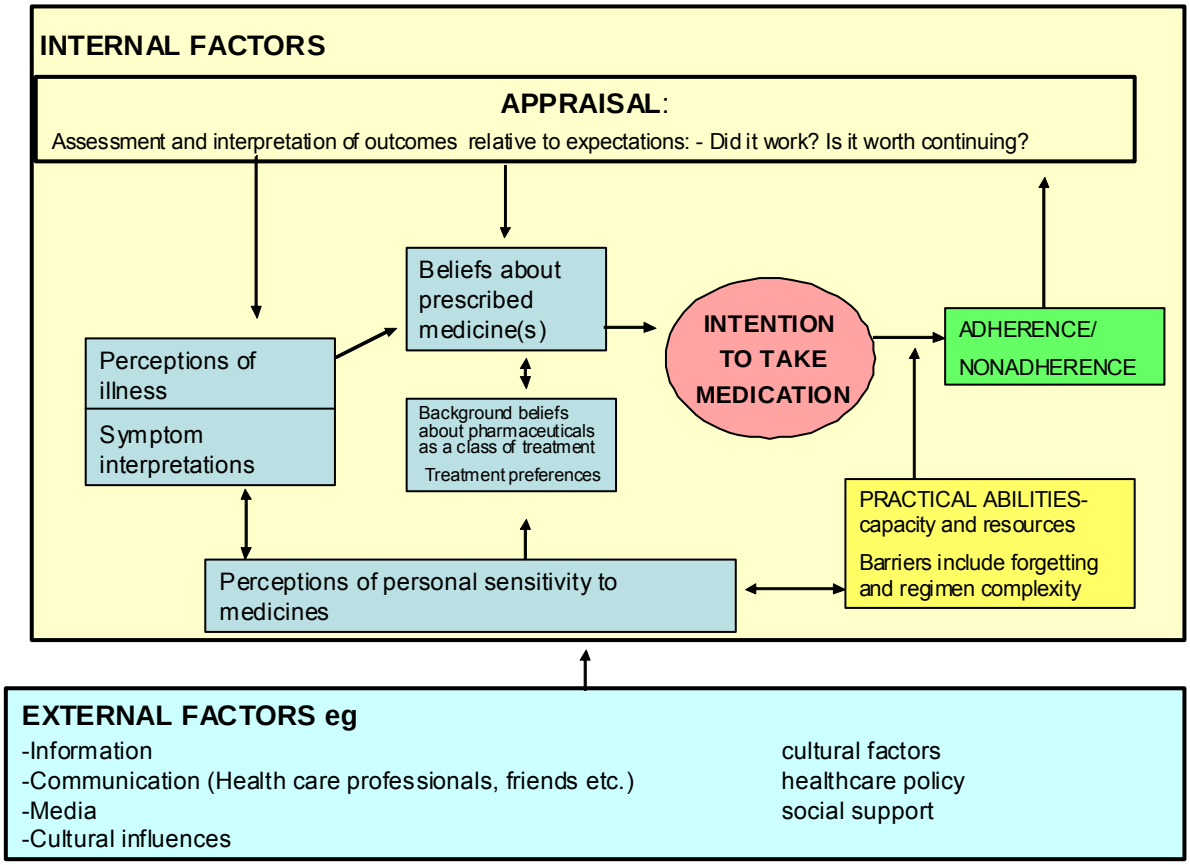

Figure 1. Horne, R. Concordance, Adherence and Compliance in Medicine-Taking. Report for the National Co-ordinating Centre for NHS Service and Delivery Organisation R&D (NCCSDO) (2005), pp 139.

In routine clinical terms the factors included in figure 1 that are barriers to medicine-taking can be considered as either practical barriers or perceptual barriers. Perceptual barriers are ways in which individual patients think about their illness or condition and treatments both in general and specifically. Practical barriers are those such as cost, memory or dexterity that affect individuals' ability to use the medicine recommended to them.

3.6 Terminology and structure of guideline

The terminology used in the area of medicine-taking highlights the changing understanding of medicine-taking behaviour and the changing relationships between health care professionals and patients. The terms compliance, adherence and concordance are now often used interchangeably and inappropriately to describe medicine-taking by patients. The approach taken by this guideline is to use terminology as recommended in the Report for the National Co-ordinating Centre for NHS Service Delivery and Organisation R&D on Concordance, Adherence and Compliance in Medicine-Taking (2005) (NCCSDO) [1].

Compliance has been the most commonly used term in relation to medicine-taking and can be defined as 'the extent to which the patients' behaviour matches the prescriber's recommendations' [21]. The term has been criticised as it is suggested it carries an implicit assumption that it is the prescriber's role to decide on the correct medicine and the patient has a passive role which is to take the medicine as he/she has been instructed. Non-compliance indicates a failure to follow instructions and can be used as a pejorative term indicating a patient who is unwilling to do as instructed by a prescriber who knows what the patient needs.

Adherence is defined as 'the extent to which the patient's behaviour matches agreed recommendations from the prescriber'. Adherence shifts the balance between professional and patient to suggest there should be agreement between prescriber and patient about the prescriber's recommendation. In this understanding adherence is referring to behaviour matching an agreed recommendation but patients may agree to take medicine and yet not take it precisely as prescriber intended. Adherence is not binary.

Concordance is less easily defined and its meaning has changed. It was initially used to describe the consultation process by which agreement about therapeutic decisions was reached by prescribers and patients. It presumed an exploration of patients' views and their incorporation into the decision made. The term therefore addresses consultation processes and does not include any aspects of medicine-taking as do compliance and adherence.

Some uses of the term have included both communication and support for patients in medicine taking. While the term concordance has been useful in drawing attention to the need to engage patients in decisions there is currently no agreed way in which one can judge whether a consultation has been concordant. Concordance does reflect current social values where patients are seen as active participants in their own healthcare but does not address medicine-taking and may or may not lead to improved adherence.

We have chosen to discuss the consultation process regarding medicines separately from actual medicine taking. We use the term 'shared decision-making about medicines' to refer to the healthcare professional–patient/carer consultation and the term adherence to describe patients' medicine-taking behaviour. The guideline has looked separately at evidence about interventions to increase patient involvement in the decision to take medicine within the consultation and at evidence about interventions to support patients in taking of medicines. While this division is useful when examining the literature and making recommendations, the dynamic nature of medicine-taking must not be forgotten. Patients' perceptions and beliefs will change over time and the experience of taking a medicine will also influence patients' intentions to continue taking that medicine and others prescribed.

From a therapeutic perspective concepts of persistence and forgiveness of a medicine are also important. Persistence refers to how long the patient takes the medicine for and forgiveness refers to whether or not medicines will provide some benefit even if not taken all the time at the recommended dosage and timing.

Fig 2 provides a representation of the patient's pathway. The patient comes to the consultation with their own beliefs and experiences (see section 5). In the meeting with the health professional the patient's complaint is assessed and a prescription may be recommended by the health professional. Within the consultation the decision as to whether or not the patient leaves with a prescription may be led completely by the health professional or negotiated between health professional and patient. If the patient leaves the consultation

with a prescription they may or may not take the prescription to be dispensed, and even if the medicine is dispensed they may or may not take the medicine.

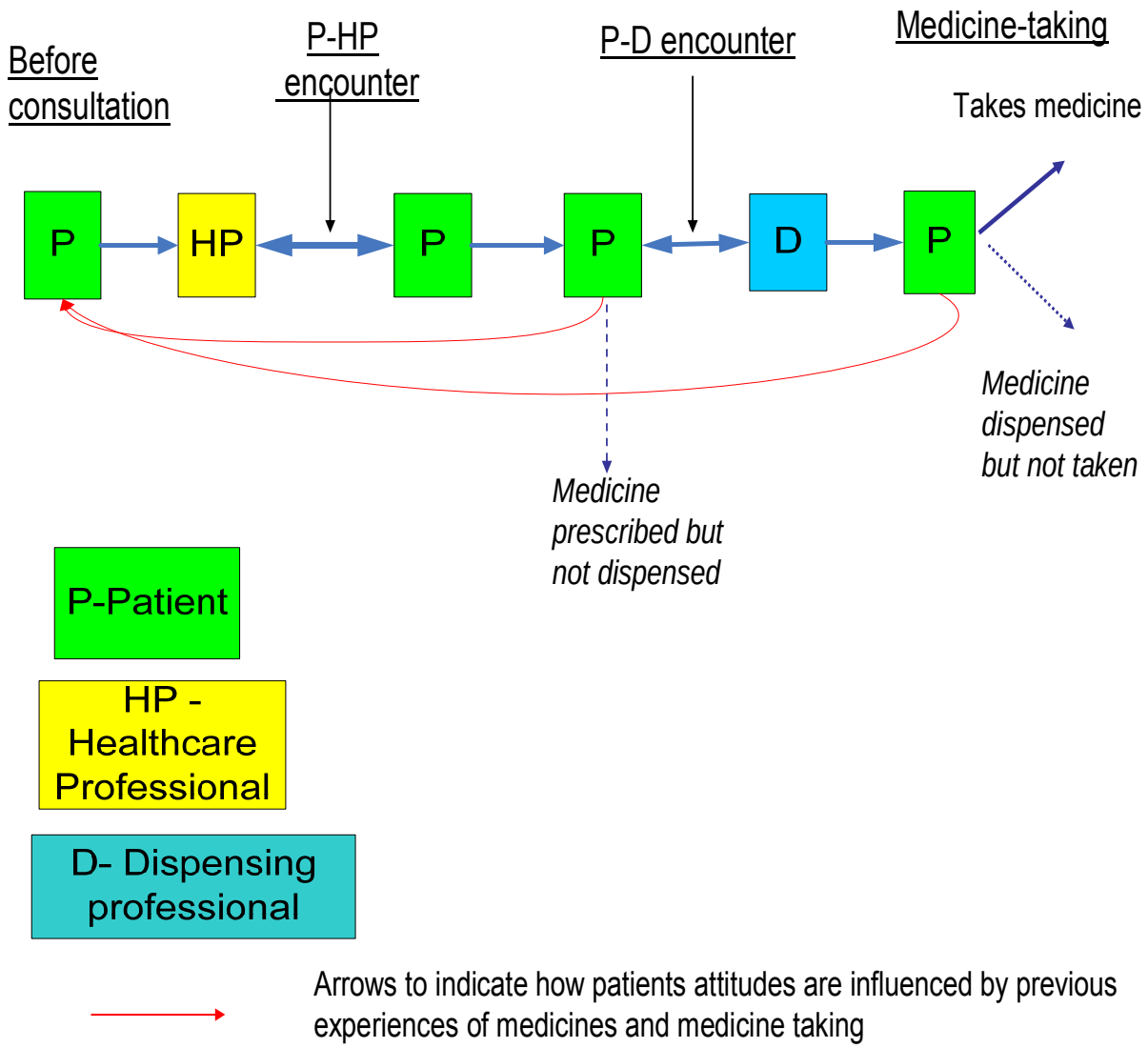

Fig.2 Simplified representation of patient pathway

3.7 Shared decision-making about medicines

Models of shared decision-making for use in clinical practice have been developed. Towle (1997) [22] suggested steps for shared decision-making and these have been adapted by Elwyn (1999) [23] following exploratory research with general practitioner registrars. They suggest that population surveys cannot predict preference of individual patients for involvement and patients' preferences for involvement may vary according to clinical situation so the

involvement of patients in decision-making has to be explicitly addressed. Neither can patients consider their role in actual making of a decision until they have information about their options and the risks and benefits of those options. The following stages are suggested by Elwyn (1999) to involve patients in healthcare decisions and by implication this also describes the competencies required by practitioners to involve patients (Elwyn 1999) [23].

- Implicit/explicit involvement of patients in decision-making process
- Explore ideas/fears and expectations of problem and treatments
- Portrayal of options
- Identify preferred format and provide information
- Checking process: understanding of information and reactions
- Acceptance of process and role in decision-making
- Make, discuss, or defer decisions
- Arrange follow-up

While these models have been developed when considering a variety of decisions we have used this model to provide an outline structure for our discussion and recommendations about sharing decisions about medicines in consultations. While a treatment can never be understood without reference to the underlying disease, illness or symptom it is beyond the scope of this guideline to make recommendations about general communication and about how diagnosis and prognosis should be explained to patients. These do overlap with our recommendations on communication about medicines but we have not examined these areas explicitly.

Although we have used the term SDM in this guideline and have used literature relating to SDM the understanding of the Guideline Development Group is that this is a process and that we are addressing the 'sharing' of decisions rather than defining what a shared decision is. Edwards (2006) [24]

have suggested that it is the process of involving patients in decisions that delivers benefits for patients rather than attaching importance to defining who makes the decision. Given the difficulties in defining precisely what a shared decision is we cannot advocate that the outcome from this process has to be a 'shared – decision'. For many patients this may be the preferred outcome, other patients will prefer to give the decision to the professionals and others to make their own 'informed' decision. Cox (2007) [25] in a study about prescribing of medicines in general practice, found that 39% of patients wanted the GP to share the decision, 28% wanting the GP to be main decision-maker, 17% wanted the GP to be the only decision-maker, 14% preferred that the patient be the main decision-maker and 2% the only decision-maker. Given the evidence that patient involvement in choices about medicine is lower than desired by patients and that prescribers are not good at recognising which patients want involvement our recommendations aim to make the process of involvement more explicit and to increase overall patient involvement.

4 Interventions to increase shared decision-making about medicines

4.1 Recommendations

Hyperlink to recommendations section on Patient Involvement in Decisions About Medicines

Hyperlink to recommendations section Communication Between Healthcare Professionals

4.2 Introduction

Shared decision-making can be broadly defined 'as a decision-making process jointly shared by patients and their health care provider' (Legare 2008) [26]. As discussed in chapter 3 the concept of shared decision-making evolved as a development from a predominantly paternalistic model of professional and patient interactions. Makoul and Clayman (2006) [27] found that the most commonly occurring themes in discussions of concepts of shared decision making were patient values and preferences, options, partnership and patient participation, with 17 other concepts also given considerable weight. In a review of communication about medicines Cox (2004) [28] sets out how patients and professionals need to have two way discussions in which they exchange information and views about medicines.

Hyperlink to section 3.3 What we are trying to achieve in involving patients in decisions about medicines

4.3 Process of shared decision-making

Hyperlink to section 3.7 Shared decision-making about medicines

4.4 Methods

Searches were conducted to gather the most relevant evidence relating to the key clinical questions on shared decision-making. Reviews of the evidence using systematic methods relating to searching and appraisal were conducted to answer the clinical questions in line with the NICE Technical Manual. The GDG and project teams agreed appropriate inclusion and exclusion criteria for each topic area in accordance with the scope. Initially an overall search of relevant Randomised Controlled Trials (RCTs) and Systematic Reviews was

conducted using shared decision-making terms. The articles retrieved were then separated under the relevant key clinical questions. Reviews of the evidence using systematic methods relating to searching and appraisal were conducted to answer the clinical questions. However, this did not answer all the Key Clinical Questions succinctly so further searches were done using lower grades of study design.

After the key terms were searched we generated a list of abstracts which were sifted to find relevant articles. Full articles of those deemed to have relevance to the question were obtained. These were then further assessed with regards to our inclusion and exclusion criteria for the question and either included or excluded. We were specifically looking for studies regarding medicine-taking. There is a wide body of evidence relating to decision-making in oncology and surgery but these were excluded.

We extracted the evidence from each included article for study quality, and then brought together the results into an evidence review for each key clinical question. The evidence reviews were structured into explanatory narratives for each article. These were then combined to provide evidence. It was difficult to separate out the content of some of the interventions contained in systematic reviews. For example there was overlap of interventions which explored the improvement of communication between patients and practitioners and interventions exploring those exploring how information should be presented and discussed between practitioners and patients. We have therefore included some studies in more than one section and have indicated this where appropriate.

4.5 Is it possible to increase patient involvement in decisions about medicines?

Related References	Evidence Statements (summary of evidence)
Patient-centred communication in the consultation	
Rao (2007) [29]	One systematic review of how to improve the communication behaviours of physicians and patients found that the interventions studied statistically significantly improved the patient-centred communication behaviours of physicians and residents. Interventions had modest effects in improving patients' communication behaviours. Interventions had modest effects in improving patients' communication behaviours.
Rao (2007) [29]	In one systematic review there was a mix of statistically significant and statistically non-significant results, depending on the communication behaviour studied – e.g. 5/7 found statistically significant changes in patients' communication patterns. All of these included skills practice as part of the intervention, the other 2 studies were low intensity;
Rao (2007) [29]	One systematic review investigated the intensity of interventions and found that higher intervention intensity was clearly related to improvements in physician communications. This was less pronounced for patient communication interventions.
Lewin (2001) [30]	One systematic review found that some interventions

	to promote patient-centred care in consultations led to statistically significant increases in the patient-centredness of the consultation process. They concluded that there is limited and mixed evidence on the effects on health care behaviours or health status.
Patient involvement in the consultation	
Rao (2007) [29]; (Harrington (2004) [31]; Kinnersley (2007) [32]; Loh (2007) [33]	Three systematic reviews found mixed results as to whether or not interventions increased patient involvement in the consultation (described below). One RCT study found an increase in patient participation.
Harrington (2004) [31]	In one systematic review, 10 RCTs found a statistically significant increase in participation, while 5 RCTs found a statistically non-significant increase.
Kinnersley (2007) [32]	In one systematic review patient participation was increased in 8 out of 14 RCT studies and no effect was found in 5 RCT studies.
Wetzels (2007) [34]	One systematic review found limited evidence (three RCTs) of interventions aimed specifically at improving older patients' involvement in consultations.
Wetzels (2007) [34]	Those RCT studies that did investigate older patients' involvement found that the interventions resulted in the patients asking more and different questions, and so they may become more active in consultations due to pre-visit preparation.
Type of behaviour evoked	

Harrington (2004) [31]; Kinnersley (2007) [32]; Wetzels (2007) [34]	Question-asking was the most targeted behaviour found by one systematic review (Harrington, 2004). 5 of the studies found statistically significant increases in this behaviour and 5 studies found statistically non-significant effects (Harrington 2004). In another systematic review (Kinnersley 2007) 6 out of 17 studies found statistically significant increases and the other 11 studies found no statistically significant effects on question-asking. Another systematic review (Wetzels 2007) found one study where more participants asked questions and one study where few prepared questions.
Harrington (2004) [31]	In one systematic review there was a statistically significant increase in clarifying issues.
Harrington (2004) [31]	One systematic review found a statistically significant increase in patients' perception of control over health and for an active role in health care, recall of information, adherence to recommendations, attendance and clinical outcomes.
Harrington (2004) [31]; Kinnersley (2007) [32]; Loh (2007) [33]	One systematic review (Harrington 2004) found a statistically significant increase in satisfaction for only two RCTs however there was high satisfaction found overall. In one systematic review (Kinnersley 2007) 14 out of 23 studies showed no change and 5 had increased satisfaction. In another RCT (Loh 2007) patient satisfaction was statistically significantly higher in the intervention 29.8 (s.d=2.7) than the control group 27.0 (s.d=3.6), p=0.014.
Type of intervention	

Rao (2007) [29]; Harrington (2004) [31]; Kinnersley (2007) [32]; Wetzels (2007) [34]	In 4 systematic reviews most of the interventions were written, e.g. booklet/checklists, while some were videotapes or face to face coaching.
Harrington (2004) [31]; Kinnersley (2007) [32]	One systematic review found that face-to-face and video interventions showed more statistically significant results than written interventions (Harrington 2007). Another systematic review found a small to moderate statistically significant increase for writing alone and coaching.
Wetzels (2005) [35]	One consultation leaflet RCT (including open and pre-structured questions) to improve involvement of older patients, showed an increase in satisfaction but no effect of the leaflet on involvement, enablement or satisfaction. There was a statistically significant result of reporting more psychological symptoms to their GPs.
Little (2004) [36]	One RCT found that a general leaflet which asked patients to list issues they wanted to raise questions led to a statistically significant increase in satisfaction but not in other aspects. The leaflet was statistically significantly more effective when consultations were short. The leaflet increased the number of investigations by the doctor.
Wilkinson (2002) [37]	One RCT of an education guidebook to encourage and support participation found no statistically significant differences in the effectiveness of their primary care visit. There were statistically significant differences for those receiving preventative health care interventions.

Ross (2004) [38]	One RCT found the use of a patient-accessible online medical record found no statistically significant results for self-efficacy, adherence, health status or patient satisfaction. General adherence to medicines advice was statistically significantly improved.
Loh (2007) [33]	One RCT found no statistically significant differences in treatment adherence.

4.5.1 Evidence to recommendations

The GDG were interested in what evidence was available to indicate that patient involvement in decisions about medicines can be increased. The evidence is complex and difficult to interpret because of the lack of standardisation of interventions, the use of multiple interventions in some trials and lack of transparency in reporting of studies. A significant proportion of studies included in systematic reviews were carried out in US settings and the majority of interventions for patients and practitioners were carried out before consultations. The GDG were convinced from the evidence reviews that practitioner skills could be improved and that these improvements as well as some patient interventions did result in increased patient involvement. The GDG considered it important that practitioners were aware that skills could be improved through further training. The GDG considered that the evidence did not allow them to make specific recommendations about how practitioners should increase patient involvement and requested further searches to look at specific aspects of increasing patient involvement.

4.5.2 Methods of the evidence review

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies: Systematic reviews of randomised controlled trials (RCTs) or Randomised controlled trials of interventions involving shared decision-making in the clinical context.

Types of participants: people prescribed medicine for a medical condition.

Duration of studies: no time limit specified.

Types of interventions: any interventions involving shared decision-making in a consultation between a health care professional and patient.

Types of outcome measures: Patient-centred communication in the consultation; consultation process outcomes: patient involvement, question asking, preparedness; patient care outcomes: satisfaction, knowledge, self-efficacy. type of interventions involved and type of information.

It should be noted that the remit of the guideline is for conditions with prescribed medicine and this excludes conditions which require chemotherapy or screening. All RCTs are within this remit, however many of the systematic reviews included populations outside the remit, this is noted where applicable.

4.5.3 Evidence review

The narratives for this question are not grouped because they cover various aspects of the question. The evidence review has been constructed under the above sub-headings of patient-centred communication, patient involvement, type of behaviour, type of intervention and type of information. It should also be noted that RCTs which were included in the systematic review were not narrated separately so as not to duplicate results.

Rao (2007) [29] conducted a systematic review of interventions to enhance communication behaviours among physicians and patients in an outpatient setting. They included RCTs of interventions which were designed to improve the communication behaviours of physicians and patients. The primary outcome was an assessment of the patient-centred verbal communication behaviours. They rated the intensity of the interventions based on how often it was delivered and the personnel involved in the delivery. Thirty-six RCTs met

the inclusion criteria, 18 trained physicians or residents and 15 trained patients, 3 intervened with both. The majority (26 RCTs) were conducted in primary care clinics while 10 were conducted in medical specialty settings. Twenty of the RCTs were conducted in the USA. Half of participants were assessed before and after the physician-patient interaction. Most of the studies were conducted on audiotapes or videotapes and coders were blinded to group assignment. There were a variety of types of physician/resident interventions (e.g. information, feedback, modelling, and practice). Nearly all interventions included written instructions. Some (10 interventions) included videotapes which modelled desirable communication behaviours. Most RCTs showed statistically significant improvements in the communication behaviours of the physicians/residents. The higher intensity interventions resulted in physicians asking more open-ended questions and less biomedical questions than the comparison groups. They were more likely to elicit the patients' concerns they had prior to the visit, and show a more patient-centred communication style overall. There were statistically significant improvements in the information provision to patients. Rao noted that few RCTs (6) checked for patients' understanding of the information received. 18 studies intervened with patients and showed modest effects. Most of the RCTs were informational (17), often written. In some instances the written information included models of desirable communication with examples of questions to ask (8). Eight RCTs included practicing or coaching sessions and four were feedback. Six interventions were moderately-intense, 2 were rated as high-intensity.

Seventeen of the RCTs used different measures of patient involvement. Seven assessed the degree to which patients spoke during the visit, 5 (moderate intensity interventions) of these showed statistically significant changes in communication patterns. All of these RCTs were skills practice interventions. The other two RCTs interventions were low-intensity and showed no statistically significant results. To conclude, the interventions enhanced communication behaviours with physicians compared to controls and there were modest effects with the patient interventions. Intervention

intensity had a clear relationship to improving the physicians' behaviours but this was follow suit for the patient interventions.

Harrington (2004) [31] conducted a systematic review which looked at interventions to increase patients' participation in medical consultations. There was a mix of populations including primary care and outpatient oncology patients. The inclusion criteria for the review included interventions designed to improve patients' communication with doctors in any setting; and RCTs reporting on the impact of the intervention on the patients' communication. Most of the studies were RCTs, with the others being quasi-experimental. Twenty five papers were retrieved from the search. Most of the studies were from the USA, 2 from Australia, 5 from the UK and one from the Netherlands. Most of the interventions were written followed by face-to-face coaching and videotape. Written interventions were in booklet or checklist form. The specific behaviours most encouraged were question-asking, raising concerns and requesting clarification or checking understanding. The process of communication was measured mostly using interaction analysis from audio recordings. Researchers coding the interactions were blinded in only six of the studies. Overall the effect of interventions was that they encouraged patients to be more active in their consultations. Of the 16 studies examining variables of participation, 10 reported a statistically significant increase and five reported a statistically non-significant increase. All but one of the six face-to-face interventions and all of the video interventions reported statistically significant results in increasing participation. Of the 10 written interventions, only two reported a statistically significant increase. Question-asking was equal in statistically significant increases and statistically non-significant trends. There was a statistically significant increase in requesting clarification on matters. There was no statistically significant increase in satisfaction due to the interventions apart from in two studies. There was overall a high level of satisfaction reported. There was a statistically significant increase in perception of control over health and preferences for an active role in health care, recall of information, adherence to recommendations, attendance and clinical outcomes.

Lewis, Butow, Ford, Street and Brown were studies with cancer patients exclusively.

Kinnersley (2007) [32] conducted a Cochrane review of the effects of interventions before consultations designed to help patients address their information needs. The settings and populations varied, but most were conducted in the USA. The author's stated that this review complemented other Cochrane reviews by Wetzels (2007) [34] and Lewin (2001) [30]. The inclusion criteria was RCTs of interventions which were intended to help the patients, representatives or carers address their information needs in a consultation. This was done by encouraging question-asking, expression of information needs, overcoming barriers to communication and clarifying understanding of the information provided. Outcome measures included the consultation process, consultation outcomes and service outcomes. Thirty-three trials described in 35 studies met the inclusion criteria. Of the studies that assessed single interventions for patients,15 included written materials and four included coaching. Of the multiple component single interventions studies, 4 had coaching and written materials. Results: 17 studies measured question-asking and 6 found statistically significant increases and 11 studies found no effects on the intervention group compared to the control group. Patient participation was measured in 14 studies, it was increased in 8, and had no effect in five studies. Patient satisfaction was measured in 23 studies, in 14 studies there were no changes and in 5 there was increased satisfaction. Patient knowledge was measured in 5 studies, with a reduction in two studies and no changes in 3 studies. According to type of intervention, comparisons between written alone and coaching alone showed similar, small to moderate and statistically significant increases for both types of question-asking. Patient satisfaction was borderline statistically significant for written materials, and the effect of coaching was small and statistically significant. Written materials led to a small and statistically significant increase in consultation length. Coaching also showed an increase but this was not statistically significant. Interventions immediately before the consultation led to a small statistically significant increase in consultation length and patient satisfaction.

It should be noted that many of the studies were from other settings: Brown (1999, 2001), Bruera (2003), Butow (1994, 2004), Davison (1997, 2002), Ford (1995), Oliver (2001) were cancer studies. Finney (1990), Kim (2003), Lewis (1991) were from paediatric and family planning settings.

Wetzels (2007) [34] conducted a Cochrane review assessing the effects of interventions in primary care to improve older patients' involvement. The inclusion criteria included RCTs and quasi-randomised trials; older participants (65 years or over) in primary care; interventions either before during or after the consultation and the interventions had to aim to improve the patients' involvement. Studies with other health care professionals were excluded. The outcome measures included use of health care, preparation for contact with a care provider, contact with the care provider (communication), feedback of care, health status and behaviour, treatment outcomes and outcomes related to health professionals. Three studies met all inclusion criteria (Cegala 2001, Kimberlin 2001 and Tennstedt 2001). They were published in English and conducted in the USA. The interventions were either face-to-face sessions to coach patients in question-asking and participating in consultations (given before the consultation) or they were written interventions (booklet or checklist). The primary outcome measure in two of the studies was the questioning behaviour of patients, while the other study's was self-reported active behaviour. The studies used mostly qualitative analysis to assess the outcomes and these were not assessed at a later date. In Cegala (2001) the trained patients asked more medically-related questions, gained more information and provided more information than control patients. They did not verify information more than control patients and appointment length was not longer overall. In Kimberlin (2001) there was more question-asking about their medicine in the intervention group than the control group. Tennstedt (2000) found older patients were generally not involved in their GP visit. Few prepared questions or identified issues to discuss with their GP. However, only 21% found that the GP dominated the visit. The intervention group reported more active behaviours such as bringing a list of problems to the visit (statistically non-significant in intention to treat analysis but

statistically significant in those who did attend, and higher satisfaction with the interpersonal aspects of the encounter).

In conclusion, there is little evidence of interventions which specifically aim to improve older patients' involvement and thus they cannot recommend the use of the examined interventions in clinical practice. The interventions that were included resulted in patients asking more and different questions, and they became more active in consultations due to pre-visit preparation.

Wetzels (2005) [35] ran a cluster-randomised trial to assess a consultation leaflet implementation programme in which GPs and older patients were encouraged to improve older patients involvement when visiting their GP. This study was conducted in the Netherlands. All patients aged 70 years or above in the intervention practices received a consultation leaflet by mail. This leaflet included a short motivating text on patient involvement and a mixture of open and pre-structured questions to help patients prepare for the next consultation and prioritise which problems they wanted to discuss with their GP. The questions were chosen because they would help to explore patient's ideas, fears and expectations, and they encouraged them to address important issues. At pre-intervention 315 patients, and 263 patients at post-intervention, were included in the study.

Based on results from a previous qualitative study, the authors concluded that it would be important to include GPs in the implementation of patient involvement, so GPs in the intervention group received a 30 minute practice visit to motivate them to involve patients and instructed them in the use of the consultation leaflet.

The main results reported that subjects were satisfied with their involvement and the GP's behaviour during the consultation. However, there was no difference in effect as a result of the leaflet on involvement, enablement or satisfaction between the intervention and the control group. The intervention group leaflet users reported more psychological symptoms to their GP compared with non-users of the leaflet ($p=0.034$). Overall the main findings do not support the use of the implementation programme on improving involvement, enablement or satisfaction of older patients in their care.

Lewin (2001) [30] conducted a Cochrane review of interventions to promote a patient-centred approach in clinical consultations. The inclusion criteria included RCTs and controlled before and after studies. The interventions promoted patient-centred care in clinical health care consultations, not in social support or social care. Other exclusion criteria included studies that considered cultural, disability, sexuality or other sensitivity training only for health care providers; evaluating training in psychotherapy or counselling for health care providers; studies that trained health care providers to deliver a specific, secondary intervention. The outcome measures included consultation processes; other health care behaviour; health status and wellbeing including physiological measures; patient and/or carers' satisfaction with care. Interventions were grouped into the intensity of patient-centredness and teaching tactics (weak, medium and strong). Five thousand two hundred and sixty titles and abstracts were found, 135 with potential to be included, 17 were included. The studies were mainly conducted in North America; others were from the UK, Switzerland, Norway and Trinidad and Tobago. The aims, format, content of interventions and the clinical conditions on which they focused showed heterogeneity. Studies were grouped into broadly similar interventions: patient-centred training compared with no training for providers (11 studies*); patient-centred training for providers plus patient-centred training or materials for patients (3 studies**); patient-centred training for providers plus condition or behaviour-specific training or materials for providers and patients (2 studies***); patient-centred training for providers, patient-centred materials for patients plus condition- or behaviour-specific materials for providers and patients compared with condition- or behaviour-specific materials for both providers and patients (1 study****). The participants were mainly health care primary care physicians and patients were the recipients in six studies. In some of the studies the primary goal was to increase patient-centredness of care and these studies tended to focus on communication skills as important on their own right, while in other studies patient-centred care was seen as a method to change patient behaviour or improve the health outcome. Overall there is fairly strong evidence that some

interventions which promote patient-centred care in the consultation can lead to significant increases in the patient-centredness of the consultation process.

The following studies dealt with either specific populations or topics outside our main focus: Clark (1998) paediatric doctors, Cope (1986) CCT, Langewitz (1998) paediatric doctors, Lewis (1991) paediatric residents and fellows, Meland (1997) was lifestyle changes for CHD risk.

*Cope (1986), Howe (1996), Langewitz (1998), Levinson (1993), Putnam (1988), Robbins (1979), Roter (1995), Roter (1998), Smith (1995), Smith (1998), Thom (1999).**Joos (1996), Lewis (1991), Pill (1998).***Clark (1998), Meland (1997).****Kinmonth (1998).

Little (2004) [36] conducted a randomised controlled trial to assess the effect of leaflets on empowering patients in primary care consultations. Six hundred and thirty six patients were recruited in the study, aging from 16-80 years and were attendees at one of five general practices in the UK. Participants were randomised to four conditions: receipt of a general leaflet, depression leaflet, both leaflets and no leaflets (control group). The general leaflet encouraged patients to list any issues, to ask questions, talk and discuss any problems of concern with their GP. The depression leaflet listed symptoms of depression (without labelling as such) and asked the patient if they had these, and explained that the doctor would like to discuss them. The outcomes measured were patient satisfaction (the scores reflected aspects of doctor patient communication), consultation time, prescribing, referral and investigation. The only statistically significant interaction was the increase in satisfaction for those who received the general leaflet, the mean difference was 0.17 (95% CI 0.01 to 0.32, p=0.04). Consultation time and the general leaflet were statistically significantly associated with improved satisfaction. The leaflet was statistically significantly more effective when consultations were short (leaflet 0.64, 95% CI 0.19 to 1.08; time 0.31, 0.0 to 0.06. Interactions between both showed those consultations of 5, 8, and 10 minute increased satisfaction by 14%, 10% and 7%. This was also shown for subscales of satisfaction – comfort from communication 1.02 (95% CI 0.36 to 1.68), relief of distress 0.74 (95% CI 0.0 to 1.49), intention to comply with management decisions 0.65

(95% CI 0.06 to 1.23) and rapport 0.81 (95% CI 0.16 to 1.45). The general leaflet increased the number of investigations by the GP (OR 1.43, 95% CI 1.00 to 2.05), which was unlikely to be due to chance or confounders after controlling.

Wilkinson (2002) [37] conducted a randomised controlled trial to investigate the relationship between providing patients with an education guidebook (designed to encourage and support participation in the health care visit) and selected patient and system outcome measures. The study population included 277 predominantly male participants, with an average age of approximately 60 years. This study was conducted in the USA.
Patients in the intervention group were mailed the appointment guidebook with instructions prior to a scheduled routine visit with their primary care provider. The control group was mailed the standard letter informing them of their upcoming appointments. After the visit, the patients in both groups were sent a short questionnaire with instructions and a postage-paid return envelope.
No statistically significant differences were reported in the proportion of patients in the two groups that agreed with any of the six statements, which were relevant to primary care visit effectiveness. However, statistically significant differences were reported in the proportion of patients who received preventative health care interventions of influenza vaccination, pneumococcal vaccination and gender specific cancer screening.

Ross (2004) [38] conducted a randomised controlled trial that assessed the effects of a patient-accessible online medical record on patient satisfaction, adherence and health status in a randomised controlled trial conducted in the USA. The version used in the study, System Providing Patients Access to Records Online (SPPARO) provides access to clinical notes and test results, and also provides a method of sending electronic messages to the clinical staff. Patients included in the study were aged 18 years or older. One hundred and seven were enrolled in the study.

Participants in the SPPARO group were given a user identification and password to SPPARO and a written user guide to the system. The control group continued to receive standard care in practice. Periodic messages were sent by research staff to all participants and they were informed about upcoming surveys and encouraged to contact the research assistant if they had a change of address or telephone number. They were also reminded that they could contact the research assistant if they had problems using SPPARO.

No statistically significant results were found for self-efficacy, adherence to medicines, health status and patient satisfaction. General adherence to medicines advice showed a statistically significant improvement in the intervention group compared with the control group. At 6 months the difference was 2.3 (95% CI -3.7 to 8.3) and at 12 months 7.4 (95% CI 1.8 to 10.9), p=0.01, p=0.02 when adjusted for multiple comparisons. Although the number of patients who visited the emergency department did not differ significantly statistically, there was a statistically significant increase in the number of overall emergency department visits in the intervention group compared to the control group.

Loh (2007) [33] conducted a randomised controlled trial that investigated the effects of a shared decision-making intervention in primary care of depression compared to usual care on adherence, satisfaction and clinical outcomes. The study was conducted in Sudbagen, Germany with primary care physicians as the unit of randomisation. The sampling frame (n=148) were sent a letter and 30 accepted the invitation to take part. Twenty were randomly assigned to the intervention group and 10 to the control group, after drop-out 15 and 8 were left respectively. The physicians had to recruit newly diagnosed depressive patients. The intervention physicians enrolled 263 patients and the control group enrolled 142. After their diagnosis the patients completed a questionnaire measuring patient involvement, depression severity and socio-demographic characteristics. After 6-8 weeks the patients completed a second questionnaire measuring adherence and treatment outcome. At the same time, the physicians rated their assessment of the patients' adherence. The shared decision-making intervention was then implemented with the

intervention group. The intervention was a multi-faceted program including physician training; a decision board for use during the consultation; and printed patient information with specific encouragement to be active in the decision-making process. The physicians in the intervention group completed modules on guideline-concordant depression care. This included enhancing physicians' skills for improving the shared decision-making process. The outcomes measures were patient participation, treatment adherence, patient satisfaction, consultation time and clinical outcomes.

There was no difference in patient participation before the intervention compared to afterwards in the control group, whereas the intervention group had statistically significantly higher patient participation from pre to post intervention (on the doctor facilitation scale, p=0.001 and patient participation scale, p=0.010). There was no statistically significant difference for treatment adherence. Patient satisfaction was statistically significantly higher in the intervention 29.8 (s.d=2.7) than the control group 27.0 (s.d=3.6), p=0.014. There were no values taken for satisfaction before the intervention. There was no difference between groups for length of consultation. Neither group had a statistically significant reduction in depression severity from baseline to post-intervention.

4.6 How can practitioners elicit patients' preferences for involvement in decisions about medicines?

Related references	Evidence statements (summary of evidence)
	No tools designed for use in clinical practice were found.
Ende (1989) [39]; Langewitz (2006) [40]; Tortolero (2006) [41]; Neame (2005) [42]; Braman (2004) [43]; Doherty (2005) [44]; Schneider (2007) [45]; Hill (2006) [46]	The Autonomy Preference Index (API) and developments of the API have been created to elicit patients' preferences for involvement in decision-making and may be reduced to a 6-item subscale.
Cox (2007) [25]	A brief pre-consultation questionnaire may be used to elicit patients' preferences for involvement in decisions about medicines.
Caress (1997) [47]	A set of 5 sort cards can be used to elicit the patients' preferred role and perceived role within the consultation.
Doherty (2005) [44] within a hospital and Cox (2007) [25] before and after a general practice consultation.	Two of these tools have been used within routine clinical settings, but only by dedicated researchers.

4.6.1 Evidence to recommendations

The GDG had requested a specific literature search for clinical tools. No tools for use in clinical practice were found which could elicit patients' preferences for involvement. No clinical tools were found. Two of the shorter research tools had been used in routine clinical settings but by dedicated researchers.

The GDG did not consider it appropriate to recommend these tools outside research settings. The GDG used the evidence from the literature and their professional opinion to develop recommendations on eliciting patients' information needs. The GDG did not consider it could make a specific recommendation on how practitioners should elicit patients' preferences for involvement but noted that the language used in simpler research tools was relatively straightforward. The GDG considered that healthcare professionals needed to be alert to non-verbal clues from patients about their involvement and decisions in the consultation.

4.6.2 Methods of the evidence review

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies – A previous search included only randomised controlled trials (RCTs) and systematic reviews (SRs). No studies which met the criteria were found. We widened the search to include any type of studies to find relevant information to meet our inclusion criteria.

Types of participants - people prescribed medicines for a medical condition.

Duration of studies – no time limit specified for the studies.

Types of interventions - Any intervention (tool) which elicits patient preferences for involvement in decisions about medicines. The tools had to be brief enough to be utilised within a consultation between the patient and practitioner. Therefore long questionnaires were excluded as they would not be manageable.

Types of outcome measures – Any outcome relating to the use of the tool was acceptable as we were looking for a tool which could be utilised within a consultation, rather than looking for specific clinical outcomes.

4.6.3 Evidence review

No tools designed for use in clinical practice were found.

The tools in this review are research tools and not clinical tools designed for use in a consultation. We have included these research studies to illustrate brief questionnaires that have been used in research settings indicating the content of the questionnaires to inform the GDG. We have not reported in detail on development or validation of these questionnaires.

Ende (1989) [39] constructed an instrument to measure patient preferences for making medical decisions and their desire to be informed. The instrument, named the Autonomy Preference Index (API) has a questionnaire format and the scales were developed by a group of 13 clinicians, medical sociologists, and ethicists who were interested in patient autonomy. Items on the scales were tested for reliability and validity. The final API consisted of an 8-item scale on information-seeking and a 15-item scale on decision-making. Within this 15-item scale was a 6-item sub-scale which related to general items. The other 9-items were related to three clinical vignettes and were too disease-specific to be useful for this question. The 6-item scale (part A) meets our criteria (see above) but is a research tool rather than a clinical tool.

The Decision making preference scale (Part A): (responses on a 5-point Likert scale ranging from 'strongly disagree' to 'strongly agree'). The higher the score on the scale, the more patients wished to participate in the decision-making:

1.* The important medical decisions should be made by your doctor, not by you.

2. You should go along with your doctor's advice even if you disagree with it.

3.* When hospitalised, you should *not* be making decisions about your own care.

4. You should feel free to make decisions about everyday medical problems.

5.* If you were sick, as your illness became worse you would want your doctor to take greater control.

6. You should decide how frequently you need a check-up.

* Scoring for these items was reversed, and goes from 5 to 1, rather than 1 to 5.

The API was used within a variety of studies: **Langewitz (2006)** [40]; **Tortolero (2006)** [41]; **Neame (2005)** [42]; **Braman (2004)** [43]; **Schneider (2007)** [45] **and Hill (2006)** [46]. All of the studies used the 6-item subscale as illustrated above, except for Langewitz (2006) [40] who adapted the instrument into two questions and Hill (2006) [46] who adapted the questionnaire slightly to apply to psychiatric patients. Most of the studies posted their questionnaires to the participants rather than having them completed in a clinical setting.

Langewitz (2006) [40]

As part of the questionnaire, Langewitz (2006) [40] adapted the API to 4 point Likert scale: fully agree, slightly agree, slightly disagree, fully disagree.
How much do you agree with the following statements?

- One should stick to the physician's advice even if one is not fully convinced of his ideas (follow physician's advice)
- It should completely be left to physicians to decide on a patient's treatment (Physician should decide)

This was conducted at the University of Basel in Switzerland and was sent to the patients after discharge from hospital.

Degner (1992) [48] adapted the API and placed the questions on sort cards for use with patients with cancer. Their questions were adapted by **Caress (1997)** [47], **Doherty (2005)** [44] and **Cox (2007)** [25].

Caress (1997) [47] conducted a cross-sectional study at a regional renal unit in the North of England with 462 participants from a convenience sample over a 12 month period. 155 of the patients were pre-dialysis, 103 were dialysis patients and 147 were transplant patients. Using a set of sort cards, as used by Degner (1992) [48], the patients picked a single card which was closest to their preferred role in decision-making and also picked a single card closest to their perceived role in decision-making. Patients were also asked to give their rationale for their preferred role.
The 5 sort cards:

Active options

Card A: I prefer to make the final decision about which treatment I will receive.

Card B: I prefer to make the final selection of my treatment after seriously considering my doctor's opinion.

Collaborative option

Card C: I prefer that my doctor and I share responsibility for deciding which treatment is best for me.

Passive options

Card D: I prefer that my doctor makes the final decision about which treatment will be used but seriously considers my opinion.

Card E: I prefer to leave all decisions regarding my treatment to my doctor.

The key points found from the study were that: participation preference was highly individualistic, with a lot of patients wishing to remain passive. Those who did prefer an active role were unlikely to attain this preference; trust in the HCP can influence the preference; desire for information is not synonymous with desire for participation.

Doherty (2005) [44] used the adapted questionnaire to use in an acute hospital trust in England and was one study which tried to elicit the patients' responses within an actual clinical situation.

Cox (2007) [25] included 479 patients who were approached in the waiting room in general practitioner surgeries to participate. They were given an interview where they completed the pre-consultation questionnaire and were also administered a questionnaire after the consultation. The GP was given a questionnaire before, which included their preferred role in decision-making with patients and a questionnaire afterwards detailing their perceptions of the decision-making during each consultation. The doctors' assessment of patients' preference to be involved in shared decision-making was correct in 32% of the consultations, overestimated in 45% of the consultations and

underestimated in 23% of the consultations. The patients' preferences for decision-making involved: 39% wanting the GP to share the decision, 45% wanting the GP to be the main (28%) or only (17%) decision-maker and 16% wanting to be the main (14%) or only (2%) decision-maker.

The questionnaire given to the patients at pre-consultation included the following 5 statements, of which patients were asked to choose one:

- I would prefer that I make the decision about medicines I take for this problem.
- I would prefer that I make the final decision about medicines I take for this problem after seriously considering my doctor's opinion.
- I would prefer that my doctor and I share responsibility for deciding about medicines I take for this problem.
- I would prefer that my doctor makes the final decision about medicines I take for this problem, but seriously considers my opinion.
- I would prefer that my doctor makes all decisions about medicines I take for this problem.

4.7 What tools are available to help elicit patients' beliefs about medicines?

Related references	Evidence statements (summary of evidence)
Hamilton (2007) [49]	One RCT that assessed a patient self-completion agenda form on prescribing and adherence showed no statistically significant results for prescription, satisfaction scores or adherence.
Horne (1999) [50]; Menckeberg (2008) [51]; Horne (2007) [52]; Brown (2005) [53]; Khanderia (2008) [54]; Kumar (2008) [55]; Kemp (2007) [56]; Aikens (2008) [57]; Clifford (2008) [58]; Jenkins (2003) [59]; Theunissen (2003) [60]	No tools designed for use in clinical practice were found. The Beliefs about Medicines (BMQ) – Specific component is a research tool which is used to elicit beliefs about medicines.

4.7.1 Evidence to recommendations

No tools designed for use in clinical practice were found although the GDG were aware of current studies to develop such tools, in particular studies seeking to adapt the BMQ for clinical use. The GDG reviewed the research tools found but did not consider it appropriate to use these outside their research settings. The GDG used the information from the research studies and their professional opinion to make recommendations in relation to elicitation of patients' beliefs about medicines. The evidence review of patients' experience about medicines (chapter 5) was used to inform the content of the recommendations about exploring patients' beliefs and concerns.

4.7.2 Methods of the evidence review

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies – we initially included only randomised controlled trials (RCTs) and systematic reviews (SRs), however none of these types of studies were found that met the criteria. We increased the current search to include any type of study in order to find relevant information to meet our inclusion criteria.

Types of participants - people prescribed medicines for a medical condition.

Duration of studies – no time limit specified for studies.

Types of interventions - any intervention (tool) which elicits patient beliefs about their medicines. The tools had to be brief enough to be utilised within a consultation between the patient and practitioner. Therefore long questionnaires were excluded as they would not be manageable.

Types of outcome measures – any outcome relating to the use of the tool was acceptable as we were looking for a tool which could be utilised within a consultation, rather than looking for specific clinical outcomes.

4.7.3 Evidence review

No tools designed to elicit patients' beliefs about medicines for use in clinical practice were found. The tools which we found in this review were research tools. We decided to include studies which used these research tools to illustrate some questions that could be asked to the patient in a consultation. Most studies were in questionnaire form and so we included those which were shortest. We have not reported the parts of the questionnaire which were not relevant to the clinical question.

Horne (1999) [50] created a questionnaire which explicitly states the intention of assessing patients' beliefs about medicines. The beliefs about medicines questionnaire (BMQ) included two parts – the BMQ-General, which assessed beliefs about medicines in general and the BMQ-Specific, which looks at patients' specific beliefs towards their medicine. The study states that the two sections of the BMQ can be used together or separately. As the BMQ-Specific answers the question, and we are looking for brevity within the consultation, this part of the study is reported.

The BMQ-Specific includes two 5-item factors which assess beliefs of the necessity of medicines prescribed (Specific-Necessity) and concerns about medicines prescribed, based on beliefs of the danger of dependence, long-term toxicity and the disruptive effects of medicines (Specific-Concerns).

The BMQ-Specific items, which are rated 'strongly agree, agree, uncertain, disagree or strongly disagree':

- My health, at present, depends on my medicines.
- Having to take medicines worries me.
- My life would be impossible without my medicines.
- Without my medicines I would be very ill.
- I sometimes worry about long-term effects of my medicines.
- My medicines are a mystery to me.
- My health in the future will depend on my medicines.
- My medicines disrupt my life.
- I sometimes worry about becoming too dependent on my medicines.

- My medicines protect me from becoming worse.

The BMQ-Specific was used in many other studies to assess beliefs about medicines for a range of conditions (Menckeberg, 2008 [51]; Horne, 2007 [52]; Brown 2005 [53]; Khanderia, 2008 [54]; Kumar, 2008 [55]; Kemp, 2007 [56]; Aikens 2008 [57]; Clifford, 2008 [58]; Jenkins, 2003 [59]; Theunissen, 2003 [60]).

We did retrieve one study, **Hamilton (2006) [49]**, which was a randomised controlled trial conducted to test the effect of patient self-completion agenda forms on prescribing and adherence in general practice. This RCT was considered relevant as one of the items of the self-completion form was related to expectations of medicines and it was considered a clinical tool.

1610 patients at 10 general practices in Devon and Dorset (UK) were involved in the trial for up to 12 weeks. All patients were given a letter and an envelope when attending their GP. Half the group received an agenda form which they could fill out while waiting for the doctor. The other half received usual care. The agenda form called the SCAF (self completion agenda form) included five questions:

1. What made you decide to come to see the doctor? Please describe the problem you have e.g. symptoms or current illness.
2. Your ideas about your illness: what do you think is wrong with you?
3. Your concerns: have you any particular worries about your illness?
4. Your expectations: how do you think your problem should be treated? What do you hope the doctor will do?
5. Do you think you should receive a prescription for your problem?

The GP was handed this form when the patient went into their appointment, to use in whichever way they thought appropriate. There were no statistically significant differences between proportion of patients who received a prescription, or in satisfaction scores or adherence to prescribed medicines.

4.8 What tools are available to help elicit patients' information needs?

Related references	Evidence statements (summary of evidence)
	No tools designed for use in clinical practice were found.
Kinnersley (2007) [32]	One systematic review found that 17 RCTs measured question asking with 6 finding statistically significant increases and 11 finding no effects.
Kinnersley (2007) [32]	One systematic review found that patient satisfaction in 14 RCTs showed no changes but in 5 RCTs there were statistically significant increases in satisfaction.
Strydom (2001) [61]	One questionnaire has been developed which can assess information needs of people with learning disabilities.
Agård (2004) [62]	One study used 4 open-ended questions to elicit patient's information needs.
Duggan (2000) [63]; Astrom (2000) [64]; Zwaenepoel (2005) [65]	Three studies included 5 open questions from the Intrinsic Desire for Information (IDI) scale which can elicit information needs from patients.
Ende (1989) [39]; Langewitz (2006) [40]; Tortolero (2006) [41]; Neame (2005) [42]; Braman (2004) [43]; Doherty (2005) [44]; Schneider (2007) [45]	Seven studies use the Autonomy Preference Index 8-item scale to elicit the information needs of patients.

4.8.1 Evidence to recommendations

No tools validated for use in clinical practice were found. The GDG used the evidence from the literature and their professional opinion to develop recommendations on eliciting patients' information needs. The GDG considered that good communication skills are needed to elicit patients' information needs and there is particular importance in considering how best to overcome barriers to communication such as language difficulties.

4.8.2 Method of the evidence review

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies – we initially included only randomised controlled trials (RCTs) and systematic reviews (SRs) however none of these types of studies were found to meet the criteria. We increased the search to include any type of studies to find relevant information to meet our inclusion criteria.

Types of participants - people prescribed medicines for a medical condition.

Duration of studies – no time limit specified for the studies.

Types of interventions - any intervention (tool) which elicits patients' information needs. The tools had to be brief enough to be utilised within a consultation between the patient and practitioner. Therefore long questionnaires were excluded as they would not be manageable.

Types of outcome measures – any outcome relating to the use of the tool was acceptable as we were looking for a tool which could be utilised within a consultation, rather than looking for specific clinical outcomes.

4.8.3 Evidence review

No tools designed for use in clinical practice were found. The tools in this review were research tools opposed to clinical tools which could be used in a

consultation. We decided to include studies which used these research tools to illustrate some questions that could be asked to the patient in a consultation. Most studies were in questionnaire form and so we included those which were shortest – and so could possibly be used in a consultation. We have not reported the parts of the questionnaire which were not relevant and feasible in a consultation.

One Cochrane review (included in section 5.4) addressed ways of eliciting patients' information needs. **Kinnersley (2007)** [32] conducted a Cochrane review of the effects of interventions before consultations designed to help patients address their information needs. The settings and populations varied but most were conducted in the USA. They stated that it complemented other Cochrane reviews by Wetzels (2007) [34] and Lewin (2001) [30]. The inclusion criteria were RCTs of interventions intended to help the patients, representatives or carers address their information needs in a consultation. This was done by encouraging question-asking, to express their information needs, to overcome barriers to communication and to clarify their understanding of the information provided. Outcome measures were the consultation process, consultation outcomes and service outcomes. 33 trials described in 35 studies met the inclusion criteria. Of the studies assessing single interventions for patients 15 included written materials, four were coaching. The multiple component single interventions studies four had coaching and written materials. Seventeen studies measured question-asking with 6 finding statistically significant increases and 11 studies finding no effects of the interventions compared to controls. Patient participation was measured in 14 studies, it was increased in 8, showed no effect in 5 studies, and in one study it increased initially then decreased. Patient satisfaction was measured in 23 studies, in 14 studies there were no changes and in 5 there was increased satisfaction. Patient knowledge was measured in 5 studies with reduction in two studies and no changes in 3 studies. According to type of intervention, comparisons between written alone and coaching alone showed similar, small to moderate and statistically significant increases for both types for question-asking. Patient satisfaction was borderline statistically significant for written materials, for coaching the effect was small and statistically

significant. Written materials led to a small and statistically significant increase in consultation length, for coaching the increase was smaller but was not statistically significant. Interventions immediately before the consultation led to a small statistically significant increase in consultation length and patient satisfaction.

It should be noted that many of the studies were from other settings: Brown (1999, 2001), Bruera (2003), Butow (1994, 2004), Davison (1997, 2002), Ford (1995), Oliver (2001) were cancer studies. Finney (1990), Kim (2003), Lewis (1991) were from paediatric and family planning settings.

Strydom (2001) [61] conducted a study of a service-user questionnaire to find gaps in medicines knowledge and information sources. This study specifically involved finding out the views of those with learning disabilities. Twenty-one participants were included who were either currently taking prescribed medicines (GP or specialist health services) or had taken in the recent past. Two thirds of the subjects received help with taking their medicines. A questionnaire was designed by the authors using previously published guidelines. They used structured and semi-structured sections, including open questions. The questionnaire was delivered by one of the research team with experience of communicating with people with learning disabilities. The questionnaire was designed to find out their experiences and opinions of using medicines.

A table was given in the paper to show the questions relating to medicines knowledge. Please note that it is unknown as to whether this was exhaustive. The open questions were not reported in the paper.

- Can you read the label? (yes, no)
- What is written on the label? (don't know, name, my name, chemist's name, dose, other)
- What is your medicine called? (don't know, brand or generic name, approximate name, description)

- What are you taking medicine for? (don't know, knew indication, approximate indication)
- Is there anything you should not do while taking this medicine? (don't know, yes, plus example)
- Are there any side-effects? (don't know, one, two or more)

The resulting answers led to the framework for a structure of a patient information leaflet for people with learning disabilities who take medicine for psychiatric conditions. It is not clear as to whether the service users who filled in the questionnaire were taking psychiatric medicine or another type of medicine. The subjects were 'selected for their range of experiences of taking medicines'. Therefore this study does not elicit patients' information needs in total, but how to elicit the knowledge gaps of those with a learning disability.

Duggan (2000) [63] developed and evaluated a survey tool (intrinsic desire for information) to find out patients' perceptions and information needs in regard to their medicines. It was tested for reliability and by factor analysis and was used with 2 cohorts of patients in East London (sample of 500).

Astrom's (2000) [64] paper refined and validated the IDI into a 12-item scale. They included 5 open questions which were a joint construction of the project aims and questions from Lindegren (1999), which was a Masters thesis at the Department of Bio pharmaceutics at Uppsala University. The open questions were transcribed at the bedside of 299 patients in the wards of three medical hospitals in London. Astrom (2000) concluded that the desire for information may be more complicated and involve an emotional or behavioural component, which was not included. It should be noted that this is a desire for information which may differ from information needs.

The 12-item scale was deemed too long to meet our inclusion criteria, however some of the open questions may be of relevance.

The IDI (for reference only):

Part 1 – Demographic details.

Part 2 – Questionnaire items (scored from strongly agree through strongly disagree on a 5-point Likert scale).

1. I always speak to my pharmacist when I want information about my medicines.
2. Sometimes I feel a little inhibited when I ask for information…they might think I should know already.
3. If there is anything I need to know, it's most convenient to ask at the surgery.
4. It's not really my place to ask for information, they have enough to do.
5. The people at the hospital can easily give me information when I go for my appointment.
6. I need as much information about my medicines as possible.
7. Too much knowledge is a bad thing.
8. You can never know enough about these things.
9. I don't need any more knowledge about my medicines/illness.
10. I read about my medicines/illness as much as possible.
11. What you don't know (with respect to medicines/illness) doesn't hurt you.
12. I find information about my medicines/illness confusing.

Open questions:

13. What kind of information about your medicines do you want? Why?
14. How do you want your information to be presented (written, oral, both, other)? Why?
15. Who would you like to give you information about your medicines? Why?

16. When would it be best to have the information about your medicine presented (at hospital, at home, at the community pharmacy, at the GP's)? Why?
17. Would you like to sit down and talk about your medicines with a pharmacist at the hospital?

Zwaenepoel (2005) [65] used the IDI scale and 5 open questions in a survey of the need for information of 279 psychiatric in-patients in Flanders.

Ende (1989) [39] created the Autonomy Preference Index (API) which, as well as a decision-making preference scale had an eight-item information-seeking preference scale. The instrument was in questionnaire format and the scales were developed by a group of 13 clinicians, medical sociologists, and ethicists who were interested in patient autonomy. Items on the scales were tested for reliability and validity. The final API consisted of an 8-item scale on information-seeking scale (ISS) and a 15-item scale on decision-making.
The 8-item ISS consisted of the following items for information-seeking preference, with responses on a five-point Likert scale from 'strongly disagree' to 'strongly agree':

1. As you become sicker you should be told more and more about your illness.
2. You should understand completely what is happening inside your body as a result of your illness.
3. Even if the news is bad, you should be well informed.
4. Your doctor should explain the purpose of your laboratory tests.
5. *You should be given information only when you ask for it.
6. It is important for you to know all the side effects of your medicines.
7. Information about your illness is as important to you as treatment.
8. When there is more than one method to treat a problem, you should be told about each one.

* Scoring for this item is reversed and goes from 5 to 1, rather than 1 to 5.

Five further studies used the Autonomy Preference Index to elicit patients information needs (Langewitz, 2006 [40]; Tortolero, 2006 [41]; Neame, 2005 [42]; Braman, 2004 [43]; Schneider, 2007 [45]; Hill, 2006 [46]). All of the studies used the full length (8-item) information-preference scale except for **Langewitz (2006)** [40] who incorporated only one question from the API to target information needs: 'Even when the news is bad the patient must be informed (information)'. Hill (2006) [46] slightly altered the API questions for psychiatric patients to use.

Agard (2004) [62] conducted a qualitative analysis of semi-structured interviews in Gothenburg, Sweden on 40 patients 60 years and over who were receiving treatment after a heart failure diagnosis. The semi-structured qualitative interview had 4 open-ended questions as an interview guide. The questions were:

1. What is your opinion about the medical information that you have been given?

2. What kind of information is lacking?

3. What information have you been given about heart failure?

4. What is your attitude toward receiving prognostic information?

They were also encouraged to speak about the questions and to raise other issues related to them to ensure their major personal concerns really emerged. To avoid respondents feeling ignorant or embarrassed about not being able to adequately answer questions relating to knowledge they were asked first about the information they had been given, rather than asking directly about their knowledge of diagnosis, treatment and prognosis.

Many patients had a limited understanding of their disease but said they were still satisfied with the information they received. Some were indifferent to, accepted, or were unaware of their low level of knowledge.

They concluded that 'to inform the patient adequately, physicians and nurses should determine the patient's level of knowledge and explore why those patients who have a limited understanding do not assimilate or request information. The information they provide should also be adapted to the patient's capacity, wishes and emotional reactions.'

4.9 How can information about medicines be provided for patients in order to enhance SDM in regard to medicines?

Related references	Evidence statements (summary of evidence)
Trevena (2006) [66]	A systematic review of systematic reviews and RCTs found that communicating with patients about evidence does increase their understanding regardless of what tools used. There was a greater effect if information was structured (either written, verbal or video) or interactive, especially if tailored to the individual.
Trevena (2006) [66]	One systematic review of systematic reviews and RCTs found that probabilistic information is best represented as event rates, rather than words, probabilities, or summarised as effect measures such as relative risk reduction. Illustrations, such as cartoons or graphs appear to aid understanding.
Wills (2003) [67]	One systematic review of information formats concluded that decision support/aids can address patient information needs for shared decision-making. They enable patients to better understand treatment options, including probability information.

4.9.1 Evidence to recommendations

Information provided to patients about treatments increases their understanding whatever the format (verbal, written or video) particularly if the information is structured or interactive and especially when tailored to the individual. The GDG considered that health care professionals need to be aware that individuals will vary in the amount and type of information they require and in how they can best access that information. It was the professional opinion of the GDG that undue emphasis is currently placed on use of leaflets and written information and there is inadequate access to pictorial and graphic information. Examples of useful websites were presented to the GDG showing information presented in a variety of ways and the GDG believed it important to widen knowledge and access to such resources. The GDG considered that information should be provided before prescription and dispensing. The GDG were concerned about possible over reliance on PILs which in their professional opinion were not often appropriate for patients and caused concern and problems after medicines had been dispensed. The GDG were aware of pilot work taking place to improve PILS. The evidence review reported in 4.10 also informed recommendations in this area.

4.9.2 Method of the evidence review

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies: Systematic reviews of randomised controlled trials (RCTs) or randomised controlled trials of interventions involving shared decision-making in the clinical context.

Types of participants: people prescribed medicines for a medical condition.

Duration of studies: no time limit specified.

Types of interventions: any interventions involving shared decision-making in a consultation between a health care professional and patient.

Types of outcome measures: patient-centred communication in the consultation; consultation process outcomes: patient involvement, question asking, preparedness; patient care outcomes: satisfaction, knowledge, self-efficacy; type of interventions involved and type of information.

It should be noted that the remit is for conditions with prescribed medicines and this excludes conditions which require chemotherapy or screening. All RCTs are within this remit, however many of the systematic reviews included populations outside the remit, this is noted where applicable.

4.9.3 Evidence review

Trevena (2006) [66] conducted a systematic review of RCTs and review of reviews structured around three aspects of communication with patients about evidence: patients' preferences and actions; research evidence; and the clinical state and circumstances. These were then translated into three main questions:

- What are the most effective communication tools to improve patient understanding of evidence?
- What are the most effective formats to represent probabilistic information to improve patient understanding of evidence?
- What are the most effective strategies to elicit patient preferences/beliefs/values relating to evidence?

The authors excluded studies that did not address their question; were about patient education; were focused on skills and behaviour outcomes without attempting to increase understanding or knowledge; were concerned with counselling as a therapeutic intervention; or were specific to communication regarding clinical trial participation.

Overlap between the trials included in the systematic reviews and those identified independently was verified and duplicated studies were excluded. Ten systematic reviews of RCTs and 30 additional RCTs were retrieved.

The review concluded that communicating with patients about evidence does increase their understanding regardless of the tools used. The authors also found that there was a greater effect if information was structured (either written, verbal or video) or interactive (computer, touch screen, question

prompts) and particularly if the information was tailored to the individual. Probabilistic information was found to be best represented as even rates in relevant groups of people, rather than words, probabilities or summarised as effect measures such as relative risk reduction. Written information was reported to be more effective if illustrations and graphs were used.
The authors did however remark that there could be difficulty in generalising from the literature as the trials were conducted in a wide variety of clinical settings using a range of clinical problems and outcomes.

Wills (2003) [67] conducted a systematic review of patient health information provision and use for treatment decision-making. It included research from the past 10 years focusing on testing different formats of information presentation for patient decision-making. The three types of formats looked at were probability presentations, graphic formats and words vs numbers. They found two studies where participants preferred presentation of medicine in terms of relative risk rather than absolute risk format. They found that people place relative risk information into a simplified format of small or large risks and there is a tendency to seriously under or overestimate their personal risks for health outcomes. There is a need to tailor the format of risk communication to the individual's level of numeracy. In routine clinical encounters information should be presented as balanced, in both positive and negative frames. Graphics can improve the understanding of numerical probability information. However some people may dislike some types of displays or misunderstand them. Consistent finding of individual differences in preferences for probability information in words, numbers of both formats implies a need for routine individualised assessments of patient preferences for format. In conclusion, decision support/aids can address patient information needs for shared decision making. They enable patients to better understand treatment options, including probability information.

4.10 What information about medicines should be provided for patients in order to enhance SDM in regards to medicine?

4.10.1 Evidence to recommendations

The GDG considered that the provision of information to patients is to facilitate informed choice about medicines, and achieve a clear picture of the benefits and risks. The information that should be provided to a patient is dependent on what that patient needs to make a decision and therefore a prescriptive list can not be generated. Patient Information Leaflets (PILs) provided with medicines often do not help in providing information about medicines and in any case are only received after the medicine is dispensed. The GDG did consider some broad areas of information that patients might require and used the evidence from expert reviews, in particular those with patient involvement to inform this. They also considered that sources such as the MHRA leaflet might be useful for patients. The GDG therefore made recommendations about the need to tailor the information to the patient and that practitioners should not assume that PILs will provide adequate or appropriate information for individual patients.

4.10.2 Evidence review

The evidence review is a narrative review. The GDG requested review of current national guidance and reports with a particular emphasis on those where patients' views and perspectives were given priority.

4.10.2.1 Summary of 'Always read the leaflet (2005) Report of the Committee on Safety of Medicines Working Group on Patient Information'[1]

The Working Group on Patient Information received advice from patients and experts on the quality of Patient Information Leaflets (PILs) and how to improve them. Patient organisations identified the following with regards to PILs:

- The quality is variable and language is complex with too much jargon.
- The leaflet is often too busy and the print too small.
- Leaflets are too negative and do not mention enough of the benefits
- The PIL should complement discussion with the prescriber, ideally available in the consultation.
- One PIL can not meet everyone's needs so information on patient organisations for further advice could be given.
- Helpline numbers and website addresses for further information should be mentioned.
- Comparative information and information about lifestyle issues can help in decision making.

Expert views regarding PILs:

- Too much use of jargon.
- The use of capital letters was eye-catching but hard to read.
- Inappropriate punctuation can obscure the message.
- Text in boxes may be skipped over.
- Euphemisms are not helpful when referring to serious side effects.
- Messages should be consistent.
- Language should be clear and unambiguous.

Research[2] showed that patients prioritise four key points of information about a medicine – side effects, dos and don'ts, what it does and how to take it – but different people prefer different orders of priority.

The Working Group recommended the following for an improved readability guideline:

Usability – PILs should be clear and understandable to the reader. This incorporates writing style, typeface, design and layout, headings, use of colour, use of symbols and pictograms. The use of templates so that

information is presented consistently would be useful. (See annex 6). PILS should not be too long and complex.

User involvement in PILs – user testing of patient information is recommended. This should be done under controlled conditions and meeting certain stipulations. User testing of content and impact is important. The production of PILs by companies often occurs at the end of the medicine development process, with little thought of involving patients in writing and testing the information. Views should be at all stages of development.

Communicating Risk

It is fundamental when making an informed decision to understand and weigh up the risk and benefits of a treatment. The working group suggested:

- Use of headlines to summarise the most important messages for safety and effectiveness of using the medicine.
- Information on all the side effects is required by law but must be presented logically and include a description of side effects, estimating frequency and advice on necessary actions.
- Inclusion of the potential benefits to provide balance is important.
- Provide information about the harmful effect itself; the probability of it occurring and how to minimise risk and what actions to take if a problem arises.
- Put the most important information first, include information on benefit, use the right words and use numbers to convey risk. Also a supplementary leaflet of risks and benefits in addition to PILs would be useful.

Trust in the information source is also important. Harms and benefits should be side by side and medicine side effects must legally be provided. Care should be taken to give unbiased and clear statistical information.

To increase trust in PILs transparency of data and certainty of risk estimates may be effective. To avoid unnecessary concerns the use of clear information

on a true scale and the nature of such risks are important, such as using analogies and alternative risk scales to show rarity of risk; describe baseline risk and increased risk; provide further information sources on these risks.

Headlines – It is suggested that information could be portrayed in headlines which should include: why the patient should take the product; the maximum dose or duration of treatment; potential side effects/withdrawal reactions; contraindications; important medicine interactions; circumstances in which the medicine should be stopped; what to do if the medicine does not work or where to find further information. Headlines should also include a firm encouragement for the patient to read the rest of the leaflet.

Balance - It is important to be balanced and convey information on benefits as well as risks in order for the information to be credible. The PIL should therefore include the potential benefits of taking the medicine. Research shows that short factual statements on benefits help weigh the risks and benefits. It must also be compatible with the 'summary of product characteristics', and be useful to the patient but not promotional.

Information to give a balanced account would include:

- Why it is important to treat the disease.
- Whether the treatment is for short term or chronic use.
- Whether the medicine is being used to treat the underlying disease or for controlling symptoms.
- Whether the effects will last after medicine stopped.
- Where it is to treat two or more discrete indications, all should be succinctly described as above.
- Where to obtain more information on the condition.

Side effects

Better information about side effects would include:

- Logical order - the most important information should be first e.g. situations where need to take action such as stopping medicines or getting medical help.
- What to do if encounter serious problems.
- Estimates of frequency should be mentioned – as the most serious side effects are also the rarest.
- Use the right wording – not just describe the side effect but convey seriousness/severity.
- Many side effects are dose related and so a warning statement is needed but should not alarm those prescribed high doses.
- It would be useful to have a glossary of lay terms – so there is standardised side effect lay terminology across medicines.

Expression of risk

Expressing statistical risk in PILS:

- Quantifying risk using absolute numbers.
- Verbal descriptors of risk only used if accompanied by equivalent statistical information.
- Convey uncertainty around risk estimates; frequency ranges; duration of risk; frequency estimates based on spontaneous adverse medicine reaction data; constant denominators.

Concepts deemed inappropriate by the Working Group were:

- NNT/NNH.
- positive framing and negative framing – too cumbersome and lengthy.
- use of diagrams – constraints in size.

Supplementary information - a leaflet about risks and benefits in addition to PILs would be able to go into more detail.

Meeting the needs of special groups of patients

Not everyone finds it easy to access and use information in the PIL, e.g. visually impaired people, people whose English is not their first language, people with poor literacy and numeracy, those with learning difficulties or physical difficulties.

Suggestions are made and projects described to help these patient groups:

For health literacy:

- A health search engine for healthcare staff and public.
- Patient information bank for NHS trusts to print consistent information for individuals on their care and treatment.
- Power questions to ask in consultations.

Poor basic skills:

- Clearly written in plain English.
- Signpost other sources of information.
- Helplines.

Patients with sight loss:

- Leaflets in Braille or large print.
- Audio version.
- Leaflets on the web.
- Digital television.
- Telephone helplines and automated voice systems.

Fluency in English difficulties:

- Provision of leaflets in other languages from the company in written or web-based format.

- Telephone helplines.
- The use of translator services.

Medicines for children and young people

- Information for children should be communicated by parents or carers and so leaflets should be aimed at adults.
- Information for young people should take into account their lifestyle of the age group and likely questions.

Provision of information for carers

- Carers may not be in the consultation when prescribed and may need training on administration techniques.
- Outside power of the group but use of a telephone helpline could address some concerns.

The Pharmaceutical Companies

Responsibilities:

- It is suggested that the pharmaceutical industry could promote access to the information on the PILs and other measures.
- Portfolio of Information keys for pharmaceutical companies – use these to help identify additional measures that would promote the dissemination of information on safe use of their products to ensure vulnerable groups can access it.
- Leaflets in other formats; how to signpost these other formats; translation into other languages; use of information mediators such as helplines; expert sources of advice. The PIL can be a pointer to other sources of information for vulnerable groups e.g. booklets, simplified leaflets, magazines and websites.

The information format of the patient leaflet is very important and should be clear and understandable. The information needs to be balanced, trustworthy, and include benefits as well as side effects, with the most important information highlighted. The communication of risk should be conveyed with seriousness but without alarm for the patient. Where to get extra information should be mentioned, if not a separate detailed booklet given. It would be very good practice to have patients test the leaflet to see its appropriateness. Special groups of patients should be taken into account while producing PILs.

Changes to legislation

Since publication of the document 'Always read the label' in 2005, there have been changes made to the European Commission regulations regarding patient information leaflets in response to this report. These included provision of the PIL in formats which are suitable for the blind and partially-sighted; requirement of a specific order for the appearance of the required information on the leaflet; and the requirement of consultation with target patient groups (user testing) to ensure legible, clear and easy to use PILs. These areas were important in the report and it is hoped that they will improve patient information leaflets to support the information provision by health care providers.

4.10.2.2 Raynor (2007) [68] Summary

Raynor (2007) [68] researched the role and effectiveness of written information available to patients. They conducted a quantitative review of the effectiveness of written medicines information; a qualitative review of the role and value of the information; stakeholder workshops to elicit stakeholder perceptions of the key issues surrounding information presentation to patients; and an information design review.

The workshop discussions found timing of the delivery of the information important, which was often presented after the medicine was prescribed. Sometimes no leaflet was available at all. They found too much information to be overwhelming, harder to understand, often frightening and often too much irrelevant information. Readability was the most important part of written

medicines information – the size of text and content, meaningful information and not jargon.

Other information of importance:

- Dosage and ingredients.
- When and how long to take it.
- The likelihood of it being successful.
- Side-effects e.g. how common or rare they are.
- Factors relevant to their personal medical condition.

Also the role of medicines:

- How to take the drug effectively.
- Its potential side-effects and interactions.
- How to reduce potential harm from medicines.
- How long before the medicine will have beneficial effects.
- Why it is necessary to finish the course.
- Why it was recommended not to drink alcohol.

What makes medicines information effective?

- Timing of delivery of the information – more effective during the consultation.
- Visually appealing and straightforward to read.
- No jargon.
- Basic information about what the medicine contains.
- Designed for patients or professionals.

What participants feel makes medicines information valuable?

- Looks and feels important and highlights priority information.
- Permits an informed choice.
- Is reassuring and reduces concern, conflict and anxiety about whether the medicine is the right one for them.
- Gives them confidence in taking medicines.

4.10.2.3 The 'Medicine use review: Understand your medicine' NHS report[4] summary

The 'Medicine use review: Understand your medicine' NHS report[4] suggests questions patients should ask about their medicines. These could be adapted (as below) into written information for patients:

- What the medicine does.
- Why is it important to take the medicine.
- Other treatment options.
- When and how it should be taken.
- How long it should be taken for.
- What medicines, drinks, foods or activities the patient should be aware of when taking the medicine.
- What the patient should do if they do not feel well when taking it.
- How the patient can tell if it's helping.
- How the patient can be sure it's safe to take it.
- The possible risks and side effects.
- What to do if they get one of the side effects.
- What happens if the patient stops the medicine or takes a lower dose.
- Is there anything they can do to remember to take their medicines.
- Where to go for more information.

4.10.2.4 "Taking Medicines" leaflet summary

The Medicines and Healthcare products Regulatory Agency (MHRA) have produced a leaflet for patients called 'Taking Medicines – some questions and answers about side effects'. The leaflet has 8 questions and short answers to these questions. Patients are advised that they should receive a patient information leaflet with their medicines, and to ask their doctor, pharmacist or NHS direct if they have further queries. The questions in the leaflet are:

1. What do medicines do?
2. Will my medicine cause side-effects?

3. What is meant by a common or rare side effect?
4. How much medicine should I take?
5. How can I reduce the risk of side effects?
6. Do side effects always come on straight away?
7. What should I do if I feel unwell after I take my medicine?
8. Will my medicine affect my lifestyle?

1 Always Read the Leaflet: Report of the Committee on Safety of Medicines Working Group on Patient Information (2005). The Stationery Office, London.

2 Berry, D.C. (1997) Psychol Health. As referenced in Always Read the Leaflet: Report of the Committee on Safety of Medicines Working Group on Patient Information

4 The 'Medicine use review: Understand your medicine' (2005) NHS Report by MHRA and ASK.

4.11 Mental capacity narrative

Some concern was expressed by the GDG about the potential conflicts between respecting the autonomy of the patient and the duty of care felt by practitioners towards the patients. The GDG discussed the importance of professionals' codes of conduct and the legal system in protecting both patients and professionals. The narrative below brings together the principles discussed and is a repeat of section 3.4 in chapter 3.

4.11.1 Roles and responsibilities of patients and health care professionals

Hyperlink to section 3.3 Roles and Responsibilities of Patients and Health Care Professionals

4.12 What information about shared decision-making and adherence should be recorded in patients' notes?

4.12.1 Evidence to recommendations

The GDG considered it important that a record is kept of discussions between health care professionals and patients about medicines. Prescribing and taking of medicines is a long term dynamic process which may involve multiple interactions between health care professionals and patients. Good record keeping aids continuity of care by providing information for healthcare professionals to review the discussion they or other health care professionals have had with patients about their medicines. The GDG made recommendations based on professional opinion.

4.13 What tools are available to support the patient in reaching an informed decision? How effective are these tools?

Related References	Evidence Statements (summary of evidence)
O'Connor (2003) [69]	One systematic review found that there a variety of decision aids used in studies - audio guides, CD-ROMs, web-based, interactive video-disc, lecture and handouts.
O'Connor (2003) [69]	One systematic review found that decision aids led to greater knowledge, realistic expectations, lower decisional conflict from feeling informed, more active in decision-making and less indecision after the intervention.
O'Connor (2003) [69]; Montgomery (2003) [70]; Weymiller (2007) [71]; Thomson (2007) [72]; Oakley (2006) [73]	Decision aids reduced decisional conflict (1 systematic review, 4 RCTs).
Thomson (2007) [72]	One RCT, where decision aids decreased decisional conflict, found that those who used the aid but had not started warfarin treatment were less likely to do so than the control group (who received evidence-based guidelines).
O'Connor (2003) [69];	Decision aids improved patient knowledge (1

Montgomery (2003) [70]; Weymiller (2007) [71]; Thomson (2007) [72]	systematic review, 3 RCTs).
O'Connor (2003) [69]	One systematic review found that simpler decision aids compared to detailed decision aids showed a statistically significant improvement in knowledge, more realistic expectations and greater agreement between values and choices.
Montgomery (2003) [70]	One RCT found that decision analysis decreased decisional conflict more than a video/leaflet intervention.
Fraenkel (2007) [74]	One RCT found that an interactive computer tool which generated personalised feedback statistically significantly improved decisional self-efficacy and preparedness to participate in decision-making, with greatest benefit for older adults.
Oakley (2006) [73]	One RCT found that a workshop plus a decision aid (identifying own risk and pros and cons) and worksheet did not statistically significantly improve adherence, although patients were initially satisfied with the information on medicines this was non-significant and had dissipated by the end of trial.
Hamann (2007) [75]	One RCT found that a decision aid and planned talk with doctor reduced hospitalisation for schizophrenic outpatients. However those who showed a higher preference for autonomy and better knowledge showed a statistically significant higher re-hospitalisation rate.

4.13.1 Evidence to recommendations

The literature review found a number of systematic reviews concerning decision aids and their use. The results of the trials primarily related to decisional conflict, satisfaction, involvement in decision and participation with little effect on health outcomes overall. The GDG considered the evidence supportive of the importance of structured information in a variety of formats to patients but did not feel it appropriate to make specific recommendations regarding decisions aids.

4.13.2 Methods of the evidence review

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies: systematic reviews or randomised controlled trials (RCTs) of tools to help the patient reach a decision (decision aids).

Types of participants: people prescribed medicines for a medical condition faced with a decision.

Duration of studies: no time limit specified.

Types of interventions: any interventions which aid the patient in making an informed decision.

Types of outcome measures: patient outcomes: decisional conflict, patient knowledge, and self-efficacy.

It should be noted that the remit of the guideline is for conditions with prescribed medicine and this excludes conditions which require chemotherapy or screening. All RCTs are within this remit, however many of the systematic reviews included populations outside the remit, this is noted where applicable.

4.13.3 Evidence review

O'Connor (2003) [69] conducted a Cochrane review of decision aids for people facing health treatment or screening. They included RCTs; involving those

over age of 14 making decisions about screening or treatment options for themselves, a child, or significant other; including decision aids and looking at whether the decision aids achieved their objectives. They found 131 decision aids developed within the previous five years, 94 were web-based, 14 paper-based and 12 videos with print resources, eight were audio-guided print resources, two were CD-ROMs and one a web-based with workbook. Most of the decision aids were intended for use before counselling. Decision aids were better in terms of greater knowledge, realistic expectations and lower decisional conflict related to feeling informed. They increased the proportion of people active in decision-making and reduced the proportion of people who remained undecided post-intervention. Simpler decision aids were proven to have more statistically significant improvement than more detailed decision aids in knowledge, more realistic expectations and greater agreement between values and choices. There was no improvement compared to comparisons for affecting satisfaction with decision making, anxiety, and health outcomes.

Only a few of the studies in this systematic review were relevant to the guideline as the majority of studies included were surgery, screening, or other populations not included in the medicines concordance remit. The studies that were relative to the guideline were seven trials of hormone replacement therapy* (audio guides, booklet and interactive videodisc, mix of lecture and handouts); two trials involving Ischaemic heart disease**, interactive videodisc and a videocassette; and one study of atrial fibrillation treatment*** (audio guide deciding whether to change from aspirin to warfarin). All studies except five of the HRT trials compared a decision aid with usual care. The other five studies compared a multiple element design with a simple decision aid.

*McBride 2002, Murray HRT 2001, O'Connor, 1998-RCT, Dodin 2001, O'Connor Wells 1999, Rothert 1997, Rostrom 2002.**Morgan 1997, Bernstein 1998.***Man-Son-Hing 1999.

Montgomery (2003) [70] conducted a factorial randomised control trial to evaluate two interventions to help hypertensive patients decide whether to start medicines to reduce blood pressure. This was carried out in 21 general

practices in SW England with 217 patients aged 32 to 80 years (mean age 59 years), who were newly diagnosed with hypertension. Patients were allocated to decision analysis or no decision analysis, they were then further randomised to video/leaflet or no video/leaflet groups. The decision analysis in this case was a decision tree for hypertension which used a computerised self-completed interview to assess patients' utilities with minimal input from researcher and the absolute cardiovascular risk was calculated. The video was informational about high blood pressure. The information booklet included four fact sheets from the British Hypertension Society. The primary outcome was the total score on the decisional conflict scale, a questionnaire measuring how uncertain about the course of action to take and factors which could be changed that lead to the uncertainty. Secondary outcomes were subscales of the Decisional Conflict Scale and intentions about starting treatment, state anxiety, knowledge of hypertension, actual treatment decision.

Both interventions successfully reduced patients' total decisional conflict at follow-up. Decision analysis decreased the decisional conflict more than the video/leaflet. Total decisional conflict mean for decision analysis was 27.6 (s.d=12.1), no decision analysis 38.9 (s.d=18.3) adjusted difference -9.4 (95% CI -13.0 to -5.8) p<0.001; video/leaflet 30.3 (s.d=13.4) and no video/leaflet was 36.8 (s.d=18.8), -4.2 (95% CI -7.8 to -0.6), p=0.021. The Decisional conflict subscales showed a clear reduction in three of the five subscales - uninformed 23.7 (s.d=11.8) compared to no decision analysis 40.7 (s.d=23.1) adjusted difference -15.7 (95% CI -20.2 to -11.2), unclear values 28.4 (s.d=14.7) vs 43.8 (s.d=24.3) adjusted difference -13.1 (95% CI -18.0 to -8.1) and unsupported 24.4 (95% CI 13.4 vs 34.8 (18.3) adjusted difference -8.7 (95% CI-12.8 to -4.7) and some evidence for reduction in uncertainty and no evidence for decision quality. The video/leaflet intervention showed no evidence in these last two subscales and there was only clear evidence on the uninformed subscale. For the intention to start treatment when followed up the adjusted risk ration: yes versus unsure 1.19 (95% CI 0.59 to 2.40) for decision analysis and 1.80 (95% CI 0.89 to 3.63) for the video/leaflet. No versus unsure 3.15 (95% CI 0.91 to 10.98) and 0.52 (95% CI 0.15 to 1.77) respectively. The overall p values were 0.09 and 0.17 respectively. Actual

prescription of medicine was not different for either intervention or controls. There was a suggestion (p=0.055) that anxiety may be reduced by decision analysis although the evidence there was weak and no evidence of this for the video/leaflet intervention. Both interventions statistically significantly increased knowledge of hypertension. Those who received both interventions had the lowest decisional conflict (27.1 compared with 28.2 and 33.3 and 44.2 for decision analysis only, video/leaflet and control). They had a high knowledge score – the same as video/leaflet. Within the regression models there was a statistically significant (antagonistic) interaction between decision analysis and video/leaflet, so the effect of each was reduced by the presence of the other (interaction coefficient 12.5, 95% CI 5.4 to 19.5, p=0.001 for decisional conflict and -9.1, 95% CI -16.3 to -1.9, p=0.013 for knowledge. This study was followed up in 2005 by Emmett, who found that there was no evidence of any difference in blood pressure, cardiovascular disease risk for either intervention or between them. There were also no effects on medicine prescribing, self-reported adherence, consulting behaviour or management changes.

Weymiller (2007) [71] conducted an RCT study of the effect of a decision aid on statin medicine decision-making. The study was conducted in a diabetes referral clinic in Minnesota, USA. Ninety-eight participants were included with a mean age of 64 (s.d=12) for the decision aid group and 66 (s.d=8) for the control group. Participants were randomised to either receive usual care plus a standard pamphlet on cholesterol management or a statin choice decision aid. The decision aid included name, cardiovascular risk factors, an estimated level of cardiovascular risk (3 levels) and the absolute risk reduction with statins and the potential disadvantages of taking them. A question prompted patients to express whether they were ready to make a decision and if they wanted to take statins, discuss the issues with their clinician or other. After the consultation the participants were given a questionnaire to complete. The outcomes of interest were improvement in patient knowledge and reduction in decisional conflict. Seventy-four% would recommend the decision aid to others compared to 53% of control patients recommending the pamphlet, (OR 2.6, 95% CI 0.8 to 8.0), 68% would want to receive similar support for future decisions compared to 58% of control patients (OR 1.5, 95% CI 0.6 to 3.8).

Those receiving the decision aid had higher knowledge scores than the control group and those allocated to receive the intervention during the visit achieved better knowledge than those who received before the consultation. The intervention group had statistically significantly less decisional conflict afterwards than the control group, and at 3 months (although not statistically significant). Those in the DA group felt more informed. Thirty percent of the DA group (6/7 were from the DA during the visit group) decided to start statin therapy immediately after, compared to 21% of the control group. At 3 months 63% of the DA group and 63% of the control group reported taking statins (OR, 1.4, 95% CI, 0.8 to 2.4). Overall, there was no difference in adherence to patient choice at 3 months.

Thomson (2007) [72] conducted a randomised controlled trial of a decision aid for anti-thrombotic treatment of patients with atrial fibrillation. One hundred and nine patients aged over 60 years from 40 general practices in the Northeast of England. The intervention involved the doctors in the clinic delivering either the decision aid or guidelines to the patient. The decision aid was a computerised aid which presented the individualised benefits and potential harms of warfarin treatment and participants were invited to weigh up the advantages and disadvantages of treatment before coming to a shared decision with the doctor. This involved personalised risk assessment using the Framingham equation for stroke risk and the presentation used graphical and numerical formats followed by a shared decision-making component. The evidence-based guidelines group applied decision analysis derived guidelines according to the participants' risk factor profile and the recommendation made directly to the participant by the clinic doctor. The primary outcome measure was decisional conflict immediately after the consultation. Secondary outcomes were anxiety, knowledge and decision-making preferences. The computerised decision aid group had lower decision conflict immediately after the clinic (mean -0.18, 95% CI -0.34 to -0.01) and mean -0.15 (95% CI -0.37 to 0.06) at three month follow-up. Both groups had less decision conflict after the consultation but the difference between groups was statistically significant at 5% level. Subscales suggested this was due to feeling more informed and clearer of their personal values for the risks and benefits of alternative options.

The reduction in anxiety fell statistically significantly but was not different between groups. Knowledge scores improved slightly after the consultation but at three months were back at baseline level. Participants in the decision aid group were less likely to start warfarin than those in the guideline arm (39/53, 73.6%) compared to guidelines (50/56, 81.7%), RR 0.82, 95% CI 0.68 to 0.99. This was mainly caused by the group who were not already on warfarin. The differences in starting warfarin for this group was 4/16 (25%) in the decision aid group, compared to the guideline group15/16 (93.8%), RR 0.27, 95% CI 0.11 to 0.63. There was no difference in health outcomes 3 months after the clinic.

Fraenkel (2007) [74] conducted a randomised control trial which tested the efficacy of a computer tool to improve informed decision-making for patients with knee pain in an outpatient clinic. The trial was conducted in a primary care outpatient clinic in the USA. Eighty-seven participants over the age of 60 were randomised to receive an Arthritis Foundation information pamphlet (control group) or to perform an Adaptive Conjoint Analysis (ACA) (intervention group). The ACA is an interactive computer tool which could generate immediate feedback to the participant and help them construct treatment preferences by means of trade-offs by rating tasks. The treatment characteristics in the ACA task included route of administration, likelihood of expected benefit, and risk of adverse effects. Questionnaires were given to assess outcomes. Decisional self-efficacy and preparedness to participate in decision-making remained statistically significantly higher in the intervention group than the control group after controlling for race and health status. Arthritis self-efficacy was of borderline significance. Outcomes by age and education suggest older adults may be the most likely to benefit. Ninety eight percent of the participants thought the ACA task was very easy/easy to do. The patients in the intervention group had greater self-confidence in their ability, felt more prepared to participate in shared decision-making and felt they had greater self-efficacy over arthritis than the control group.

Oakley (2006) [73] assessed the effectiveness of a decision aid on patient adherence to oral biphosphonate medicine. They conducted an RCT with

postmenopausal women over the age of 65 who were diagnosed with osteoporosis. Thirty-three participants were included in the study, with a mean age of 77 years (range 61-90). The intervention group attended an osteoporosis workshop, where they were given a decision aid and group discussion on a worksheet. This included working through the decision-making process and identifying their own lifetime risk of hip fracture, personal and family health issues which may influence their decision, and self-care options already using or willing to try. They were to consider the pros and cons and their personal values regarding therapy and noted any questions for the GP on a worksheet. Two weeks later they returned with their worksheets for a follow up with a GP osteoporosis specialist. Questionnaires were then administered to establish compliance. The difference in adherence improvement was not statistically significant. Satisfaction with information about medicines improved initially in the intervention group but by the final questionnaire this effect had dissipated to non-significance. The decisional conflict scale showed a reduction in decisional conflict from baseline measures (total DCS score pre-intervention, median 2.5 (1.8-3.4) v 2.0 (1.0-2.4) post-intervention, $p<0.001$, however this cannot be compared to the control group as they were not assessed for this measure. The decision aid improved their ability to make a decision about which treatment was best and to discuss their medicine with the GP. However it had no obvious effect on adherence.

Hamann (2007) [75] conducted an RCT to assess whether shared decision-making in antipsychotic medicine choice would influence long-term outcome. 86 patients with a diagnosis of schizophrenia were included and followed up, 58% female with mean age of 38 years (s.d=11.4), mean duration of illness 9.2 years (s.d=8.5). The study was conducted in Germany. The intervention group received a decision aid program and the control group received usual care. The decision aid was a 16 page booklet with the pros and cons of oral versus depot formulation, first versus second generation antipsychotics, psycho-education and a type of socio-therapeutic intervention. Twenty-four hours after working through the booklet with the trained nurses the patients consulted with the psychiatrists on further treatment. The patients then filled

out questionnaires relating to patient involvement, satisfaction and psychopathology. Patients were followed up at 6 and 18 months after discharge from hospital. Univariate analysis found no statistically significant differences between groups. When multivariate analysis was conducted to control for the re-hospitalisation rate it showed that there was a positive trend for the decision aid and planned talk in reducing rehospitalisation. Higher participation preferences (OR=1.06, p=0.03) and better knowledge (OR=1.23, p=0.03) rates statistically significantly predicted rehospitalisation. No other effects were shown.

4.14 How can a practitioner elicit whether a patient agrees with the prescription recommended by the practitioner?

Related references	Evidence statements (summary of evidence)
	No evidence was found on specific clinical tools that can aid the practitioner in eliciting whether patient agrees with the recommended prescription.

4.14.1 Evidence to recommendations

No tools designed for use in clinical practice were found. The GDG used the information from the research studies and their professional opinion to make recommendations in relation to elicitation of agreement with decision to prescribe.

4.14.2 Methods of the evidence review

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies – no restrictions on study design.

Types of participants - people prescribed medicine for a medical condition.

Duration of studies - no time limit specified.

Types of interventions - any interventions intended to assess tools that can aid a practitioner in eliciting whether a patient agrees with recommended prescription.

Types of outcome measures – agreement with prescription, patient satisfaction with issued prescription.

4.14.3 Evidence review

No study was found that assessed a clinical tool that could aid a practitioner in eliciting whether a patient agrees with the recommended prescription. One prospective observational study (Bikowski 2001) [76] that aimed to characterise the degree of disparity between physicians' perceptions of older patients' medicine regime and patients' perceptions of their regime within a community family medicine residency setting.

Eligible patients were aged 65 years and older, non-institutionalised, visiting the clinic on the index day for a routine visit, had seen the index physician at least three times in the past calendar year, and, by brief review of the medicine flow sheet, were taking at least four prescriptions medicines. The study sample comprised 50 physician-patient pairs.

Physicians were given the patient's chart, with a request to complete a questionnaire that asked for information on all prescriptions and non-prescription medicines, with dosages and frequencies of administration. Patients were interviewed at home by first year medical students who received specific training for the study.

Percentage congruence - defined as agreement between physician and patient regarding all prescriptions medicines, dosages and frequency, was calculated for each pair. Complete congruence was showed for 14% of the 50 physician-patient pairs; 74% had at least one medicine that either the physician was unaware the patient was taking or the physician thought the patients was taking but that was not part of the patients regime; 12% had dose and/or frequency differences, however they agreed upon the medicines in the regime.

Antihypertensive medicines were the most commonly prescribed medicine, accounting for 36% of the total. The highest congruence was found for diabetic and other endocrine medicines. Pain medicines and gastrointestinal medicines showed the lowest congruence.

4.15 What aspects of consultation style increase patient involvement in decision-making?

Related References	***Evidence Statements (summary of evidence)***
McKinstry (2006) [77]	One high quality systematic review found that there is insufficient evidence to conclude that any intervention may increase or decrease trust in physicians.
van Dam (2003) [78]	One systematic review of RCTs found that supporting patient participation in diabetes care and self-care behaviour (i.e. by assistant-guided patient preparation for visits to doctors, empowering group education, group consultations, or automated telephone management) is more effective than changing provider consultation style for improving patient self-care and diabetes outcomes.
Edwards (2004) [79]	One RCT reported statistically significant effects of the research clinic group (which provided more consultation time) in confidence in decision and expectation to adhere to chosen treatments.
Cohen (2004) [80]; Edwards (2004) [79]	Two studies from the same randomised controlled trial found that training GPs in SDM or combined with risk communication yielded conflicting results in the probability of a prescription being issued to patients.

Cohen (2004) [80]; Edwards (2004) [79]	Two studies from the same randomised controlled trial found that training GPs in SDM or combined with risk communication yielded no effect on the probability of investigations, referrals or follow-up GP visits for any of the conditions.
Savage (1990) [81]	One RCT found that a directing style of consultation yielded statistically significantly higher levels of satisfaction on almost all the outcome measures compared to a sharing style. This was particularly relevant for patients with physical problems.
Shields (2005) [82]	One RCT reported a statistically significant likelihood of a physician promoting collaboration in treatment decision-making and exploring issues around the disease and illness with patients rather than with companions of the patients e.g. physicians were more likely to be responsive to being patient-centred when the patient raised the issue than when their companion raised it. There was no difference in level of patient-centeredness between the unaccompanied and accompanied visits.
Shields (2005) [82]	One RCT reported a statistically significant responsiveness of a physician to explore the disease and illness when the issues were raised by the patient compared with the companion of the patient.

4.15.1 Evidence to recommendations

The GDG were aware that there is anecdotal evidence that practitioners and patients report that the quality of the practitioner-patient relationship is important in decision–making. The quality of the practitioner-patient relationship was reported as being important in some studies of patients' medicine-taking behaviour as outlined in chapter 3. The quality of a practitioner–patient relationship is likely to be influenced by a number of factors that relate to previous consultations and problems under discussion. The consultation skill of an individual practitioner is also likely to be important regardless of length of professional-patient relationship. It was considered that the level of trust between practitioner and patient may be a key factor in this relationship and the GDG wished to review whether this could be specifically increased in practitioner-patient encounters. The evidence from a recent systematic review suggested that there is insufficient evidence to recommend any specific intervention. The GDG felt that consultation style should be tailored to individual patients to allow full communication.

4.15.2 Methods of the evidence review

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies: systematic reviews or randomised controlled trials (RCTs) that focus on aspects of consultation style that may increase patient involvement in decision-making.

Types of participants: people prescribed medicines for a medical condition faced with a decision.

Duration of studies: no time limit specified.

Types of interventions: any interventions which assess which aspects of the consultation style may increase patient involvement in decision-making.

Types of outcome measures: Patient-centred communication in the consultation; consultation process outcomes: patient involvement, question

asking, preparedness; patient care outcomes: satisfaction, knowledge, self-efficacy, type of information.

It should be noted that the remit is for conditions with prescribed medicine and this excludes conditions which require chemotherapy or screening. All RCTs are within this remit, however many of the systematic reviews included populations outside the remit, this is noted where applicable.

4.15.3 Evidence review

Our searches retrieved two systematic review and 4 RCTs that were considered relevant to the key clinical question. All the studies looked at the patient-provider interaction, either by exploring the impact of different provider styles or by focusing on patient behaviour changes.

McKinstry (2006) [77] conducted a Cochrane review of interventions to improve the trust of patients in their doctors. They searched 10 databases including the Cochrane Central Register of Controlled Trials, Medline and Embase. The inclusion criterion for studies was RCTs, CCTS, controlled before and after studies and interrupted time series studies. The interventions were any that influenced patients trust in their doctors, or where trust was an outcome of an intervention. The participants were doctors, adults or children using healthcare or those related to them. Outcome measures were an increase or decrease in patients' trust and the components of trust; other healthcare behaviours; health status and well-being; use of resources; satisfaction with care; perception of doctors' communication skills; perception of doctors' humanistic attributes; perception regarding patients' trust; perceptions of doctors trustworthiness. Studies were excluded if they did not measure change in trust or were not the right type of study. Two authors independently assessed whether the titles and abstracts were relevant and four authors assessed the retrieved articles for inclusion. Two authors assessed the quality of each study according to EPOC criteria. A multi-disciplinary advisory group was set up to assess whether there was anything that had been left out of the review. 2099 titles and abstracts were found, five met all the criteria, but two of these referred to the same study and one had insufficient data points before and

after the intervention, therefore leaving three studies. Two of the studies had a primary aim of assessing the impact of the intervention on patient trust. Thom (1999) coached doctors in behaviours known to be associated with trust and Hall (2002) looked at the impact of disclosing financial incentives physicians received for compliance with managed health care protocols on the trust patients had in physicians. In the third study (Thompson 2001), trust was a secondary outcome and compared the impact of three different types of induction visit for new patients of an HMO to those who received no intervention. The trust was in any health care professional. The review detailed the quality of studies including allocation concealment, blinding and protection from contamination. On assessment of study quality all three RCTs provided baseline measures and within and between group differences for measures. Thom (1999) used computer allocation to groups but it was not clear if the researcher was blind to this allocation. The interviewer was blind to the status of the physician but it was unclear if the patients were blinded. Hall (2002) conducted a stratified random sample study and used a computer for allocation with no input from researchers. The interviewers were blind to the patients' status but the patients were aware of their own status. Thompson (2001) did not report how the randomisation was applied. Patients were aware of their status but it is not clear if interviewers were blind to the status of the interviewees. The study by Thom (1999) showed no effect on trust (74.4 for the intervention and 76.2 for the control group, statistically non-significant). Satisfaction or humaneness scores were also statistically non-significant. Hall found a small increase in trust for both groups from baseline and when adjusted this was a 1.4% increase in physician trust ($p<0.05$). Thompson (2001) found the trust in the health plan health professionals rose statistically significantly following the enrolment visit with health personnel compared to control group $p<0.001$). The author concluded that there is insufficient evidence to conclude that any intervention may increase or decrease trust in physicians.

Van Dam (2003) [78] developed a systematic review of RCTs that looked at the effects of interventions on provider-patient interaction on patient diabetes

health behaviour, patient self-care, delivered diabetes care and health outcomes, and to disentangle those that are the most effective. Eight studies were included after a rigorous methodological quality assessment, and these showed different interventions on different levels of the provider-patient interaction in diabetes care. Four studies focused on provided consulting behaviour modifications (studies 1-4), and four studies focused directly on patient behaviour change (studies 5-8). All studies were conducted in practical diabetes care, three in hospital outpatient clinics and five in general practices.

The main findings suggest that the most effective interventions are those with a direct approach to support patient participation (i.e. by assistant-guided patient preparation for visits to doctors, empowering group education, group consultations, or automated telephone management) in diabetes care and self-care behaviour, while interventions which focus on change of provider behaviour were less effective. Thus, the authors advocate a shift from the traditional medical model to a more patient-centred, patient participation and empowerment paradigm of delivery of diabetes care. The authors pointed out that the review did present some limitations, illustrated by the small number of reviewed papers; the differences between the studies; and the focus on RCTs.

Cohen (2004) [80] and **Edwards (2004)** [79] conducted a cluster randomised crossover trial with the aim to explore the costs of training GPs in developing SDM competences and in the use of risk communication (RC) aids and to evaluate the effects of such training on a range of service resource variables. Edwards (2004) published the main trial results that focused on the doctor patient interaction, patient outcomes and satisfaction with the decision. Within each cluster, patients were also allocated randomly to consult with the doctor at one of three points in the study. The study comprised three phases. Phase 1 was pre-training. Phase 2 included training for half of the GPs and the other half in RC. In phase 3, each GP received training in the other element making them fully trained in both. The authors argued that in this way, the design offered the greatest potential to gain understanding about the effects of each form of training alone and in combination and if the sequence

of skill acquisition was important. A further randomisation allocated patients to attend either in usual surgery time or in a research clinic- audio taped, including fewer interruptions and more time for each consultation (up to 15 minutes each).

SDM training involved GPs attending two workshops where standardised and previously piloted skill development processes were used. SDM competences were described and demonstrated by means of consultation simulation and pre-prepared scenarios involving the four study conditions. RC also involved attendance at 2 workshops, and the aids consisted of tabulated data and visuals displays of risk estimates for the four study conditions. Patients with one of four conditions (menorrhagia, atrial fibrillation, menopausal symptoms or prostatism) were invited by their GP to attend a "review consultation" to discuss their continuing treatment. Twenty GPs from 20 different practices in South Wales were recruited. Costs of training for both RC and SDM included time of trainers, of those being trained and of the simulated patients used as part of the training exercise. Information on prescriptions, investigations and referrals was obtained from questionnaires completed by each clinician at the review consultation.

Main results published by Cohen (2004) indicated that Training in SDM or combined with RC statistically significantly affected the probability of a prescription being an issue to women with menopausal symptoms and menorrhagia (despite RC alone not having any effect). However, there was no statistically significant change in prescribing for patients with prostatism or atrial fibrillation. There was also no effect on the probability of investigations, referrals or follow-up GP visits for any of the conditions. Training cost was £1218 per GP, resulting in an increase of cost of consultation by £2.89.

Edwards (2004) reported statistically significant effects of the research clinic (which provided more time) in confidence in decision ($p<0.01$) and expectation to adhere to chosen treatments ($p<0.05$). Anxiety scores approached statistical significance for the RC intervention, as did expectation to adhere to the chosen treatment for both interventions. No statistically significant effects of the risk communication or SDM interventions were seen on the whole range of patient-based outcomes.

Cohen (2004) concluded that due to the explanatory nature of the study, no assessment could be made on how training could affect the length of a consultation.

Savage (1990) [81] sought to compare the effects of a directing and sharing style of consultation by a GP on patient's satisfaction with the consultation in a deprived inner city area. Patients were aged 16 to 75 years of age and were randomised to receive a directing or sharing style in the part of the consultation regarding treatment, advice and prognosis. Three hundred and fifty nine patients were randomised, however 120 patients failed to complete the assessment that took place a week later.
There were no statistically significant differences in the mean length of consultations between the two experimental groups. Patients who had the directing style of consultation reported statistically significantly higher levels of satisfaction on almost all the outcome measures, and was particularly strong for patients with physical problems (excellent explanation $p<0.02$; excellent understanding $p=0.04$). There was no statistically significant difference in the responses to the directing and sharing styles in longer consultations, where the main treatment was advice and among patients with psychological or chronic problems. Statistical significance values were not reported. This study was conducted in England.

Shields (2005) [82] evaluated the influence of accompanied visits on physician-patient communication, particularly on patient-centred communication. Thirty patients were included in the study. The participants were aged above 65 years, were not cognitively impaired and had a companion who could accompany them to their next visit. Companions were not assigned a specific role during the session and physicians were not asked to conduct the sessions in any particular way.
There were no statistically significant differences between accompanied and unaccompanied visits for the number of issues raised by patients. However patients did raise more issues in unaccompanied visits. No statistically significant differences were observed for levels of patient-centeredness, or

satisfaction, even if patients who were accompanied reported being slightly more satisfied.

Physicians were more likely to promote collaboration in treatment decision making with patients than with companions ($p<0.0001$). Physicians were also more responsive to issues regarding exploring the disease and illness when the issues were raised by the patient compared with the companion ($p<0.03$). There was no difference in level of patient-centeredness between the unaccompanied and accompanied visits.

4.16 Do interventions to increase patient involvement increase length of the consultation?

Related References	Evidence Statements (summary of evidence)
Evidence from the UK	
McCann (1996) [83]; Middleton (2006) [84]	Two RCTs from the UK found that interventions to increase participation in the consultation (leaflet and agenda form) statistically significantly increased consultation length. The intervention group in the McCann study increased consultation length by 72 seconds (p=0.02). The agenda form group in the Middleton study increased consultation length by 54 seconds, p<0.004. The consultation length increased by 114 seconds for the combined group (education and agenda form (p<0.001).
Little (2004) [36] McLean (2004) [85]	Two RCTs from the UK found interventions to increase participation in the consultation (a prompt to elicit patient concerns and a leaflet) did not statistically significantly increase consultation length.
Middleton (2006) [84]	In one RCT that reported a statistically significant increase in consultation length, the increase was more pronounced when using an agenda form than when using the agenda form in combination with an educational intervention. When using the educational intervention alone no difference was found.
Little (2004) [36]	One RCT reported that the use of a general leaflet

	in the consultation was statistically significantly more effective in increasing satisfaction when consultations were shorter.
Edwards (2004) [79]	Adherence was increased in clinics where more time was available than usual surgery times.
Evidence including the rest of the world	
Kinnersley (2007) [32]; Harrington (2004) [31]; Cegala (2001) in Wetzels review (2007) [34]; Loh (2007) [33]; Hamann (2006) [86]	Evidence from two systematic reviews and three RCTs suggest that interventions designed to improve patient participation in consultations do not increase overall length of consultations. One review (Kinnersley 2007) found 14 RCTs with no statistically significant increase in consultation length and 3 RCTs with a statistically significant increase (Hornberger 1997; McCann 1996 and Middleton 2006 – 2 UK studies reported earlier).
Hornberger (1997) in Kinnersley (2007) [32]	In one of the RCTs that reported a statistically significant increase in consultation length, this increase was due to time spent discussing diagnoses and physical examination.
Kinnersley (2007) [32]	Written materials had a small and statistically significant increase in consultation length compared to coaching where the small increase was not statistically significant.*
Kinnersley (2007) [32]	Interventions immediately before the intervention led to a small and statistically significant increase in consultation length. Whereas those some time before had no effect. **

Kinnersley (2007) [32]	There was no difference in the effect on consultation length (Kinnersley review) in RCTs whether they had additional clinician training or not.***
Hornberger in Kinnersley (2007) [32]	One RCT (from Kinnersley review) reported that overall quality of care showed a statistically significant effect on the intervention group which had a longer consultation time than the control group.

*This result is from a comparison of written materials and coaching for the consultation length of all studies which included written materials or coaching (thirteen), three of which were not relevant to the population of interest in this evidence review.

**This result is from a comparison of studies some time before consultation (2) and immediately before consultation (11), of which three of the immediately before consultation were not the relevant population.

***This result included studies of Clinician training (2) compared to 12 studies where Clinicians were not trained. One of the Clinician training studies and three of the Clinicians not trained studies were not the relevant population

4.16.1 Evidence to recommendations

The GDG were concerned that interventions to increase patient involvement in the consultation might result in longer consultations and have impact resource implication and impact on service delivery more generally. The evidence was mixed. The studies included different health-care settings and different specialities and decisions. The GDG were primarily interested in simple interventions and the evidence indicated that simple interventions might result in increase in consultation length but this did not always occur. The interventions in the studies were however more complex than the recommendations the GDG were making which primarily centre on how practitioners consult. The GDG considered it important to reassure clinicians that increasing patient involvement may not affect consultation length.

4.16.2 Methods of the evidence review

The aim of the literature review is to identify the most relevant, published evidence to answer the key clinical questions generated by the GDG. Due to time constraints, exhaustive systematic reviews (see the Methods of the Cochrane review) were not undertaken. However, the evidence reviews were undertaken using systematic, transparent approaches following the Guidelines Manual 2007 (www.nice.org.uk).

The titles and abstracts of records retrieved by the searches, suggested by the GDG or submitted by stakeholders were scanned for relevance to the key questions. Any potentially relevant publications were obtained in full text. These were then reviewed to identify the most appropriate evidence to help answer the key questions and to ensure that the recommendations are based on the best available evidence. This process required four main tasks: selection of relevant studies; assessment of study quality; synthesis of the results; and grading of the evidence.

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies: systematic reviews or randomised controlled trials (RCTs) that assess whether interventions to increase patient involvement increase length in consultation.

Types of participants: people prescribed medicine for a medical condition faced with a decision.

Duration of studies: no time limit specified.

Types of interventions: any interventions which aim to increase patient involvement and include details of consultation length.

Types of outcome measures: Patient-centred communication in the consultation; Consultation process outcomes: patient involvement, question asking, preparedness; Patient care outcomes: satisfaction, knowledge, self-efficacy in relation to consultation length.

It should be noted that the remit is for conditions with prescribed medicine and this excludes conditions which require chemotherapy or screening. All RCTs are within this remit, however many of the systematic reviews included populations outside the remit, this is noted where applicable

4.16.3 Evidence review

This review was stratified to firstly present the RCTs research from the UK and secondly present systematic reviews and RCTs which include research from other areas of the world.

4.16.3.1 RCTS from the UK

Little (2004) [36] conducted a randomised controlled trial in the UK to assess the effect of leaflets in empowering patients in primary care consultations. Participants were randomised to four conditions: receipt of a general leaflet, depression leaflet, both leaflets and no leaflets (control group). The general leaflet asked patients to list issues they wanted to raise and explained that the doctor wanted them to ask questions, talk and discuss any problems of

Middleton (2006) [84] conducted a randomised controlled trial in the UK of agenda forms completed by the patient and doctors' education about the agenda on the outcome of the consultation. The intervention group were asked to think of a list of their concerns, arrive five minutes earlier and bring spectacles and an interpreter if those were required. The intervention doctors were given a one day educational workshop to allow the doctors to have awareness of the patient agenda model of the consultation. The model involved identifying the agenda (ideas, concerns, expectations and reasoning). The doctors reflected on their own agenda and negotiation of action with patients. Half of the patients in this group filled in an agenda form in the preceding time before their consultation, half did not. The control group included GPs not given the educational programme, and this group was split into half the patients using the agenda form and half not using it. The consultation length for the control group was 7.1 minutes (95% CI 6.5 to 7.7 minutes). The agenda form statistically significantly increased the duration of consultation by 0.9 minutes (95% CI 0.3 to 1.5, p=0.004) and the combined intervention by 1.9 minutes (95% CI 1.0 to 2.8, p<0.001). The educational intervention on its own did not statistically significantly change the length of consultation (0.7 minutes, 95% CI -0.2 to 1.6 minutes). There was a statistically significant increase in both interventions for number of problems identified. The only change in patient satisfaction was increase in depth of doctor-patient relationship from the agenda form group.

McCann's (1996) [83] randomised controlled trial in the UK was of a brief written intervention leaflet 'Speak for Yourself' to increase participation in the consultation read before the consultation compared to those given a control leaflet. The first part asked patients to identify the nature of their problems and to consider their ideas to causes, treatment and effects of the problems. They had space to write down ideas. The second part of the leaflet advises to state their ideas and concerns about the illness to the doctor and ask questions. The intervention group had statistically significantly longer consultations (8.43 minutes, s.d=2.97 versus 7.22 minutes, s.d=2.42, 95% CI -0.44 (0.08, 0.81) and they asked more questions than controls.

McLean (2004) [85] conducted an open randomised controlled trial to see whether a prompt to elicit patients' concerns for minor illness would be beneficial and the costs of doing so. One hundred and ten patients from four training semi-rural general practices in the South-East of the UK took part in the study. The written prompts were 'May I ask if you have any concerns about this "…." (illness/pain) you have come about today?' followed by: 'Anything in particular about the "…"?' and, if still unforthcoming: 'What is it about the "…" that concerns you?' A consultation satisfaction questionnaire regarding the professional care component was given. The doctor had to record the consultation length (estimated to the nearest minute using a clock to note start and end of consultation) and the diagnosis made. The control group received the consultation as normal. The doctor depending on whether the top sheet of a randomly arranged pile of papers said 'control' or 'intervention'. [However it must be noted that the same doctor was conducting both control and intervention and the control condition may inadvertently receive a more patient-oriented consultation]. Patient satisfaction was 80.9 for controls and 88.2 for intervention patients (s.d=11.8), mean difference 7.2 (95% CI 2.0 to 12.6). The consultation length of intervention consultations was on average 1 minute longer for intervention group than controls (11.0 vs. 10.0 minutes), but this was not statistically significant.

Cohen (2004) [80] and **Edwards (2004)** [79] conducted a cluster randomised crossover trial in the UK with the aim to explore the costs of training GPs in developing SDM competences and in the use of risk communication (RC) aids and to evaluate the effects of such training on a range of service resource variables. Edwards (2004) published the main trial results that focused on the doctor patient interaction, patient outcomes and satisfaction with the decision. Within each cluster, patients were also allocated randomly to consult with the doctor at one of three points in the study. The study comprised three phases. Phase 1 was pre-training. Phase 2 included training for half of the GPs and the other half in RC. In phase 3, each GP received training in the other element making them fully trained in both. The authors argued that in this way, the design offered the greatest potential to gain understanding about the effects of each form of training alone and in combination and if the sequence of skill acquisition was important. A further randomisation allocated patients to attend either in usual surgery time or in a research clinic- audio taped, including fewer interruptions and more time for each consultation (up to 15 minutes each).

SDM training involved GPs attending two workshops where standardised and previously piloted skill development process was used. SDM competences were described and demonstrated by means of consultation simulation and pre-prepared scenarios involving the four study conditions. RC also involved attendance at 2 workshops, and the aids consisted of tabulated data and visuals displays of risk estimates for the four study conditions. Patients with one of four conditions (menorrhagia, atrial fibrillation, menopausal symptoms or prostatism) were invited by their GP to attend a “review consultation” to discuss their continuing treatment. Twenty GPs from 20 different practices in South Wales were recruited. Costs of training for both RC and SDM included time of trainers, of those being trained and of the simulated patients used as part of the training exercise. Information on prescriptions, investigations and referrals was obtained from questionnaires completed by each clinician at the review consultation.

Edwards (2004) reported statistically significant effects of the research clinic (which provided more time) in confidence in decision ($p<0.01$) and expectation

to adhere to chosen treatments ($p<0.05$). Anxiety scores approached significance for the RC intervention, as did expectation to adhere to chosen treatment for both interventions. No statistically significant effects of the risk communication or SDM interventions were seen on the whole range of patient-based outcomes.
However, Cohen (2004) concluded that due to the explanatory nature of the study, no assessment could be made on how training could affect the length of a consultation.

4.16.3.2 RCTs conducted outside the UK

Kinnersley (2007) [32] conducted a Cochrane review to find interventions which aimed to increase patient involvement by enabling patients to address their information needs within the consultation. Most of the RCTs were from the USA, 2 from Australia, 5 from the UK and one from the Netherlands. Most of the interventions were written followed by face-to-face coaching and videotape. Written interventions were in booklet or checklist form. The specific behaviours most encouraged were question-asking, raising concerns and requesting clarification or checking understanding.

Seventeen RCTs in the Kinnersley review (2007) looked at consultation length, 3 studies found a statistically significant increase (Hornberger, 1997; McCann, 1996 and Middleton, 2006) and 14 RCTs found no effect. Bolman (2005) found a decrease in the first consultation and an increase in the last consultation. The meta-analysis showed a small but not statistically significant increase in consultation length (SMD 0.10 95% CI -0.05 to 0.25).
Fifteen RCTs reported that the use of written materials during the consultation led to a small and statistically significant increase in consultation length (SMD 0.13, 95% CI 0.05 to 0.21). There was a small and statistically significant increase in consultation length for interventions immediately before the consultation (SMD 0.16, 95% CI 0.03 to 0.29) compared to those carried out some time before (SMD -0.04, 95% CI -0.93 to 0.86). RCTs with coaching

found a statistically non-significant increase (SMD 0.07 95% CI -0.07 to 0.20). In studies where there was additional clinician training there was little impact on consultation length for written and coaching materials. RCTs with clinician training SMD 0.17 (95% CI 0.01 to 0.32) compared to studies without clinician training SMD 0.17 (95% CI 0.10 to 0.24). It should be noted that of these seventeen RCTs only eleven of these related to our population of interest, the results for these are detailed below.

4.16.3.3 RCTs included in the Kinnersley (2007) [32] review

Hornberger (1997) conducted a two-armed, randomised trial of whether a self-administered pre-visit questionnaire enhanced awareness of patients concerns in the USA. They completed the Patient Concerns Form while waiting for their visit. This covered 25 items of concerns of five categories: desire for medical information, psychosocial assistance, therapeutic listening, general health advice and biomedical treatment. After the interview the patients completed a post-visit questionnaire which assessed their perceptions of the concerns addressed by the physician. The net effect of the intervention compared to the control group was a difference of 6.8 minutes (95% CI 0.4, 13.3) for total time in consultation. With most of the extra time spent discussing diagnoses (3.35 minutes, 95% CI 0.00 to 6.72) and in performing the physical examination (2.7minutes, 95% CI 0.5 to 4.9). The number of diagnoses increased by 30% in the intervention group compared to the control group (increase of 1.7 diagnoses per visit). Those in the intervention group had marginally higher satisfaction but this was not statistically significant except for overall quality of care (0.35, +/- 0.23, p=0.05).

Greenfield (1985) conducted a randomised controlled trial of an intervention to increase patient involvement in their care in the US. The intervention group received a treatment algorithm as a guide to help them read their medical record and a behaviour-change strategy. The participants were coached in

appropriate question-asking and negotiation of decisions. The intervention occurred in a 20 minute session before their regular consultation with their GP. The control group also saw a clinic assistant just before their regular appointment for a similar amount of time as the intervention group. They received a standard protocol of receiving information and review of ulcer disease and were given copies of these materials. They did not get to see their medical records. There was no statistically significant difference between groups in length of consultation after the interventions, both groups averaged 16 minutes per encounter. The time of the encounter before was 16.8, (s.d= 8.2) whereas the control group was 15.1 (s.d=7.6), a difference of 1.7 (95% CI -2.92 to 6.32). The time of the encounter after was 15.7 (s.d=6.7) for the intervention and 16.3 (s.d=9.7) for the control, -0.6 (95% CI -5.49 to 4.29). However, they differed in how they spent their time with the intervention patients spending more time involved in the interaction than controls.

Greenfield (1988) conducted a randomised controlled trial in a diabetic clinic in the USA. This intervention was the same as in Greenfield (1985) but delivered twice, before the initial and follow up consultations. There was no change in question-asking, patient satisfaction, knowledge or consultation length (30.30 s.d=13.80 intervention group versus 32.50 s.d=13.90 for the control group). Participation and the preference for active involvement increased.

Maly (1999) conducted a randomised controlled trial in a family medicine clinic in the US where patients received copies of their medical record progress notes and produced two main questions to ask their physician. Control group received health education sheets and made suggestion lists for their clinic care. The consultation length did not differ between groups.

Roter's (1977) randomised control trial in a family medicine clinic in the US involved 10 minutes with a health educator to identify questions from a question asking protocol. The participants were encouraged to ask questions and took a list in to the consultation. Question asking and patient satisfaction

increased and there was no difference between consultation length (29.90, s.d=12.70) vs 40.50 (s.d=92.70).

Thompson (1990a) conducted a randomised controlled trial in an obstetric and gynaecologist clinic in the USA. Participants received a question prompt sheet with instructions to write at least 3 questions to take to the consultation. Question asking increased and there was no change in patient satisfaction and consultation length 7.70 (s.d=2.90) vs 8.70 (s.d=4.70), 95% CI -0.26 (-0.80, 0.29).

Martinali's (2001) randomised controlled trial in the Netherlands used a checklist to prepare coronary patients for visiting their cardiologist. The short checklist which was to be completed at home was aimed towards structuring the exchange of information in the consultation and to concentrate on those issues that caused most concern to the patient. A brochure was also developed with instructions for the checklist. A brochure was also given from the Dutch Heart Foundation, which both groups received. The consultation length was 12 minutes (s.d=4.2) in the experimental group and 10.3 (s.d=3.8) in the control group, f=1.82, p=0.18.

Bolman's (2005) randomised controlled trial in cardiology clinics in the Netherlands involved a checklist of 49 questions on 10 issues (as Martinali 2001). This was mailed to the patient a week before each of three linked consultations. There was no change in patient satisfaction. Consultation length was reduced at first visit but increased at third visit (13.73, s.d=3.73 vs 16.22, s.d=5.84, 95% CI -0.49, -0.88, -0.10)

4.16.3.4 Other systematic reviews of RCTs

Harrington's (2004) [31] systematic review, which investigated how to improve communication in a consultation showed that studies overall found that by involving patients there was not a resultant increase in consultation length.

Five out of seven studies that included consultation length (and were our population of interest) found there was not a statistically significant increase in the length of consultation except for Hornberger (1997) and McCann (1996). All of these studies are in the Kinnersley (2007) review except for **McGee (1998)**, (a study conducted in the USA) which did not find any difference in consultation length.

The **Wetzels (2007)** [34] systematic review, which looked at interventions to improve older patients' involvement, reported findings related to consultation length. Only one of the three studies meeting the inclusion criteria of the review included consultation length (Cegala 2001). In **Cegala (2001)** the trained patients asked more medically-related questions, gained more information and provided more information than control patients. They did not verify information more than control patients and appointment length was not longer overall. (18.81 vs 22.59, p=0.46) and time engaged in talk 16.25 vs 14.41, p=0.68). This study was conducted in the USA.

4.16.3.5 RCTs (not included in any systematic reviews)

Loh (2007) [33] investigated the effects of a shared decision-making intervention in primary care of depression compared to usual care on adherence, satisfaction and clinical outcomes. The study was conducted in Sudbagen, Germany with primary care physicians as the unit of randomisation. The sampling frame (n=148) were sent a letter, 30 accepted the invitation to take part, 20 were randomly assigned to the intervention group and 10 to the control group, after drop out 15 and 8 were left respectively. The physicians had to recruit newly diagnosed depressive patients. The intervention physicians enrolled 263 patients and the control group 142. After their diagnosis the patients completed a questionnaire measuring patient involvement, depression severity and socio-demographic characteristics. After 6-8 weeks the patients completed a second questionnaire measuring adherence and treatment outcome. At the same time, the physicians rated their assessment of the patients' adherence. The shared decision-making intervention was then implemented with the

intervention group. The intervention was a multi-faceted program including physician training, a decision board for use during the consultation given to the patients after the consultation, printed patient information with specific encouragement to be active in the decision-making process. The physicians in the intervention group also completed modules on guideline-concordant depression care which included content on enhancing skills for improving the shared decision-making process. The outcomes measures were patient participation, treatment adherence, patient satisfaction, consultation time and clinical outcomes. There was no difference for the control group in patient participation before and after, whereas the intervention group had statistically significantly higher patient participation from pre to post intervention for the doctor facilitation scale (p=0.001) and there was an increase in the patient participation scale (p=0.010). There were no statistically significant differences in treatment adherence. Patient satisfaction was statistically significantly higher in the intervention 29.8 (s.d=2.7) than the control group 27.0 (s.d=3.6), p=0.014. There were no values taken for satisfaction before the intervention. There was no difference between groups for length of consultation 29.2 (s.d=10.7) versus 26.7 (s.d=12.5). Neither group had a statistically significant reduction in depression severity from baseline to post-intervention.

Hamann (2006) [86] conducted a randomised controlled trial which aimed to assess an intervention for shared decision-making in patients with acute schizophrenia. 107 patients from 12 acute psychiatric wards of two hospitals in Germany were included in the study. Before the consultation participants were given a talk on their treatment options and to prepare them for their GP consultation. A 16 page booklet decision aid covering the pros and cons of oral vs depot formulation, first vs second generation antipsychotics, psycho-education, and type of socio-therapeutic intervention. Trained nurses assisted the patients to work through the booklet and gave answers to any information requests. They had to write down their experiences with antipsychotic medicine and to indicate their preferences. They met with physicians within 24 hours of working through the decision aid. The control group received routine care. There was no difference reported in the time spent in individual

consultations as reported by the psychiatrists - mean 64 min/weeks for the intervention group compared to 60 min/weeks for the control group, $p>0.05$.

4.17 Cost–effectiveness of interventions to increase shared decision-making

The GDG were very aware of the importance of considering cost-effectiveness when reviewing interventions to increase shared decision making. The GDG were reassured that the systematic review on consultation length indicated that this did not necessarily increase as this was perceived by the GDG to be the area where cost effectiveness analysis might be important. The interventions recommended by the GDG generally involve improving communication and the targeting of information resources to the patients who need them.

While involvement in decisions can be considered a right the opportunity costs have to be considered. The process of shared decision-making can increase patient wellbeing by improving patient satisfaction with the consultation, as well as the wellbeing possibly of doctors and carers. This benefit is termed process utility in the literature [87] . However, any such benefits are likely to be relatively small in comparison to the health benefits emanating from the medical treatment. However, although many people may perceive involvement in their care decisions as beneficial, not everybody will value shared decision making in this way. As a result, a change in process utility may both be positive or negative. Although the current cost-effectiveness literature tends not to consider process utility, patient preferences in SDM can be investigated using discrete choice experiments including conjoint analysis. There are published studies which investigate the relative importance of features of a health care consultation. This evidence has not been formally reviewed as part this guideline, however, the following papers have been identified as examples of conjoint analyses. [88] [89] [90] [91] [92] [93] [94] [95] [96] [97] [98] [99] [100] [101] [102] [103] [104]

Increasing patient involvement in decisions may result in the agreement to prescribe and take a medicine, or equally, to not prescribe and take a different

medicine or no medicine. A programme that facilitates shared decision making between a HCP and a patient can be seen as an intervention to increase adherence to joint decisions including prescribed medicine, and thereby health of the population. The current evidence is very limited but it seems likely that the shared decision making process would improve cost-effectiveness by enabling patients to make a prediction of their individual valuation of harms and benefits and subsequently opt in or out of treatment. Theoretically it is likely to be of economic benefit to enable patients to decline a suggested prescription as it prevents people from accepting and filling prescriptions they might otherwise not have taken. No formal cost-effectiveness analyses of interventions to increase shared decision-making were found. Any analysis would have to include the effect on adherence and subsequent clinical outcomes. A discussion of the issues relevant to health economic evidence for interventions to improve adherence can be found in chapter 10.

5 Patients' experience of medicine-taking

5.1 Recommendations

Hyperlink to recommendations section Understanding the Patients Knowledge, Beliefs and Concerns about Medicines

5.2 Introduction

If health care professionals are to facilitate patient involvement in decisions about medicines it is helpful and necessary to understand how patients approach the taking of medicines, in particular the ongoing appraisal of medicines that continues after a consultation. Investigation into why patients do not take medicines as prescribed indicates that the decision to take medicines and the continuing taking of medicines should be considered as a complex behaviour [1].

5.3 What are the barriers and facilitators for individuals in medicine-taking

Related references	Evidence statements (summary of evidence)
Pound (2005)[7]; Munro (2007) [105]; Mills (2006) [106]; Carrick (2004) [107]; Deegan (2005) [108]; Lewis (2006) [109]; Cooper (2002) [110]; Ogedegbe (2004) [111]; Lukoscheck (2003) [112]; Wilson (2002) [113]; Bollini (2004) [114]; Adam (2003) [115]; Scotto (2005) [116]; Alfonso (2006) [117]; Sidat (2007) [118]; Lewis (2006) [109]; Pyne (2006)	Patients wish to minimise medicine intake where possible. They may wish to do this to decrease adverse effects and potential for addiction, to make the regimen more acceptable or for financial reasons. Patients may decide to use prescribed medicine to alleviate symptoms or strategically, to replace or supplement medicines sometimes or all the time with non-pharmacological treatments. Patients will commonly evaluate prescribed medicines by trying out the medicines and

[119]; Kikkert (2006) [120]; Vinter-Repalust (2004) [121]; Campero (2007) [122]; Reid (2006) [123]; Elliott (2007) [124]; Aronson (2005) [125]; Garcia Popa-Lisseanu (2004) [126]; Erwin (1999) [127]; Mutchler (2007) [128]; Lawton (2005) [129]; Morgan (2005) [130]; Ring (2007) [131]; Campero (2007) [122]; Chen (2007) [132]; Gascon (2004) [133]; Vermeire (2003) [134]; George (2003) [135]; Fraenkel (2007) [136]; Field (2006) [137]; Badger (2006) [138]; Givens (2005) [139]; Attebring (2005) [140]; Nair (2007) [141]; Gordon (2007) [142]; Bajcar (2006) [143]; Taylor (2002) [144]; Enriquez (2004) [145]; Gray (2006) [146]	weighing up the costs and benefits. They will consider adverse effects and acceptability of regimen. They may stop the medicine and see what happens and obtain information from non-medical sources and observe the effect of medicines on others. Both subjective and objective indicators may be used to evaluate medicines. Patients do not generally disclose their beliefs and change of regimen to HCPs. Patients may not be able to recognise the difference between effects of medicine and effects of disease and have difficulty in evaluating long term preventative medicine where there are no symptoms. Patient on multiple medicines may make choices between medicines.

5.3.1 Evidence to recommendations

The GDG discussed the appropriate research methodology to provide evidence of patients' actual medicine-taking behaviours. The GDG considered it important to provide health care professionals with evidence of how patients actually use medicines to sensitise professionals to issues that may be relevant for discussion with individual patients. The GDG accepted the use of qualitative evidence for this and considered the Pound synthesis provided the type of evidence they were looking for. The description of patient behaviours and factors influencing patients medicine-taking behaviours were used to inform the recommendations about exploring patients' beliefs and concerns,

the type of information that patients' may require and to describe common medicine-taking behaviour that healthcare practitioners might wish to discuss with patients.

5.3.2 Methods of the evidence review

Searches of the literature revealed a large number of studies that set out to explore patients' experience of medicine taking. The majority of these studies are qualitative studies. One of the current challenges in qualitative research is how to bring together the findings from individual qualitative studies. One approach is to present a narrative of these studies describing their findings individually. More recently the field of qualitative synthesis has attempted to synthesise the findings from different studies into a common set of findings that includes the findings from individual studies but that may also provide additional levels of understanding that may not be apparent when each study is looked at individually. A synthesis of medicine-taking has already been conducted using a meta-ethnography [7]. The Pound (2005) [7] review is methodologically sound and systematic synthesis developed by a panel of experts within the field of medicines adherence. Following discussion with the GDG it was agree that rather than conduct an alternative summary or synthesis of the qualitative studies of patients experience of medicine-taking we used the synthesis as the basis for our evidence review. The findings of the synthesis were updated by searching for evidence published since the review was conducted and a narrative summary of these presented. The GDG requested additional search for systematic reviews.

5.3.3 Evidence review

Pound (2005) [7] aimed to conduct a synthesis of qualitative studies of lay experience of medicine-taking. The study was part of a Health Technology Assessment project to evaluate meta-ethnography as a method of synthesizing qualitative research studies of health and health care. This narrative has used the paper published in Social Science and Medicine [7]. The authors of the HTA report kindly allowed us to read a draft copy of their report for the HTA which primarily concerned the detail of their methodology. Studies

using both qualitative methods of data collection and qualitative methods of data analysis and published in English were included. Studies published between January 1992 and December 2002, were eligible for inclusion. Medline, Embase, Cinahl, Web of Science, Psychinfo and Zetoc were searched. The electronic search was supplemented by extensive hand-searching. Papers were appraised for quality using a version of CASP 1988 criteria. Thirty-eight papers were included in the synthesis. Papers were organised into medicine groups. The initial synthesis brought together papers looking at similar medicine/disease groups and these findings were then synthesised. The medicine groups were antiretroviral therapy, anti-hypertensive medicine, psychotropic medicine, proton-pump inhibitors, asthma, miscellaneous medicines and medicines in general.

The paper reports a summary of the findings of the individual studies and the results of the synthesis of these studies. The authors developed the concept of ‘resistance’ to medicines to describe lay-peoples’ response to medicines. One of the main conclusions of the synthesis is that people do not take medicines as prescribed because of patient concerns about medicines themselves. Their interpretation is that nonadherence is not necessarily a result of failures from the professionals, patients or systems, but because of concerns about the medicines themselves. Drawing on issues such as patient reports of testing for adverse effects; worries about dependence; the potential harm from taking medicines on a long term basis; and issues with disclosure and stigma, the authors’ conclude that many patients ‘resist’ the taking of medicines. Patients can be described as ‘acceptors‘ of medicines, some uncritically, others following their own enquires and experimentation. People’s medicine-taking may change with different medicines and the illness in question, which illustrates the relative nature of the concept of “resistance”. Those that may “resist” a certain type of medicines may “accept” a different medicine.

The findings of the synthesis fell into three parts (1) the way people evaluate their medicines and the difficulties they encounter in doing this (2) the interaction between medicines and patient identity (3) the ways people take

their medicines. The themes that make up each part are listed under each heading.

5.3.4 The evaluation of medicines and the difficulties encountered by people in evaluating medicines

Trying out the medicines and weighing up the costs and benefits

The most common way of evaluating medicines was to try it out and weigh up the benefits of taking it against the cost of doing so. The majority of the studies focused more on the problems associated with medicine and less on the benefits of medicine, but it was clear that people had hope that their medicines would help with the symptoms; avoid relapse and hospitalisation; for minimisation of disease progression or for prevention of future illness.

Adverse effects

Adverse effects were a key criterion in the evaluation of medicines. This was found in several studies including those about treatments for cancer, rheumatoid arthritis, asthma, diabetes, schizophrenia and digestive disorders. Adverse effects were very prominent in studies of patients taking anti-HIV medicine. The frequency and nature of adverse effects experienced by these patients, particularly as adverse effects were severe and unpredictable, resulted in distrust and fear of the medicines. These adverse effects affected social activities, relationships and work.

Acceptability of regimen

People reported the evaluation of the suggested regime in terms of how it fitted in with daily schedules and life in general. The frequency of doses and number of pills was also a challenge, as also taste, smell, size and shape of the pills. Regimes that required disruption of schedules resulted in patients reporting that they were no longer in control of their lives and people varied as to whether they fitted the world around their regime or resisted the demands of the regime and missed doses.

Weighing and balancing

A process of weighing and balancing was carried out by people, mainly where the advantages of treatment in terms of symptoms or effect on disease was balanced by side effects and disruption. Adverse effects and disruption would lead people to question if it was worth taking medicine or not.

Stopping the medicine and seeing what happens

In some cases, patients test the medicines by either changing the doses or stopping the medicine as to observe what happens. Some authors suggest that this process can either be explicit or subconscious and tends to occur more frequently in long term conditions.

Observing others, obtaining information

Patients used a variety of sources of information with some patients relying more on their observations of how other people dealt with medicines such as HIV medicines rather than the advice/information given by the doctor. People use a variety of sources of information (e.g. internet, books and support groups) as well as that provided from their GPs.

Objective and subjective indicators

People used both objective and subjective indicators to evaluate efficacy of medicine. In the studies in the synthesis, blood pressure monitoring appeared to be used widely as a means of evaluating efficacy of antihypertensive medicine. The perception of symptom minimisation could be as important as objective indicators such as an increase in T-cell count in the case of HIV patients.

Gender differences in evaluating medicines

Some studies suggested that women with HIV do not belong to certain social networks like gay men or injecting drug users and thus could be less informed about the medicines. Also, some women were reported to show scepticism towards the medicines used for HIV with arguments that the clinical trials had not been conducted with women.

Difficulties with evaluating medicines

In some studies it was noted that patients could not distinguish between the effects of their illness from the effects of the medicine. This could even lead to patients rejecting treatments mistakenly. Other authors pointed out that evaluation can be dependent on the individuals understanding of how a medicines works and its function and this can be difficult for certain people due to lack of information and understanding. This is particularly relevant in the case of preventative medicine, as there are no immediate symptoms that can be used as indicators of efficacy.

Worries about medicines that lay testing and evaluation cannot resolve

Fear of dependency and tolerance were pointed out as issues for patients. Fear of addiction was reported when taking psychotropic medicines and general concern over taking medicines on a long term basis was present with hypertensive medicines. Some authors noted that those who worried over the long term effects of medicines were those most likely to change their regimen to the lowest possible dose.

5.3.5 Medicines and identity

Non-acceptance

Since taking medicine is equated with having an illness people may not take medicine if they do not accept their illness. This was particularly strong in the asthma studies in the synthesis. The relationship with acceptance of disease was, however, complex with some patients using medicines to keep their problem under control and downplay its significance. In the case of neuroleptic medicine and HIV medicine an acceptance of the diagnosis was crucial in determining whether the patient would take their medicine as prescribed. Medicine was seen as a reminder of illness.

Disclosure and stigma

People with potentially stigmatising illnesses such as HIV and mental health problems were particularly concerned that their medicines marked them out as individuals with those particular health problems. This could lead to avoiding taking medicine in public and either postponing or foregoing their

medicine intake. Some people were reported to not initiate treatment which would reveal them as having HIV. Patients with mental health problems also reported feeling stigmatized by their intake of medicines, and some felt ashamed.

5.3.6 Ways people take their medicine

Motivation to minimise intake

The majority of studies illustrate how people wish to minimise their intake of medicines with patients spontaneously reporting dislike of medicines to researchers. This was also true in the case of medicines commonly reported as being overused by patients, such as benzodiazepines.

To decrease adverse effects and addiction

People often reduce or skip doses, or take tablets separately rather that all at once. Others may temporarily stop their medicine intake as a way of cleansing their body and minimise toxicity.

To make the regimen more acceptable

This section related to how people modified their regimen in order to fit with their daily schedule, alleging that to have some clinical gain, complete adherence was not required. Other argued that the optimum regimen was not known anyway, and that strict adherence was not possible.

For financial reasons

Some people were reported to have decreased their doses as they could not afford the prescribed amounts.

Using medicine symptomatically

Some patients were reported to use medicines accordingly to symptoms displayed. Patients associated symptoms with their medical problem and when these symptoms indicated that the problem was not controlled they would take their medicines. An example was symptoms of tiredness or weakness in treatment for high blood pressure. People with rheumatoid arthritis modified their doses according to their symptoms as did patients on neuroleptic medicines.

Using medicine strategically

People adjusted their dose or did not take their medicine when planning to drink alcohol as they feared possible interactions. This was also reported for those on neuroleptic medicines and antihypertensive medicine. PPIs were also altered according to what people planned to eat.

Replacing or supplementing medicines with non-pharmacological treatments

In varying ways, people often complemented their treatment with home remedies. On a more specific level, some patients who worried about the harmful effects of medicines would sometimes take a break and use natural remedies for a certain period.

Doctor-patient communication about regimen modifications

Some patients reported being scolded by their doctors if making their own decisions about their care. Rather than confronting them, they would then switch doctors. Also, many patients do not reveal their beliefs to the doctors, but once outside the surgery and in control, people would then change or refute their regimen. Some authors noted that patients who had changed their regimen would not disclose this to the HCPs due to previous experience of coercion or recognition of their powerless position. Authors argue that as patients self-regulate anyway, doctors need to recognize this and even support them in the process, as well as helping people feel in control.

Imposed compliance

One issue that was found exclusively in studies relating to mental health was that of ‘imposed compliance’. Patients with mental health problems felt surveyed for signs of ill health and under pressure or even coercion from friends, relatives and health care professionals to take medicines. Patients felt that medicine was used to make them acceptable to society and was part of an unwritten social contract that required the taking of medicines to allow patients to be acceptable to the community.

5.4 Update of qualitative evidence synthesis - Pound 2005 synthesis

5.4.1 Methodology of update

The aim is to update the synthesis of qualitative evidence of medicine-taking in a similar methodological approach as when updating a Cochrane review. The titles and abstracts of records retrieved by the searches were scanned and any potentially relevant publications obtained in full text. The studies were reviewed to identify the most appropriate evidence to help answer the key questions and to ensure that the recommendations are based on the best available evidence. Qualitative synthesis is considered a process where the analysis of a number of qualitative studies may result in new findings not contained in the individual studies. It was felt therefore inappropriate to do additional synthesis to that undertaken by Pound et al. This update is a narrative review which discusses the studies found in the update particularly where the findings add to the existing synthesis.

Types of studies - studies with both qualitative methods of data collection and analysis published in English.

Types of participants - people aged above 16 years prescribed medicine for a medical condition (3 studies included in the synthesis relate to children and/or adolescents).

Duration of studies - there was no limit on the duration of studies.

Possible challenges - One of the first challenges of the process of developing a systematic review on qualitative evidence is how to find the evidence. Qualitative evidence is catalogued on a wide range of databases or sometimes not at all and indexes and search filters require substantial improvement if they are to be rigorous and systematic. Secondly, is the lack of agreement of appropriate methods for appraising the quality of qualitative evidence. We will use the same CASP criteria as those used in the original synthesis.

5.4.2 Evidence review from update searches

Update searches

Our update searches produced 381 references. Based on abstract information, eighty five studies were ordered. Further exclusions were made if the study turned out not to be relevant for the topic, or did not have qualitative data collection and analysis. CASP criteria were used to assess the quality of the studies. The details of all the studies are in Appendix C. Forty-five studies were included in the update. The studies covered a wide range of medical conditions and patient groups but did cluster around long term conditions. Twelve were concerned with HIV medicine, 8 with medicine for psychiatric conditions and 4 for patients with diabetes. Five studies focused on patients from low income and/or ethnic groups. A shift could be seen in that most recent studies discussed the issue of patient-health care professional communication more explicitly than those included in the Pound synthesis. Many papers, as in the Pound synthesis, accepted a medical paradigm that medicine-taking was a good thing and some sought to understand patients' beliefs and experience with a view to improving adherence. Patients' readiness to negotiate with health care professionals and to disclose their medicine-taking behaviour to health care professionals was discussed [147] as was the challenges facing health care professionals in supporting the integration of patients' needs and preferences [148]. In general the findings fitted well into the categories elaborated in the Pound synthesis although studies often developed their own terminology and categories. As described in the Pound synthesis many studies did not reference each other. The findings in this update are described under the themes as described in the Pound synthesis i.e. (1) the evaluation of medicines and the difficulties people encountered in this, (2) medicines and identity and (3) the ways people take their medicine.

5.4.2.1 The evaluation of medicines and the difficulties encountered by people in evaluating medicines

The findings of the update searches were similar to the findings of the Pound synthesis in how patients evaluated medicines. The themes of trying out the

medicines and weighing up the costs and benefits were present as well as the importance of adverse effects and the acceptability of the regimen. The studies elaborated different terminology. **Carrick (2004)** [107] developed a core concept of 'well being'. The study was an interview study of 25 adults taking antipsychotic medicine. The findings were that patients sought to maximise 'well-being' which was normality of function, feeling and appearance. 'Well being' was defined personally by patients and was their goal in taking treatment. The achievement of well-being was a net effect of symptoms and side effects. Some patients preferred the effects of their disease to the side effects of treatment. This was achieved by interplay of evaluating treatment, managing treatment and patients' understanding of the situation. Patients considered medicine in the context of their beliefs about their illness and its causes. While the maximising of 'well-being' was relevant for all patients interviewed there was a spectrum of behaviour in relation to how active the patient was in engaging with their doctors and talking through their views about medicine. **Deegan (2005)** [108] again in the field of psychiatric problems developed a concept of 'personal medicine'. She interviewed 29 patients with psychiatric problems and considered that psychiatric medicines are considered in relation to 'personal medicine' i.e. non-pharmaceutical activities that gave meaning and purpose to life and that serve to raise self-esteem, decrease symptoms and avoid unwanted outcomes. Examples of personal medicine were the ability to work, and to parent appropriately and to engage in social activities. Her analysis was that medicines that conflict with patients' 'personal medicine' are unlikely to be used by patients.

Balancing the benefits of medicine against the side effects of treatment was a theme also in studies of patients on medicine for HIV**. Lewis (2006)** [109] interviewed patients who were 100% adherent to HAART and found that they performed a trade off between the benefits and side effects of medicine. In this sample of adherent patients the interviewees reported that they did not have many other options for treatment and HAART was important in keeping them well. **Cooper (2002)** [110] interviewed 26 patients who had declined HAART treatment and found that they used their own interpretations (which

often differed from professional interpretations) of indicators such as CD4 counts to inform their decision, preferred non-pharmacological treatments and also found the lack of symptoms an issue in considering treatment. The paper uses the concept of patients' perceived 'personal necessity' of treatment as a factor in their decision. Patients also had concerns about medicines from previous personal experiences or from seeing and talking to others taking HIV medicines.

The methods by which people evaluate medicines and the difficulties experienced by patients in doing so were present in the studies. **Ogedegbe (2004)** [111] interviewed 106 African –American patients in urban primary care clinics. Patients had difficulties in evaluating treatment due to the lack of symptoms of raised blood pressure. Many used their own indicators to consider if and when they should take any treatment. **Lukoschek (2003)** [112] interviewed 92 African-American patients about their beliefs and attitudes to hypertension and anti-hypertensive medicine. Patients held differing understandings of high blood pressure and hypertension. Patients' beliefs about problem influenced their approach to treatments including diet, exercise and medicine. Patients' weighed beliefs about advantages of medicines against the side effects and many patients preferred herbal and alternative remedies. Patients with HIV interviewed for the study by **Wilson (2002)** [113] found it difficult to understand and assess their medicine as they did not know whether any symptoms were related to their disease or the medicine. **Bollini (2004)** [114] in a study of patients taking anti-depressant medicine indicated that patients would test treatment by stopping once they felt better to see what would happen and if they really needed the medicine.

For HIV patients to derive benefit from HAART medicine, high adherence to the prescribed regime is required. The acceptability of the regimen and fitting it into schedules was a significant issue in all studies which examined patients' experience of taking HAART medicine. **Adam (2003)** [115] interviewed patients who were taking HAART but found the required schedule difficult and altered the dosing regime and associated eating rules to fit the regime into their schedules. This paper concludes that the nature of HAART medicine and

its regime should be seen as the problem with this medicine and nonadherence not seen as a patient problem.

5.4.2.2 Medicines and identity

The meta-ethnography synthesis indicated that for many patients the taking of medicines interacted with issues of identity. Non–acceptance of diagnosis and issues around disclosure and stigma were significant issues in studies found in Pound synthesis. Medicines challenged patients to consider themselves as someone with a disease or could provide external evidence of a stigmatizing disease. These issues recurred in the studies included in the update. **Scotto (2005**) [116] interviewed 14 patients who had required hospitalization for a relapse of heart failure symptoms. In this sample the acceptance of the diagnosis of heart failure resulted in an altered self-image for patients but this acceptance and its integration into patients' lives was an important part of managing medicine. Behaviours to support adherence worked when the illness and its management could be integrated into ordinary life. **Alfonso (2006)** [117] interviewed 15 people who were HIV positive who were not taking medicine and explored their reasons not to take medicine. Many had prior experience of taking HAART. Not taking medicine allowed some to deny that they were HIV positive. For some either taking HIV medicine per se or the occurrence of side effects of this treatment risked exposing their HIV status. Many already felt isolated and separate and did not want to exacerbate this**.** Similar issues of taking HAART were reported in an interview study by **Sidat (2007)** [118] where patients delayed in starting treatment while dealing with issues of identity and denial. **Lewis (2006)** [109] interviewed 13 patients who were known to be 100% adherent to HAART treatment and a prominent theme in this sample was transcending their identity as someone with HIV which for the patients was associated with feelings of self-blame and moving on from that to take control of their health and its' maintenance. In an interview study by Wilson and colleagues [113] issues of identity are more dynamic and are part of an ongoing appraisal of medicines and medicine taking. **Pyne (2006)** [119] explored explanatory models of schizophrenia and treatments for schizophrenia held by professionals and

5.4.2.3 Ways people take their medicine

The ways in which patients take their medicines were similar in the update studies as in the Pound synthesis. Patients changed their medicines and used medicines in strategic ways but did not necessarily disclose this to health care professionals **Deegan (2005)** [108]. In the sample interviewed by **Ogedegbe (2004)** [111] the cost of prescriptions and the effort involved in getting prescriptions reordered and refilled meant people did not take their medicine continuously. Studies of patients prescribed HIV medicine similarly indicated patients making adjustments to their regimes in keeping with their own beliefs and experiences and not reporting these to health care professionals **Campero (2007)** [122].

In general patients would not report their treatment modifications to health care professionals unless they saw themselves as expert patients. The ubiquity of patients' alteration of their regimes is indicated by the findings of **Aronson (2005)** [125]. This was a small study of 11 patients, who were described as completely adherent to medicine. They were all prescribed short

term courses of antibiotics and all patients took all the medicine. These patients however did alter the timing of doses to fit in with their schedules. Doses were forgotten and then taken when remembered. **Wilson (2002)** [113] describes HIV patients making decisions about how they take their medicine almost on a dose-by dose basis. This was for a number of reasons and in this study patients' medicine-taking behaviours are described as a result of reconciling incompatibilities which included illness beliefs, the difficulty of the regime and its impact of life. Patients generally described themselves as adherent to health care professionals. **Reid (2006)** [123] describes the strategic use of diuretic medicine by patients with heart failure- patients changing the timing of medicine or omitting the dose according to social and other activities.

5.4.2.4 Additional findings from update search

The findings of the qualitative studies included in the update of the Pound synthesis (2005) fitted largely within the themes found in the original synthesis. A finding not elaborated in the synthesis and not found in other update studies was medicine-taking experience and behaviours in older adults on complex regimes. **Elliott (2007)** [124] interviewed 20 patients aged 67-90 about their experience of medicine-taking. Patients were all members of one HMO and took 4-12 medicines. The researchers were particularly interested in how patients on multiple medicines make decisions about medicines. The general findings from the study did not differ from themes found in synthesis – patients wished to minimise medicine overall, they stopped and started medicine to take a break from medicine, to check if they were working, to determine the cause of side effects and generally did not disclose this behaviour to their physicians. The patients interviewed did report having made choices between which medicines they would decide to take, this included choices between medicines for different disease and choices within diseases. When choosing between medicines for different diseases patients chose to take the medicine for the disease they feared most or that which gave symptomatic relief. Choices otherwise were influenced by symptom control, side effects, medicine cost, negative health experience, illness beliefs and acceptability of medicine (i.e. taste etc). Illness beliefs

dominated more general factors such as influence of family, friends, health providers and the media. Complexity of regime did not affect choice. Cost was a factor even when not related to financial hardship, and patients appeared to resent the cost of medicines. Choices were generally influenced by one dominant factor and less likely to be a result of analysis of multiple factors.

Two studies reported on structural issues that interfered with patients' ability to appraise medicine and to receive the information they required to do this. **Garcia Popa-Lissenau (2004)** [126] reported on the difficulties patients from low incomes with rheumatological disorders had in physically accessing appointments with professions. **Mutchler (2007)** [128] reported how for non-English speaking Latinos in the US the difficulty in engaging with health care professionals results in reduced information available to those patients and poorer relationships with professionals which of itself could reduce trust in treatment.

5.4.2.5 Experience of medicine-taking of minority groups in UK

We specifically searched for papers examining experience of patients from minority groups in the UK. Overall their use and experience of medicines was similar to that already described in the evidence review. One additional finding in **Erwin (1999)** [127] was a belief by patients of African origin that they had different physiology from white people and that medicines used for treatment of HIV might not be appropriate for them and that they were being discriminated against. This was an issue also raised by African American patients interviewed. **Sidat (2007)** [118] found that this patient group were also often involved in church activities and some churches were against use of medicine. **Lawton (2005)** [129] explored the perceptions of diabetic patients of Indian and Pakistani origin of taking oral hypoglycaemic medicines. These patients' beliefs and use of medicines was influenced by their experience of the health system in their country of origin. They distrusted this system and admired the NHS but consequently considered that the medicines available in the UK were likely to be stronger and more efficacious than those available in their country of origin and so they reduced dose and sought to balance effect of medicines by taking in 'strong' foods. People of African origin living in South

London were interviewed about their use of malaria prophylaxis **Morgan (2005)** [130]. One of the factors influencing use of anti-malarial was the practice of leaving medicines in Africa for family members.

5.5 Systematic reviews of barriers and facilitators for individuals in medicine-taking

5.5.1 Methods of the update

The GDG requested an additional search for any further systematic reviews of barriers and facilitators for individuals in medicine taking. The search strategy used for the Pound updates searches was applied to this review together with a systematic review filter. The titles and abstracts of records retrieved by the searches were scanned and any potentially relevant publications were obtained in full text. Cross-referencing of all the studies was undertaken to ensure that the search is as comprehensive as possible. The studies were then reviewed to identify the most appropriate evidence to help answer the key questions and to ensure that the recommendations are based on the best available evidence.

Types of studies: Systematic reviews.

Types of participants: people aged above 16 years prescribed medicine for a medical condition.

Duration of studies: no limit on duration of studies.

5.5.2 Evidence review

The search for systematic review of barriers and facilitators of medicine-taking produced two eligible reviews in very diverse patient populations. No systematic reviews examining statistical associations between patient reported factors and actual medicine-taking were found. The systematic reviews that were found examined medicine-taking in particular population subgroups – patients with TB and patients with HIV on retroviral treatment.

Although there was potential overlap in terms of type of studies informing a synthesis between medicine-taking in these areas and medicine-taking in the Pound synthesis there was little overlap in papers included in each synthesis highlighting the issues raised by authors of Pound synthesis about difficulty of locating qualitative literature.

The first of these **Munro (2007)** [105] is a review of qualitative studies which aimed to understand the factors considered important by patients, caregivers and health care providers in contributing to TB medicine adherence. The authors used meta-ethnography as in Pound synthesis. The majority of the studies in this review were conducted in developing countries. The emphasis on adherence and inclusion of carers and health care providers' perspectives as well as the methodology resulted in an analysis which included structural factors that influence patients' medicine-taking as well as patient factors.

The primary themes that emerged from the included studies were: 1) Organization of treatment and care including access to care, treatment requirements and relationship with the provider; 2) Interpretation of illness and wellness; 3) Financial burden including impact on work, cost of treatment, general poverty; 4) Knowledge attitudes and beliefs about treatment; 5) Law and immigration; 6) Personal characteristics and adherence behaviour including substance abuse, gender ,religion, motivation; 7) Side effects; 8) Family, community and household influence.

A systematic review by **Mills (2006)** [106] examined patient reported barriers and facilitators to adhering to antiretroviral therapy. This analysis included 37 qualitative studies and 47 surveys using structured questionnaires or structured interviews. Seventy-two studies were conducted in developed countries. Fifty-six were from the US and only 3 from the UK. A systematic approach was taken to extracting themes from the qualitative studies and synthesizing the quantitative data and pooling the results. Briefly the authors extracted themes from the qualitative studies and then reviewers examined the quantitative surveys to determine if the same issues had been addressed in the surveys. The authors used their own criteria to assess the surveys and

these related to the development process and face validity of the questionnaire and the population surveyed. The authors used the prevalence of themes as reported in the surveys for their statistical analysis. This technique is called meta-study and is one of a series of methods being developed to bring together findings of qualitative and questionnaire studies.

Barriers identified in both economic settings (developed and developing world) included: fear of disclosure, concomitant substance abuse, forgetfulness, suspicions of treatment, regimens that are too complicated, number of pills required, decreased quality of life, work and family responsibilities, falling asleep and access to medicine. Important facilitators reported by patients in developed nation settings included having a sense of self work, seeing positive effects of anti-retroviral medicines, accepting their seropositivity, understanding the need for strict adherence, making use of reminder tools, and having a simple regimen. In a further study of adherence rates in sub-Saharan Africa and North America [149] Mills comments that the most prevalent barriers to adherence in sub-saharan Africa are cost, not disclosing HIV status to a loved one or fear of being stigmatised, alcohol abuse and difficulty in following complex medicine regimens.

6 Information for inpatients and practitioners when patients are transferred between services

6.1 Recommendations

Hyperlink to recommendations section Providing Information

Hyperlink to recommendations section Communication Between Healthcare Professionals

6.2 Introduction

Patients are frequently started on medicines when in hospital as an inpatient or when attending outpatient clinics. Transitions between care settings have been recognised as a time when potential errors in medicine can occur. NICE and the National Patient Safety Agency (NPSA) have recently produced joint guidance on medicines' reconciliation when adult patients are admitted to hospital (www.NICE.org.uk/PSG001). Literature reviews suggest unintentional variances of 30-70% between medicines which patients were taking before admission and those prescribed on admission. The GDG considered that patients have the same rights to information and choice regardless of setting but acknowledged that this is not always possible when patients are acutely unwell.

6.3 What information regarding medicines should be provided for patients and practitioners when patients are discharged from secondary care?

6.3.1 Evidence to recommendations

The GDG recognised that medicines may be initiated in hospital settings in emergency situations and when patients are unwell. They recognised that in these situations discussions of details of medicines may not be possible. However as patients' condition improves and patients are prepared for discharge they should be offered a full explanation of their medicine. This explanation should allow patients to make informed choices about their continued use of the medicine prescribed. The experience of the GDG was of considerable confusion and lack of information provided to patients and to subsequent providers of care when patients are discharged. Difficulties arise not only in knowledge of what medicines have been prescribed for patients but what information patients have been given about their illness and medicines. The GDG based these recommendations on professional opinions and information from expert sources.

6.3.2 Methods of the evidence review

The evidence review is a narrative review. The GDG requested a review of available guidance and reports with a particular emphasis on those where patients' rights to information and involvement were given priority.

6.3.3 Evidence review

The Academy of Royal Medical Colleges is currently preparing consensus guidance on what should be included in hospital discharge summaries. This guidance which will include advice on information about medicines will be available late in 2008. The WHO produced a report in 2007 on Assuring Accuracy of Medicines at Transitions of Care (www.jcipatientsafety/org/). The emphasis on reports and guidance about medicines reconciliation is on the

reduction of medicines errors. Patients' rights to information and involvement in decisions about medicines are not the primary concern of these reports. The WHO report does however state that effective involvement of patients and families in medicines reconciliation is vital to reducing errors. They suggest that:

- The patient is in the best position to be aware of all the medicines prescribed by multiple caregivers.
- Consideration should be given to asking patients to put all their medicines in a bag and bring it with them whenever going to the hospital or a doctor visit.
- Patients, family, and caregivers should be encouraged to keep and maintain an accurate list of all medicines, including prescription and non prescription medicines, herbal and nutritional supplements, immunisation history, and any allergic or adverse medicine reactions. These medicine lists should be updated and reviewed with the patient/family/caregiver at each care encounter.
- Patients should be taught about the risks of medicines, both individually and in combination, with particular attention to patients on multiple medicines prescribed by multiple caregivers.

7 Assessment of adherence

7.1 Recommendations

Hyperlink to recommendations section Assessing Adherence

7.2 Introduction

Many patients take medicines over long periods of time and discussions about these medicines need to consider the patients experience of taking the medicine. This includes an assessment or discussion about whether or not the patient is taking the medicine and if they are doing this exactly as prescribed or in some other way.

A number of ways of assessing adherence have been developed. These can generally be described as direct methods or indirect methods. Direct methods are examinations of blood, urine or other bodily fluids for the presence of the medicine or a metabolite. Indirect methods do not measure the presence of the medicine but use methods such as self report from patients, pill counts, prescription reordering, pharmacy refill records, electronic medicine monitoring and therapeutic effect to form an assessment of adherence. In the context of routine clinical practice and of involving patients in decisions about medicines the GDG considered that indirect methods were the most commonly used. Self-report is the most available method for reporting adherence in a clinical context. The GDG wished to consider the advantages and disadvantages of self report in routine clinical practice to recommend how it should be used by practitioners. We conducted an evidence review to explore specifically the advantages and disadvantages of self-report for assessing adherence. Other types of measures of adherence were not explored.

7.3 What are the advantages and disadvantages of self-report in assessing patient's adherence?

Related references	Evidence statements (summary of evidence)
Advantages	
Hawkshead (2007) [150]; Gagne (2005) [151]; Paterson (2002) [152]; Miller (2000) [153]; Turner (2002) [154]; Farmer (1999) [155]; Bender (1997) [156]; LaFleur (2004) [157]; Rand (1994) [158]	Self-reporting is the most simple and inexpensive method of measuring adherence.
Miller (2000) [153]; Farmer(1999) [155]; Paterson (2002) [152]; Bender (1997) [156]; Rand (1994) [158]	Self-reporting is quick and easy to administer, avoiding the use of sophisticated methodology or equipment.
Hawkshead (2007) [150]; Bender (1997) [156]	Self-reporting methods which are validated can feasibly be used in clinical settings.
Hawkshead (2007) [150]; Paterson (2002) [152]; Farmer (1999) [155]; Hecht (1998) [159]; Bennett Johnson (1992) [160]; George (2007) [161]	Self-reporting can identify those who are nonadherent. It is most likely those reporting nonadherence are being truthful.
Hawkshead (2007) [150]; Miller (2000) [153]; Rand (1994) [158]; Bennett Johnson (1992) [160]	Self-reporting can gather social, situational and behavioural factors including revealing patterns of medicine use and what leads to non-compliance.
Disadvantages	

George (2007) [161]; Hawkshead (2007) [150]; LaFleur (2004) [157]; Turner (2002) [154]; Miller (2000) [153] Hecht (1998) [159]; Bender (1997) [156]	Self-reporting has the problem of over-estimating adherence.
Hawkshead (2007) [150]; Gagne(2005) [151]; LaFleur (2004) [157]; Turner (2002) [154]; Farmer(1999) [155]; Bennett Johnson (1992) [160]	Inaccurate self-reporting can be caused by recall bias, social desirability bias and errors in self-observation.
Paterson (2002) [152]; Hecht (1998) [159]; Bennett Johnson (1992) [160]	The timeframe of the adherence recollection can affect the accuracy of the recall. Specifying the time period can help.
Hawkshead (2007) [150]; Farmer (1999) [155]; Hecht (1998) [159]	Wording of questions, the way a question is asked and the skills of the interviewer can either facilitate or be detrimental to gaining accurate responses.
Turner (2002) [154]; Bennett Johnson (1992) [160]	Being non-judgmental, giving a preamble before adherence questions, and asking about specific behaviours can help validity.

7.3.1 Evidence to recommendations

The GDG considered that self-report is the most widely used method of assessing adherence and that although direct measures of adherence are relevant in some situations they were more interested in making recommendations for routine clinical practice. Indirect methods such as therapeutic effects and prescription ordering and refills are methods which should alert prescribers and dispensers to problems of adherence. In these situations and as part of medicine reviews health care professionals need to be able to discuss medicine-taking with patients. The GDG made recommendations on how professionals should assess adherence using the review of advantages and disadvantages of self-report.

7.3.2 Methods of the evidence review

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies – We included literature reviews and systematic reviews only.

Types of participants - People prescribed medicine for a medical condition.

Duration of studies – No time limit was specified.

Types of interventions - Any interventions intended to change adherence to prescribed medicine which reviews studies which focus on self-report advantages and disadvantages.

Types of outcome measures - No outcome measures specified.

7.3.3 Evidence review

The searches mainly returned literature reviews, rather than systematic reviews, therefore details (of the various studies mentioned in these reviews) were not always given and some only mentioned the studies briefly.

Garber (2004) [162] produced a systematic review on the concordance of self-report with other measures of medicine adherence. They searched a number of databases and identified 2757 articles. The inclusion criteria included studies where at least 2 adherence measures were used, one of which was a self-report measure, the other a non self-report measure. The self-report measures included questionnaires, diaries or interviews and were categorised under these. They found 86 unique comparisons, mostly interviews (57%), questionnaires (27%) and diaries (17%). The non-self-report measures were electronic measures (35%), pill count or canister weight (26%), a plasma drug concentration (20%) a claims-based measure (13%) and a clinical opinion (6%). 43% of the pairings of self-report and nonself-report measures were highly concordant.

Concordance levels were categorised by the following: Kappa results (for categorical variables) over 0.6 were high, 0.6 to 0.4 were moderate and below 0.4 were low. Pearson correlation co-efficient (for continuous variables) over 0.8 were high, 0.8 to 0.4 were moderate and below 0.4 were low. When sensitivity and specificity of the measure was given the measure was as a likelihood ratio (LR). A positive LR greater than 10 was categorised as high, a LR+ of 3 to 10 was moderate and LR+ below 3 was low. If there was no statistical analysis given the authors used an algorithm to categorise.

In the majority (45/59) of those which were not highly concordant, the self-report measure showed higher adherence compared to the nonself-report measure, but this varied widely depending on type of self-report measure. 31% of the interviews were highly concordant with nonself-report measures. Diaries (71%) and questionnaires (55%) were much more likely to be highly concordant with non self-report measures. The difference in concordance by the type of self-report measure was significant (chi-square=8.47, p=0.01). It also depended on the non-self-report measures. Self-reporting had higher concordance with other types of non self-report measures (58%) than electronic measures (17%) (chi-square 14.3, $p<0.01$). Interviews showed the least concordance with electronic measures, where none of the 15 comparisons were highly concordant. The authors noted that this was a

comparison between measures which could not fully evaluate the accuracy of any of the measures.

The authors concluded that questionnaire and diary methods were preferable over interviewing for measuring adherence. They note that many of the studies did not explicitly compare adherence measures statistically and those that did used simplistic analyses. They also note that the categorisation of concordance was based on arbitrary cut-off points, so different cut-off points could change the levels of concordance between methods.

In summary, questionnaires and diaries were more concordant with other measures.

George (2007) [161] conducted a literature review to assess adherence of COPD patients with disease management programs. They searched OVID and International Pharmaceutical Abstracts. They did not report the inclusion/exclusion criteria or how many studies were retrieved. The adherence measures that were included in the review were self report, inhaler weights, electronic monitoring, inhalation technique assessment, medicine/pill count, pharmacy refill data/claims data and biological assays.

They found that self-reporting of missed doses (by questionnaire) underestimated nonadherence compared to more objective measures e.g. capsule count (Dompeling, 1992), inhaler weights (Rand, 1995) and electronic monitoring (Rand, 1992; Braunstein, 1996; Simmons, 2000). Self-report was shown to have moderate reliability (25% to 67%) compared to objective measures such as canister weight (Rand, 1995) and electronic monitoring (Gong, 1988; Nides, 1993; Bosley, 1995).

Self-reporting of nonadherence of medicine for COPD has shown satisfactory reliability, when compared to objective measures (Dolce, 1991; Nides, 1993; Rand, 1995). Self-report is commonly criticised for overestimating adherence and poor reliability yet those who report nonadherence are likely to be telling the truth (Haynes, 1980; Inui, 1981; Choo, 1999; Erickson, 2001).

The author's concluded that even though electronic monitoring is regarded as the gold standard it is more suited to a clinical trial setting. Self-reporting is the cheapest, simplest and easiest method to assess adherence. Self-report can identify the reasons for nonadherence and therefore the issues can be addressed.

Hawkshead (2007) [150] presented a narrative review of the advantages and limitations of methods for measuring adherence in hypertensive patients. No mention is given to how they searched for these studies or decided to include/exclude. The types of adherence measures were self-report, electronic monitoring, pill counts, pharmacy refill rates, bioassays/biomarkers and direct observation.

They state that self reporting is the simplest method for assessing medicine adherence and can include patient diaries, interviews during office visits and adherence-specific questionnaires. 'Several multi-item questionnaires have been developed and tested in outpatient settings with the explicit aim of ascertaining valid and reliable estimates of adherence to antihypertensive medicines', of which many have reported high measures of validity and reliability (Morisky, 1986; Kim, 2000; Shea, 1992; Krousel-Wood, 2005; Hyre, 2007). There are three previously validated self-reported medicine adherence instruments – the Medication Adherence Survey (MAS), the Brief Medication Questionnaire (BMQ) and the Medical Outcomes Study (MOS). Cook (2005) compared the level of agreement between these and pharmacy refill rates and found correlations between of 0.23, 0.26 and 0.21 between the refill rates and the MAS, MOS and BMQ respectively.

Validated self-report measures can feasibly be used in clinical settings and help to identify those who are nonadherent, and intervene to increase this (Harmon, 2006). The advantages stated are that self-report is simple and economical; it can also gather social, situational, and behavioural factors which can impact on adherence. The disadvantages are the possibility that there could be recall bias, over-estimation of compliance and responses which are socially acceptable. Validity can also depend on the skills of the

interviewer as well as the question construction and timeframe (Farmer, 1999 and Wang, 2004). It is suggested that self-report could be combined with objective information, e.g. prescription-fill data, to improve adherence measurement.

The authors' concluded that selecting the type of measure for clinical practice depends on the intended use of the information, the resources available, patient acceptance and the convenience of the method. A combination of methods may be best to give an accurate assessment of adherence and should be tailored to individual needs.

In summary, some self-reporting questionnaires have been validated and can be simple and feasible to use in clinical settings and identify non-adherers. However they can have biases and overestimate adherence.

Gagne (2005) [151] reported on how to improve self-report measures for nonadherence to HIV medicines, with particular attention to techniques that can be applied with questionnaires administered in clinical practice. Questionnaires are inexpensive and convenient and can be conducted in clinical and research settings, but can vary in terms of accuracy. According to many authors, forgetfulness (Brooks, 1994; Hayes & DiMatteo, 1987; Holzemer, 1999; Rand, 2000; Svarstad, 1999) and social desirability (Felkey, 1995; Gordis, 1969; Gray, 1998; Rand, 2000; Svarstad, 1999) are main factors leading to inaccurate self-reporting of nonadherence. Social desirable answers can depends on how much the patient perceives the desirability of the behaviour to be. Those behaviours perceived as undesirable are under-reported and behaviours perceived as desirable can be over-reported (Cannell 1979; Fowler, 1995). There are techniques suggested for minimising forgetfulness and social desirability (Cannell, 1979; Fowler, 1995; Sudman & Bradburn, 1974; Sudman & Bradburn, 1982) although methods to reduce these are not well-documented, are often derived from clinical practice than controlled experimental studies and their reported effectiveness is inconsistent.

Suggestions were made to reduce socially desirable answers:

- Assuring confidentiality and that information will not be available to HCPs (Eldred, 1998; Gordillo, 1999).
- Explaining that there are no right or wrong answers (Des Jarlais, 1999; Chesney, 1990).
- How the question is asked (Ickovics, in Eldred, 1998; Chesney, 1999; Svarstad, 1999).
- Wording the question to increase the likelihood of gaining certain desired answers, such as nonadherence (loading the question) (Sudman, 1982; Bradburn, 1982; Allaire, 1988).
- Open-ended questions can avoid the pitfalls of response categories (Schwarz, 1985; Sudman, 1982).

Open-ended questions have been used in studies of HIV (e.g. Chesney, 1990) and for measuring adherence/nonadherence (e.g. Svarstad, 1999). Open-ended answers have shown to be less affected by social desirability than close-ended answers (Sudman, 1974). Sudman (1974) also found that open-ended questions were less affected by forgetfulness and recall errors.

Recall can be aided by:

- Item wording, using familiar words and words that have only one meaning and one idea (Sudman, 1982);
- Words should not have blame implications (Averitt, in Eldred, 1998).
- Aided-recall techniques such as memory cues may be useful (Sudman, 1982).
- Specifying a reference time period, especially a recent and short time frame can aid forgetfulness (Brooks, 1994; Chesney, 1999; Holzemer, 1999; Sudman, 1982).

However there is the problem of the time period being too short and not accurately representing the adherence level, as adherence varies over time (Chesney, 1997b; Gray, 1998; Kastrissios, 1998). This could be solved by using a short period of time and administering the questionnaire a number of times over the period. However, this could lead to less motivation and could be costly. Shorter periods of reference could be used when administering the questionnaire only once. According to episodic and semantic memory it may be best to ask more precise information about the past few days and less specific information from a longer time period.

The author concluded that most of the HIV literature used multiple measures of adherence. Adherence to HIV measures could be enhanced by improving self-report measures of nonadherence. Questionnaire designs may have surprisingly beneficial results.

In summary, self-reporting by questionnaire can have biases such as social desirable responses and recall bias. These biases can be minimised using certain techniques.

LaFleur (2004) [157] conducted a brief narrative review of methods to measure compliance with medicine regimens. No search or inclusion/exclusion criteria were given. They state that self-report is the most popular method for assessing compliance as it is inexpensive but is often unreliable (Myers, 1998). Self-report can include patient interviews or self-report surveys. When compared to objective measures e.g. electronic monitoring devices or medicine level monitoring of compliance self-reporting has shown to over-report compliance over 50% of the time (Spector, 1986; Gordis, 1969; Waterhouse, 1993; Straka, 1997). It is also often inaccurate for those reporting non-compliance with medicine-taking. In Kwon (2003) a comparison of self-reporting of antidepressant use with prescription claims showed a 20% difference in those reporting nonadherence to antidepressants. The reasons for any discrepancies with other measures could be that patients do not understand regimens, do not know indications for their medicine, or do not

report behaviours perceived as not socially-acceptable, or forgetting of non-compliance. No references were given for these assertions.

In summary, self-report by interviews or surveys can be inexpensive but can be unreliable and over-report compliance. Those who report non-compliance can also be inaccurate. There could be biases such as social desirability, recall and not understanding medicine regimes.

Turner (2002) [154] reviewed literature, to compare various measures of adherence to antiretroviral therapy. This was a narrative review with no details of search/inclusion criteria. The types of adherence measures in the review were self-report, health care provider estimation, pill counts, pharmacy-based measures, electronic monitors and biological/laboratory markers. They state that self-reports are less complex but that there can be problems with recall over long time periods. Many studies use self-report over the past 4 days but additional questions may be needed, e.g. about weekends, as this tends to be a difficult time for adherence.

All types of self-reporting overestimate adherence compared to other measures (Arnsten, 2001; Golin, 1999; Melbourne, 1999). Even those who report missing doses tend to overestimate adherence compared to other measures (Wagner, 2000). Social desirability biases can also contribute. Those who report problems with adherence usually have poorer adherence with other measures (Haynes, 1980). Those who report nonadherence appear responsive to interventions, and are important to identify (Haynes, 1980).

The validity can be increased with a preamble before the questions about adherence in order to reassure patients that information will not be held against them and that nonadherence is common. Audio computer-assisted self-interviewing is suggested for more sensitive topics (Metzger, 2000; Gribble, 2000).

A study by Bangsberg (2000) compared adherence measured by self-report (by patient interview) with provider estimation and unannounced pill counts. A comparison of pill counts with estimates of and patient self-reporting of

medicines adherence showed that the physician estimates explained 26% of the variation of pill count adherence, and patients' estimates explained 72%. They found that the sensitivity and specificity of estimates of nonadherence (<80% of pills taken according to pill count) were 72% and 95% respectively for patient interview but only 40% and 85% respectively for provider estimates.

They conclude that self-report is more easily obtained but has relatively poor sensitivity but good specificity. However electronic measures have better sensitivity but poorer specificity.

In summary, all types of self-report overestimate adherence, even with those who report nonadherence and biases such as social desirability can occur. Certain techniques could be used to minimise these biases.

Paterson (2002) [152] conducted a brief narrative review to ascertain how adherence to antiretroviral medicine should be measured. The methods reported were electronic monitoring, pill counts, pill recognition, review of pharmacy records, patient self-report, biological parameters, and medicine monitoring and provider prediction of adherence. They noted that how a question is asked can influence self-report of adherence (i.e. in face-to face inquiry or patient-completed questionnaires). A non-judgemental stance can help and this can be achieved by a preamble before the questions to show that they are not being judged and are looking for honest answers (Turner, 2001).

Another disadvantage of self-report (face-to-face interview) is that periods shorter than 7 days are not long enough to determine the percentage of adherence likely, however some patients may not correctly report adherence for 7 day periods. They state that additional questions may be necessary to counteract this e.g. about adherence at the weekend.

One method to counteract the problems of gaining honest answers is computer-assisted self-interviewing (Bangsberg, 2001) or diary. Diaries hold

an advantage as they can be inexpensive and accurate. Their disadvantage is that some may complete them retrospectively or not at all.

Paterson (2002) asserts that self-report is 'likely to be the simplest means of assessing adherence' and so the reliability is important to assess. Adherence was found to be 'considerably higher' than that measured by electronic monitoring or pill count (Liu, 2001). Self-report overestimates adherence. It is most useful in those who admit to being poor adherers (Murri, 2000). They conclude that electronic monitoring devices are the closest to a gold standard in adherence measurement.

The authors conclude that there is no gold standard for measuring adherence and that electronic monitoring, in their opinion, may be the closest, yet it has some limitations. If a patient is failing to respond to treatment, self-report or pill identification should be the first option. If they report adherence this could be confirmed by electronic monitoring.

In summary, various self-reporting measures were reported. Interviews may be too late for accurate recall or may be too early to gain useful adherence information. Diaries are inexpensive and can be more accurate as there is no recall bias, however they may not be completed or completed retrospectively. Self-report can overestimate adherence but can identify those who report nonadherence.

Miller (2000) [153] reviewed current literature of measures of adherence of antiretroviral medicines in clinical trials. The types of measures of adherence were self-report, clinician estimates, pill counts, pharmacy records, clinic attendance, plasma levels, surrogate/indirect laboratory markers and electronic monitors. They report that the simplest method of measuring adherence is self-report. But there is no standardised instrument. Self-reported surveys are quick and avoid sophisticated methodology or equipment and are inexpensive compared to other methods of measurement. They have limitations, such as significantly exceeding adherence measured by other objective methods (Bond, 1991; Stratka, 1997; Cramer, 1991). HIV studies confirm this (Golin, 1999; Arnsten, 2000; Paterson, 1999; Bangsberg,

1999). Interviews and surveys often promote socially acceptable responses (DiMatteo, 1982). Less adherent patients report higher adherence than they actually had (Bond, 1991). Memory can also affect the accuracy of reporting adherence. Most surveys use broad response categories to report the proportion of pills taken, thus small degrees of nonadherence is hard to distinguish with self-report. The information is useful, but accuracy is limited and biased towards higher adherence.

Self-reported nonadherence has been associated with worse virologic outcomes (Demasi, 1999; Bangsberg, 1999; Duong, 1999; Murri, 1999; Le Moing, 1999) and as an independent predictor of clinical response to HAART when controlling objective virologic and immunologic markers (Montaner, 1999). They assert that even though it is an imperfect measure it can provide information that explains variation in clinical response to antiretroviral therapy which is not explained by other clinical factors.

The authors concluded that each method of adherence measurement has its own strengths and weaknesses. Caution should be taken when extrapolating adherence measured in clinical trials into clinical practice. Many measures have been independent predictors of clinical outcome. They may identify slightly different nonadherent populations. The different measures may complement each other and they would recommend using more than one measure, where possible.

In summary, self-report surveys are simple and inexpensive but can overestimate adherence. Interviews and surveys can have social desirability and recall biases. Also as categories are large, small degrees of nonadherence are hard to detect. There is no standardised instrument. However it can explain variation in clinical responses to ART.

Farmer (1999) [155] conducted a review of methods for measuring and monitoring medicine regimen adherence in clinical trials and clinical practice. They searched Medline for the years 1990 to 1999 and retrieved 2630 articles regarding patient compliance. The types of adherence measures included were self-report, biomarkers, direct patient observation, pill counts,

prescription record review (manual and electronic) and electronic monitoring. Types of self-report included questioning/interrogation and the use of diaries and survey instruments. They tabulated the various methods for assessing adherence and their advantages and disadvantages. Patient interviews are easy to use and inexpensive but the patient can be influenced by question construction and interviewer's skill. Adherence questionnaires are easy to administer (on site, mail, telephone), can be validated and may explain patient behaviour. However there is a lack of continuous data and the accuracy is instrument-dependent.

Patient interviews are generally considered the most unreliable for assessing adherence (Grymonpre, 1998; Matsui, 1994; Craig, 1985; Straka, 1997; Park, 1964; Inui, 1981; Gordis, 1969). Those who report nonadherence are usually correct, whereas those who say they are adherent may not be (Cramer, 1991). However it can depend on the method used and how it is used. Assessing self-reporting is difficult mainly because there are so many methods. The interviewer's skill and the construction of the questions can affect the accuracy and validity of self-report. The relationship and communication between the HCP and patient can statistically significantly affect compliance (Davis, 1969). Highest compliance was found with those who joked, laughed and sought suggestions from their GP. The wording of questions can affect the response, and implications of blame can encourage biased responses (Ross, 1991). Some answers are socially desirable and concealed their real behaviour (Sherbourne, 1992). It is hard to assess studies of interviews as the way they are asked could bias the result.

Stewart (1987) looked at 2 compliance questions in an interview to assess medicine-taking behaviour. Comparing the results to pill counts, the questions had a specificity of 69.8% and sensitivity of 80%, therefore an overall 74.5% accuracy. The time frame used for recall can differ, some researchers do not specify, others are 7-10 days and some are a month (Grymonpre, 1998; Dirks, 1982; Straka, 1997). To correct these problems some researchers have tried to construct a standardised questionnaire for measuring adherence. For example Morisky (1986) developed a 4-item questionnaire specific to

medicine regimen adherence. It was assessed on unidimensionality, reliability and concurrent validity with blood pressure control. The instrument's sensitivity was 81% and specificity 44%. It was not found to be efficient at predicting poor adherence (Morisky, 1986).

Svarstad (in press at time of review) developed a self-administered instrument called the Brief Medication Questionnaire. The accuracy was assessed using MEMS. There were 3 sets of questions – 5 regimen screen items, 2 belief screen items and 2 recall screen items. The sensitivity for repeat nonadherence was 80% for the regimen screen, 100% for the belief screen and 40% for the recall screen. The specificity for repeat adherence had 100% for the regimen, 80% for the belief and 40% for the recall screen. The accuracy of reported repeat nonadherence was 95% for the regimen, 85% for the belief and 40% for the recall screen.

The authors concluded that each method has strengths and weaknesses depending on the intended use. When selecting a specific method an assessment of each method's validity should be undertaken. A combination of methods is recommended.

In summary, several methods of self-report were examined. Interviews are simple and inexpensive, but can depend on the interviewer. Questionnaires can be administered in a variety of methods, but are considered the most unreliable. Those who say they are nonadherent are usually being truthful but many who say they are adherent may not be.

Bender (1997) [156] conducted a literature review to assess nonadherence in asthmatic patients. A search of Medline was made from 1990 to 1997 of all pertinent articles, preferably controlled studies. Types of adherence measures were biochemical measurement, clinical judgement, medicine measurement, pharmacy database review and electronic medicine monitoring. Self-report measures can be collected by interview, diaries and questionnaires but no validated adherence-specific questionnaire is commonly used as they are often specific to the studies. Self-report measures are simple, inexpensive and usually brief and so they are commonly used to measure adherence.

Especially in the clinical setting they are the best measure for collecting information on beliefs, attitudes and experiences with medicine regimes. Accuracy with other measures is highly variable. Spector (1986), Coutts (1992) and Gibson (1995) compared asthmatics self-reporting of inhaler usage with electronic medicine monitoring devices and they showed that asthma diaries usually overestimate adherence. Demands of the setting can influence the usefulness and reliability of the information gained from self-reporting. These can be a desire to please on the part of the patient and the Health Care Professional's skill and sensitivity in eliciting self-reports. When collected well it can give good insight into patients' problems with adherence. As they are unlikely to identify themselves as non-adherers unless they are this helps identify them (Coutts, 1992; Spector, 1986; Dolce, 1991; Morisky, 1990).

The authors state that while self-report may not be a sufficient measure of adherence in many settings and particularly in research, it is probably a necessary measure in all settings.

In summary, self-report measures are simple, inexpensive, brief and the best way of collecting information in the clinical setting. However diaries overestimate adherence and the demands of the setting can influence the usefulness and reliability of the measure.

Rand (1994) [158] reported in a narrative review on measuring adherence to asthma medicine regimens. They did not state search or inclusion criteria. The types of adherence measures included in the review were biochemical measures, observation of MDI technique, clinical judgement, medicine measurement and medicine monitors.

They state that self-report is the most inexpensive and quick way of measuring adherence (Soutter, 1974). The possible advantage of diary cards is that they can measure adherence across time and can reveal patterns between the disease exacerbation and compliance with the medicine. As there are many medicines used within asthma prescribing, it can help to see the adherence of certain medicines rather than just overall. It can also

specifically assess overuse, inappropriate use or erratic use of medicines as well as triggering events for the need for medicine e.g. in Kesten (1991). Asthma diaries may share commonalities but there is no standardised diary as such in research. A disadvantage of asthma diaries is they may be be complex and time-consuming. Also criteria of acceptable adherence may differ from patient to patient. One way to evaluate the level of adherence is to use trained, masked, medical personnel to score the compliance. It is preferable to develop standardised compliance criteria for all raters and train them by a standardised protocol and make sure there is inter-rater reliability.

Many studies have used questionnaires to collect clinic or follow-up data for patient adherence (Bailey, 1987; Kinsman, 1980; Dolce, 1991), mainly designed for a particular research project. Many include adherence questions within a larger questionnaire, such as the 76-item Revised Asthma Problem Behaviour Checklist (RAPBC) and the 72-item Asthma Problem Behaviour Checklist (APBC). These have been found to be reliable with test-retest correlation coefficients of r=0.95 and r=0.80 respectively. However no reliability and validity information was available for those items specifically measuring adherence to medicine.

Rand (1994) points out that both asthma diaries and self-report are the most common methods for assessing asthma medicine adherence but these instruments, because they are not standardised or not published, rarely have their validity and reliability assessed. Except for Adherence Scale and Inhaler Adherence Scale (Kinsman, 1980; Dolce, 1991; Bailey, 1990), which are six-item scales based on Morisky's work (1990). This instrument was found to have a Chronbach's alpha of 0.76 and 0.69 and was concordant with outcome measures in the UAB adult asthma study.

The limitations of self-report have been mentioned by many authors (Masur, 1981; Mawhinney, 1991; Cramer, 1989; Rand, 1992). When compared to objective measures it varies highly on the degree of accuracy (Gordis, 1966; Mattar, 1974). Diary self-reports were compared to an electronic medicine monitoring device to measure adherence to asthmatic medicine by Spector

(1986). The findings were that all patients self-reported using the inhaler on certain days, whereas the measured medicine suggested just over half (52.6%) actually did so. Adding a diary can add more complexity to the patient regime than there all ready is. It has been shown that the greater the complexity of a regime the lower the compliance (Masur, 1981). Some participants alter their records of medicine use to appear compliant (Mawhinney, 1991; Rand, 1992). This can be improved if they also have reporting by the family/partner of the patient (Paulson, 1977).

Self-reporting can also depend on the individual patient or practitioner. For example elderly patients may have memory impairment, especially when taking many medicines and therefore do not report accurately. Long-term usage may be forgotten but they may be able to recall recent usage. The skill and sensitivity of the Health Care Practitioner can also play a role in how much information is given and the reliability of it. When collected carefully it could be very good insight into the problems of a patient's adherence. Also it is unlikely that patients will represent themselves as non-adherers (Gordis, 1976) so it will identify non-adherers correctly.

In summary, self-report is generally inexpensive and quick. Diaries can measure adherence across time and reveal any patterns and overuse of medicine. However there is no standardised diary and it can sometimes be complex and time consuming. If there is no standardised questionnaire or diary then no validity or reliability are assessed. Therefore there is variation in accuracy and it can depend on the individual or practitioner.

Bennett-Johnson (1992) [160] conducted a narrative literature review of adherence measurement in diabetes management. No search or inclusion criteria were given. The types of adherence measures used were health-status indicators, health provider ratings, behavioural observations and pill counts.

They point out that self-report of regimen adherence is often mistrusted. Patients may say one thing but do something completely different, often because of what they think the professional wants to hear. However

noncompliance self-reporting appears more valid than self-reporting of compliance (Diehl, 1987). Asking about specific behaviours can lead to better adherence data (Cerkoney, 1980; Cox, 1984; Shlenk, 1984; Brownlee-Duffeck, 1987; Hanson, 1987; Hanson, 1988; Hanson, 1990). There have only been a few that have looked at the reliability of these reports (Hanson, 1987 and Hanson, 1988). If asked to report their specific behaviours over a certain time period, the data can be good quality (Glasgow, 1987; Johnson 1986). Glasgow (1987) used written diaries successfully to measure adherence and Johnson (1986) adapted the 24-hour recall interview (which is a standard dietary assessment method) to use as a general adherence assessment strategy with IDDM patients. The authors state that 'in a series of studies the authors have demonstrated both the reliability and validity of this technique' (Bennett Johnson, 1992). These studies referred to are Johnson (1986); Johnson (1990); Spevack (1991); Reynolds (1990); Johnson (1990) and Freund (1991). Multiple interviews are recommended to ensure representation of adherence behaviours.

One disadvantage with self-reporting is problems of memory recall. Where possible a significant other should additionally be interviewed regarding the patient's behaviour.

The advantages of self-report are numerous, as reliable information can be obtained; interviews can be done over the telephone making them accessible; the patient does not have to do very much apart from give their time for an interview. They however do need trained interviewers, or with multiple interviews and multiple patients the process can take a lot of time and effort. No references were made for these assertions.

In summary, self-reporting of non-compliance is likely to be more valid, whereas compliance reporting is not valid. They can ask about specific behaviours and find out about what leads to non-compliance. It is easy for the patients to do and interviews can be done by telephone call. However there are biases with recall and people may say one thing but do another and there can be errors in reporting e.g. self-observation skills.

Dunbar (1989) [163] reviewed the methods to assess adherence to arthritis medicine with a review that included '16 representative studies of compliance'. No inclusion/exclusion criteria or search details were given. The review included self-report, clinician judgement, therapeutic outcome, direct observation, biological measures, pill counts, pharmacy refills and electronic monitors.

They noted that a major problem is the accuracy of reporting, with poor compliance usually underreported. One issue is the memory decay when assessing adherence (Farr, 1987). Effects, such as not realising the diminishment of higher adherence levels has occurred and moving past events forward in perception can all lead to inaccuracy. Motivational factors are also important, errors in reporting can be due to self-observation skills, especially when the compliance behaviour is itself variable. Misconceptions of the regimen may lead to errors through inaccurately labelling events compliant or noncompliant.

Self report has advantages in that it can identify some noncompliance in a cost-efficient manner and permits an in-depth study of the types of errors that patients can make which leads to non-compliance. It also has been shown to have reasonable sensitivity and specificity in discriminating those who comply from those who do not. In one study of medicine adherence self-report showed 100% sensitivity and 40% specificity when serum levels were used as a standard (Craig, 1985). The authors assert that 'self-report can be a useful measure. However, it is important to attend to the collection of accurate information.'

The authors conclude that self-report can be a useful measure and interviewers' skills are very important. Clinical measures are fraught with problems and there is no perfect measure.

In summary, self-reporting can mean poor compliance is underreported, there can be recall bias and self-observation skills may be erroneous. It is cost-efficient and can identify non-compliers.

Hecht (1998) [159] reported briefly with a narrative review on measures for HIV adherence in clinical practice. The types of adherence measures mentioned were self-reporting, medicine levels, physician judgement, MEMS, pill counts and prescription refills.

Sackett (1975) compared self-report to pill counts. Of those that reported having less than 80% adherence, 95% were found nonadherent by pill count. Those reporting that they were adherent over 80% of the time, were shown to be nonadherent by pill count 34% of the time. Gilbert and Sackett's studies, suggest that self-report is more accurate than physician assessment. Thus if HCPs want to know if patients are taking anti-retroviral therapy, they need to ask them rather than relying on their judgement. When they say they are missing medicine, believe them, as this is mostly the truth. Patient self-report tends to overestimate adherence. Those who report missing doses infrequently may have a significant problem of nonadherence.

Hecht (1998) says that what matters is how Health Care Practitioners ask the questions. Stating it should be in a specific, non-judgmental way and one that allows them to disclose nonadherence. Therefore, questions should not imply that they are wrong if they do not take their medicine the way they are 'supposed to'. A time period must also be specified. No references given for these conjectures. Measuring medicine levels should be regarded as a supplementary measure. Electronic pill monitoring, pill counts, reviewing prescription refills can be useful adjuncts to self-report in certain contexts, but every method has its limitations.

In summary, self-report is more accurate than Health Care Practitioners' judgement alone. It tends to overestimate adherence. It depends on how the questions are asked and a time period must be specified.

Overall summary

This evidence review focused on the advantages and disadvantages of self-report for assessing adherence. These were primarily narrative reviews rather than systematic reviews.

These reviews reported that all measures of adherence have strengths and weaknesses. There is no gold standard. Self-report can vary in reliability, yet it was thought generally to be a useful measure of adherence. Those who report nonadherence are likely to be telling the truth. It is also good for finding out the reasons for nonadherence. In a couple of studies it was suggested that self-report could be the first measure of adherence and for those who report adherence it could be supplemented by other measures. It is primarily a clinical tool, whereas other measures may be more relevant to clinical trials.

Any questionnaire which measures self-report should be well-designed and validated. Many of the reviews reported that the success of interviews as a measure largely depended on the skills and communication of the interviewer. It could depend on the way a question is asked.

8 Interventions to increase adherence to prescribed medicine.

8.1 Recommendations

Hyperlink to recommendations section Interventions to Increase Adherence

8.2 Introduction

Adherence is defined as 'the extent to which the patient's behaviour matches agreed recommendations from the prescriber' [1]. Adherence describes patient behaviour in the actual taking of medicines. This definition of adherence presumes that the patient has reached some agreement with the health care professional about the prescribed medicine. The Guideline Development Group was interested in interventions that would support patients in taking medicines following agreement with the health professional.

Nonadherence can be intentional or unintentional. Nonadherence is unintentional if the patient does not take the medicine, for example, due to forgetfulness or not being able to access the medicine because of problems with packaging and dexterity. Nonadherence is intentional when the patient makes a decision to not take the medicine as previously agreed or to take it in a way other than recommended by the prescriber because of their own beliefs and appraisals of the medicine and medicine-taking. Both intentional and unintentional nonadherence can occur regarding the amount or duration of missed medicine e.g. a single dose may be missed, a patient may miss several days of medicine or a patient may permanently stop taking medicine. In some patients nonadherence takes the form of the patient reducing or increasing the dose of prescribed medicine rather than omitting it.

8.3 Methods

The aim of the evidence review is to identify the most relevant, published evidence to answer the key clinical questions generated by the GDG. Reviews of the evidence using systematic methods relating to searching and

appraisal were conducted to answer the clinical questions in line with the NICE Technical Manual. The GDG and project teams agreed appropriate inclusion and exclusion criteria for each topic area in accordance with the scope. Additional evidence reviews were developed as an update to the 2005 Cochrane review[7] titled: "interventions for enhancing medicine adherence". The Haynes review aimed to summarise the results of randomised controlled trials (RCTs) of interventions to help patients follow prescriptions for medicines for medical problems, including mental disorders but not addictions. The review was organised by disease except for short-term treatments where not enough studies were retrieved on any individual disease condition to allow grouping by disease.

The main results of the Cochrane review were: For short-term treatments, four out of nine interventions (reported in eight RCTs) showed an effect on both adherence and at least one clinical outcome, while one intervention reported in one RCT significantly improved patient compliance, but did not enhance the clinical outcome. For short-term treatments, the main characteristics of the interventions were:

- counselling patients about importance of adherence, reinforced with written instructions.
- counselling from a hospital pharmacist and a follow-up phone call compared to a standard advice sheet and referral to a family physician that prescribed the same medication.
- comparing pre-packed chloroquine tablets versus chloroquine syrup.
- comparing dispensing azithromycin for infections free in the emergency department with a prescription that could be filled for free at a pharmacy.
- comparing nasal spray with varying levels of training and instructions.

For long-term treatments, 26 out of 58 interventions reported in 49 RCTs were associated with improvements in adherence, but only 18 interventions led to improvement in at least one treatment outcome. Almost all of the interventions that were effective for long-term care were complex, including combinations of

[7] first published in 2002

more convenient care, information, reminders, self-monitoring, reinforcement, counselling, family therapy, psychological therapy, crisis intervention, manual telephone follow-up, and supportive care. Even the most effective interventions did not lead to large improvements in adherence and treatment outcomes. Six studies showed that telling patients about adverse effects of treatment did not affect their adherence.

These results led the authors to conclude that for short-term treatments several quite simple interventions increased adherence and improved patient outcomes. Current methods of improving adherence for chronic health problems are mostly complex and not very effective, so that the full benefits of treatment cannot be realised and that further research concerning innovations to assist patients to follow medicine prescriptions for long-term medical disorders is required.

A more recent version of this Cochrane review has now been published in 2008. The main results were: for short-term treatments, four out of ten interventions reported in nine RCTs showed an effect on both adherence and at least one clinical outcome, while one intervention reported in one RCT significantly improved patient adherence, but did not enhance the clinical outcome.

For short-term treatments, the main characteristics of the interventions were:

- counselling patients about importance of adherence, reinforced with written instructions.
- counselling from a hospital pharmacist and a follow-up phone call compared to a standard advice sheet and referral to a family physician that prescribed the same medication.
- comparing pre-packed chloroquine tablets versus chloroquine syrup.
- comparing dispensing azithromycin for infections free in the emergency department with a prescription that could be filled for free at a pharmacy.
- comparing nasal spray with varying levels of training and instructions.

For long-term treatments, 36 out of 81 interventions reported in 69 RCTs were associated with improvements in adherence, but only 25 interventions led to improvement in at least one treatment outcome. Almost all of the interventions that were effective for long-term care were complex, including combinations of more convenient care, information, reminders, self-monitoring, reinforcement, counselling, family therapy, psychological therapy, crisis intervention, manual telephone follow-up, and supportive care. Even the most effective interventions did not lead to large improvements in adherence and treatment outcomes. In this update the authors also reported that for short-term treatments where several quite simple interventions increased adherence and improved patient outcomes the challenge is that there are inconsistent results from study to study with less than half of studies showing benefits.

The evidence in the Cochrane review was organised by disease, however as this guideline is intended to be a generic document we re-arranged the evidence according to the type of intervention. We also conducted additional specific searches for several questions. This is described below.

The titles and abstracts of studies retrieved by electronic searches were scanned for relevance to the topic on interventions to increase adherence. Any potentially relevant publications were obtained in full text. These were then reviewed to identify the most appropriate evidence and were then allocated to the relevant key clinical questions. Following this, the assessment of study quality; synthesis of the results; and grading of the evidence was undertaken.

While the GDG were interested in any intervention that might be useful in supporting adherence, the key clinical questions agreed by the GDG included questions on a number of specific interventions. We initially conducted one broad search in order to find evidence on interventions to increase adherence. This search allowed us to pick up any intervention designed to increase adherence and then allocate the evidence to the respective clinical question. This reduced the duplication of sifting and reviewing of the evidence. This search was supplemented by specific searches in areas considered important

by the GDG where we also included some observational studies. These were areas where the broad search left considerable uncertainty but the interventions were considered either potentially important in clinical practice or areas where popular preconceptions may exist.

These were:

- Does change in dosing regime affect adherence to prescribed medicine?
- Does drug formulation/packaging affect adherence to prescribed medicine?
- Do prescription charges affect adherence to prescribed medicine?
- Does the use of multi-compartment medicine systems increase adherence to prescribed medicine?
- Do medicine reviews affect adherence to prescribed medicine?

8.4 Evidence to recommendations : difficulties in interpreting studies on interventions to improve adherence

Given the advances of medical therapies and the increase in prescribing and medicine use in the last decades, it could be expected that this has been accompanied by a greater understanding of the processes of adherence and nonadherence and the effectiveness of interventions to promote adherence. In general however the current body of literature on adherence is of poor methodological quality and was considered inadequate to answer many of the GDG questions on interventions to increase adherence. Medicine-taking does not appear to be recognised by many researchers as a complex human behaviour which should be studied using complex interventions in line with the MRC framework (2000) [164]. The GDG considered that the difficulties with studies on interventions to increase adherence were common across studies.

The issues affecting quality of the studies appraised for interventions to promote adherence are outlined below:

(a) The content and method of delivery of the components of the intervention are not well described and differ in different studies.

(b)The lack of distinction between content of intervention and how it was delivered makes it impossible to understand the overall poor and contradictory outcomes.

(c)The majority of the studies do not assess a single intervention but include multi-component interventions. In a trial the two interventions being compared may each have a different set of components. This means it is not possible to compare one trial with another and even when an intervention works it is not possible to know which component or combination of components is effective.

(d) Studies do not report whether the planned interventions took place as intended in the study protocol.

(e) No standard method of assessing adherence is used.

(f) There is infrequent justification of the relevance of certain interventions in improving adherence e.g. there is no theoretical framework informing the studies and this precludes development of understanding of phenomena of adherence/nonadherence.

(h) Studies had frequently small sample sizes and inadequate description of settings and existing rates of adherence; generalising of these interventions to routine clinical practice is therefore not possible.

(i) Many of the interventions are extremely complex and labour-intensive and are carried out by paid research staff and thus it is unknown whether they could be carried out in a non-research setting.

(i) Within the long-term conditions, even the most effective interventions did not lead to substantial improvements in adherence and treatment outcomes.

(k) Interventions are not targeted to causes of nonadherence – it is likely therefore that some interventions may be more effective than evidence suggests if directed to actual cause of non–adherence in individual patients.

(l) Comment is not made on patient involvement in decision to prescribe medicines.

(m) Few studies mention whether raters of outcome or adherence were blind to whether subjects were in the intervention or control group.

(n) Despite the comprehensive and detailed searching, some trials that met our criteria may have been missed. The literature on patient adherence is not well indexed as it sprawls across the traditional disease areas and as a result of all these, there is little information available to fully understand why one intervention works and other very similar ones did not. Our concern about the evidence in this area is mirrored in other key reviews and trials [3].

(o) The evidence reviews on cost effectiveness of interventions to improve adherence is discussed in chapter 10. The GDG considered these when making recommendations. The GDG noted that interventions to increase adherence may or may not lead to improved clinical outcomes. Increased adherence may result in more adverse effects. Differences in clinical outcomes will depend on the effectiveness of the adherence-enhancing intervention, as well as the dose-response related efficacy of the medicine. Increased adherence was generally associated with increased efficacy but did not have a consistent relationship with costs in the reviews. Assuming the intervention is effective and raises adherence rates, it still remains uncertain what the incremental treatment effect of the medicine will be. The intervention may result in a potential QALY loss due to side effects of the medicine (where before non adherence would have prevented them).

The GDG considered that results of the reviews need to be interpreted with caution, as some of the elements that have worked within some of the trials are present in other studies that have not yielded significant improvements. The GDG were interested in simple interventions that might be targeted to

individuals but the majority of the studies are complex interventions with an extremely wide range of components.

8.5 Does change in dosing regime affect adherence?

Related references	Evidence statements (summary of evidence)
Shi (2007) [165]; Schroeder (2004) [166]; Iskedjian (2002) [167]; Claxton (2001) [168] Baird (1984) [169]; Brown (1997) [170]; Girvin (1999) [171]; Portsmouth 2005 [172]; Molina (2007) [173]	Systematic reviews and RCTs show that simplification of dosing frequency can increase adherence to prescribed medicine.
Schroeder (2004) [166]; Iskedjian (2002) [167]; Portsmouth 2005 [172]; Molina (2007) [173]; Baird (1984) [169]; Girvin (1999) [171]	Two systematic reviews and four RCTs show that reducing twice-daily to once-daily dosing may increase adherence to prescribed medicine.
Claxton (2001) [174]; Rudd (2004) [175]; Parienti (2007) [176]	Evidence from one low quality systematic review and two RCTs showed that once-daily dosing compared to twice-daily did not increase adherence to prescribed medicine.

8.5.1 Evidence to recommendations

For general discussion of limitations of evidence see section 8.3.

The GDG were interested in whether there was evidence to indicate that changes in dosing regime would improve adherence. The findings of the evidence review were that reducing the complexity of a regime can increase adherence but the quality of evidence was low. The evidence from the qualitative interviews indicated that the difficulty for patients is integrating the regime into their lives rather than dose complexity per se and the GDG

recommendation is that changes to dosing regime need to be tailored to needs of individual patients. The GDG considered that the evidence does not support that developing once-daily formulations and combined pills will necessarily improve adherence.

One area of interest for the GDG was the use of medicines by injection particularly antipsychotic medicines and contraceptives. This option could be classified as changes to dose regime or medicine formulation. The GDG were clear that using medicines by injection in this way may be an appropriate choice where patients have non-intentional adherence i.e. they forget to take their medicines. As such this choice should be offered to patients. The GDG were aware of evidence from qualitative synthesis that patients with mental health problems can feel coerced to take medicine and wished it made clear that the aim of our recommendations is to support informed adherence.

8.5.2 Methods of the evidence review

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies – We initially included only randomised controlled trials (RCTs) of interventions to increase adherence. The excluded studies list from the Cochrane review was checked as we have included those studies with less than 80% follow-up of participants. As with the Cochrane review we found only a small number of studies that fulfilled our criteria. For this evidence review we excluded any randomised controlled trials that evaluated changes in dosing regimes but did not assess the same medicine in all comparative groups. The GDG requested a further search to pick up any systematic review published after the Cochrane review search cut-off. However, the included systematic reviews did not follow this criterion.

Types of participants - people prescribed medicine for a medical condition.

Duration of studies - six months follow-up from the time of patient entry for long-term regimens for the RCTs. No time limit specified for short-term conditions.

Types of interventions - any interventions intended to change adherence to prescribed medicine. As the Cochrane review is presented by condition, we have used the evidence extracted in that review and reconfigured it by intervention.

Comparator - a comparison of different dosing regimes, for the same medicine to ensure no confounding of results.

Types of outcome measures – inclusion criteria (as defined in the Cochrane review) were expanded by including studies that used adherence as the only outcome variable as opposed to adherence and treatment outcome variables. The excluded studies list of the Cochrane review was cross-referenced to ensure that no potentially relevant study was missed out.

8.5.3 Evidence review

8.5.3.1 Does change in dosing regime affect adherence?

We found many studies comparing dosing regimes but these were often comparisons of different medicines. It was necessary to only include studies that compared the same medicine so that the results would not be confounded.

Systematic Reviews

One recent review of systematic reviews and empirical studies **(Shi 2007)** [165] looked at the impact of dose frequency on compliance and health outcomes, particularly for injectables. Inclusion criteria were that the studies should compare different dose frequencies, including injectable medicines and be published in a peer reviewed journal. Exclusion criteria were that the article should not focus solely on dosage forms, dose administration or dose timing.

Full text reviews were conducted on a total of 64 empirical studies and 25 literature/systematic reviews. No details were given on overall methodological quality of the studies.

Results were presented through five main areas: cardiovascular diseases, diabetes, nephrology/urology, neurology/psychiatry and rheumatoid/muscle. Of the 21 studies that measured compliance, 17 reported a positive impact (no details of significance given) of reducing dose frequency on compliance, whilst inconclusive results were seen in four. Details of the dose frequency reductions contained in the studies were not provided by the review.

Articles not measuring compliance as the main outcome looked at efficacy and other outcomes of extended-release medicines in comparison to the immediate-release forms. The studies also supported the general benefits of reducing dosing frequency on improved quality of life or patients' satisfaction (6 studies), greater control over side effects (5 studies) and improved economic outcomes using extended-release formulation (2 studies).

Schroeder (2004) [166] used the Cochrane methodology to review dosing regimes and adherence in hypertensive patients. The methodological quality of the primary included studies was assessed to be generally low. Many RCTs showed marked heterogeneity in terms of participants, interventions and outcomes. A pooled analysis was considered inappropriate as results on adherence were reported in many different ways. Simplifying dosing regimens improved adherence in 7 of 9 studies with relative improvement in adherence increasing by 8% to 19.6%. All of the studies that used objective outcome measurement (Medicine Event Monitoring System) showed an improvement in adherence through the use of once-daily instead of twice-daily dosing regimens, although four of these compared two different medicines. Only 1 study showed an increase in adherence (90% vs. 82%; $p<0.01$) together with a reduction in systolic blood pressure of 6 mm Hg ($p<0.01$).

A weak meta-analysis conducted by **Iskedjian (2002)** [167], combined comparative studies of different research designs including prospective trials (RCTs and cohort studies), retrospective chart reviews and database

analyses. Adherence was defined differently in various studies and different instruments were used to measure patient adherence. In this meta-analysis, all variables that could affect adherence other than daily dose-frequency were assumed to be equal between comparators.

Eight studies involving a total of 11,465 observations were included (1830 for daily [OD] dosing, 4405 for twice a day dosing [BID] and 4147 for dosing >2 times daily [>BID] and 9655 for multiple daily dose [MDD]). The primary objective was to assess adherence. The average adherence rate for OD dosing (91.4%, s.d=2.2%) was statistically significantly higher than for MDD (83.2%, s.d=3.5%; p<0.001). The difference between adherence rates for OD dosing (92.7%) and BID dosing (87.1%) was also statistically significant (p=0.026), although the difference in this analysis was smaller than in the OD-versus-MDD analysis (5.7% vs. 8.2%). The difference in adherence rates between BID dosing (90.8%, s.d=4.7%) and >BID dosing (86.3%, s.d=6.7%) was not statistically significant (p=0.069). However, a subgroup analysis using a stricter definition of adherence (≥90% intake) did reveal a statistically significant difference between BID and >BID dosing (respective adherence rates of 76.1% and 67.0%, p<0.001).

Another systematic review published by **Claxton (2001)** [168] also found that simpler, less frequent dosing regimes resulted in better compliance. This systematic review appeared to include several study designs. This review showed strong methodological limitations particularly in terms of data analysis. The study did not give full details of inclusion/exclusion criteria and thus possibly including studies that compared different dosing regimes in different medicines. The results should therefore be viewed with caution.

Seventy-six studies were included in the review. By combining all data it was found that increasing the number of daily doses was statistically significantly related to a decline in compliance (p<0.001 among dose schedules). Comparisons between dose regimens showed that compliance was statistically significantly higher with once daily regimens vs. 3 times daily (p=0.008) or 4 times daily regimens (p<0.001). Compliance with twice daily

dosing was statistically significantly higher than 4 times daily dosing (p=0.001). There were no statistically significant differences in compliance between once daily and twice daily regimens or between twice daily and 3 times daily.

Randomised controlled trials

Three RCTs **Baird (1984)♦** [169]; **Brown (1997)** [170] and **Girvin (1999)♠** [171] from the Cochrane review (2005), assessed the effect of the simplification of a dosing frequency. **Baird (1984)** [169] compared twice a day 100mg Betaloc tablets to once daily 200mg Betaloc Durules, in a sample comprising 389 participants. Mean age of the participants was 52.7 years for the twice daily group, compared to 54.5 years. Over the total study period, compliance exceeded 80% in 96.4% of patients in the Durules group and 90% of patient in the Betaloc tablets group (p=0.0591). When to 90% levels of compliance were compared, overall compliance exceeded this level in 92.8% of patients on Durules and in only 81.5% of patients on tablets (p=0.009). A statistically significant effect in increasing adherence was reported. **Brown (1997)** [170] tested controlled-release niacin twice daily to regular niacin, four times daily, in the treatment of hyperlipidemia and coronary artery disease, in 29 male participants aged ≤65 years. Compliance was 95% with the controlled-release niacin versus 85% with regular niacin (p< 0.001). **Girvin (1999)** [171] tested enalapril 20 mg once daily versus enalapril 10 mg twice daily in the treatment of high blood pressure. Sample size comprised of 27 patients. Mean age of participants was 62 years. Overall medicine adherence was improved with once-a-day dosing. The difference in percentage of doses taken by pill count between the two periods was statistically significantly in favour of the once daily regimen (p<0.01), as was the percentage of doses taken as measured by a pill container that recorded lid openings (MEMS) (p< 0.001).

♦ Study information indicates that duration is less than 6 months, however this is not stated in Cochrane Review.

♠ Study with less than 6 months duration that was included in the Cochrane Review as results for blood pressure outcomes were negative.

One RCT **Portsmouth (2005)** [172] included in the 2008 revision of the Cochrane review assessed whether virologically controlled HIV-1-infected individuals switched from a twice-daily antiretroviral regimen to a once-daily regimen demonstrate improved adherence and quality of life while maintaining virological control. Forty-three patients were included in this study, with 22 in the once daily (intervention) group, and 21 in the twice daily (control) group.

The once-daily group (intervention): the prolonged release capsule group (PRC) were assigned to take d4T PRC/3TC/EFV all once-daily (24 h apart); Twice daily (control group): participants in the control group were assigned to continue either d4T IR/3TC/EFV or Combivirs/EFV as per their screening regimen. Note: participant weighing less than 60 kg were prescribed either 30 mg of d4T IR or 75 mg of d4T PRC.

After randomisation, patients allocated to the PRC (intervention) maintained this high adherence, while those allocated to IR (control) showed a statistically significantly reduced adherence in 'taking compliance' (p=0.0237) (percentage of prescribed number of doses taken), 'correct dosing compliance' (p=0.0104) (percentage of days with correct number of doses taken) and 'timing compliance' (p=0.028) (percentage of doses taken within 3 hours of the prescribed dosing intervals) at both weeks 12 and 24.

One RCT, **Rudd (2004)** [175], from the Cochrane updated review that was included in the evidence review on the effects of self-monitoring on adherence reported some results in regard to once-daily regimens compared to twice-daily regimens. This RCT assessed a system for patients to monitor their own blood pressure. Seventy-six patients received routine care while the intervention group (n=74) received an automated blood pressure device for use at home with management by a nurse care manager. The patients recorded their own blood pressure then the device printed these which were mailed to the nurse care manager in order to guide medicines. The adherence measures by a medicine event monitor were found to be statistically significant (80% for the intervention group and 69% for the control group, p=0.03). One of the outcomes found that once-daily regimens had higher

adherence 82% (s.d=28%) than twice-daily 69% (s.d=34%) or more frequently 49% (s.d=41%). None of these differences were statistically significant.

Update searches

From the conducted update searches, we retrieved two RCTs that were considered important as they would contribute to modifying the recommendations drafted for the topic of the impact of changes of dosing regimes on adherence to prescribed medicine. These were Molina (2007) and Parienti (2007).

The safety, efficacy and adherence to lopinavir/ritonavir (LPV/r) dosed OD or BID in antiretroviral-naive, HIV-1-infected subjects was evaluated in an RCT **Molina (2007)** [173]. A randomised, open-label, multicenter comparative study was conducted through 96 weeks of treatment. A total of 190 antiretroviral-naive subjects with plasma HIV-1 RNA above 1000 copies/ml and any CD4(+) T cell count were enrolled. Subjects were randomised (3:2) to LPV/r 800/200 mg OD (n=115) or 400/100 mg BID (n=75). Subjects received TDF 300 mg and FTC 200 mg OD. Adherence to LPV/r through 96 weeks was measured using MEMS((R)) monitors. Median baseline VL and CD4(+) T cell count were 4.8 log(10) copies/ml and 216 cells/mm(3), respectively. Prior to week 96, 37% (OD) and 39% (BID) of subjects discontinued, primarily due either to adverse events (17% OD, 9% BID) or to loss to follow-up or nonadherence (12% OD, 17% BID). The proportion of subjects with VL <50 copies/ml (57% OD, 53% BID; p=0.582 (ITT NC = F)), change in CD4 count (244 cells/mm(3) OD, 264 cells/mm(3) BID; p = 0.513), and evolution of resistance did not differ between groups through 96 weeks. Diarrhoea (17% OD, 5% BID, p=0.014) was the most common moderate or severe, study medicine-related adverse event. Adherence to LPV/r was higher for the OD group than the BID group and declined over time in both groups.

Parienti (2007) [176] aimed to determine the effect of once-daily dosing on adherence to nevirapine. This RCT was comprised of three-phase (3-month observational, 4-month randomised, 5-month interventional) open-label, clinical trial at four French academic medical centres during 2005-2006

among 62 chronically HIV-1- infected subjects with long-lasting viral suppression under a twice-a-day nevirapine-based antiretroviral combination. Participants were randomly assigned to switch to nevirapine 400 mg once-daily (n = 31) or continue nevirapine 200 mg twice-a-day (n = 31). After the randomised phase, participants had an opportunity to choose their antiretroviral dosage.

Fifty-two patients qualified for electronic data analysis. During the randomised phase, the mean adherence rate was not statistically significantly superior by 0.5% in once-daily versus twice-a-day dosing (p=0.68), adjusting for previous twice-a-day adherence rate (p<0.0001). Once-daily group increased days without dose (odds ratio (OR) 1.7; 95% CI 1.0, 2.8; p=0.04), adjusting for previous medicine interruptions (p<0.0001). In the longitudinal analysis, once-daily dosing was statistically significantly associated with at least two consecutive days without dose (OR 4.4; 95% CI 1.9, 10.3; p<0.001). The authors concluded that changing from twice to once-daily nevirapine did not improve adherence.

8.6 Effect of prescription charges on adherence to prescribed medicine

Related references	Evidence statements (summary of evidence)
Hirth (2008) [177]; Atella (2005) [178]	Some UK patients may have difficulty affording medicines. The most common strategies for patients with problems affording medicines is to delay the dispensing of medicines, to not visit the GP and to lower the dose below that prescribed to extend the duration of the prescription.

8.6.1 Evidence to recommendations

For general discussion of limitations of evidence see section 8.3

The GDG considered cost an important issue to address. The majority of patients do receive prescriptions free on the NHS but a substantial minority do not.

Most of the evidence for cost as a barrier to adherence comes from the US and these are not relevant to NHS settings. Only a few studies have been conducted in the UK. These indicate that for some patients costs are a concern. Cost concerns may also indicate doubts by the patient about the value of the prescription.

When cost is a concern for patients a variety of options are available each of which have advantages and disadvantages.

The GDG noted that there are a number of schemes in existence which aim to provide free or reduced cost of prescriptions e.g. prescription pre-payment certificates and exemption certificates.

Prescription length may be increased giving the patient longer prescription for the same cost but this may reduce the opportunity for review. Quite short dispensing time frames may be important for example when patients are suicidal or need careful monitoring of medicine and its effects. Instalment dispensing is possible for certain medicine items but in general it seems unreasonable to ask a patient to pay for each dispensing point. However the GDG was also mindful of the fact, that it might also be unreasonable for the pharmacist to make serial dispensings for a single dispensing fee. Costs and value of prescriptions should be considered not just at the point of prescribing but at all stages of the process.

The GDG did not consider it appropriate to make a specific recommendation on how healthcare professionals should act when cost is a problem for the patient as the response is likely to be dependent on patient circumstance and condition.

8.6.2 Methods of the evidence review

This question was included because although the issue of setting a prescription charge is outside the scope of this guideline, cost may be an issue for individual patients and the prescriber may be able to intervene if costs influence adherence.

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies – no restrictions on study design. However, due to the nature of the question, the requirement was that the studies needed to be conducted in the UK.

Types of participants- people prescribed medicine for a medical condition.

Duration of studies - no time limit specified.

Types of interventions - any interventions intended to assess the correlation between prescription charges and the impact on adherence to prescribed medicine.

8.6.3 Evidence review

Types of outcome measures – adherence to prescribed medicine, cost reducing strategies.

We retrieved one observational study **(Hirth 2008)** [177] that examined out of pocket medicine spending and cost-related medicine nonadherence among dialysis patients in twelve countries including the UK.

Data were gathered from 2002 to 2004 as part of the dialysis outcomes and practice patterns study (DOPPS), an observational study of haemodialysis practices and outcomes in twelve countries- Australia, New Zealand, Belgium, Canada, France, Germany, Italy, Spain, Sweden, United Kingdom, Japan, and the United States. A random sample of patients were selected, totalling n=7766. Of the selected 83 per cent who agreed to enrol and have their medical records abstracted, 85 per cent of these enrolled patients also completed the patient questionnaire. A total of 70 per cent of patients provided both medical and questionnaire data. Local currencies were converted to US Dollars.

Questionnaires and medical record abstraction techniques were standardised across countries and languages. Patient questionnaires were administered soon after recruitment. They were asked about the total out-of-pocket spending for prescription and over the counter (OTC) medicines in the previous month. They were also asked “Do you sometimes decide not to purchase medicines because of cost?” and to report their out-of-pocket spending for haemodialysis treatments.

Whilst the United States reported 86 per cent of out-of-pocket spending for medicines, only patients in Australia/New Zealand, Belgium, and Sweden

were statistically significantly more likely to face out-of-pocket spending, while those in France, Japan, Spain and the UK were statistically significantly less likely to do so.

Mean monthly spending for prescription and OTC medicines ranged from $8 in the UK to $114 to the United States. Among patients with medicine spending, only 10 per cent faced monthly costs greater than $30 in the United Kingdom, whereas 10 per cent incurred costs greater than $310 in the United States.

Observed cost-related nonadherence, indicated by the proportion of patients who reported that they sometimes did not purchase medicines because of cost, was statistically significantly less than expected in France, Japan, Spain, Sweden and the UK.

Nonadherence was associated with the percentage of patients reporting any out-of-pocket spending and the average out-of-pocket cost. Although the US had high out-of-pocket spending burdens, their nonadherence was still clearly higher than would be expected on the basis of the percentage facing any costs or the mean cost burden. On the other hand, Sweden and Belgium had lower levels of nonadherence than would be expected given either measure of out-of-pocket spending burden. The lowest nonadherence rates existing in France, Japan, Spain and the UK were correlated with low out-of-pocket spending.

Atella 2005 [178] aimed to explore how and to what extent costs incurred by patients influence their decision-making behaviour in accessing medicines, both in the UK and in Italy.

Based on findings from focus groups, a questionnaire was designed to assess medicine cost issues. As such, several hypotheses were tested regarding patients' decision-making behaviour and how it was influenced by health and socio-demographic status and the novel concept of a self-rated affordability measure. Patients were eligible if they had either dyspepsia or mild hypertension. They were sampled as successive patients who visited 51

physicians in Italy and 21 community pharmacists in the UK. Samples were drawn from the areas of Manchester and Rome. Of the 550 dyspepsia and 600 hypertension questionnaires distributed, 122 and 153 were returned- a response rate of 22.2% and 25.5%, respectively. In the UK, 296 dyspepsia and 277 hypertension questionnaires were distributed, targeting dyspepsia patients who bought OTC medicines, and dyspepsia and hypertension patients who had to pay prescription charges; 110 dyspepsia and 134 hypertension questionnaires were returned, giving a response rates of 37.5% and 48.4%. In both countries the majority of the respondents were not exempt.

The self-rated affordability measure showed that 70.3 per cent of the UK sample and 66.5 percent of the Italian sample had to think about the cost of medicines at least sometimes. Also, 24.3 per cent and 16.3 per cent, respectively said they always have to think about how much money they have available to spend when they obtain medicines. According to the results, the patient initiated strategy most commonly used by UK respondents with affordability problems is (1) to delay the dispensing of medicines until they get paid, (2) not visiting the GP to avoid incurring the cost of prescribed medicine and (3) reducing the dose below that prescribed to extend the course of medicine.

Affordability issues were also strong when examining the use of self-medicine strategies. The UK respondents were particularly cost conscious when considering the price of an OTC product before buying it, or they would ask for something cheaper if they could not afford a particular OTC product.

The authors point out that affordability seemed to play a more important role in the UK sample than in the Italian, however they do point out that Italian patients with dyspepsia were sampled only through GPs and may be those more severely affected and/or less likely to be disposed towards self medicine. Also, OTC products are much more expensive in relation to the prescription charge that they are in the UK where the prescription charge is high.

8.7 Does medicine packaging affect adherence?

Related references	Evidence statements (summary of evidence)
Medicine packaging	
Orton (2005) [179]	One systematic review found that unit-dose packaged medicines (blister packs and polythene bags with separate pockets compared to envelopes or bottles), as part of multi-component interventions showed higher adherence. However these results were drawn from trials with methodological limitations, one RCT with possible confounding and 3 quasi-RCT studies.
Schneider (2008) [180]	One RCT found that the use of blister packaging (Pill Calendar), for one medicine (lisinopril), compared to medicine in a bottle statistically significantly increased adherence.
Becker (1986) [181]	One RCT where all medicines were prepared together in a blister package, compared to receiving medicine in separate vials for each medicine, showed a statistically non-significant improvement in adherence to prescribed medicine.
Lee (2006) [182];	One RCT showed that blister packaging of multiple medicines as part of a multi-component intervention given to an elderly population (≥65 years) statistically significantly increased adherence to prescribed medicine.

8.7.1 Evidence to recommendations

For general discussion of limitations of evidence see section 8.3. The GDG considered the evidence review did not provide convincing evidence that medicine packaging per se increases adherence. The GDG recognised that individual patients may have practical difficulties in using medicines depending on packaging and considered that health care professionals should explore with patients whether the way in which a medicine is packaged causes difficulty and respond to individual problems.

8.7.2 Methods of the evidence review

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies - We initially included only randomised controlled trials (RCTs) of interventions to increase adherence. The excluded studies list from the Cochrane review was cross-referenced as we included studies with less than 80% follow-up of participants. After the GDG voiced concerns over the possibility of missing out important studies by only having included a small amount of studies, the search was redone to pick up any systematic review published after the Cochrane review search cut-off.

Types of participants - people prescribed medicine for a medical condition.

Duration of studies - six months follow up from the time of patient entry for long-term regimens for the RCTs. No time limit specified for short-term conditions.

Types of interventions - any interventions intended to change adherence to prescribed medicine. As the Cochrane review is presented by condition, we have used the evidence extracted in that review and reconfigured it by intervention.

Types of outcome measures - inclusion criteria (as defined in the Cochrane review) were expanded by including studies that used adherence as the only

outcome variable as opposed to adherence and treatment outcome variables. The excluded studies list of the Cochrane review was cross-referenced to ensure that no potentially relevant study was missed out.

8.7.3 Evidence review

8.7.3.1 Effect of medicine packaging on adherence

Medicine packaging

In this evidence review the GDG were wishing to find out whether the packaging that medicine came in would affect adherence. The only relevant systematic review that we found was a Cochrane review by Orton (2005). It looked at blister packs and sectioned polythene bags for the medicine. Other RCTs that we looked at included blister packs that had multiple medicines in a blister pack that were produced specifically for the patient. It should be noted that these technologies are not available in the UK at present and the evidence did not address the question the GDG were most interested in.

Blister packaging is where the medicines are sealed in a blister pack, which often has a calendar of days of the week or month. One blister can hold either one single medicine or can be a combination of several medicines.

Systematic Reviews

One Cochrane review **Orton (2005)** [179] that aimed to assess the effects of unit-dose packaged treatment and treatment adherence in people with uncomplicated malaria was retrieved. Any type of programme that included unit-dose packaging of antimalarial medicines packed in units of a single dose was incorporated in the review. Treatment adherence was a secondary outcome, however all four included studies measured it.

Interventions and control arm groups had to received the same antimalarial medicine and any other intervention. The interventions that were assessed in this systematic review ranged from labelled and boxed blister packs of chloroquine and primaquine tablets and capsules, simple labelled and

sectioned polythene bags of chloroquine tablets, tablets or capsules in paper envelopes or loose and chloroquine syrup in bottles.

Three quasi RCTs and one cluster RCT met the inclusion criteria, and overall trials were of poor methodological quality.

A meta-analysis of two trials (with 596 participants) showed that participant reported treatment adherence was higher with blister-packed tablets compared with tablets in paper envelopes (RR 1.18, 1.12 to 1.25). Two trials using tablets in sectioned polythene bags as the intervention also reported an increase in participant reported treatment adherence: in one study (cluster RCT) it was compared with the tablets in paper envelopes whilst the other trial compared it with syrup in bottles (RR 2.15, 1.76 to 2.61; 299 participants).

It appears that unit-dose packaging medicines (in combination with prescriber training and patient information) was associated with higher participant reported treatment adherence, however this conclusion is drawn from trials with methodological limitations.

Heneghan (2006) [183] conducted a systematic review of reminder packaging which included blister packaging. This review is already included in the 'multi-compartment medicine systems' key clinical question and only one blister package RCT with adherence data was included in the Heneghan review, therefore we have not included Heneghan in the packaging question. The blister pack RCT (with adherence outcomes) from Heneghan (2006) has been included for this question (see Becker, 1986).

Randomised Controlled Trials

Becker (1986) [181] from the Cochrane review delivered an intervention whereby patients aged 20 to 80 years were assigned to the experimental group received all their medicines in the special packaging format (all pills taken together were packaged in a single plastic blister sealed with a foil backing on which was printed the day of the week and the time of day at which each medicine was to be taken). One hundred and eighty patients were

included in the study. Patients in the control group received all of their antihypertensive medicines in the conventional pill vials (separate vials for each pill that were labelled with the medicine name, the dosage, the medicine instructions, and the physician's name). All medicines for both groups were provided free of charge to ensure that all patients would receive their medicines. This study was conducted in the USA. No statistically significant effects on adherence were reported.

Schneider (2008) [180] conducted a randomised controlled trial to assess the impact of one medicine packaging type on adherence and treatment outcomes of older patients. The study was conducted at 3 sites in Tucson and Columbus in the USA. 85 participants aged 65 years or older, prescribed lisinopril (antihypertensive medicine) were randomised to receive daily-dose blister packaged medicine (pill calendar) as the intervention compared to traditional bottles of loose tablets as the control group. Patients returned for refills every 28 days during a 12 month period where the pharmacist would record the time between prescription refills for the medicine and any study-related problems. At 6 and 12 months after enrolling the patients visited the physician to find out blood pressure management; the occurrence of morbidity in the past 6 months e.g. angina, myocardial infarction and stroke; and any medical services they had required in the past 6 months e.g. hospitalisations or emergency department visits. Medical charts were reviewed by two pharmacists to gather this information. The percentage of times prescriptions were refilled on time (within 5 days before or after due date) were statistically significantly higher 80.4% (s.d=21.2) for the intervention group than the control group, 66.1% (s.d=28), p=0.012. The medicine possession rate (the sum of the day's supply for all prescriptions received during the study divided by the number of days between the first and last prescription dispensed) was also statistically significantly higher for the intervention group, 0.93 (s.d=11.4) and 0.87 (s.d=14.2) for the control group, p=0.039. No differences were found between the groups for systolic blood pressure and diastolic blood pressure measures.

Lee (2006) [182] compared a comprehensive pharmacy care program which was delivered to one group for 3-8 months and a second group for 3-14 months in 200 patients aged 65 years or over, taking four or more chronic medicines daily with positive results. The first group returned to usual care after 8 months. The care program consisted of 3 elements, including individualised education on medicines; medicines dispensed using an adherence aid (blister packs) and regular follow-up with clinical pharmacists every 2 months. This study was conducted in the USA.

Mean baseline adherence overall was 61.2% (s.d=13.5%) with an overall level of adherence of 96.9% at 8 months of intervention. At 14 months, medicine adherence was 95.5% (s.d=7.7%) in the continued intervention group and 69.1% (s.d=16.4%) in the control group ($p<0.001$). Proportions of people who had at least 80% adherence rates were 97.4% in the intervention group and 21.7% in the control group ($p<0.001$).

8.8 Does the use of multi-compartment medicine systems increase adherence to prescribed medicine?

Related references	Evidence statements (summary of evidence)
Heneghan (2006) [183]	A high quality systematic review suggests that some types of multi-compartment medicine systems may improve adherence to prescribed medicine. It should be noted that only four RCTs were multi-compartment compliance aids which reported adherence data. These RCTs were classed as having a high risk of bias. Some of these RCTs were part of a multi-component intervention.
Henry (1999)[184]	One RCT showed that a multi-compartment medicine system as part of multi-component intervention showed no statistically significant effects on adherence.
Peterson (1984) [185]	One RCT showed that that a multi-compartment medicine system as part of a multi-component intervention showed statistically significant effects on adherence to medicine.

8.8.1 Evidence to recommendations

For general discussion of limitations of evidence see section 8.3.

Despite the frequent use of multi-compartment devices that are refilled regularly by pharmacists and individuals, there was little evidence on their use. For patients who have practical problems in managing complex regimes or who may be forgetful these devices may have a value. The GDG considered that many individuals develop their own strategies and that the

evidence on these devices was not strong enough to make recommendations for widespread use.

8.8.2 Methods of the evidence review

This review was originally titled ‘does the use of dosette boxes increase adherence to prescribed medicine’. Dosette box is an example of a device which holds a patient’s medicine and is labelled with periods of time. Although the term is derived from a particular brand of device it is widely used in routine clinical practice. The evidence search using a variety of terms returned no studies. After consultation it was brought to our attention that devices like dosette boxes may be classified under different headings and that some researchers label them as ‘reminders’ or as ‘packaging’. We therefore re-examined the papers included in the packaging review and reminder reviews and extracted those relevant to dosette-type devices. The review by Heneghan (2006) and some RCTs/systematic reviews which had been incorrectly placed with the packaging and reminder questions are now relocated to the question. These we have termed multi-compartment medicine systems although there is no agreed term in the published literature. The term ‘dosette’ is no longer used in the final recommendations. The original search terms matched the terms needed for this restructured multi-compartment medicine system question. For example the search terminology included ‘dosette’, ‘nomad’ or ‘manrax’ ‘monitored dosage system’ and ‘compliance aid’.

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies – no restrictions on study design.

Types of participants- people prescribed medicine for a medical condition.

Duration of studies - no time limit specified.

Types of interventions - any interventions intended to assess the correlation between the use of multi-compartment medicine systems and the impact on adherence to prescribed medicine.

8.8.3 Evidence review

Multi-compartment medicine systems

Reviews differed in the terminology of these systems and also grouped multi-compartment medicine systems together with packaging methods such as blister packaging.

Multi-compartment medicine systems are devices which hold a patients' medicine (single and multiple medicines) and are labelled with periods of time (day/days of the week/month). They can be re-used and can be filled by the pharmacist or by the patient themselves. This differs from the evidence review of blister packaging as this is a device rather than a type of packaging. Some studies included in the reviews considered the use of non-reusable blister or compartment packaging which was done by individual pharmacists for individual patients.

Systematic Reviews

One high quality systematic review by **Heneghan (2006)** [183] aimed to determine the effects of 'reminder packaging' to increase patient adherence with self-administered long-term medicines.

The systematic review included eight studies containing 1137 participants. All types of setting were included and no age limits were set. Studies where direct observation of therapy occurred through a health professional were excluded. Interventions that were included required a medicine system for the day of the week or the time that the medicine was to be taken, and it had to form part of the packaging.

The primary outcome of importance was adherence to medicine which was measured by pill counts and/or self-reporting. Three of the RCTs included in the review did not have any adherence data, these were Simmons (2000),

Binstock (1988) and Winland-Brown (2000). Simmons (2000) was the only RCT from Heneghan to meet all the quality criteria and to be judged as having a low risk of bias.

The authors refer to the findings under the term ‘reminder packaging’. Therefore we have split this into two categories of packaging – blister packs and multi-compartment medicine systems. Blister packaging is discussed in the section on packaging.

Heneghan (2006) conducted a combined analysis of the studies of pill count (the 6 interventions using multi-compartment medicine systems, within 4 RCTs) and found that there was a statistically significant increase in the percentage of pills taken within the groups that had ‘reminder packaging’, Weighted mean difference 11% (95% CI 6% to 17%, p<0.0001). Heneghan (2006) concluded that ‘reminder packaging’ (multi-compartment medicine systems and blister packaging) is a simple method for improving adherence but can be problematic and have errors. They state that, while awaiting further trials, there is justification for use of these systems with patients where need is identified.

Randomised controlled trials from the Heneghan (2006) study

Azrin (1998) conducted a RCT with 39 participants who had mental illness, with a mean age of 38.5 years in Florida, USA. One group received a pamphlet of information on types of medicine, their action, efficacy, potency and side effects. Another group received a ‘guidelines to taking medicines’ pamphlet. All participants received a pill box with 28 compartments (4 time periods/day). The guideline pamphlet covered the correct use of the pill box. There was a change in adherence to medicine (proportion of pills taken) from pill counts and self-reported measures.

Huang (2000) conducted a RCT of 184 participants (aged 20 to 80 years) who were to take vitamin pills for two months. The intervention group received medicines in bottles and a pill organiser with seven compartments (for each day of the week). The participants had to remove the pills from the bottles and

place them in the organiser. The control group received the pills in two bottles and did not receive an organiser.

Skaer (1993) NIDDM-a conducted a RCT of 258 non-insulin dependent diabetes mellitus (NIDDM) patients (aged <65 years) from South Carolina, USA receiving Medicaid benefits. The intervention group received standard pharmaceutical services and with every prescription refill request they were provided with a sequentially numbered 30-day supply inventory tray with easy access compartments. The control group received standard pharmaceutical care.

Skaer (1993) NIDDM-b conducted a RCT with 258 medicaid beneficiaries (aged <65 years) with NIDDM which had not been previously treated. The intervention group received pharmaceutical care, unit of use packaging and a medicine refill reminder 10 days before their refill date.The control group received the pharmaceutical care and mailed medicine refill reminders.

Skaer (1993)a conducted a RCT of 304 medicaid patients (aged <65 years) who had mild to moderate hypertension. The intervention group received pharmaceutical care and unit of use packaging (30-day supply inventory tray with easy access compartments). The control group received standard pharmaceutical care.

Skaer (1993)b conducted a RCT of 304 medicaid beneficiaries (aged <65 years) who had mild to moderate hypertension. The intervention group received standard pharmaceutical care, unit of use packaging and a mailed medicine refill reminder ten days before their refill date. The control group received standard pharmaceutical care and mailed medicine refill reminders.

It should be noted that the four Skaer studies represent only two randomised controlled trials.

Randomised Controlled Trials (not included in the systematic reviews)

Henry (1999) [184] from the Cochrane review delivered an intervention where verbal advice on medicine use and possible side-effects were employed along

with information sheets on the treatments and medicines with the dose-dispensing unit. The control group were given treatment only, along with verbal advice and information sheets. A total of 119 patients were included. Mean age of patients was 58 years for the control group and 57 for the intervention group. Compliance in intervention group patients was also encouraged by a phone call 2 days after the start of therapy. This study was conducted In Australia. No statistically significant effects on adherence were reported.

In **Peterson's (1984)** [185] (from the Cochrane review) RCT, the intervention group received several adherence-improving strategies: patients were counselled on the goals of anticonvulsant therapy and the importance of good adherence in achieving these goals; a schedule of medicine-taking was devised that corresponded with the patient's everyday habits; patients were given a copy of an educational leaflet; each patient was provided with a 'dosette' medicine container and counselled on its utility; patients were instructed to use a medicine/seizure diary; and patients were reminded by mail of upcoming appointments and of missed prescription refills. The control group received none of these interventions. Patient compliance improved statistically significantly with the intervention group patients. At follow-up the proportion of compliant patients in each group differed statistically significantly (according to their prescription refill frequencies), 88% of the intervention group and 50% of the control group were considered compliant (chi-square=8.79, df=1, $p<0.01$). Fifty three adults and teenagers were enrolled in the study, and the median age was 35 years for the control group and 28 years for the intervention group. The study was conducted in Australia.

8.9 Does medicine formulation affect adherence?

Related references	Evidence statements (summary of evidence)
Bangalore (2007) [186]	One highly biased systematic review suggests that fixed dose combination compared to free medicine component regimen may increase adherence to prescribed medicine.
Brown 1997 [170]	One RCT showed that controlled release medicine along with simplified dosing compared to regular medicine may increase adherence to prescribed medicine.

8.9.1 Evidence to recommendations

For general discussion of limitations of evidence see section 8.3

The GDG considered the evidence review did not provide convincing evidence that changes to medicine formulation will improve adherence. Changes to medicine formulation should be considered with changes to dosing as a response to individual patient problems only.

8.9.2 Methods of the evidence review

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies - We initially included only randomised controlled trials (RCTs) of interventions to increase adherence. The excluded studies list from the Cochrane review was cross-referenced as we included studies with less than 80% follow-up of participants. After the GDG voiced concerns over the possibility of missing out important studies by only having included a small

amount of studies, the search was redone to pick up any systematic review published after the Cochrane review search cut-off.

Types of participants - people prescribed medicine for a medical condition.

Duration of studies - six months follow up from the time of patient entry for long-term regimens for the RCTs. No time limit specified for short-term conditions.

Types of interventions - any interventions intended to change adherence to prescribed medicine. As the Cochrane review is presented by condition, we have used the evidence extracted in that review and reconfigured it by intervention.

Types of outcome measures - inclusion criterion (as defined in the Cochrane review) was expanded by including studies that used adherence as the only outcome variable as opposed to adherence and treatment outcome variables. The excluded studies list from the Cochrane review was cross-referenced to ensure that no potentially relevant study was missed out.

8.9.3 Evidence review

8.9.3.1 Does medicine formulation affect adherence?

Systematic Reviews

The possibility of bias was assessed to be high in a systematic review by **Bangalore (2007)** [186] which included RCTs and retrospective reviews of data bases. Nine studies were combined in a meta-analysis which included three RCTs and four retrospective data bases of pharmacy claims. There was marked heterogeneity in the compliance measures among the studies evaluated and the patient group had different conditions which were being treated. In the meta-analysis a total of 11,925 patients on fixed dose combination were compared against 8317 patients on free medicine component regimen. Fixed dose combination resulted in a 26% decrease in the risk of non-compliance compared with free medicine component regimen (pooled RR 0.74 (CI 0.69-0.80; p<0.0001). There was no evidence of

heterogeneity in this analysis (p=0.07). A subgroup analysis of the four studies on hypertension showed that fixed dose combination (pooled RR 0.76 CI 0.71-0.81; p<0.0001) decreased the risk of medicine non-compliance by 24% compared with free medicine combination regimens. Due to methodological concerns about the conduct of the meta-analysis, the results of this study should be viewed with caution.

Randomized Controlled Trials

Brown (1997) [170] from the Cochrane review looked at the effect of different formulations as they compared regular niacin versus polygel controlled release niacin. All patients received lovastatin 20mg, colestipol 10g, and niacin 500mg for 12 months, with dosage adjustment to target cholesterol of 150 to 175mg/dl, and to minimize side effects. Twenty-nine male participants were enrolled aged ≤65 years At 12 months, patients were randomly assigned to 1) continue with regular niacin at a dose identical to that established during the 12 month dose-finding period, or 2) change to polygel controlled-release niacin at that daily dosage, but given twice rather than 4 times/day. At 20 months, groups 1) and 2) were reversed (crossover). This study was conducted in the USA. Adherence was statistically significantly greater for the controlled-release preparation.

8.10 Do reminders (and what types of reminders, text messaging etc) increase adherence to prescribed medicine?

Related references	Evidence statements (summary of evidence)
Stewart (2005) [187]; Urien (2004) [188]; Piette (2000) [189]	Three RCTs show that a reminder given via a telephone call in a multi-component intervention can increase adherence to prescribed medicine.
Beaucage (2006) [190]	One RCT showed no statistically significant results on the effect of a reminder given via a telephone call in a multi-component intervention in increasing adherence to prescribed medicine
Hamet (2003)[191]; Peterson (1984) [185]	There is conflicting evidence on the effect of reminders via mail in a multi-component intervention in increasing adherence to prescribed medicine.
Vrijens (2006) [192]; Mannheimer (2006) [193]; Sackett (1975) [194]	There is conflicting evidence on the effect of electronic reminders in a multi-component intervention in increasing adherence to prescribed medicine.
Guthrie (2001) [195]	One RCT showed that using a combination of postal and telephone reminders in a multi-component intervention showed no effect on adherence to prescribed medicine.

8.10.1 Evidence to recommendations

For general discussion of limitations of evidence see section 8.3

The type of reminders varied – telephone, mail, electronic or a combination of telephone and mail. The benefit of any type of reminder was not clear from the available evidence. The GDG did not consider the evidence sufficient to make any recommendations about reminders.

8.10.2 Methods of the evidence review

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies - randomied controlled trials (RCTs) of interventions to increase adherence. The excluded studies list from the Cochrane review was checked as we have included those studies with less than 80% follow-up of participants.

Types of participants - people prescribed medicine for a medical condition.

Duration of studies - six months follow up from the time of patient entry for long-term regimens. No time limit specified for short-term conditions.

Types of interventions - any interventions intended to change adherence to prescribed medicine. As the Cochrane review is presented by condition, we have used the evidence extracted in that review and reconfigured it by intervention.

Types of outcome measures - inclusion criterion (as defined in the Cochrane review) was expanded by including studies that used adherence as the only outcome variable as opposed to adherence and treatment outcome variables. The excluded studies list of the Cochrane review was cross-referenced to ensure that no potentially relevant study was missed out.

8.10.3 Evidence review

8.10.3.1 Telephone reminders

Stewart (2005) [187] compared four once-monthly educational sessions, the prescription of a home-based walking program and once-monthly phone calls

with four once-monthly educational sessions, the prescription of a home-based walking program without once-monthly phone calls in patients attending a hypertension clinic with positive results at week 24 but not 36. Sample size was comprised 83 participants. During the phone calls patients (or a family member) were asked about the exercise program and reminded about diet and medicine. In total 5 (pairs) of telephone calls (to patient and family member) were made once monthly over 24 weeks by a physiotherapist. This study was conducted in South Africa.

At week 24 statistically significantly more patients in the group receiving telephone calls (65%) were taking their medicines as prescribed compared to the group not receiving telephone calls (44.7%, p=0.05), however, there was no difference between the groups at week 36 (82.4% vs 86.7%) [187].

Urien (2004) [188] compared a telephone-delivered intervention plus educational advice with educational advice alone in patients receiving antibiotic treatment. The sample was comprised of 128 participants aged ≥18 years. The telephone call was undertaken on the 4th day after the start of treatment, when the first box of antibiotics should have been finished. The patient was advised to continue the treatment according to the dosage and number of days that had been prescribed. The patient was also reminded that although he or she may feel better or even cured, the treatment was to be continued for 10 days. This study was conducted in Spain.

Adherence was statistically significantly higher in the intervention group (78.3%) than in the control group (54.1%) (p=0.005) [188].

Beaucage (2006) [190] compared a pharmacist telephone intervention with usual care in patients on antibiotic treatment with negative results. A telephone call was made to patients in the intervention group by a pharmacist 3 days into treatment. The pharmacist asked about the patient's general condition, on the presence of adverse effects and the participants understanding of dosing. The pharmacist emphasised the importance of adherence and offered motivation to the patient. The patients were offered an opportunity to ask questions and were given the pharmacist's contact details

in case they wanted to make contacted their pharmacist at a later time. This study was conducted in Canada.

Mean adherence to treatment was 94% (s.d=9%) and 94% (s.d=12%) in the intervention and control groups respectively (p=0.803). The proportion of patients with less than 80% adherence was similar in the two groups (Intervention group: 8%, control group: 9%).

Piette (2000) [189] compared a telephone intervention with usual care in patients with diabetes (n=280) with positive results. Patients were excluded if they were above 75 years of age. The intervention consisted of, "…a series of automated telephone assessments designed to identify patients with health and self-care problems (TeleminderModel IV automated telephone messaging computer). Calls were made on a bi-weekly basis, up to 6 attempted calls, and involved a 5 to 8-minute assessment. During each assessment, patients used the touch-tone keypad to report information about self-monitored blood glucose readings, self-care, perceived glycaemic control, and symptoms of poor glycaemic control, foot problems, chest pain, and breathing problems, with automated prompts for out-of-range errors. The automated telephone calls were also used to deliver, at the patient's option, 1 of 30 targeted and tailored self-care education messages at the end of each telephone session. Patients only received a 1-page instruction sheet on the use of the phone. Each week, the automated assessment system generated reports organised according to the urgency of the reported problems, and a diabetes nurse educator used these reports to prioritise contacts for a telephone follow-up. During follow-up calls, the nurse addressed problems reported during the assessments and provided more general self-care information. After several months, intervention group patients were offered additional automated self-care calls that focused on glucose self-monitoring, foot care and medicine adherence. In the medicine adherence part of these sessions, patients were asked about their adherence to insulin, oral hypoglycaemic medicines, antihypertensive medicines, and antilipidemic medicines. For each type of medicine, patients without adherence problems received positive feedback and reinforcement. Patients reporting less than optimal adherence were asked

about specific barriers and were given advice from the nurse about overcoming each barrier. The nurse was located outside the clinic and had no access to medical records other than the baseline information collected at enrolment and her own notes. She did not have any face-to-face contact with patients. The nurse addressed problems raised by patients in the automated calls and also gave general self-care education. The nurse also checked on patients who rarely responded to automated calls. A small number of patients initiated calls to the nurse by a toll free number. She referred these to the primary care physician as appropriate [196]. This study was conducted in the United States.

Compared with usual care, patients in the intervention group reported fewer problems with medicine adherence ($p < 0.003$).

8.10.3.2 Mail reminders

Hamet (2003) [191] compared the Avapromise intervention (designed to modify behaviour by medicine adherence through reinforcement and lifestyle modification) with usual care in patients with high blood pressure. This was a study that comprised a total of 4864 participants. The ages of participants ranged from 16 to 89 years. The intervention was made up of two elements that were delivered together. The first element attempted to reinforce medicine behaviours by using medicine reminder letters, blood pressure diaries and telephone nurse counselling sessions. The second element addressed lifestyle management through educational brochures. Patients assigned to the intervention group were mailed the material at one, two, three, four, six and 12 months. This study was conducted in Canada.

A total of 25.4% (95% CI 23.7 to 27.2) of patients discontinued their treatment from the intervention group and 25.5% (95% CI 23.8 to 27.3) from the control group ($p=0.94$). There was no statistically significant difference in the duration of Irbesartan compliance between the treatment groups [191].

In **Peterson's (1984)** [185] (from the Cochrane review) RCT, the intervention group received several adherence-improving strategies: patients were

counselled on the goals of anticonvulsant therapy and the importance of good adherence in achieving these goals; a schedule of medicine-taking was devised that corresponded with the patient's everyday habits; patients were given a copy of an educational leaflet; each patient was provided with a 'dosette' medicine container and counselled on its utility; patients were instructed to use a medicine/seizure diary; and patients were reminded by mail of upcoming appointments and of missed prescription refills. The control group received none of these interventions. Patient compliance improved statistically significantly with the intervention group patients. At follow-up the proportion of compliant patients in each group differed statistically significantly (according to their prescription refill frequencies), 88% of the intervention group and 50% of the control group were considered compliant (chi-square=8.79, df=1, p<0.01). Fifty three adults and teenagers were enrolled in the study, and the median age was 35 years for the control group and 28 years for the intervention group. The study was conducted in Australia.

8.10.3.3 Mail and telephone reminders

Guthrie (2001) [195] delivered an intervention involving postal and telephone reminders regarding coronary risk reduction and medicine compliance, which were sent during the first 2 months of pravastatin treatment, or usual care. This was a large study that comprised a total of 13,100 participants. Mean age was 58.0 years. Both groups received reminder postcards at 4 and 5 months, in addition to counselling by physicians about coronary risk reduction. At study discontinuation, patients completed and mailed (to the program-coordinating centre) questionnaires concerning compliance with care, as well as self-reported adoption of other lifestyle modifications. This study was conducted in the USA. Neither early reminders nor baseline patient characteristics were statistically significantly associated with reported pravastatin compliance rates.

8.10.3.4 Electronic reminders

Vrijens (2006) [192] compared a supportive intervention program with usual care in patients who had been taking atorvastatin with positive results. Four

hundred and twenty nine participants aged >18 years entered the study. As part of the supportive intervention program participants were supplied with a 'beep-card' that reminded the patient of the dosing time, and also gave educational reminders. The supportive intervention program also provided patients with a medicine review by the patients' pharmacist of their electronically compiled dosing history (through MEMs). At each follow-up visit the pharmacist delivered an educational message, updated the patients' compliance passport and analysed with the patient their electronically compiled dosing history over the previous month/3 months (depending on the gap between follow-up appointments). Baseline adherence was statistically significantly higher in the intervention group compared to the control group (96.43% vs. 94.33%, p=0.003). At 12 months, the intervention group had an increased adherence of 6.5% compared to the control group (95.89% vs. 89.37%, p<0.001). The analyses were stratified by baseline compliance and language region. Over time, the difference between groups increased, with approximately 17% difference in adherence between groups at 300 days. 13% (n=25) of the intervention group discontinued medicine before 300 days, compared to 25% (n=51) in the control group. Persistence was statistically significantly higher in the intervention group compared to the control group (87% vs. 74%, p=0.002). This remained statistically significant when adjusted for multiple baseline variables. This study was conducted in Belgium [192].

In a study conducted by **Sackett (1975)** [194] (from the Cochrane review), subjects in one of the interventions (augmented convenience) groups visited company physicians, rather than their family physicians, for hypertensive and follow-up care during paid working hours. Two hundred and thirty Canadian steelworkers were enrolled. The ages of the participants were not reported in the study. The second intervention, mastery learning, aimed to give the facts about hypertension, its effects upon target organs, health, and life expectancy, the benefits of antihypertensive therapy, the need for adherence with medicines and some simple reminders for taking pills (which was provided in a slide-tape format, and reinforced by a secondary-school graduate). No

statistically significant results were reported. This study was conducted in Canada.

Mannheimer (2006) [193] conducted a cluster randomised controlled trial (2x2 factorial design) to assess two interventions to increase adherence in 928 patients who were taking anti-retroviral therapy in the USA. One intervention is the Medicine Manager (MM) which involved a trained research staff member working with the participants individually to provide tailored adherence support according to a standardised protocol, identifying and addressing information, motivation and skills for antiretroviral adherence (using detailed questionnaires). The second intervention was the electronic medicine reminder system, a small portable alarm (ALR) which was programmed to flash and sound when antiretroviral doses were due. Participants were followed up with assessments at 1 and 4 months after randomisation and 4 months thereafter. The MM group had statistically significantly higher reporting of 100% adherence over time compared to non-MM interventions (OR=1.42, p<0.001). There were no statistically significant differences between the ALR group and the non-ALR groups for adherence.

8.10.3.5 Type of reminders used not stated

De Geest (2006) [197] compared a nurse-led intervention and usual care with usual care alone in patients who had undergone a kidney transplant with negative results. This was a small study that comprised a total of 18 participants aged > 18 years. The intervention group received one home visit and three telephone interviews, one at the end of the month for three consecutive months. During the home visit printouts were discussed with the patient for problem detection, and adherence goals were set. All patients received self-efficacy interventions. Nurses also implemented additional educational, behavioural (e.g. the use of reminders) and/or social support interventions if they felt this would help the patient. Telephone calls served to discuss adherence in the previous month, to check on health status, and discuss and change, if appropriate, adherence interventions. This study was conducted in Switzerland.

Adherence increased in both groups over the first 3 months (p=0.04). The overall difference between groups was statistically non-significant at 3 months (p=0.31) and at 9 months (p=0.58) with a gradual decline over the total 9 months to a level still higher than initial levels [197].

8.11 Is there any evidence on interventions that aim to minimize side-effects in order to increase adherence?

Related references	Evidence statements (summary of evidence)
Rickles (2005) [198]; Collier (2005) [199]; Kemp (1998) [200]	There is conflicting evidence with regard to whether discussing side effects, as part of a multi component intervention, increases adherence.
Rathbun (2005) [201]; Chaplin (1998) [202]; Canto De Cetina (2001) [203]; Tuldra (2000) [204]; Peveler (1999) [205]	There is conflicting evidence with regard to whether educating patients about side effects, as part of a multi-component intervention, increases adherence.
Howland (1990) [206]	One RCT showed that informing patients about side effects did not have a statistically significant effect on adherence.
Vivian (2002) [207]; Finley (2003) [208]; Katon (2002) [209]	There is conflicting evidence with regards to whether giving an intervention deliverer (e.g. a pharmacist) the power to adjust a patient's medicine and/or dosage, as part of a multi component intervention, increases adherence.
Chisholm (2001) [210]; Adler (2004) [211]	There is conflicting evidence with regard to whether giving an intervention deliverer (e.g. a pharmacist) the power to make recommendations about the treatment to the patient's practitioner, as part of a multi component intervention, increases adherence.

8.11.1 Evidence to recommendations

For general discussion of limitations of evidence see section 8.3

Interventions relating to side effects primarily involve providing information for patients on side effects. No single way of providing information on side effects with a view to increase adherence to prescribed medicine can be recommended. This is mainly due to the evidence not assessing the impact of minimising side effects independently, thus not being able to ascertain their true effect.

The GDG considered that there are a number of ways to manage side effects to support patient adherence. These include adequately informing patients about side effects, exploring how a patient wants to manage side effects, reducing the dose of medicine and changing the medicine to an alternative.

8.11.2 Methods of the evidence review

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies - randomised controlled trials (RCTs) of interventions to increase adherence. The excluded studies list from the Cochrane review was checked as we have included those studies with less than 80% follow-up of participants.

Types of participants - people prescribed medicine for a medical condition.

Duration of studies - six months follow up from the time of patient entry for long-term regimens. No time limit specified for short-term conditions.

Types of interventions - any intervention intended to change adherence to prescribed medicine. As the Cochrane review is presented by condition, we have used the evidence extracted in that review and reconfigured it by intervention.

Types of outcome measures – inclusion criteria (as defined in the Cochrane review) were expanded by including studies that used adherence as the only outcome variable as opposed to adherence and treatment outcome variables. The excluded studies list of the Cochrane review was cross-referenced to ensure that no potentially relevant study was missed out.

8.11.3 Evidence review

Although a number of RCTs were found which addressed side effects, we did not find many where the interventions' sole purpose was to address side effects. Within the RCTs which did address side effects there was a lot of variability in how they did this and to what extent side effects were a focus of the intervention. What follows is a summary of the RCTs which addressed side effects with information on interventions limited to those parts of the study which addressed side effects. For further details please see evidence tables for the RCTs retrieved from update searches, or the Cochrane review.

8.11.3.1 Discussing side effects with patients

RCTs were excluded from this section if side effects were only discussed, and if no further details were given on how to educate the patients in managing their side-effects with a view to increase adherence. Other RCTs were excluded if addressing side effects was potentially part of a multi-component intervention but when the actual decision to address side effects was the choice of the intervention provider (therefore meaning it was impossible to tell how many patients in the intervention group had side effects addressed and how many did not have this issue addressed).

3 RCTs addressed side effects by clearly discussing them with patients. **Rickles (2005)** [198] had pharmacists address adverse events during telephone calls in 98 patients with a mean age of 38 years. The pharmacist could probe or explain issues not understood by the patient and make recommendations. The intervention had positive effects. The difference at six months in adherence with the rate of missed doses was statistically significantly lower in the intervention group (30.3%, s.d=36.4 vs. 48.6%, s.d=39.2, p=<0.05). This study was conducted in the USA. **Collier (2005)** [199] had nurses address

participants' medicine-related behaviour and barriers to adherence during telephone calls in 282 patients. Advice around side effects was offered. Over 24 months, rates of adherence were high in both groups (>72% reported at least 95% adherence). No difference was seen between groups (OR 0.86, 95% CI 0.57 to 1.29). This study appears to have been conducted in the USA.
Kemp (1998) [200], an RCT from the Cochrane review, as part of "compliance therapy", had 2 sessions where intervention group participants focused on symptoms and the side effects. This study had 74 participants. The mean age in the intervention group was 34 years (s.d=10.6) and 37 years (s.d=11.9) in the control group. This study was conducted in the UK.

Patients receiving compliance therapy demonstrated higher adherence ratings ($p < 0.001$) than control group patients.

8.11.3.2 Educating patients and follow-up

5 RCTs addressed side effects through educating the patient about them and then following up on this education.

Rathbun (2005) [201] provided patients with a mean age of 38 years with education about adverse-event management strategies, among other things. A total of 43 patients were included in this study. Telephone follow-up was provided to identify early problems. At week 28, adherence rates were 74% (s.d=31%) in the intervention group and 51% (s.d=41%) in the control group (p=0.080, difference between groups 23%, 95% CI: 1% to 44%). Mean decline in adherence between weeks 4 and 28 were 12% (p=0.15) in the intervention group and 22% (p=0.002) in the control group. Patients in the intervention group were more likely to take their medicine at the prescribed dosing schedule: at 4 weeks, 69% in the intervention group vs 42% in the control group (p=0.025) and at 28 weeks, 53% in the intervention group vs 31% in the control group (p=0.046). No statistically significant difference was seen between the groups based on patient self-report (94% vs 89% intervention vs control, p=0.51). This study was conducted in the USA.

Chaplin (1998) [202], an RCT from the Cochrane review, had intervention group participants, "…participate in a discussion about the risks and benefits of neuroleptic medicines based on individual semi-structured educational sessions with reference to a standardised information sheet. The patients were asked whether they had heard of tardive dyskinesia. The common movements of TD were modelled and the patients were asked whether they thought they had the condition or had seen others with it. They were informed that they were receiving an antipsychotic medicine and were given information about extrapyramidal symptoms and TD, its risk factors, prevalence, treatment, potential irreversibility and the 1% risk of TD in non-antipsychotic-treated patients. They were told that gradual discontinuation of antipsychotic medicine was the best way to prevent the condition but if done abruptly carries a high risk of relapse and of precipitating TD. It was stated that the optimum maintenance treatment, taking into account its risks and benefits, was to use the lowest dose of antipsychotic medicine that would keep them well. Most importantly, they were asked not to make any changes to their treatment without discussion with their psychiatrist. Finally, they were given the opportunity to ask questions in an informal interactive session lasting 30 minutes, and were given an information sheet for reference" [196]. This study included 56 participants (age range not given) and was conducted in the UK. The intervention did not increase adherence relative to the control condition.

Canto De Cetina (2001) [203], an RCT from the Cochrane review, had women in their intervention group (counselling group) receive, "…a structured pre-treatment counselling with indications about the mode of action of DMPA, the common side effects of the medicine, including the possibility of irregular menstrual periods, heavy bleeding, spotting, and amenorrhea. To mentally prepare users for potential side effects, it was stressed that these side effects would be not detrimental to their health. These indications were repeated at each follow-up visit" [196]. This study included 350 participants. The mean age in the counselling group was 33.9 years with a 20-35 range and 34 years in the control group with also a 20-35 range. This study was conducted in

Mexico. There was a positive effect of the intervention in terms of cumulative termination rates.

Tuldra (2000) [204], an RCT from the Cochrane review, investigated a psycho-educative intervention part of which involved participants being taught how to manage medicine and tackle problems such as forgetting, delays, side effects and changes in the daily routine. During follow-up participants were provided with skills to deal with minor adverse effects. This study had 116 participants. The mean age in the intervention group was 39 years (s.d=10) and 38 years (s.d=7) in the control group. It appears this study was conducted in Spain. "In an intention to treat (ITT) analysis, no improvements were found in adherence (the p-values were slightly above the 0.05 significance level). However, when a per protocol analysis was conducted, the intervention resulted in improvements in compliance to HAART at 48 weeks. The lack of statistical significance observed using the ITT analysis might be a reflection of a low power to detect differences due to the relatively small sample size for each arm (n=55 for intervention, n=61 for control). The per protocol analysis is suspect in any adherence study as it ignores patients who dropped out, the most severe form of nonadherence." [196].

Peveler (1999) [205], an RCT from the Cochrane review, compared four treatment groups, "…treatment as usual, leaflet, medicine counselling, or both interventions. The information leaflet contained information about the medicine, unwanted side effects, and what to do in the event of a missing dose. Patients were given medicine counselling by a nurse at weeks 2 and 8, according to a written protocol. Sessions included assessment of daily routine and lifestyle, attitudes to treatment, and understanding of the reasons for treatment...The importance of medicine treatment was emphasized, and side effects and their management discussed." [196]. This study had 213 participants with a mean age of 45.3 years with a range of 21-83. This study was conducted in the UK. "The treatment leaflets had no effect on adherence…This study was only 12 weeks in duration, which is shorter than our usual 6 months follow-up criterion. However, because the results were negative for adherence and clinical outcomes with the leaflet intervention, the

paper was included for this review. (Counselling about medicines, however, did result in statistically significant improvements in adherence and clinical outcomes. Nonetheless, because the follow-up was less than six months in duration, the results for counselling are not considered in the conclusions of this review.)" [196].

Howland (1990) [206], an RCT from the Cochrane review, informed intervention group patients of six possible side-effects of treatment with erythromycin, while control (uninformed) patients were not made aware of potential side effects of treatment. This study had 98 participants. The mean age in the intervention group was 50 years and 48 years in the control group. It appears this study was conducted in the USA. The intervention did not increase adherence relative to the control condition nor did it decrease adherence.

8.11.3.3 Adjusting medicine and/or dosage

3 RCTs addressed side effects by giving the intervention deliverer power to adjust medicine and/or medicine dosage.

In a study by **Vivian (2002)** [207] intervention patients saw clinical pharmacists who could make changes in the prescribed medicines and dosages and provided medicine counselling centred around the discussion of side effects, lifestyle and adherence (note we have made an assumption here that the discussion of side effects and changes in medicine are related, this is not explicitly stated in the study). Fifty seven patients aged above 18 years were included in this study. The majority of the study population were African American (77%). There were no statistically significant differences in compliance (from self report measure) between ($p>0.25$, mean and s.d not given for adherence) or within ($p=0.07$) the two groups at baseline or at the end of the study. This study was conducted in the USA.

Finley (2003) [208] had pharmacists provide a detailed explanation of the role of antidepressants (including potential therapeutic effects and adverse effects). Care managers were permitted to titrate antidepressant medicines in a fashion consistent with the HMO's clinical guidelines and current

recommended practices (note we have made an assumption here that the discussion of side effects and changes in medicine are related, this is not explicitly stated in the study). During follow-up phone calls and clinic appointments pharmacists followed a standardised set of questions that assessed adverse effects, among other things. One hundred and twenty five patients were included in the study. The majority of the study population was female 42 (84%) in the control group and 64 (85%) in the intervention group; and the mean ages were 54.1 (s.d=17.3) years in the control group and 54.4 (s.d=14.1) years in the intervention group. After 6 months, the intervention group demonstrated a statistically significantly higher medicine adherence rate than that of the control group (67% vs. 48%, p=0.038). This study was conducted in the USA.

As part of a multifaceted intervention, **Katon (2002)** [209] scheduled two sessions for intervention patients with a psychiatrist in a primary care clinic. The study included 228 patients aged between 18 and 80 years. Mean ages were 47.2 (s.d=14) years in the intervention group and 46.7 (s.d 13.4) years in the usual care group. When severe side effects or inadequate response to treatment occurred, the psychiatrist helped the patient and primary care physician alter the dosage or choose an alternative medicine. There were no differences between the four study groups in either adherence to the care suggestions, combined or individually. There were no inter-group differences in medicine adherence. This study was conducted in the USA.

8.11.3.4 Recommendations to health care professionals

2 RCTs addressed side effects by giving the intervention deliverer power to make recommendations to other health care professionals involved in the patients care.

Chisholm (2001) [210] examined an intervention which included a pharmacist taking medicine histories and reviewing medicines with the patient, with an emphasis on optimising medicine therapy to achieve compliance outcomes while minimising adverse events related to medicine. Twenty four patients aged between 18 and 60 years were included in the study. The majority of the

study population was male (75%). The clinical pharmacist also provided recommendations to the nephrologists with the goal of achieving desired outcomes. Counselling involved discussion of patients concerns around their medicine therapy and instructing them how to properly take their medicines. Counselling was both verbal and/or in writing. At 12 months the mean compliance rate in the intervention group was 96.1% (s.d=4.7%) compared to 81.6% (s.d=11.5%) in the control group ($p<0.0001$). For 6 of the 12 months, higher rates of compliance were seen in the intervention group ($p<0.05$). Also, 75% (n=9) of the intervention patients were compliant each month compared to 33.3% (n=4) of the control group. This study was conducted in the USA.

Adler (2004) [211] employed a pharmacist intervention which emphasised, among other things: assessing a patient's medicine regimen for medicine-related problems (such as side effects or medicine interactions); monitoring medicine efficacy and toxicity; and educating patients about depression and antidepressants. This study included 533 patients aged above 18 years. The mean age was 42.3 years, and the majority was female. After an initial appointment with the patient, pharmacists provided the patients primary care practitioner with a thorough medicine history (including adherence to prescribed medicines and medicine-related problems) and whatever recommendations the pharmacist may have suggested to improve the regimen. For patients using antidepressants at study entry (n=227) there were no significant differences in antidepressant usage between the intervention and control groups either at 3 (90.7% vs. 87.2, p=0.50) or 6 months (83.4% vs. 78.4%, p=0.33). This study was conducted in the USA.

8.12 How does the way the information is presented (e.g. pictorial vs. written) affect adherence?

Related references	Evidence statements (summary of evidence)
Raynor (2007) [68]	One high quality systematic review of quantitative and qualitative research on the role and effectiveness of written information available to patients about individual medicines stated that no robust evidence was found that the information (delivery) had an effect on patient satisfaction or compliance.
Schaffer (2004) [212]	One RCT showed that written information alone and written and verbal information resulted in greater improvements in adherence to prescribed medicine compared to verbal information alone.
Segador (2005) [213]	One RCT showed that verbal and written information compared to verbal information alone resulted in statistically significantly greater improvements in adherence to prescribed medicine.
Atherton-Naji (2001) [214]	One RCT showed that simple tailored information (mailed leaflets with written and pictorial information) did not significantly improve adherence to prescribed medicine compared to usual care.

8.12.1 Evidence to recommendations

For general discussion of limitations of evidence see section 8.3

While there is no conclusive evidence about the effectiveness of the mode of delivery of information affects adherence, in certain cases/diseases it made a difference. The GDG considered from what is know about information provision in other areas that this needs to be individualised to each patient.

8.12.2 Methods of the evidence review

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies - randomised controlled trials (RCTs) of interventions to increase adherence. The excluded studies list from the Cochrane review was checked as we have included those studies with less than 80% follow-up of participants.

Types of participants - people prescribed medicine for a medical condition.

Duration of studies - six months follow up from the time of patient entry for long-term regimens. No time limit specified for short-term conditions.

Types of interventions - any interventions intended to change adherence to prescribed medicine. As the Cochrane review is presented by condition, we have used the evidence extracted in that review and reconfigured it by intervention.

Types of outcome measures - inclusion criteria (as defined in the Cochrane review) were expanded by including studies that used adherence as the only outcome variable as opposed to adherence and treatment outcome variables. The excluded studies list of the Cochrane review was cross-referenced to ensure that no potentially relevant study was missed out.

8.12.3 Evidence review

A health technology assessment report of a “Systematic review of quantitative and qualitative research on the role and effectiveness of written information available to patients about individual medicines” [68] was retrieved. This report

aimed to address the role and value of written information given to patients; and how effective this information is in improving patient's knowledge of their treatment and health outcomes. The inclusion criteria of this review was broader than those applied in our reviews, as members of the public not currently taking medicine; general public using over the counter medicines and some addiction therapies were included. Also, studies did not necessarily need to have an aim to increase adherence. Despite these differences, it was felt that due to the high quality of this document, it would be relevant to refer to it in this section to support the evidence included in the reviews and inform the decision making process.

Key findings of the report show that:

- the majority of people do not value the written information they receive, and
- no robust evidence was found that the information had any effect on patient satisfaction or compliance.

Most patients did not value the current package insert patient information leaflets (PILs) and did not consider information written by medicine manufacturers to be sufficiently independent.

The (PILs) supplied had deficiencies in the content (e.g. complexity of language) and layout (e.g. print size). However, it did show that patients valued written information that contained condition-based details along with the medicines information, in addition to alternative treatments for the condition.

In addition, the qualitative evidence included in the report did not show that patients perceive improvement of compliance as a function of PILs. This can be explained by how an informed decision not to take medicine is a legitimate and acceptable outcome. In contrast, some health care professionals viewed that the increase of compliance was one of the main PIL uses.

The key points for improvement of written medicines information outlined by the review were:

- The need to involve patients in all stages of the process, as to reflect better their needs.
- To incorporate the findings from the review to improve future information design and content.
- To present risk information numerically instead of verbal descriptions.

8.12.3.1 Verbal vs. written vs. verbal and written vs. usual care

Schaffer (2004) [212], a study from the Cochrane review, compared two interventions and a combination of the two control groups in patients with asthma aged 18-65 (n=46) with results dependant on the measure of adherence used. There were 4 groups, "…standard provider education (control group); (b) audiotape alone; (c) National Heart Lung and Blood Institute (NHLBI) booklet alone; and (d) audiotape plus NHLBI booklet". This study was conducted in the United States.

"The results showed a statistically significant increase in adherence by pharmacy-refill measure (but not by self-report) for NHLBI booklet versus control, and for NHLBI booklet plus audiotape versus control, but not for audiotape versus control at six months".

8.12.3.2 Verbal and written information vs. verbal information alone

Segador (2005) [213] compared the effect of written information in addition to verbal information in patients receiving antibiotic treatment for acute sore throat (n = 158) with statistically significant results. Patients in the written information group were given written information at the time of their first visit to their GP. The written information emphasised the importance of completing the antibiotic treatment, of respecting intervals between doses and the drawbacks of an early drop-out, and was given only at the time of initial consultation. The control group was given verbal information only. This study was conducted in Spain.

The pill count average was 87.4 +/- 25.2% and it was higher in the intervention group (93.7 +/- 24.5%) than in the control group (81.1 +/- 24.5%) ($p < 0.05$).

8.12.3.3 Written and/or pictorial information given vs. usual care

Atherton-Naji (2001) [214] compared an educational intervention to routine care in patients (n=45) with depression with statistically non-significant results. Patients in the intervention group received simple tailored information (mailed leaflets with written and pictorial information) at 1, 6 and 16 weeks after the initial prescription. The leaflets contained basic information about the condition, treatment and general problems people may have with adherence to the treatment. Leaflets were personalised for each patient and their specific medicine. This study was conducted in the UK. Over 6 months, 35.6% (n=16) collected prescriptions at each month (no statistically significant difference between groups). The proportion decreased over time from month 1 (intervention group: 95.8% (n=23) vs. control group: 100% (n=21)) to month 6 (intervention group: 58.3% (n=14) vs. control group: 52.4% (n=11)).

8.13 Do specific forms of therapy (e.g. CBT) affect adherence?

Related references	Evidence statements (summary of evidence)
All studies included in evidence review	There is some evidence that elements of CBT or psycho-behavioural can help but the quality of the evidence does not allow us to generalise these results.
Gray 2006 [215]; Wyatt 2004 [216]; Bechdolf 2004 and 2005 [217] [218]; Weber 2004 [219]; Antoni, 2006 [220]; Wagner 2006 [221]; Lam, 2003 [222]	The majority of evidence suggests that CBT approaches do not improve adherence relative to other forms of treatment.
Strang (1981) [223]	One RCT showed that family therapy increased adherence to prescribed medicine when compared to individual support sessions.
Xiong (1994) [224]; Zhang (1994) [225]	Two RCTs showed that family therapy did not increase adherence to prescribed medicine when compared to standard care.
Miklowitz, 2003 [226]	One RCT showed that family therapy and pharmacotherapy increased adherence to prescribed medicine when compared to crisis management and pharmacotherapy.
Razali, 2000 [227]	One RCT showed that culturally modified family therapy increases adherence when compared to behavioural family therapy.
Remien, 2005 [228]	One RCT showed that couple based therapy

	increases adherence compared to usual care.
Ruskin, 2004 [229]	One RCT showed that telepsychiatry did not increase adherence compared to face to face psychiatry.
Kemp 1996, 1998 [230] [200]; O'Donnell 2003 [231]	There is conflicting evidence with regards to whether compliance therapy increases adherence compared to counselling.
Pradier, 2003 [232]; Van Servellen (2005) [233]	There is conflicting evidence to suggest that multi-component interventions mainly based on motivational principles increase adherence.
Weber 2004 [219]	One RCT showed that CBT and usual care did not increase adherence compared to usual care alone.
Gray, 2006 [215]	One RCT showed that CBT and health education did not increase adherence compared to health education alone.
Bechdolf, 2004 and 2005 [217] [218]	One RCT showed that CBT and health education did not increase adherence compared to psycho-education.
Antoni 2006 [220]	One RCT showed that cognitive behavioural stress management in addition to antiretroviral medicine adherence training did not increase adherence compared to medicines adherence training alone.

8.13.1 Evidence to recommendations

For general discussion of limitations of evidence see section 8.3

The evidence concerning specific forms of therapy and their effect on adherence is inadequate. Conclusions from a variety of single studies with ill defined content and delivery are inconclusive. The GDG noted that definitions of CBT and other therapies were often unclear. It was also argued that some of these interventions may not be salient to medicine-taking behaviour. The available evidence is that patients make their own appraisal of medicines based on factors important to them and in this context their behaviour is rational and coherent and as such not appropriate for CBT.

Therapies which worked with patients and families addressing social and cultural issues do provide evidence of specific principles of engaging with patients that may be of value. The evidence for CBT/other forms of therapy comes from patients with severe mental illness and HIV. Evidence from these populations might not be generalised to other medicine-taking populations.

8.13.2 Methods of the evidence review

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies - randomised controlled trials (RCTs) of interventions to increase adherence. The excluded studies list from the Cochrane review was checked as we have included those studies with less than 80% follow-up of participants.

Types of participants - people prescribed medicine for a medical condition.

Duration of studies - six months follow-up from the time of patient entry for long-term regimens. No time limit specified for short-term conditions.

Types of interventions - any interventions intended to change adherence to prescribed medicine. As the Cochrane review is presented by condition, we have used the evidence extracted in that review and reconfigured it by intervention.

Types of outcome measures – inclusion criteria (as defined in the Cochrane review) were expanded by including studies that used adherence as the only outcome variable as opposed to adherence and treatment outcome variables. The excluded studies list of the Cochrane review was cross-referenced to ensure that no potentially relevant study was missed out.

8.13.3 Evidence review

8.13.3.1 Family Therapy

Miklowitz (2003) [226] compared family focused therapy and pharmacotherapy with crisis management and pharmacotherapy (serving as control group) in patients with bi-polar disorder with positive results. The study included 101 participants with ages that ranged from 18 to 62 years (mean age 35.6 ± 10.2 years). Family focused therapy involved three modules: 1/ psycho-education, which involved passing on information about the disorder, its aetiology, signs, symptoms and also information on how to prevent relapse; 2/ communication training where, through role play, skills of listening, offering feedback, and requesting changes in behaviour were passed on; and 3/ problem solving skills, where participants identified potential problems, came up with and evaluated various solutions. Family focused therapy involved approximately 21 sessions over a nine month period and was conducted with the whole of the patient's family at the patients/family's home. This study was conducted in the USA.

Patients in the intervention group had higher mean medicine adherence scores during follow up (2.77 +/- 0.43) than patients in the control group (2.56 +/- 0.48, p=0.04). This study was conducted in the USA.

Razali (2000) [227], a RCT from the Cochrane review, compared the effects of "culturally modified family therapy"(CMFT) to the effects of "behavioural family therapy" (BFT serving as the control condition) in patients with schizophrenia. This study included 166 participants, with ages ranging from 17 to 55 years. The majority of the patients came from a low socio-economic background. The CMFT was delivered by a psychiatrist and sessions were given monthly for the first 3 months and then every 6 weeks in the following months. The

CMFT consisted of a "….Socio-cultural approach of family education, medicine intervention programme and problem-solving skills. The socio-cultural approaches to family education include explanations of the concept of schizophrenia from a cultural perspective and an attempt to correct negative attitudes toward modern treatment. The family education and medicine intervention was delivered as a package. The medicine intervention programme included medicine counselling, clear instruction about dose, frequency and possible side effects, the role of carers in supervision of medicine-taking at home, and close monitoring of compliance by a medicine intake check-list presented in every follow-up visit [196]." This study was conducted in Malaysia.

At six months there was no significant difference in compliance but at 1 year the intervention (CMFT) group had statistically significantly higher compliance than those in the control (BFT) group. Ninety percent compliance was achieved by 85% of the CMFT group and 55% of the BFT group, $p<0.001$.

Strang (1981) [223], a RCT from the Cochrane review, compared family therapy or individual support sessions in patients with schizophrenia with positive results. Thirty two patients were enrolled in this study. No information on the ages of the patients was given. All patients had scheduled therapy and monthly medicine appointments. Patients were allocated to family therapy or individual support sessions. This study was conducted in the UK.

The patients in the family therapy group were statistically significantly more adherent than those in the individual support group.

Xiong (1994) [224], a study from the Cochrane review, compared a family based intervention with standard care in patients with schizophrenia with negative results. Sixty three families were enrolled in this study and mean age was 31 years (ranging from 17 to 54 years). The family based intervention "…included monthly 45 minute counselling sessions focused on the management of social and occupational problems, medicine management, family education, family group meetings, and crisis intervention" [196]. This study was conducted in

China. There was no difference in terms of adherence between the two groups.

Zhang (1994) [225], a study from the Cochrane review, compared a family intervention with no additional care above standard care in patients discharged after their first admission to the hospital for schizophrenia with negative results. This study included 83 patients. Mean ages were 23.5 (sd=7.6) for the intervention group and 24.1 (sd=8.1) for the control group Families and patients in the family intervention group were "…assigned to one of two counsellors for their ongoing care, were invited to come to a discharge session that focused on education about the management of the patient's treatment, asked to come to a family group counselling session with other families three months after discharge, and then attend three-monthly group sessions with other families with similar patient problems. Non-attendance triggered a visit from study staff. Each family was contacted at least once during the 18-month follow-up." [196] This study was conducted in China. There was no difference in terms of adherence between the two groups.

8.13.3.2 Couples Therapy

Remien (2005) [228] compared a couple-based ART adherence intervention with usual care in HIV-serodiscordant couples with positive results. The intervention included structured discussions and instruction, as well as specific problem-solving and couple-communication exercises. A total of 215 couples aged >18 years were enrolled in the study. The mean age of the participants was 42 years. The study sample mainly consisted of lower-income racial/ethnic minorities. Key components included education about the importance of adherence to avoid viral resistance and maintain health, identifying patterns of nonadherence, developing communication and problem-solving strategies to overcome adherence barriers, optimising partner support and building confidence in the couple for achieving and maintaining improved adherence. In addition the intervention sought to help couples to address issues of sex and intimacy. The intervention was administered to each couple by a nurse practitioner through 45-60 min sessions held over 5 weeks. The study was conducted in the USA.

At 6 months there were statistically significant differences in adherence change between the 2 groups.

Statistically significant group differences in adherence change from baseline to week 8 in terms of proportion of prescribed doses taken (p=0.021) and proportion of doses taken within specified windows (p<0.001). At 3 months only the proportion of doses taken within specified time windows was statistically significant (p=0.028).

8.13.3.3 Telepsychiatry

Ruskin (2004) [229] compared patients being seen by a psychiatrist, either in person or by means of telepsychiatry, who had one of the following five diagnoses: major depressive disorder, dysthymic disorder, adjustment disorder with depressed mood, mood disorder due to a general medical condition, or depressive disorder not otherwise specified with negative results. One hundred and thirty one patients were enrolled in the study. Mean age of participants was 49.7 (sd=12.8) years. Treatment sessions lasted approximately 20 minutes and consisted of antidepressant medicine management, psycho-education, and brief supportive counselling. Treatment consisted of eight sessions with a psychiatrist over a 6-month period. This study was conducted in the USA.

There was no difference in the percentage of adherent patients between the two treatment groups.

8.13.3.4 Compliance Therapy

Kemp's (1996, 1998) [230] [200] RCTs from the Cochrane review, compared "compliance therapy" with supportive counselling sessions (serving as the control group) in patients with psychotic disorders with statistically significant results. Forty-seven patients aged 18 to 65 years were included in the 1996 study and 74 patients also aged 18 to 65 years in the 1998 study. Compliance therapy consisted of 4 to 6 sessions and was defined as, "…a strategy that borrows from motivational interviewing. During session 1 and session 2, patients reviewed their illness and conceptualized the problem. In the next 2 sessions, patients focused on symptoms and the side effects of treatment. In

the last 2 sessions, the stigma of medicine-taking was addressed [196]". This study was conducted in the UK.

At 12 months patients receiving compliance therapy received higher adherence ratings ($p< 0.001$) than those patients receiving non-specific counselling.

O'Donnell (2003) [231], a RCT from the Cochrane review compared "compliance therapy" with non-specific counselling (as the control group) in patients with schizophrenia, with negative results. The study included 94 patients aged between 18 and 65 years. The mean age for both of the groups was 32 years (s.d=9). The intervention lasted 5 sessions, each session lasting 30-60 minutes. It is reported that, "…the sessions covered a review of the patient's illness history, understanding of the illness and his or her ambivalence to treatment, maintenance medicine and stigma. Compliance therapy is a cognitive behavioural intervention with techniques adapted from motivational interviewing, other cognitive therapies and psycho-education." [196]. This study was conducted in Ireland.

There was no difference in terms of adherence between the two groups.

8.13.3.5 Multicomponent intervention

Pradier (2003) [232], a RCT from the Cochrane review, compared a combined educational and counselling intervention with a control condition in patients with HIV with positive results. The study included 244 patients aged >18 years. Median age of the participants was 40 years in the intervention group and 38 years in the control group. The intervention consisted of 3 individual sessions delivered by nurses lasting 45-60 minutes. The intervention was, "…founded on the principles of motivational psychology, client centred therapy and the use of an "empathic therapeutic to enhance participants' self efficacy". The intervention focused on cognitive, emotional, social and behavioural determinants affecting adherence." [196] This study was conducted in France.

Self-reported adherence between baseline and six months was statistically significantly improved in the intervention group, versus control. 75% of the

intervention group and 61% of the control group reported adherence at 6 months (p=0.04). Compared to 58% vs 63% at baseline (p=0.59).

Van Servellen (2005) [233] compared an enhanced adherence intervention with standard clinical care in patients (n = 85) taking antiretroviral medicines for at least 3 months with negative results. To be eligible to take part in this study participants must be able to speak Spanish. The enhanced adherence intervention consisted of two parts the first being modular instruction which was aimed at increasing patients HIV knowledge and ability to communicate with medical staff and was delivered over 5 sessions by health educators and nurses. These were followed up by case management sessions, delivered either face to face or via a telephone by a nurse, which concentrated on addressing the patient's potential or actual risks for nonadherence using motivational interviewing techniques. Content involved going over things misunderstood in the modular instruction stage, identifying barriers to adherence and finding strategies to challenge these and helping to find community, treatment and social support/referrals to help address adherence barriers. This study was conducted in the USA. There were no statistically significant differences between the group at 6 months.

8.13.3.6 Cognitive Behavioural Treatment

Antoni (2006) [220] compared cognitive behavioural stress management (CSBM) in addition to antiretroviral medicine adherence training (MAT) with MAT alone in patients with HIV with negative results. CSBM sessions included a didactic component, as well as group discussion, with opportunities provided to apply newly learned techniques. One hundred and thirty patients aged between 18 and 65 years were included in the study. The mean age was 41.6 (s.d=8.3) years. Homework was assigned to provide opportunities for participants to practice techniques and increase their self-efficacy. The treatment was focused extensively on eliciting participant experiences with adherence and medicine side effects. Throughout the 10-week, 135-minute group sessions (90 minute stress management and 45 minute relaxation), facilitators encouraged participants to examine potentially distorted cognitions and how these may influence adherence to HAART (as well as other relevant

self-care behaviours). During cognitive restructuring exercises, participants were asked to examine medicine-relevant thoughts both in session and through homework exercises. Adherence was also a key target during the skills training sessions. This study appears to have been conducted in the USA (not explicitly stated).

The experimental conditions did not differ statistically significantly in participant-reported medicine adherence throughout the 15-month investigation period.

Bechdolf (2004 and 2005) [217] [218] compared group CBT with group psycho-education (PE) in patients who had suffered an episode of a schizophrenia or a related disorder with negative results. Eighty-eight patients aged between 18 and 64 years were included in the study. Only a minority of patients were employed. Group CBT focused on assessment and engagement (sharing information about voices and delusions, models of psychosis), improving self-esteem, formulation of key-problems and developing interventions directed at reducing the severity and the occurrence of key problems, relapse prevention/keeping well and enhancing medicine compliance. There was a specific focus on the component "improving self-esteem" to foster feelings of hope and engagement with therapy. Group CBT involved 16 sessions in 8 weeks by a psychiatrist or clinical psychologist. This study was conducted in Germany.

Compliance was high initially (group CBT mean: 3.9 (s.d=0.3) vs. PE group: 3.8 (s.d=0.5)). At 8 weeks post-treatment, there was no statistically significant difference between groups (3.9 (s.d=0.3) vs. 3.7 (s.d=0.7)) nor at 6 months (3.5 (s.d=0.9) vs. 3.2 (s.d=1.0). This remained statistically non-significant when corrected for pre-treatment scores. At 24 month follow-up again no statistically significant differences were seen (3.4 (s.d=0.7) vs. 2.9 (s.d=1.1).

Weber (2004) [219], a RCT from the Cochrane review, compared cognitive behavioural therapy in addition to usual care to usual care alone in patients with HIV with negative results. The study included 60 patients, and the median age was 41 years. The intervention was delivered by a

psychotherapist. The Cochrane Review informs that, "…protocol defined a minimum of three and a maximum of 25 sessions within the one year study period. The participant and psychotherapist determined the frequency of appointments and set their own goals for future interventions. The intervention had to be based on concepts of cognitive behavioral therapy" [196]. This study was conducted in Switzerland.

There was no statistically significant difference in mean adherence between the two groups, but both groups had very high mean adherence rates (92.8% versus 88.9%), and a higher proportion of intervention group patients were at or above 95% adherence (70% versus 50%, p=0.014).

There was no difference in terms of adherence between the two groups.

Lam (2003) [222] compared cognitive therapy and minimal psychiatric care v minimal psychiatric care alone in patients with bi-polar disorder with positive results. One hundred and three patients with ages ranging from 18 to 70 years were enrolled in the study. Mean age was 46.4 (sd=12.1) years for the intervention group and 41.5 (sd=10.8) for the control group. Traditional cognitive therapy for depression was provided by clinical psychologists with new elements highlighting the need for combined psychological and medicine treatment, CBT skills for monitoring mood and preventing relapse and highlighting the importance of sleep and routine. The therapy also addressed illness beliefs. Cognitive therapy involved 12 to 18 individual sessions within the first 6 months and 2 booster sessions in the second 6 months. This study was conducted in the UK.

At 14 months, medicine adherence was 95.5% (sd=7.7%) in the cognitive therapy group and 69.1% (sd=16.4%) in the control group (p<0.001). Proportions of people who had at least 80% adherence rates were 97.4% in the cognitive therapy group and 21.7% in the control group (p< 0.001).

Gray (2006) [215] compared adherence therapy (AT) with health education (HE) (serving as the control group) in patients with schizophrenia with negative results. Adherence therapy is a brief, individual CBT approach. Six elements formed the core of the therapy: assessment, medicine problem solving,

medicine timeline, exploring ambivalence, discussing beliefs and concerns about medicine and using medicine in the future. Three hundred patients were included in the study, and the mean age was 41.5 (s.d=11.5) years. Key therapy skills that the therapists use included exchanging information, developing discrepancies between participant's thoughts and behaviours about medicines and working with resistance to discussing psychiatric medicine and treatment. The overall aim of process was to achieve a joint decision about the medicine. Participants were offered a maximum of 8 sessions lasting 30-50 minutes over a 5 month period and the intervention was delivered by 9 therapists (four psychologists, three psychiatrists and 2 mental health nurses). The study was conducted in 4 countries: The Netherlands, Germany, England and Italy.

At 12 months, there were no statistically significant differences between the groups using either patient assessment (AT group: 3.20 (s.d=1.07), HE group: 3.33 (s.d=1.02), 95% CI -0.35 to 0.08) or clinical assessment (AT group: 5.22 (s.d=1.57) HE group: 5.03 (s.d=1.55), 95% CI -0.12 to 0.52) of adherence.

Wagner (2006) [221] compared a cognitive behavioural treatment with an enhanced condition of the treatment (a 2 week pre-treatment practice trial) and a control group, for the effect on adherence to a new regime of antiretroviral therapy. The study included 230 patients with a mean age of 39 (ranging from 21 to 70 years), 80% were male, 49% were Latino(a) and 65% were unemployed. The study was set in the USA. The intervention involved five sessions of cognitive behavioural therapy. Questionnaires were administered and blood was drawn at screening (four weeks before treatment baseline), and periodically up to 48 weeks from the start of treatment. There was no difference in adherence between the intervention and the enhanced intervention group. There was initially a statistically significant increase in attaining 'good' adherence (90% of prescribed dose) for the intervention groups compared to the control group (82% versus 65%, p=0.01). The difference reduced in the following weeks and was not statistically significant. At week 48 the difference was reversed to 57% (intervention group) versus 65% (control group), but this was also statistically non-significant (p=0.52).

Wyatt (2004) [216] compared a cognitive behavioural approach (the Enhanced Sexual Health Intervention) to usual care for risk reduction and treatment adherence for 147 women who had HIV and a history of childhood sexual abuse. The mean age was 41 (s.d=8.2), 25-65 years, 51% were African American and 49% were Latina and primarily unemployed. The study was set in the USA. The intervention involved 11 weekly sessions for 2.5 hours per week of psycho-educational content relating to child sexual abuse and HIV status. They were followed up at the end of the 11 weeks and then again at 3 and 6 months. Although an effect was found for risk reduction there was no increase in adherence to medicine in the intervention group (75.6% versus 73.3%, OR=1.13, p=0.41). However a statistically significant effect was found for adherence for those who attended at least eight sessions (91.3%) compared to seven or fewer (49.7%), OR=4.90, p=0.044. The difference in adherence of the high attendees was 91.3% compared to the control group was 74.7%, this was statistically significant.

8.14 Would a contractual agreement between HCP and patient affect adherence?

Related references	Evidence statements (summary of evidence)
Bosch-Capblanch (2007) [234]	Evidence from one high quality systematic review of RCTs suggests that the use of contracts within a healthcare setting does not appear to increase adherence to prescribed medicine. These RCTs included hypertension (2 RCTs), acne, acute bacterial infection, asthma, depression, diabetes and tuberculosis. Only one RCT, for hypertension, and one RCT for acute bacterial infection, showed a statistically significant increase in adherence.

8.14.1 Evidence to recommendations

For general discussion of limitations of evidence see section 8.3.

It should be noted that patients with substance abuse issues are considered to fall outside the scope of this guideline and therefore are not included in this evidence review.

There is no evidence to show that contractual arrangements have any impact in improving adherence and the GDG did not wish to make a recommendation in this area.

8.14.2 Methods of the evidence review

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies - Randomised controlled trials (RCTs) of interventions to increase adherence. The excluded studies list from the Cochrane review was checked as we have included those studies with less than 80% follow-up of participants.

Types of participants - people prescribed medicine for a medical condition.

Duration of studies - six months follow-up from the time of patient entry for long-term regimens. No time limit specified for short-term conditions.

Types of interventions - any interventions intended to change adherence to prescribed medicine. As the Cochrane review is presented by condition, we have used the evidence extracted in that review and reconfigured it by intervention.

Types of outcome measures - inclusion criteria (as defined in the Cochrane review) were expanded by including studies that used adherence as the only outcome variable as opposed to adherence and treatment outcome variables. The excluded studies list of the Cochrane review was cross-referenced to ensure that no potentially relevant study was missed out.

8.14.3 Definitions of contracts

Contracts can be generically viewed as reciprocal agreements between two or more parties in which one or more will need to do something.

From a behavioural strategy perspective, a contract to increase patient's adherence can be defined as "a process of specifying a set of rules regarding some behaviour of interest and formalising a commitment to adhere to them" [21].

Contracts can be written or verbal. Most contracts are between healthcare practitioners and patients, but they may also occur between practitioners and carers, carers and patients or by a patient with him/herself.

8.14.4 Evidence review

We retrieved one Cochrane review that aimed to assess whether contracts between healthcare practitioners and patients had an effect on patients' adherence to treatment, prevention and health promotion activities Bosch-Capblanch (2007) [234]. Although this review included settings other than clinical settings, we decided to include this high quality systematic review of RCTs on the grounds that the results were reported in groups, thus allowing us to make conclusions from those settings relevant to the guideline. It also included other treatment groups that are outside the remit of the guideline, such as substance addiction treatments and interventions for hypertension and overweight without prescribed medicine. Other areas that were included were acne, acute bacterial infections, arthritis, asthma, breast self examination, contact lens care, depression, diabetes, phobias, promotion of healthy diet and exercise and tuberculosis.

The Cochrane review also assessed the effects of contracts on other outcomes, including patient participation and satisfaction, health practitioner behaviour and views, health status, harms, costs, and ethical issues.

Seven trials assessed contracts between HCPs and patients, nine trials assessed contracts between patients and carers, peers or others, and between HCPs and carers in one trial. Four trials assessed contracts between HCPs, patients and carers, two trials assessed self-contract and the other seven trials did not report which type of contract was being used. Twenty one trials included some type of financial incentive.

Several of the trials were of poor quality and included small numbers of people. Most were conducted in the USA and were conducted in specialised services.

Two trials that examined the effects of contracts in the context of hypertension management reported adherence outcomes. However, only one showed statistically significant results in favour of the group with contracts.

In the miscellaneous section, six trials in the contexts of acne, acute bacterial infection, asthma, depression, diabetes and tuberculosis reported adherence outcomes. However, in some cases it was not possible to determine whether adherence was also related to prescribed medicine or with an overall treatment regime (depression, and diabetes). From these, five trials did not report any statistical significance in favour of the contracts groups, whilst the acute bacterial infection trial reported statistically significantly better results (based on pill count) in the contract group. However, there was no difference between groups in self-reported adherence, nor in the number of additional prescriptions to finalise the treatment.

Based on the results for the trials that included an assessment of patients' adherence to medicine, the use of contracts does not appear to improve adherence.

Overall, the conclusions from the Cochrane authors state that there is limited evidence that contracts can have a positive effect in improving adherence. In addition they argue that there is insufficient evidence from large, good quality studies to routinely recommend contracts for improving adherence to treatment or preventive health regimens [234].

8.15 Does being involved in self-monitoring (e.g. of own blood pressure) increase adherence to prescribed medicine?

Related references	Evidence statements (summary of evidence)
Haynes (1976) [235]; Sadik (2005) [236]; Tsuyuki (2004) [237]	The majority of evidence suggests that involving patients in the self-monitoring of their medicine adherence (e.g. through recording adherence in diary logs) appears to increase adherence as part of a multi-component intervention.
Sadik (2005) [236]; Bailey (1990) [238]; Cote (1997) [239]; Cote (2001) [240]; Friedman (1996) [241]; Haynes (1976) [235]; Johnson (1978) [242]; Morice (2001)[243]; Peterson (1984) [185]	There is conflicting evidence in regard to whether having patients record information (e.g. in a diary log) relevant to their condition (e.g. symptoms) can increase adherence as part of a multi-component intervention.
Haynes (1976) [235]; Cote (1997) [239]; Morice (2001) [243]; Bailey (1990) [238]; Bailey (1999) [244]; Cote, (2001) [245].	There is conflicting evidence with regard to whether providing participants with information on how to adjust their treatment based on their own self-monitoring affects adherence.
Morice (2001) [243]; Cote (1997) [239]; Bailey (1990) [238]; Cote (2001) [245]; Levy (2000) [246]	There is conflicting evidence that involving patients more in their care through the self-monitoring of respiratory function through measurement of PEF increases adherence as part of a multi-component intervention.
Friedman (1996) [241]; Haynes (1979) [235]; Johnson (1978) [242]; Marquez-Contreras (2006) [247]; Rudd	There is conflicting evidence with regard to whether involving patients in the self-monitoring of their blood pressure improves adherence as part of a multi-component intervention.

(2004 [175]	

8.15.1 Evidence to recommendations

For general discussion of limitations of evidence see section 8.3

The evidence of the value of self-monitoring in increasing adherence was conflicting. The GDG considered that this was perhaps not surprising given that qualitative evidence had indicated that patients may use such measures to inform their own decisions and evaluations of treatments rather than to ensure they follow a previous decision. Self-monitoring is also used in conditions where the patient can alter treatment according to results and this group will have different characteristics and needs than a general patient group.

8.15.2 Methods of the evidence review

This paper includes a narrative summary of the included evidence, structured according to the category of the intervention, following the agreed reviewing protocol:

Types of studies - randomised controlled trials (RCTs) of interventions to increase adherence. The excluded studies list from the Cochrane review was checked as we have included those studies with less than 80% follow-up of participants.

Types of participants - people prescribed medicine for a medical condition.

Duration of studies - six months follow-up from the time of patient entry for long-term regimens. No time limit specified for short-term conditions.

Types of interventions - any interventions intended to change adherence to prescribed medicine. As the Cochrane review is presented by condition, we have used the evidence extracted in that review and reconfigured it by intervention.

Types of outcome measures – inclusion criterion (as defined in the Cochrane review) was expanded by including studies that used adherence as

the only outcome variable as opposed to adherence and treatment outcome variables. The excluded studies list of the Cochrane review was cross-referenced to ensure that no potentially relevant study was missed out.

8.15.3 Evidence review

Although a handful of studies were found which addressed self monitoring we did not find any study where the study interventions sole purpose was to address self monitoring (although arguably a few appear in the Cochrane review studies). Within the studies which did address self monitoring there was variability in how they did this and to what extent self monitoring was a focus of the intervention. Narratives of each study, which give full details of the entire intervention used in each individual study, are summarised below.

Tsuyuki (2004) [237] compared a patient support program with usual care in patients with heart failure with negative results. Seven hundred and sixty six patients aged above 18 years were enrolled in the study. The mean age of the patients was 74 years. Patients in the support group received educational material consisting of information about heart failure, non-drug treatment, medicine information (with special emphasis on proven benefits of therapies) and self-monitoring, all written at a grade 8 reading level. Patients also received adherence aids including a medicine organiser, medicine administration schedule, and daily weight log. Community follow-up in the patient support program consisted of telephone contact by the local research coordinator at 2 and 4 weeks and then monthly there after for 6 months after discharge. The telephone contact was to reinforce education and adherence relating to heart failure and other self-care activities, focusing on the 5 essential components: salt and fluid restriction, daily weighting, exercise alternating with rest periods, proper medicine use and knowing when to call their physician. This study was conducted in Canada. ACE inhibitor adherence over 6 months after discharge was 86.2 ± 29% in the usual care group vs. 83.5 ± 29% in the patient support group (p= ns).

Sadik (2005) [236] compared a pharmacist-delivered intervention with usual care in patients with heart failure with positive results. A total of 221 patients were enrolled in the study. Mean age of participants was 58 years. For the

intervention group patients the research pharmacist discussed with their physicians if rationalisation of medicine therapy or simplification of dosage regimens were considered appropriate. Intervention patients were also educated (in a structured fashion) on heart failure, their prescribed medicine and the management of heart failure symptoms by the research pharmacist. A printed booklet developed for this type of education programme was used and each patient was given a copy to take home. The booklet contained information on heart failure, its symptoms, the aims of treatment, the types of medicine used and their possible side-effects, diet and lifestyle changes, advice to stick to one brand of digoxin (it having a narrow therapeutic index) and information on the action to take if doses of medicine were missed. Intervention group patients were also instructed on a self-monitoring programme (signs and symptoms of heart failure; compliance with prescribed medicine) in which they were asked to become involved; a monitoring diary card (covering 1 month) was used. Patients were asked to complete their monitoring diary cards at home and to show them to their physicians when attending an appointment. The patients were asked to return their completed diary cards to the research pharmacist for review when they visited the hospital to receive medicine refills. Reinforcement of the educational message was carried out by the pharmacist as deemed necessary. This study was conducted in the United Arab Emirates.

The number of intervention group patients vs. control patients who exhibited self-reported compliance with the prescribed medicines (85 vs. 35) and lifestyle adjustment (75 vs. 29) was higher than in control group patients at 12 months ($p<0.05$).

Bailey (1990) [238], a study from the Cochrane review, compared a multi-faceted intervention with standard care in patients with recurrent episodes of wheezing with positive results. A total of 267 patients aged above 18 years were enrolled in the study. Patients in the intervention group were, "…provided with the standardised asthma pamphlets and were provided with a skill-oriented self-help workbook, a one-to-one counselling session, and were subject to several adherence-enhancing strategies, such as attending an

asthma support group and receiving telephone calls from a health educator. Physicians emphasised these skills at regular clinic visits." [196] The Cochrane review also states that the intervention included involving patients more in their care through self-monitoring of their respiratory function. This study was conducted in the USA. The intervention group were statistically significantly more adherent than the control group.

Bailey (1999) [244], a study from the Cochrane review, conducted a randomised controlled trial of asthma self-management. 236 patients stratified by moderate or severe asthma in Alabama, USA, were randomised to the University of Alabama Birmingham (UAB) asthma self-management group, the UAB core-elements group and usual care group. The core components involved a skill-oriented self-help asthma workbook, which the patients were counselled in for one hour. The participants also received 2 telephone calls and a letter at 1, 2 and 4 weeks to discuss problems and peak flow readings (see Bailey 1990). The core elements program involved a shorter version of the workbook of which counselling was given briefly (15-20 minutes). They were trained to use inhalers and peak flow meters. Participants were followed up by telephone a week later and a letter 2 weeks later. The usual care group received usual education from their GP and informational leaflets. There were no statistically significant differences between groups in adherence.

Cote (1997) [239], a study from the Cochrane review, compared two intervention groups and one control group in patients with moderate to severe asthma with negative results. A total of 188 patients aged above 16 years were enrolled in the study. The intervention was an "…asthma education program with an action plan based on peak-flow monitoring (Group P) or an action plan based on asthma symptoms (Group S). The control group (Group C) received instructions from their pulmonologists regarding medicine use and influence of allergenic and non-allergenic triggers. They were taught how to use their inhaler properly by the educator. A verbal action plan could be given by the physician. Groups P and S received the same education as the controls plus individual counselling with the specialised educator during a 1-hour session. All participants received a book titled "Understand and Control Your Asthma"

at no extra charge. Group P received a self-management plan based on peak expiratory flow (PEF). They were asked to continue measuring PEF twice a day and to keep a diary of the results. Each time, subjects only recorded the best of three measurements. Every attempt was made to ensure that patients knew how to interpret the measurement and how to respond to a change in PEF. At each follow-up visit, the patient's diary card was reviewed, and if the action plan had not been implemented when required, further explanations were given regarding when treatment should be modified. Group S received a self-management plan based on asthma symptom monitoring. These patients were asked to keep a daily diary of asthma symptom scores, using a scale of 0 (no symptoms) to 3 (night time asthma symptoms, severe daily symptoms preventing usual activities), and adjust their medicines according to the severity of respiratory symptoms using the guidelines of the action plan." [196] This study was conducted in Canada. Neither intervention had a statistically significant effect on participants' adherence.

Cote (2001) [245], a study from the Cochrane review, compared two different educational interventions with usual care for adult patients consulting with an acute asthma exacerbation with negative results. A total of 126 patients aged above 18 years entered the study. Patients in the Limited Education (LE) group were given a self-action plan that was explained by the on-call physician. The action plan used "traffic lights" (green, yellow, red) to describe specific states of asthma control based on Peak Expiratory Flow and symptoms and actions that the patient should take for each state. Patients in a "Structured Educational group (SE)", in addition to what patients in Group LE received, participated in a structured asthma educational program based on the PRECEDE model of health education. This model took into consideration three different issues that were important when dealing with health-related behaviours: predisposing factors (belief, attitude, knowledge), enabling factors (community resource, family support), and reinforcement. Reinforcement was provided at the 6-month follow-up visit and the teaching was provided individually or in small groups according to patient preference. Both intervention groups also received usual care." [196] This study was conducted in Canada.

Neither intervention had a statistically significant effect on participants' adherence.

Levy (2000) [246] compared a nurse-delivered intervention with usual care in patients with asthma (n=211) with positive results. The intervention group were, "…invited to attend a 1h consultation with one of the nurses beginning 2 weeks after entry to the study, followed by two or more lasting half an hour, at 6-weekly intervals. The second and third could be substituted by a telephone call. Patients were phoned, by the nurse before each appointment in order to improve attendance rates. Patient's asthma control and management were assessed followed by education on recognition and self-treatment of episodes of asthma. The patients were taught to step-up medicine when they recognised uncontrolled asthma using PEF or symptoms. The advice was in accordance with national guideline. Prescriptions were obtained from one of the doctors in the clinic or by providing the patient with a letter to their general practitioner. Patients presenting with severe asthma (severe symptoms of PEF below 60% of their best/normal) were referred immediately to the consultant." [196] This study was conducted in the UK

Self-reported compliance was statistically significantly higher in the intervention group for use of inhaled topical steroids and rescue medicine for severe asthmatic attacks, but there was no statistically significant difference between the groups for use of these medicines for mild attacks.

Friedman (1996) [241], a study from the Cochrane review, compared a telephone-linked computer system (TLC) intervention for monitoring and counselling patients with usual care in patients with hypertension with positive results. Two hundred and sixty seven patients aged ≥ 60 years were recruited for the study. The mean age was 76 years for the TLC group and 77 years for the usual care group. TLC is, "…an interactive computer-based telecommunications system that converses with patients in their homes, using computer-controlled speech, between office visits to their physicians. The intervention patients would call the TLC on a weekly basis. Before calling, subjects would record their own blood pressure using an automated sphygmomanometer with a digital readout. During the conversation, subjects

would answer a standard series of questions and the TLC would provide education and motivational counselling to improve medicine adherence. The TLC then transmitted the reported information to the subject's physician". [196] This study appears to have been conducted in the USA.

The unadjusted results did not demonstrate a statistically significant improvement in compliance or clinical outcome in patients using TLC as compared to those patients receiving usual care. However, when the data were adjusted for age, sex, and baseline adherence, the patients using TLC demonstrated a greater improvement in medicine adherence than those receiving usual care ($p<0.05$). Sub-group analysis showed, in people who were nonadherent at baseline, patients using TLC had greater improvement in medicine compliance ($p<0.05$) than those receiving usual care. In people who were adherent at baseline, TLC showed no statistically significant difference in adherence between the two groups over the course of the trial.

Haynes (1976) [235], a study from the Cochrane review, compared a multi-component intervention with usual care in patients with high blood pressure with positive results. Thirty nine patients were enrolled in the study. It is not clear from the study the ages of the patients. Patients in the intervention group were, "…all taught the correct method to measure their own blood pressures, were asked to chart their home blood pressures and pill taking, and taught how to tailor pill-taking to their daily habits and rituals. They also visited fortnightly (at the worksite) a high-school graduate with no formal health professional training who reinforced the experimental manoeuvres and rewarded improvements in adherence and blood pressure. Rewards included allowing participants to earn credit, for improvements in adherence and blood pressure, which could be applied towards the eventual purchase of the blood pressure apparatus they had been loaned for the trial". [196] This study was conducted in Canada. There was a statistically significant increase in adherence associated with the intervention.

Johnson (1978) [242], a study from the Cochrane review, compared four groups (1) self-recording and monthly home visits, (2) self recording only, (3) monthly home visits, and a control group consisted of (4) neither self-recording nor

home visits with negative results. One hundred and forty patients aged between 35 and 65 years were included in the study. Patients receiving antihypertensive medicines were studied. Participants, "…in groups (1) and (2) received a blood pressure kit and instruction in self-recording. Patients in the self-recording groups were to keep charts of their daily blood pressure readings and were instructed to bring these charts to their physician at each appointment. Subjects in groups (1) and (3) had their blood pressure measured in their homes every four weeks, and the results were reported to both the patient and the physician" [196]. This study was conducted in Canada. There was no effect on adherence from either intervention.

Marquez-Contreras (2006) [247], included in the Cochrane updated review, conducted a randomised controlled trial of a programme of home blood pressure management (HBPM) in patients with mild-to-moderate arterial hypertension. This study was conducted in 40 primary care centres in Spain. 250 patients were included with data for 226. Mean age of participants was 59 years, and around 50% females/males. The no. of diseases was statistically significantly higher in the intervention group 2.6 (s.d=1.6) vs 2.2 (s.d=1.2), p=0.023). Patients in the control group received usual GP care and the intervention group received the intervention from GPs plus an OMRON automatic monitor for HBPM. The programme was measuring their blood pressure 3 days a week (Tuesdays, Thursdays and Saturdays), twice before breakfast and twice before supper and record the results on a card. 74% of the control group and 92% of the intervention group were compliant (measured by MEMS) (95% CI 63.9 to 84.1 and 86.7 to 97.3, p=0.0001); the mean percentage compliances were 87.6% for the control group and 93.5% for the intervention group (95% CI 81.2 to 94.0 and 88.7 to 98.3, p=0.0001); the percentage of days the medicine was taken correctly were 83.6% and 89.4; the percentages of participants taking medicine at the correct time was 79.89 vs. 88.06.

Rudd (2004) [175] (included in the Cochrane updated review) conducted a RCT of a system for patients to monitor their own blood pressure. Patients of two medical clinics in California were randomised to receive routine care (n=76) or

an automated blood pressure device at home with management by a nurse care manager (n=74). The mean age for the intervention was 59 and 60 for the control group. Fifety percent of the intervention and 56% of the control group were female. Patients recorded their blood pressure twice a day at the same time using the semi-automated portable device. At the end of the week the device printed a report of up to 14 measurements and every two weeks patients were to mail the values on the printout to the nurse care manager who used the data to guide medicine therapy. Any new blood pressure medicine initiation was requested from the doctor. The primary outcome was change of BP at 6 months. Secondary analyses were made for frequency of medicine changes and adherence. Adherence was measured by a medicine event monitor (a microchip in the pill bottle lid of the most frequently used medicine) and the patients were required to return to the clinic at 3 and 6 months so this data could be downloaded, although this was not used as feedback to patients, physicians or nurse care managers. The mean daily adherence rate was 80% (s.d=23%) for the intervention group and 69% (s.d=31%) for the control group, p=0.03).

Morice (2001) [243], a study from the Cochrane review, compared an asthma nurse-led intervention with routine care in patients with asthma with negative results. A group of 80 patients (53 women) aged between 16 and 72 years were included in the study. Mean age was 36.1 years. Compared with the control group, patients in the educational intervention group had a minimum of two separate sessions, lasting on average 30 minutes each. These were carried out on an individual basis. The first session involved discussion on the basic mechanisms of asthma, including common triggers and an explanation of the changes which occur to the airways resulting in the symptoms experienced by the patient. This was supported by illustrations in the 'Regular Therapy with Asthma' booklet which was given to each intervention group patient. Lifestyle influences, such as occupation and leisure activities were discussed where appropriate to the individual. The need for 'preventer' and 'reliever' medicine was also emphasised during this session. Patients were encouraged to actively participate in the session and relatives were included at the patients' request. The second session took place on the following day.

Previously given information was briefly summarised with input from the patient as a means of checking understanding. An agreed individualised self-management plan was determined, with written instructions using the 'Sheffield Asthma Card'. This also contained a telephone contact number. Each patient was given a peak low meter to take home and instructions on monitoring, with documentation of predicted peak low measurement and parameters for altering treatment, as well as clear written guidelines on when to seek emergency care. Home intervention was based upon a combination of symptoms, and peak low recordings, and all guidance offered throughout the educational programme was based on the BTS guidelines for the management of asthma in adults [196]. This study was conducted in the UK. There were no statistically significant improvements in compliance at six months.

9 Reviewing medicines

9.1 Recommendations

Hyperlink to Reviewing Medicines

9.2 Introduction

Review of medicines and medicine-taking is seen as an important aspect of health care. Professionals involved in prescribing and dispensing of medicines are currently reimbursed for reviewing medicines. General practitioners in the UK are remunerated for medicine review via the Quality and Outcomes Framework (QOF). Community pharmacists are reimbursed for carrying out reviews which are called Medicines Use Reviews (MURs). The Dispensing Review of Use of Medicines (DRUM) is part of the Dispensing Services Quality Scheme for GP surgeries.

The terminology in this area is not standardised and is subject to change. The Medicines Partnership Programme [8] defined medicine review as 'a structured, critical examination of a patient's medicines with the objective of reaching an agreement with the patient about treatment, optimising the impact of medicines, minimising the number of medicine-related problems and reducing waste'. It is implicit in this definition that the patient is involved. In 'Room for Review' in 2002 they suggested four levels of medicine review – level 0 which is an ad-hoc opportunistic review; level 1 a prescription review which is a technical review of a patients list of medicines; level 2 is a treatment review which is a review of medicines with the patients full notes and level 3 which is a clinical medicine review which is a face-to face review with patients of medicine and condition. A review with the patient's notes but not necessarily with the patient (as in level 2 as described above) fulfils the criteria for QoF. An MUR is described as a one-one conversation between people and pharmacists that are designed to identify any problems a person is experiencing with their medicines (Pharmacy in England White paper 2008) [2]. Community pharmacists carrying out these reviews will not generally have

[8] http://www.npc.co.uk/med_partnership/assets/room_for_review.pdf

access to clinical information about patients. The recent Pharmacy in England White Paper (2008) [2] reports that many people report satisfaction with this service but longer term impacts can not be assessed. The White Paper reports that government plans for MUR services to be prioritised to meet health needs and ensuring funding rewards health outcomes.

The National Prescribing Centre has recently revisited the topic in A Guide to Medicine Review (2008). The guide aims to advise those providing and commissioning medicine reviews. This characterises 3 types of medicine review with an emphasis on the purpose of the review: Type 1 prescription review; Type 2 concordance and compliance review and Type 3 clinical medicine review. The three types of medicine review replace the earlier levels of medicine review. This reclassification appears to make clearer the role of the review and the place of the patient and clinical information in different types of review.

The GDG were interested in whether there was any evidence that medicine review improved either shared decision-making or adherence. In this context medicine review has to involve a face-to-face meeting with professionals and patient. The professional involved was not pre-defined. The evidence search used ‘medicine review’ as a generic term.

9.3 Does medicine review increase shared decision–making or adherence?

Related references	**Evidence statements (summary of evidence)**
All retrieved evidence	There is conflicting evidence with regards to whether medicine review increases adherence.
Lowe (2000) [248]; Sturgess (2003) [249]; Bernsten (2001) [250]; Begley (1997) [251]; Nazareth (2001) [252]	Four RCTs conducted in the UK shows that medicine review increased adherence to prescribed medicine. One RCT showed no statistically significant difference in adherence.
Lipton (1994) [253]; Hanlon (1996) [254]; Chisholm (2001) [210]; Taylor (2003) [255]; Grymonpre (2001) [256]; Sookanekun (2004) [257]	There is conflicting evidence from six RCTs conducted outside the UK that medicine review increases adherence to prescribed medicine.
Grymonpre (2001)[256]	Medicine review was carried out by pharmacists in all of the RCTs, except for one RCT where a trained volunteer undertook the review which was then reviewed by a pharmacist consultant.
Lowe (2000)[248]; Hanlon (1996)[254]; Grymonpre (2001)[256]; Nazareth (2001)[252]; Taylor (2003)[255]; Bernsten (2001) [250]; Begley (1997) [251]; Sturgess (2003)	Most of the RCTs included only participants over 65 years old.

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9.3.1 Evidence to recommendations

The GDG considered that review of prescribed medicines is most commonly undertaken in clinical settings as part of management of patients and their medical problems. In this setting it is seen as integral to continuing care and not separate from it. The GDG considered that all levels of medicine review as described in 'Room for Review' take place in this setting and have a role. Revisiting a decision to prescribe medicines and exploring patients medicine-taking behaviour was considered by the GDG to be part of the dynamic process that long-term medicine prescribing required.

The research evidence primarily addresses medicine reviews that take place separate from the delivery of clinical care, often by practitioners who do not have access to clinical history and notes. These have been a recent development and have primarily involved pharmacists. Most of the evidence on reviews by pharmacists comes from studies that targeted older adults on multiple medicines. Many studies include quite complex pharmaceutical care programmes where the interventions consists of a number of components including education and follow-up which the GDG considered more intensive than is currently provided in any type of medicine review provided in the UK.

Medicine review can have benefits for the patient but evidence was conflicting whether this led to improvements in adherence to prescribed medicine.

The GDG were particularly concerned that reviews of medicine carried out remote from the clinical settings needed to feed back to clinicians who were involved in prescribing and other aspects of care. Increasing the number of medicine reviews and the personnel involved in carrying them out might not be effective if communication and follow up is not achieved.

The GDG were clear that the lack of research on reviews conducted as part of clinical care should not indicate that these were not of value. Review of medicines will continue to be part of delivery of health care. As responses to medicine can change over time, both in terms of patient behaviour

(adherence) and clinical outcomes, a process of medicine review is likely to be necessary and be part of on-going processes of decision-making and medicine-taking. An informal review of medicine should continue as part of good clinical practice but it is not possible to recommend precise timings for formal medicine reviews outside the clinical setting.

9.3.2 Methods of the evidence review

The titles and abstracts of studies retrieved by an electronic search for medicine review were scanned for relevance to the question of whether medicine review increases adherence to medicines. Any potentially relevant publications were obtained in full text. These were then reviewed to identify the most appropriate evidence to help answer the question and to ensure that the recommendations are based on the best available evidence. This process required four main tasks: selection of relevant studies; assessment of study quality; synthesis of the results; and grading of the evidence.

This paper includes a narrative summary of the included evidence, following the agreed reviewing protocol:

Types of studies - randomised controlled trials (RCTs) of medicine review interventions to increase adherence.

Types of participants - people prescribed medicine for a medical condition. Medicine review performed by any healthcare professional or trained personnel.

Setting - carried out in the community.

Duration of studies - no time limit specified for this evidence review.

Types of interventions - any medicine review (as implying face to face meeting between the patient and the health care professional doing the review) interventions intended to change adherence to prescribed medicine. The content and delivery of interventions are not standardised in the literature. The term ‘pharmaceutical care programme’ is used and this applies to pharmacist led programmes which assess medicine use, develop an

intervention and provide long term follow-up to patients including liaison with the prescriber. Some of these interventions provide intensive support. Some subjective assessment of studies was required as content is often not well defined. Many of studies on interventions to increase adherence used pharmacists to carry out the intervention but we have included here only studies that were carried out in the community and were providing general review rather than disease specific support.

Types of outcome measures - any prescribed medicine adherence outcomes which changed as a result of the medicine review. Outcomes relevant to patient involvement were reported as part of the evidence review.

9.3.3 Evidence review

Of the RCTs found relating to medicine review, many had to be excluded as they did not have adherence outcomes. Instead they focused on hospital re-admissions, care home admissions, death and cost-effectiveness. One high quality RCT conducted by **Zermansky (2002)** [258] for HTA could not be included as there were no specific adherence outcomes. Zermansky (2002) studied whether a trained pharmacist could conduct effective clinical medicine reviews of elderly patients who were on repeat prescriptions from their GP. The participants were 65 years or over on repeat medicine, who were not resident in a nursing or residential home and were not terminally ill. The study lasted 12 months and the intervention involved the pharmacist assessing the patient, their illnesses and their medicine regimen and making recommendations. The primary outcome measure was the number of repeat medicine changes per patient, which was 2.2 in the intervention group and 1.9 in the control group (Difference of 0.31, 95% CI 0.06 to 0.57), p=0.02). The secondary outcome was the effect on cost of medicine. There was a rise in repeat medicine items for both groups, but this was statistically significantly less for the intervention group (intervention mean 0.2, s.d=1.55; control mean 0.4, s.d=1.53, difference -0.2, 95% CI, -0.4 to-0.1). The cost saving for the intervention group compared to the control group was £4.75 per 28-day month, a total of £61.75 per patient per year.

A systematic review **(Holland 2007)** focusing specifically on pharmacist-led medicine review was found. However the primary outcome of interest was reduction of hospital admissions and deaths in older people and adherence was a secondary outcome. The studies included all forms of medicine review for checking and optimising the patients' medicine regimens apart from those with only knowledge and/or adherence outcomes. They reported that 14 of the trials included adherence, with 7 reporting a statistically significant effect and 7 reporting a statistically non-significant positive effect.

The term 'pharmaceutical care programme' is also used in the literature and this generally applies to pharmacist-led programmes which assess medicine use, develop an intervention and provide long term follow up to patients. Although more intensive that any programmes currently delivered in the UK we included these studies as it was important to assess whether such structured and intensive support was either clinically or cost-effective.

Some subjective assessment of the studies was necessary as the content of the reviews and pharmaceutical programmes is not always clearly defined.

9.3.3.1 RCTs conducted in the UK

Sturgess (2003) [249] measured a structured pharmaceutical care programme provided to elderly patients by community pharmacists 191 elderly patients with a mean age of 73.1 ± 5.0 for the intervention group and 74.2 ± 6.3 for the control group. This RCT was conducted in Northern Ireland. In the intervention pharmacists assessed patients to identify medicine-related problems. A number of information sources were used by intervention pharmacists during this assessment procedure including: the patient (via informal questioning), the patient's GP, study questionnaires and computerised medicine records. During the assessment, pharmacists were asked to document any identified medicine-related problems and to form with the patient an intervention and monitoring plan e.g. education, implementation of adherence improving strategies. Pharmacists visited patients at home to assess storage of medicines where problems were identified.

Self-reported compliance: between-group analysis at each assessment point indicated that a statistically significantly higher proportion of intervention patients were compliant with their medicine at 12 (intervention group: 40.4%, control group: 24.4%) and 18 (intervention group: 47.3%, control group: 14.7%) months compared to control patients ($p<0.05$) (6 months: intervention group: 34.5%, control group: 29.4%). Analysis of change in compliance during the study (change in compliance status compared to that reported at baseline) showed that a statistically significantly higher proportion of intervention patients changed from non-compliant to compliant compared to control patients (intervention 13.4% vs. control 9.1%) and a statistically significantly higher proportion of control patients changed from compliant to non-compliant compared to intervention patients at 18 months (control 36.4% vs. intervention 4.5%).

Lowe (2000) [248] determined whether a medicine review and education programme influenced elderly patients' compliance and knowledge compared to a control group in a RCT. 161 participants, mean age 77.5 (sd=65-96) for the intervention group and 75 (sd=65-88) for the control group, mainly female (67%), living with spouse or relative 55% (intervention group) and 57% (control group) and prescribed an average of 4 medicines (ranging from 1 to 8). The RCT was conducted in a GP practice in Leeds, UK. An investigator visited patients and filled in a structured questionnaire regarding their medicines, which medicine had been used and patients' understanding and ability to take medicines. The investigator then reported the findings to doctors where there was a need to reduce dosage and discontinue medicine, then liaised with the pharmacist for modifications to medicine containers. At the second visit after a month they delivered 1 months supply of medicine and removed any other prescribed medicines. They discussed the regimen, the purpose of the medicines and the correct way to take them, with the use of a reminder chart if needed. At 3 weeks follow-up participants were given a further months supply and assessed on their knowledge and compliance, by counting the medicines left from the last visit. The mean compliance score was 91.3% for the intervention group (95% CI, 89% to 94%) and 79.5% for

the control group (75% to 84%), which was statistically significantly different ($p<0.0001$).

N.B This study was under 6 month's duration but the patients were followed up twice at 3 week to monthly intervals and the study was of particular relevance.

Begley (1997) [251] assessed the influence of domiciliary pharmacy visits on medicine management in sample of elderly people recently discharged from hospital to their own homes. Patients were aged 75 years or older. The study included one intervention group receiving home visits and counselling, in which structured patient interviews were conducted during the domiciliary visits and consisted of six sections: patient information; medicine knowledge; Patient dexterity; abbreviated mental test; medicine management; and compliance with medicine regimen. Patients were seen during 12 months. There were two control groups: one which was the control and received visits only (called V group), and other which was the control group that received traditional pharmaceutical services with no visits except for the beginning and the end of the study (NV group).

At each visit there were statistically significant differences between the groups in terms of distribution of patients at the various levels of compliance ($p<0.001$). Compliance was higher at 3 months and 12 months for the intervention group compared to the other control groups ($p<0.001$), despite the low compliance value for the intervention group at the 12 month visit. Patients in the intervention group who increased their compliance rates between visits also increased their medicine knowledge scores ($p<0.005$). Mean scores for medicine knowledge did not differ significantly (statistically) between the groups at any of the visits, although the mean score for the intervention group increased significantly (statistically) between the initial and the two weeks visits ($p=0.001$). There were no changes for patient dexterity scores between groups at any point of the study. Contacts with GP and health workers was lower for the intervention group than for the control (V) in each of the four time periods ($p<0.01$).

Bernsten (2001) [250] conducted a multicentre RCT in seven European countries including the UK that evaluated a pharmaceutical care programme provided to elderly patients (aged 65 or older) taking 4 or more medicines by community pharmacists. A total of 1290 intervention patients and 1164 control patients were recruited. The programme interventions included: 1) educating the patient about their medicine regimen and their condition; 2) implementing compliance-improving interventions such as medicine reminder charts; 3) rationalising and simplifying medicine regimens in collaboration with the patients GP. This was a continuous process throughout the 18 months of the study.

Generally, the programme had some positive effects on humanistic health outcomes such as satisfaction with treatment, and sign and symptom control, and on economic outcomes, but had less impact than anticipated on medicine therapy, medicine knowledge and compliance with medicine. An analysis of changes in compliance during the study indicated that at 18 months a statistically significantly higher proportion of the intervention patients changed from being noncompliant to compliant compared with the control groups ($p=0.028$). Intervention patients rated the services provided higher that the control at 6 and 18 months ($p<0.05$). There was a small statistically significant increase in satisfaction in the intervention group over time (baseline vs. 12 months $p=0.039$).

Nazareth (2001) [252] compared patients who had been discharged from hospital with a discharge plan with those who had a standard discharge letter. This RCT included 362 patients from four hospitals in central London. The participants had a mean age was 84 years in both groups (s.d=5.2 and 5.4 respectively), mainly female (62% and 66%), white (97%) with a mean of three chronic medical conditions and prescribed a mean of 6 medicines (s.d=2). The discharge plan included assessing the prescribed medicine, rationalising the medicine and assessing patients' medicine management, knowledge and support. The participants were then followed up 7 to 14 days later at home by community pharmacists who compared medicine-taking with prescribed medicines and their understanding and adherence to the medicine

regimen. They intervened when necessary and provided medicine counselling, disposal of excess medicines and liaison with GPs. There was no statistically significant difference in adherence to medicines for either group at 3 months or at 6 months.

9.3.3.2 RCTs conducted outside the UK

Lipton (1994) [253] assessed the impact of clinical pharmacists' consultations on medicine regimens, compliance, and health service use of 706 geriatric hospitalized patients discharged on 3 or more medicines. The RCT was conducted in the USA. Mean age was 74.6 in the experimental group and 74.4 in the control group. Pharmacists consulted with experimental patients at discharge and 3 months thereafter, and with physicians as needed. Controls received usual care. At 6-8 weeks after enrolment, experimental patients were more knowledgeable about regimens than controls. At 12-14 weeks, they were on fewer medicines and less complex regimens, and had better compliance scores $p<0.001$). There was no effect on service use or charges, perhaps due to inadequate sample size and lack of targeted medicine group's analysis.

Hanlon (1996) [254] was an RCT which compared the effects on elderly outpatients who had an additional pharmacist intervention with those who received usual care from their physician. Most of the patients were male (98% in the intervention and 100% in the control group), white (79% and 75% respectively), married (65.7% intervention, 85.4% control), with baseline compliance rates of 73% and 74% respectively. The mean age of participants was 70 years old. The RCT was conducted in Durham, North Carolina. Before attending the physician the pharmacist reviewed their medical records and medicine lists to ascertain their current medicine use, medicine-related problems and to evaluate their needs by applying the Medicine Appropriateness Index. Their findings were then reported to the physician. The Pharmacist educated the patient on medicine-related problems and encouraged compliance through strategies such as medicine reminders and written patient materials. They reviewed safe medicine use and the importance of discussing medicines with physicians. There were no

statistically significant differences between the groups at the end of the follow-up period with regard to medicine compliance (77.4% of intervention group and 76.1% of control group complied, p=0.88).

Chisholm (2001) [210] studied the compliance rates of patients who received a clinical pharmacist intervention in addition to usual care compared to control patients after a renal transplant. The RCT included 24 participants, 75% male with a mean of 49 years (s.d=10 years) and 58.3% Caucasian, 37.5% African-American and 1 Hispanic. The RCT was conducted in Augusta, Georgia, USA. The Pharmacist obtained medicine histories and reviewed medicines monthly. They made recommendations to the nephrologists and counselled the patients on their medicine, including instructing how to use the medicine. Patients were encouraged to call them with any questions. The patients were assessed on their understanding of their medicine and advised on how to enhance compliance.

At 12 months the compliance rate was statistically significant for the intervention group 96.1% (s.d=4.7%) compared to the control group 81.6% (s.d=11.5%), p<0.001. For 6 of the 12 months there were differences in compliance rates (64 to 100% for control group and 89 to 100% for the intervention group) with the intervention group always at a higher rate (p<0.05). The duration that patients complied for also differed with the intervention group remaining 75% compliant each month compared to only 33.3% of the control group (p<0.05).

Taylor (2003) [255] conducted an RCT of patients attending a community-based physician and compared those who additionally received a Pharmacist intervention to a control group. The majority of participants were women (63.6% in the intervention group vs 72.2% in the control group, p=0.445), most were white (60.6% vs 61.1%, p=.966) with a mean age of 64.4 and 66.7 years respectively (p=0.467), the majority were married 75.8% vs 72.2 (p=0.935) with 12 years mean education. They were taking on average six medicines each. The RCT was set in medicine clinics in Alabama, USA.

The pharmacists evaluated the patients' medicine, reviewed medical records and examined medicine history to determine compliance and complications with medicine. Therapeutic recommendations were made to the physicians and the pharmacists made follow-up visits to patients, gave individualised education and were available to answer questions. Patients' responses to medicines were monitored and their medicine regimens consolidated, dosage frequency was reduced and medicine reminders and techniques for using certain devices were taught.

The number within the intervention group to have compliance scores of 80-100% increased by 15% but there was no change for the control group (time period not stated). By 12 months this difference was not statistically significant, 100% of patients in the intervention group versus 88.9% (s.d=6.3) of the control group had compliance scores of 80-100%, p=0.115). At baseline this was 84.9% (s.d=6.7) and 88.9% respectively (s.d=5.8, p=0.728).

The most frequently sited reasons for not complying with medicine were forgetting to take the medicines (n=10), having too many to take (n=9), finding it hard to read or understand the directions (n=4) and too much trouble to take (n=4).

Grymonpre (2001) [256] compared the impact on geriatric patients who received pharmaceutical care compared to those patients who did not in a RCT. Most of the patients were female (75% intervention vs 83% control, p=0.254), aged 77 (s.d=8.0 to 9.0), Caucasian (100%) and lived alone 61% vs 77% respectively, p=0.018. The RCT was conducted in a community-based health clinic in Manitoba, Winnipeg, Canada. Volunteers and staff were trained to conduct a comprehensive medicine review which was utilised by the pharmacist to identify and document potential and actual medicine-related issues and to address these with the patient and they physician. Their use of prescribed and non-prescribed medicines, social medicines, home remedies, regimen, adherence and communication with GPs, problems or side effects with medicines were all assessed. The recommendations were given in a letter to physicians and the patients were followed up by the pharmacist when

required to monitor therapeutic endpoints and sort out any problems that had arisen.

The mean number of mediations adhered to at follow-up was 87 ± 46 for the intervention and 85 ± 41 for the control group, p=0.895, showing no statistically significant difference in adherence.

Sookaneknun (2004) [257] compared hypertensive patients assigned to a pharmacist-involved group with those who had no pharmacist involvement, with the objective of stabilising blood pressure. The participants of the RCT included 235 patients, mean age 63 years old and mainly female (64% in intervention and 71% in control group). The RCT was conducted in Thailand. The intervention group's blood pressure was measured every month by the pharmacist and they assessed the patients understanding of medicines, adherence and reviewed adverse effects from the medicines. Medicine counselling was given and medicine-related problems were identified, resolved and prevented. The recommendations for change of medicine regimen were given to the physicians. The adherence at pre-test was not statistically significantly different but at post-test the treatment group had statistically significantly increased adherence compared to the control group, Pre-test adherence of 80% or more was found in 51% of the treatment group and 56% of the control group. At post-test this had increased to 63% for the treatment group and had remained constant (55%) for the control group (p=0.014).

Quality of studies

The quality of many of the RCTs was low. This was mainly due to the possibility of bias occurring within the methodology.

10 Health economics and interventions to increase adherence

10.1 Introduction

Health economics is about improving the health of the population through the efficient use of resources. Economic evaluation provides a formal comparison of benefits and harms as well as the costs of alternative health programmes. It helps to identify, measure, value and compare costs and consequences of alternative treatment options. These outcomes are usually synthesised in cost-effectiveness (CEA) or cost-utility analysis (CUA), which reflect the principle of opportunity costs. For example, if a particular treatment strategy were found to yield little health gain relative to the resources used, then it could be advantageous to re-deploy those resources to other activities that yield greater health gain for the population.

The application of health economics in medicines concordance is more complex and is not as well developed as it is in its more common application to health technology assessment. There is considerable heterogeneity in the course and nature of diseases, in the types of health technologies (medicines, devices etc) used to treat them, and in the nature of possible interventions which may help to improve either decision-making or adherence.

We found that most health economic papers use adherence and compliance interchangeably, despite the conceptual difference in meaning found in the non health economic literature. In a recent economic review paper [259], the authors state that “compliance and adherence imply patient behaviour being congruent with healthcare providers’ recommendation”. In accordance with this guideline, this chapter will use “shared decision making” (SDM) to describe “a patient centred process where health care professional (HCP) makes a therapeutic alliance with a patient,” and adherence for describing “medicine-taking behaviour congruent with prescriber’s recommendation”. From a health economic perspective the concepts of persistence and forgiveness are potentially more valuable. Persistence is the length of time from initiation to discontinuation of therapy and forgiveness the benefits of a

medicine that persist even when a dose is missed. Health economics perspectives on SDM are discussed in chapter 4.

When considering the costs of interventions to increase adherence from the perspective of the NHS, a health economic evaluation will consider both the direct costs of the intervention itself, and the implications for resource use in terms of use of medicines and health services. The interventions could include, but not necessarily be limited to, one or any combination of the following: devices; packaging; or additional contact time with health care professionals.

The measurement of benefit of adherence enhancing interventions is likely to focus on the measurement of the health benefits derived from any improved adherence to the medicines themselves. The level of benefit will depend on both the effectiveness of the adherence enhancing intervention itself, and on the dose-response related efficacy of the medicine(s) (net of any disbenefits from any adverse events).

In order for an adherence enhancing intervention to be cost-effective from the perspective of the NHS for example, an economic evaluation would need to demonstrate that the intervention impacts on adherence in such a way that brings about a beneficial change in health gain at an acceptable cost or ideally a net cost saving. In accordance with NICE social value judgement criteria, interventions are usually considered to be cost-effective if:

a) The intervention dominates other relevant strategies (that is, it is both less costly in terms of resource use, and more effective compared with the alternative); or
b) The intervention has an incremental cost-effectiveness ratio (ICER) of less than £20,000 per quality-adjusted life-year (QALY) gained, compared with the next best strategy. For interventions with an incremental cost per QALY between £20,000 and £30,000 the probability of the intervention being considered cost-effective will diminish as the ICER rises.

All else being equal, adherence-enhancing interventions for medicines which are less 'forgiving' to nonadherence (**Urquhart, 1996)** [260] (**Girvin, 2004**) [261], for example, will have a higher threshold for them to be considered cost-effective compared to interventions for more 'forgiving' medicines.

The evidence on effectiveness of adherence enhancing interventions is of poor quality overall and provides inadequate evidence on long term follow-up and clinical endpoints. This guideline is a general guideline so given these complexities, and given the time available for development of this Guideline, it was not deemed possible or appropriate to try to develop de novo models designed to estimate the cost-effectiveness of interventions to improve adherence to medicines. Instead, we present an overview of the current literature which we consider to be relevant to the Guideline. In short, the available literature is primarily concerned with reviews of health economic analyses of interventions to improve adherence, whilst other reviews have addressed methodological issues around conducting evaluations concerned with measuring the impact of nonadherence on the cost-effectiveness of medicines.

This chapter is primarily concerned with presenting the methods and the results of literature reviews investigating the cost-effectiveness of adherence enhancing interventions. This is followed by a summary and discussion of the findings including a discussion of some of the methodological issues arising from the reviews. The GDG used the evidence from the reviews when considering the possible cost-effectiveness implications of their recommendations.

10.2 Which Interventions are cost effective in increasing adherence/compliance?*

Related References	***Evidence Statements (summary of evidence)***
Elliott (2005) [259]; Cleemput (2002) [262]; Hughes (2001) [263]	The evidence from the SRs revealed that a meaningful conclusion from a comparison across studies could not be achieved due to heterogeneity and the general poor quality of included studies. Definitions given for nonadherence were inadequate. Where adherence outcomes were reported, adherence measures varied greatly. A wide range of mostly disease specific health outcomes was used. Methodologies relating to costs were in most studies problematic. Most importantly, it was found that linking improved adherence to improved outcomes has proved problematic. The reviews emphasised the importance of standardising the methods to take nonadherence into account when assessing the effectiveness and cost-effectiveness of medicines. Moreover, the necessity to measure adherence and to establish a link to clinical outcome appropriately were highlighted. The need to distinguish persistence from compliance/adherence outcomes was described.

*****Please note that, from an economic perspective, adherence and compliance refer to the same concept defined as "the degree to which patient behaviour is congruent with the recommendations of health-care providers"[9], unlike concordance or persistence. For consistency, adherence was used in this review narrative regardless of the terminology choice of the original study.

[9] Haynes RB. Determinants of compliance: the disease and the mechanics of treatment. In: Haynes RB, Taylor DW, Sacket DL, editors. Compliance in Health Care. Baltimore, MD: The John Hopkins University Press, 1979:49–62.

10.2.1 Methods of the evidence review

Our primary aim was to conduct a search of the economic literature to investigate the cost-effectiveness of interventions to increase adherence, with a view to informing the key clinical questions to be considered by the GDG for this guideline.

The following literature databases were searched:

- Medline (Ovid) (1966-June 2006)
- Embase (1980-June 2006)
- NHS Economic Evaluations Database (NHS EED)
- PsycINFO
- Cumulative Index to Nursing and Allied Health Literature (CINAHL)

The electronic search strategies were developed in Medline and adapted for use with the other information databases. The clinical search strategy was supplemented with economic search terms. Titles and abstracts retrieved were subjected to an inclusion/exclusion criterion and relevant papers were ordered. No criteria for study design were imposed a priori. Papers initially included were:

- Full/partial economic evaluations.
- Considered patients over 16 years of age.
- Written in the English language.

This process yielded 88 papers, which were obtained in full text and critically appraised by a health economist using a standard validated checklist following the Guidelines Manual 2007 (www.nice.org.uk).

Types of studies: Systematic reviews of cost-effectiveness studies or comparative economic analyses based on modelling or randomised controlled trials (RCTs) of interventions to increase adherence.

Types of participants: people prescribed medicine for a medical condition from healthcare professionals in any health service setting.

Duration of studies: No time limit was applied.

Types of interventions: any interventions intended to change adherence to prescribed medicine.

Types of outcome measures: adherence levels, clinical, cost, and QALY outcomes.

A general descriptive overview of the studies, their quality, and conclusions has been presented and summarised in the form of a narrative review.

10.2.2 Evidence Review

Three systematic reviews were found. Two have been included on the grounds that they include studies which considered interventions designed to improve adherence **(Elliott 2005**[259] and **Cleemput 2002** [262]). A further review **(Hughes, 2001)** [263] investigating the impact of nonadherence on the cost-effectiveness of pharmaceuticals is included in the narrative as it was deemed highly relevant to the guideline. **Elliott (2005)** [259] reviewed 45 economic studies considering the cost-effectiveness evidence base for interventions to increase adherence. The review by **Cleemput (2002)** [262] reviewed eighteen studies with a view to investigating the economics of therapeutic nonadherence, although a number of included studies considered interventions to increase adherence.

Review 1

A UK systematic review by **Elliott (2005)** [259] included 42 studies: 30 from the US; two from the UK; and the remainder from a range of countries. The studies were conducted in 12 different clinical areas (Table 1). The reviewers used a variety of minimum quality criteria comprising economic evaluation quality criteria, standard hierarchies of evidence, and adherence-specific design issues. 21 of the original studies were based on RCTs, of which 4 used modelling techniques.

Definition of intervention

The interventions described in the reviewed studies employed a large variety of designs. They included programmes to improve convenience of care,

information, counselling, reminders, self-monitoring, reinforcement, family therapy, and other forms of additional supervision or attention. Some design issues arose, such as confounding factors on effect measures where interventions had effects that were not exclusively due to changes in medicines adherence.

Table 1. Studies included in the Elliott (2005) [259] systematic review, with number of studies by intervention and disease. Adapted with permissions from paper: Elliott (2005). Cost-effectiveness of adherence-enhancing interventions: a quality assessment of the evidence. *The annals of pharmacotherapy*, 39(3), 508-515.

Types of intervention	Asthma	Psychotic illness or depression	Hypertension	Diabetes	Tuberculosis	COAD	Malaria	HIV	Other morbidities
Health education or training	12	8	5	2		1	1		4
Specific use of health care professionals	4	4	1	2					4
Telephone calls		3	1						2
Directly Observed therapies					4				
Carers Involved		1	2						
Adverse Drug events		2							
Videos		1							
Work based care			1						
Palatable formulation							1		
Free drugs				1					
Reminders other than telephone or DOT								1	

Definition of adherence and clinical outcome

Apart from the variable and sometimes problematic definition of the intervention to increase adherence itself, the delivery of the intervention differed considerably between studies. Most interventions to increase adherence contained input by a specified health professional, an educational component, and often used of more than one component. The authors found that previously validated and unvalidated adherence measures were used combined with a range of outcome measures.

Study findings

The review does not report the cost-effectiveness findings of the individual studies, but instead concentrated on critiquing the variability and prevailing inadequacy of the methods used.

A number of health economic methodological problems, found in many of the included studies have been highlighted including:

- inappropriate or lack of incremental analysis;
- missing or inadequate sensitivity analysis and quantification of uncertainty;
- missing or unclear stating of the perspective of evaluation;
- appropriateness of statistical analysis for cost data and costing methodologies;
- missing or unclear discounting methods.

For example, of the 42 studies reviewed by Elliott (2005) [259], only nine conducted a sensitivity analysis to quantify the degree uncertainty around the base case results. Moreover, no study assessed how the use of a particular adherence measure or level influenced the base case results. The omission of sensitivity analyses is an important methodological omission which limits the generalisability of the original analyses.

Discussion

Overall, the review found that a meaningful comparison across studies was not possible due to heterogeneity and methodological weaknesses in many studies. A wide range of mainly disease specific outcomes was used. Six

studies did not report outcomes at all. Moreover, there appears to be little consensus across studies about which adherence measures to use. Twenty-four studies did not report results for adherence, or made assumptions about how adherence was improved by the intervention. Most crucially, the review found that linking improved adherence to improved outcomes has proved problematic.

Review 2

A systematic review by **Cleemput (2002)** [262] included 18 studies on the economics of therapeutic nonadherence, which were assessed according to their definition and measurement of medicines nonadherence, study design, and identification and valuation of costs and outcomes. The majority of articles dealt exclusively with medicines nonadherence. Eight studies examined the economics of adherence enhancing interventions. Of these, three were excluded from this review on methodological grounds.

Studies: methods and methodological problems

The reviewed papers included different types of economic evaluations, including cost-effectiveness, cost-benefit, and more descriptive cost-consequence analyses. Time horizons were less than 18 months in all studies, such that long-term benefits of adherence-enhancing interventions can rarely be shown. Costing methods were often found to be inappropriate. Methodological problems related to the definition and measurement of medicines nonadherence, study design, outcome measurement, and consideration of determinants of nonadherence and adherence-enhancing interventions were reported.

Definition of interventions

As set out in table 2, most interventions that represented interventions to increase adherence consisted of single components or combinations of counselling, patient education, reminders, less complex treatment regimens, and other forms of increased supervision.

Table 2: Studies from Cleemput (2002) [262] review, indicating disease group and type of intervention. Details of each study can be seen in table 3. Adapted with permissions from: Cleemput (2002). A review of the literature on the economics of noncompliance. Room for methodological improvement. *Health Policy*, 59(1), 65-94.

Disease Group	Health Education or training	CBT, cognitive approaches	Telephone calls	Directly Observed Therapy	Involve Carers	Palatable formulation	Support Group
Asthma	>		>				>
Psychotic Illness		I					
Hypertension	$	$			$		
Tuberculosis				*			
Malaria						^	

Definition of adherence and clinical outcome

Medicines nonadherence was found to be often ill-defined and not measured accurately. Interruption or cessation of therapy was often used as a definition of nonadherence, but concepts like 'taking less medicines than prescribed' and 'not starting therapy' were also found. Often, nonadherence is not specified at all. None of these five studies appear to have linked adherence to clinically relevant outcomes or QALYs.

Result from studies

No single approach has a clear advantage compared with another. Some of the reviewed studies on interventions to increase adherence show an improvement in terms of cost savings or improved adherence. The review found that one study on an intervention to increase adherence for antimalarials and one for antihypertensives showed some increase in the efficiency of treatment. However, the cost-effectiveness of an intervention to increase adherence will depend upon the costs and health effects associated with usual care and the intervention's own costs and health effects, and so the net effect on cost-effectiveness is unclear. The measures used and results found are presented in Table 3.

Table 3: Details from some of included studies representing interventions to increase adherence, taken from Cleemput (2002) [262]. Adapted with permissions from Cleemput (2002) A review of the literature on the economics of noncompliance. Room for methodological improvement. *Health Policy*, 59(1), 65-94.

ID	Subject	Design	Nonadherence Measure	Effectiveness Measure	Incremental Cost Effectiveness Ratio Results
>	Medication and inhaler compliance intervention for patients with asthma	Cost Effectiveness	Self Report	Improvement in adherence score	No ICER presented. Intervention appeared to be cost effectiveness.
I	Medication and inhaler compliance intervention for patients with psychosis	Cost Outcome Description	Self Report	Compliance, insight, attitude towards medication, global functioning	No ICER presented. No reported differences in costs – some correlations reported.
$	Medication and inhaler compliance intervention for patients with hypertension	Cost Benefit	Self Report	Prevented indirect earnings, prevented direct medical costs.	No ICER presented. Cost benefit ratios were 2.2 for family member re-enforcement and 1.24 for family member re-enforcement plus message clarification for the patient. The later was more favourable.
^	Malaria chemoprophylaxixis	Cost Effectiveness	Urine Specimen	Adherence achieved	No ICER presented. Cost Effectiveness ranged from $1.2 to $1.67

Discussion

The review described the important nonlinearity in the relationship between quality of life and nonadherence. Nonadherence may improve patients' quality of life, for instance when they deliberately adapt their medicine schedule to their own lifestyle, or it may decrease their quality of life due to increased morbidity, adverse events and/or side-effects. From a pharmacological perspective, under-dosing or extended time intervals between two medicine intakes may increase morbidity (and subsequently costs), whereas over-

dosing or shorter intervals between two medicine intakes may increase unpleasant side-effects or toxicity of the medicine.
The authors highlight the importance for clinicians, policymakers, and patients to consider the impact of nonadherence on the cost-effectiveness. Methodologies to do this adequately need to be improved and used in a standardised way in future work.

Review 3

A systematic review of pharmacoeconomic evaluations conducted in the UK by **Hughes (2001)** [263] included only studies that applied sensitivity analyses to adherence rates in order to evaluate the impact of nonadherence on the cost-effectiveness of different medicines. 22 evaluations were included in the review, of which 13 were from the US, 5 from Canada, and 2 were UK studies.

Studies: methods and methodological problems
Included studies were concerned mainly with treatments for chronic diseases, although two considered medicine regimen nonadherence with acute diseases. Decision analytic models were employed in most cases, and some of the evaluations modelling chronic illnesses adopted a Markov model approach. It was not specified if models were based on one trial exclusively or on multiple sources. Time horizons varied considerably between studies and ranged from 2 weeks to lifetime, with 3 studies spanning time up to 1 year, and 10 papers of over 10 years. Effectiveness measures varied, including disease specific outcomes such as ‘fractures avoided’ to more generic QALYs. The vast majority of studies conducted insufficient sensitivity analysis, particularly of adherence rates.

Definition of nonadherence and clinical outcome
The review indicated that definitions used for nonadherence were inadequate. Six studies made no attempt at defining the measure of adherence, or used an arbitrary proportion of doses taken to define whether patients were to be considered non-compliant. Similar to the other two reviews, inadequacy exists

in terms of sources of adherence rates used in the evaluations. Over a third of the included studies used values based on assumptions, or on medical opinion, or did not state the sources of the adherence data.

Linking nonadherence to clinical outcomes was problematic. Many studies were found to link nonadherence to changes in risk probabilities or outcomes, but only four referenced an evidence based source. Of those studies which presented sources for values and assumptions, very few used sources other than opinion. Few provided any indication of the differences in health benefits which likely to be observed when patients were non-compliant.

Discussion

It was not possible for the review to compare the magnitude of the impact of nonadherence among different medicine-disease combinations. However, it was found that the nature of nonadherence, the severity, and pathophysiology of the disease, and the extent to which a medicine 'forgives' nonadherence, (the ability of a drug to sustain its pharmacological action after a dose has been missed), all contribute to determining the extent of the clinical and economic consequences of nonadherence.

In terms of the review findings, studies showed that nonadherence generally results in a reduction in efficacy. The relationship between nonadherence and cost was less clear. While eight of the reviewed studies show that costs increase as adherence decreases, six found the opposite trend. This difference did not appear to be related to the nature of the disease, the measure of nonadherence, or the assumptions relating to the health benefits experienced by non-compliers.

The authors emphasise the need to systematically include nonadherence in pharmacoeconomic evaluations. The vast majority of studies were based upon trials designed to demonstrate efficacy, and not effectiveness. While the randomised clinical trial remains the 'gold standard' for comparing alternative treatments, the high internal validity required to demonstrate efficacy comes

at the expense of external validity, that is, generalisability of results to the 'real world' of medical practice.

10.3 Update of the systematic review by Elliott (2005)[259]

10.3.1 Methods of the evidence review

The aim of this literature search is to update the systematic review by **Elliott (2005)** [259] with relevant papers published from 2004 onwards. The titles and abstracts of records retrieved by the searches, suggested by the GDG, or submitted by stakeholders were scanned for relevance to the key questions. Any potentially relevant publications were obtained in full text. This yielded eight papers, which were then reviewed to identify the most appropriate evidence to inform consideration of the key clinical questions. This process required three main tasks: selection of relevant studies; assessment of study quality; synthesis of the results. Three of the eight references were subsequently excluded as they either failed to describe and impute adherence as an outcome measure, or did not meet the methodological requirements. The resulting five papers were reviewed using systematic, transparent approaches following the Guidelines Manual 2007 (www.nice.org.uk).

Types of studies: Systematic reviews of cost-effectiveness studies or comparative economic analyses based on modelling or randomised controlled trials (RCTs) of interventions to increase adherence.
Types of participants: people aged 16 and over prescribed medicine for a medical condition from healthcare professionals in any health service setting.
Duration of studies: No time limit was applied.
Types of interventions: any interventions intended to change adherence to prescribed medicine.
Types of outcome measures: adherence levels as well as clinical, cost and QALY outcomes.

10.3.2 Update evidence review

Five papers were found and included. One paper by **Bosmans (2007)** [264] assessed the cost-effectiveness of a pharmacy based coaching programme to improve adherence to antidepressants. Another paper by **Cleemput (2004)** [265] compared renal transplantation with haemodialysis for patients with renal failure. A paper by **Brunenberg (2007)** [266] examined the cost-effectiveness of an adherence-improving programme comprising monitoring system and adherence training for patients on antihypertensives. One US paper by **Edwards (2005)** [267] assessed the cost-effectiveness of long acting risperidone compared to other oral agents in patients with schizophrenia in a decision model. Finally **Munakata (2006)** [268] evaluated a hypothetical ceiling cost for an adherence enhancing intervention to be cost-effective for HIV positive patients on HAART.

The first Dutch based cost-effectiveness analysis by **Bosmans (2007)** [264] was based on a RCT of 151 patients with a prescription for non-tricyclic antidepressants from their GP for depressive complaints. They were randomised to receive either an intervention consisting of three personal coaching contacts with a pharmacist and an educational video to take home, or alternatively, to usual care including standard oral and written information. Adherence was measured using an electronic pill container (eDEM) and was the primary outcome, with the Hopkins depression 13 item subscale (SCL) used as a secondary outcome measure.

Mean adherence did not differ significantly between the intervention group (88%) and the control group (86%) at six months (mean difference +2.1%, 95% CI -5.6% to +9.8%). In respect to the SCL subscale, there was no statistically significant difference between the groups despite a slight improvement in the pharmacist intervention group (-0.15, 95% CI -0.54 to 0.23).
The ICER for coaching and education by the pharmacists compared with usual care was €149 per 1% improvement in adherence, and €2,550 per point improvement in the SCL depression mean item score. Uncertainty was

considerable, reflected by insignificance of mean differences. Pairs of costs and effects were distributed in all four quadrants of the cost-effectiveness plane and the cost-effectiveness acceptability curve (CEAC) for adherence showed great uncertainty. As such, the cost-effectiveness of coaching and education by pharmacists as a means of increasing adherence to antidepressants compared with usual care is unclear.

A cost-utility analysis by **Cleemput (2004)** [265] compared interventions for renal failure using a decision analytic model. The model drew on data from a prospective study of 126 adults with chronic renal failure and varying adherence levels. Of these, 23 received renal transplant. Adherence to immunosuppressants for the transplant patients was measured using an electronic event monitoring (EEM) device. Five (22%) study subjects were defined as nonadherent.

Lifetime costs after transplantation in the adherent patient group are higher than lifetime costs in the non adherent group, mainly because adherent patients live longer after transplantation. Compared with dialysis, renal transplantation offers better outcome in both adherent and nonadherent patients. Transplant was shown to be more cost-effective (dominant) than haemodialysis for all adherence levels considered. When full adherence is assumed, transplant generates a cost saving relative to dialysis and gives 5.19 additional QALYs. In a heterogeneous group of adherent and nonadherent patients, the saving was greater, but fewer additional QALYs were generated (5.06). This was mainly due to a reduced survival. Among transplant patients, adherence with immunosuppressants after transplantation is associated with a QALY gain, albeit at a higher cost which was mainly due to longer survival. Mean incremental costs per QALY in adherent patients relative to nonadherent patients after transplantation amounted to €35,021 (95%CI €26,959 to €46,620). Acknowledging that this modelling study may not be generalisable to the UK health care setting, using a threshold willingness to pay of £20,000 per QALY, this study implies that interventions to improve adherence for renal transplant patients may not be considered cost-effective using current UK thresholds.

A cost-utility study by **Brunenberg (2007)** [266] evaluated a medication events monitoring system (MEMS) plus adherence training compared with usual care alone for patients on antihypertensives. Follow-up was for 5-months only. The MEMS is a medicine container and cap equipped with a microchip that registers the date and time of each opening. This study was based on a randomised controlled trial supplemented by non-parametric bootstrapping methods. There were 164 hypertensive patients in the MEMS arm, and 89 in usual care group and they had a systolic blood pressure (BP) >160mm Hg and/or diastolic BP >95mm Hg despite being drug eligible.
Unsatisfactory adherence was defined as less than 85% of days taking the prescribed dose. From the healthcare perspective, electronic monitoring led to a reported cost saving of €100 per patient, and an additional 3.1% of patients achieved normal blood pressure than in the usual care arm. The intervention was therefore dominant over usual care. However, sensitivity analysis revealed considerable uncertainty although 55% of point estimates were in the intervention dominating south-east quadrant of the cost-effectiveness plane. The base case societal cost per QALY estimate was €15,667, which is likely to be within the current UK threshold of cost-effectiveness. 33% of bootstrap point estimates were in the south-east quadrant of the cost-effectiveness plane, although 11% were in the dominated north-west quadrant. Overall, effect sizes were small and not statistically significant.
The adherence enhancing intervention was considered to be moderately cost-effective but with considerable uncertainty around the base case result. Moreover, given the chronic nature of hypertension, the length of follow-up of five months appears insufficiently short to predict the long-term effect of the intervention on adherence and other outcomes.

Edwards (2005) [267] conducted a cost-effective analysis based on a decision analytic model that compared long acting risperidone with a range of other antipsychotic agents, including oral risperidone and depot haloperidol. The population was drawn from patients with schizophrenia in community dwellings who have previously suffered relapse requiring hospitalisation. Adherence was assumed to be improved by the long acting injectable risperidone formula. It was estimated that a 20% point difference in adherence

would predict a 3.1 point improvement in the PANSS (Positive and Negative Syndrome Scale for Schizophrenia). Such improvement in turn stabilised patients so that a further 6.1 point in PANSS was achieved by further improved medicine-taking behaviour, and aversion of relapse. The model predicts that patients receiving long acting risperidone will have the best clinical outcomes in terms of the frequency and duration of relapses over the one year duration. For example, on long acting risperidone, 26% of patients were modelled to experience relapse requiring hospitalisation, and 24% relapse not requiring hospitalisation. On haloperidol nearly two-thirds of patients are predicted to have relapses requiring hospitalisation, and over 60% relapse not requiring hospitalisation. In terms of days of relapse averted, this analysis predicts dominance of long acting risperidone over the comparators, (that is, better outcomes and lower costs), over the one year time horizon. Univariate sensitivity analysis was reported to have been robust. However, at the upper bound of the 95% CI for relapse rates requiring hospitalisation, there was an ICER of US$821 per day of hospitalisation averted for long acting risperidone compared to oral risperidone. The model also appears sensitive to the cost of hospitalisation and rates of relapse.
In summary, the analysis seems of interest, however, there are issues with its robustness and its generalisability to the UK. The outcome of cost per day of hospitalisation averted, poses a challenge for the interpretation of the findings in the context of this guideline. Values used in the sensitivity analysis seem relatively conservative. The short time horizon could be an issue, but has not been thoroughly discussed. Quantifying treatment and quality of life losses in a single measurement such as the QALY may have helped in considering the generalisability of this evaluation to the UK.

A cost-utility analysis conducted by **Munakata (2006)** [268] was based on a decision analytic model. The aim of the study was to quantify the clinical and economic effects of nonadherence, and estimate the cost-effectiveness of improving adherence in treatment naïve patients. For this, HAART treatment with an assumed good adherence was compared with HAART on 'typical' adherence. The authors drew on data from randomised controlled trials and observational data for the comparators, respectively. The model population

was HIV positive, with a mean age of 33. The assumed portion of medicines consumed of 0.98 (0.95-1.0) was defined as adherent, and 0.55 (0-0.95) as nonadherent. The proportion of adherent patients in the typical comparator arm was imputed as 0.52 (0.3-0.88). Lifetime discounted costs in the typical and ideal scenarios were $308,000 and $341,000, respectively. This gives an incremental cost of $33,000. People in the ideal scenario generated 10.2 QALYs per patient compared to 9.0 QALYs per patient in the typical scenario. This gives an incremental effect of 1.2 QALYs. The incremental cost effectiveness ratio (ICER) resulted in $29 400 per QALY. This result indicates that from a cost-effectiveness perspective, there is scope for an intervention to increase adherence. The authors calculated a willingness to pay (WTP) ceiling value for an intervention to increase adherence. They conclude that $1,600 could be spent per patient to increase adherence to ideal levels, giving 15-33% reductions in treatment failure. Univariate sensitivity analysis was conducted for all parameters, as well as multivariate SA for selected values. The analysis was described as robust in sensitivity analysis. In severe diseases where adherence and related comorbidities are influential, adherence improving interventions may be cost-effective. Given that there are interventions that are effective in increasing adherence, this analysis found that $1,600 per patient could be spent on the modelled patient group.

10.4 Summary and Discussion

The initial review included three systematic reviews of literature investigating the health economics of adherence. Only one of these Elliott (2005) [259] was specifically focused on investigating interventions to improve adherence, although the SR by Cleemput (2002) [262] also included interventions to increase adherence. A third SR by Hughes (2001) [263] focused on the investigating the influence of nonadherence on cost-effectiveness of pharmaceuticals.

The interventions described in the reviewed studies covered a range of disease areas and included a variety of designs and methods of delivery. Both validated and unvalidated measures of adherence were employed, and in

some cases the definition of nonadherence was not reported or was arbitrary. The included studies employed a range of mainly disease specific outcome measures. Some studies did not report clinical outcomes at all. There was a lack of good quality evidence linking improved adherence to improved health outcomes, with many of the studies relying on assumptions. Many of the studies had short time horizons, which could be problematic for chronic conditions where long-term adherence is of interest. None of the evaluations considered process utility. Methodological weaknesses from a health economic evaluation perspective included: inadequate use of sensitivity analysis; omission of incremental analysis; and appropriate costing methods.

The SRs indicated that because of the disparity in the nature of the outcomes, the measures of nonadherence used and time horizons of the studies evaluated, it was not possible to compare the magnitude of the impact of nonadherence among different medicine-disease combinations. However, it was evident that nonadherence impacts adversely on efficacy, but its impact on costs varies substantially. Where nonadherence impacts adversely on survival, quality of life, and, or resource usage, there is scope for an intervention that effectively raises adherence. The systematic reviews presented in this Guideline emphasised the importance of standardising the methods to take nonadherence into account when assessing the effectiveness and cost-effectiveness of medicines.

A search for economic evaluations of interventions to increase adherence undertaken for this guideline, and designed to update the search conducted by Elliott (2005) [259], found five recent economic evaluations of interventions to increase adherence. The cost-effectiveness of a pharmacist coaching intervention for patients suffering from depression is unclear, in that the outcome measure used was depression specific, and there was considerable uncertainty in the calculated ICER. The model-based analysis concerned with adherence to immunosuppressants for renal transplant patients appears likely not to be considered cost-effective, but again the direct relevance in the UK context is not certain. The adherence training intervention for antihypertension patients appears to be “moderately cost-effective” although the follow-up may

be too short and again the analysis contained considerable uncertainty and was not UK specific. The dominant result for long acting risperidone in schizophrenia patients using a US-based modelling analysis, is likely to imply cost-effectiveness in a UK context, although the limited sensitivity analysis indicated sensitivity to hospitalisation costs and assumed relapse rates. The modelled analysis for HIV patients on HAART indicates that there is likely to be scope for an adherence enhancing intervention to be cost-effective for this patient group. The absolute ceiling and the uncertainty around the base case value in the UK context is again unclear.

The picture emerging from the economic evaluations found in the update search is unclear, particularly for UK decision makers. None of the evaluations were UK-based, and some included disease specific outcome measures rather than the NICE preferred QALY outcome. A priori, we might expect that interventions to increase adherence for medicines for which nonadherence might have short term survival or more serious quality of life implications, would have a better chance of demonstrating cost-effectiveness, compared to more 'forgiving' medicines. The results of the studies examining adherence interventions for HAART (Munkata 2006) [268] and for risperidone (Edwards 2005) [267] support this supposition. On the other hand, it might therefore be surprising that the study of the use of immunosuppressants (Cleemput (2004) [265] implied that an intervention to increase adherence might not be cost-effective for renal transplant patients. An intervention to increase adherence for the relatively 'forgiving' antihypertensives was indicated to be 'moderately cost-effective.

In short, there appears to be little good quality evidence evaluating the cost-effectiveness of adherence enhancing interventions, or evaluating the impact of nonadherence on cost-effectiveness of medicines. The published systematic reviews have been critical of the quality of the existing economic evidence base, and have tended to focus on critiquing methods rather than reporting cost-effectiveness per se. In particular, there appears to be little information to support UK decision makers. Few of the published economic evaluations were conducted from the perspective of the UK NHS. Methodological weaknesses including inadequate or missing sensitivity analyses, and also the predominance of disease specific outcome measures

instead of QALYs, makes it difficult to generalise the findings of many of the studies to the UK context.

In general, and in particular for the UK context, there is a clear need for more and better research into the implications of nonadherence on the cost-effectiveness of medical interventions, and also to assess the potential of interventions to increase adherence to improve healthcare outcomes and/ or reduce healthcare costs. Future research in this area should ensure that standard principles of good economic evaluation are employed. Models might be used to investigate general or specific adherence cost-effectiveness issues, particularly for chronic conditions where medicine-taking is long-term, and where economic evaluations may need to extrapolate from shorter term clinical trial results. Any such models must ensure that parameter uncertainty is addressed adequately using appropriate sensitivity analysis. Improving the evidence base regarding the inter-relationships between adherence and health and economic outcomes, and using this information appropriately in health economic models will improve the quality of the evaluations, provide better quality information to decision makers, and hopefully lead to improved allocation of limited NHS resources.

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Appendix A
Guidelines scope

SCOPE

1 Guideline title

Medicines concordance and adherence: involving adults and carers in decisions about prescribed medicines

1.1 Short title

Medicines concordance

2 Background

(a) The National Institute for Health and Clinical Excellence ('NICE' or 'the Institute') has commissioned the National Collaborating Centre for Primary Care to develop a clinical guideline on medicines concordance for use in the NHS in England and Wales. This follows referral of the topic by the Department of Health (see appendix). The guideline will provide recommendations for good practice that are based on the best available evidence of clinical and cost effectiveness.

(b) The Institute's clinical guidelines will support the implementation of national service frameworks (NSFs) in those aspects of care where a framework has been published. The statements in each NSF reflect the evidence that was used at the time the framework was prepared. The clinical guidelines and technology appraisals published by the Institute after an NSF has been issued will have the effect of updating the framework.

(c) NICE clinical guidelines support the role of healthcare professionals in providing care in partnership with patients, taking account of their individual needs and preferences, and ensuring that patients (and their carers and families, where appropriate) can make informed decisions about their care and treatment.

3 Clinical need for the guideline

a) The number of prescription items in the NHS increased from 686 million in 2004 to 720 million in 2005, an increase of 34 million, or 5.0%. Between 2004 and 2005, the net ingredient cost of prescription items dispensed fell by £143 million from £8080 million (1.8 per cent) to £7937 million, compared with an increase of 7.6 % in the previous year.

b) Reviews conducted across disease areas and countries suggest that at least 30–50% of prescribed medication is not taken as recommended. This behaviour is often undisclosed by patients and unrecognised by prescribers, but may lead to worse health outcomes in terms of morbidity or mortality for the patient and to an increased economic burden on the healthcare system.

c) The terminology using when discussing medication-taking behaviours is complex with three commonly used definitions. The terminology is explained as follows by Horne (2005)[1]

- Compliance – 'the extent to which the patient's behaviour matches the **prescriber's** recommendations'.

- Adherence – 'the extent to which the patient's behaviour matches **agreed** recommendations from the prescriber'. Adherence emphasises the need for agreement and that the patient is free to decide whether or not to adhere to the doctor's recommendation

- Concordance – this is a recent term whose meaning has changed. It was initially applied to the consultation process in which doctor and patient agree therapeutic decisions that incorporate their respective views but now includes patient support in medicine taking as well as prescribing communication.

[1] Horne R (2005) Concepts and terminology. In: Horne R, Weinman J, Barber N et al, *Concordance, Adherence and Compliance in Medicine Taking – Report for the National Co-ordinating Centre for NHS Service Delivery and Organisation Research and Development*, pp 27–37 www.sdo.lshtm.ac.uk.

Concordance reflects normative values but does not address medicine –taking and may not lead to improved adherence.

The NCCSDO recommended using the term adherence to describe patients' medicine taking behaviour. This scope will use the terms 'shared decision-making about medicines' to refer to the health professional – patient/carer consultation and the term 'adherence' to refer to patient's medicine taking behaviour.

d) Medicines may not be taken as prescribed for many reasons. These include adverse effects, poor instructions, poor communication between healthcare professional and patient, poor memory, the effects of the illness, patients' disagreement with the need for treatment and their inability to buy the prescribed medication. Other reasons may be that patients are confused by what medicine they have been prescribed and its impact on their condition, a treatment regimen that does not fit in with the patient's daily activities has been prescribed, or the lack of a decision process that takes into account values and beliefs of the patient.

e) Current methods to improve adherence in long-term conditions are quite complex and have little effect, as reported by the latest Cochrane review on interventions for enhancing medication adherence. Similarly, the scoping review commissioned by the National Co-ordinating Centre for NHS Service Delivery and Organisation Research and Development (2005) concluded that the evidence on interventions for adherence was limited. Both the reviews showed that there was little evidence on the effectiveness of interventions to improve adherence to medication for long-term conditions within the clinical setting. Despite this, the Service Delivery and Organisation report does give some suggestions about how to improve interventions in the future.

f) There is evidence of significant differences in patterns of prescribing and of variation in application of recommended good

practice among healthcare practitioners: 'this not only relates to differences in what is prescribed for the same condition but also in the amount and level of information which is provided about prescribed medications'.[2]

4 The guideline

a) The guideline development process is described in detail in two publications that are available from the NICE website (see 'Further information'). 'The guideline development process: an overview for stakeholders, the public and the NHS' describes how organisations can become involved in the development of a guideline. 'The guidelines manual' provides advice on the technical aspects of guideline development.

b) This document is the scope. It defines exactly what this guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health (see appendix).

c) The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

a) People aged 16 years and older, including those with comorbidities, learning disabilities or language and/or cultural differences.

[2] O' Brien M (1997) Compliance among health professionals. In Baum A, Newman S, Weinman J et al. editors *Cambridge Handbook of Psychology, Health and Medicine*. Cambridge: Cambridge University Press
cited by Weinman J, Horne R (2005) Patient provider interaction and health care communication In: Horne R, Weinman J, Barber N et al, *Concordance, Adherence and Compliance in Medicine Taking – Report for the National Co-ordinating Centre for NHS Service Delivery and Organisation Research and Development*.,pp 61–8. www.sdo.lshtm.ac.uk

4.1.2 Groups that will not be covered

a) Children and young people (younger than 16 years). However, the guideline recommendations may be considered for anyone younger than 16 years who is deemed competent to express a view on their prescription.

4.2 Healthcare setting

a) All consultations with healthcare professionals in any NHS setting that relate to the initiation or review of prescribed medication.

4.3 Areas that will be covered

a) Shared decision-making about medicines and medicine taking as reported by the patient or carer. The guideline will focus on the barriers (such as communication difficulties, cultural issues, low health literacy and physical limitations), facilitators (including structural or procedural factors), beliefs and health behaviours that influence decision-making and adherence.

b) Shared decision-making about medicines and medicine taking as reported by the healthcare professional. The guideline will focus on the barriers (such as communication difficulties, cultural issues and time), facilitators (including structural or procedural factors), beliefs and health behaviours that influence decision-making and adherence.

c) The effectiveness and cost effectiveness of interventions to facilitate the process of shared decision-making about medicines (looking at time of intervention – before, during, or after the consultation with the healthcare professional; and mode of delivery). The target of the intervention may be the patient, the carer, the prescriber, any healthcare professional providing ongoing support or a combination of these.

d) The effectiveness and cost effectiveness of interventions to promote adherence in medicine taking (looking at time of

intervention – before, during, or after the consultation with the healthcare professional; and mode of delivery). The target of the intervention may be the patient, the carer, the prescriber, the dispenser or any other healthcare professional providing ongoing support or a combination of these.

e) The evidence on single or multiple medications as it relates to issues around decision-making and adherence.

f) The guideline development group will take reasonable steps to identify ineffective interventions and approaches to care. If robust and credible recommendations for repositioning the intervention for optimal use, or changing the approach to care to make more efficient use of resources, can be made, they will be clearly stated. If the resources released are substantial, consideration will be given to listing such recommendations in the 'Key priorities for implementation' section of the guideline.

Areas that will not be covered

g) Situations where direct professional involvement is required for the use or administration of medicines. Administration is defined as giving a medicine by introduction into the body (for example, orally or by injection), or by external application (for example application of an impregnated dressing). It is expected that recommendations regarding decision-making about medicines would be relevant in these situations.

4.4 Status

4.4.1 Scope

This is the final draft of the scope.

4.4.2 Guideline

The development of the guideline recommendations will begin in March 2007.

5 Further information

Information on the guideline development process is provided in:

- ‘The guideline development process: an overview for stakeholders, the public and the NHS’
- ‘The guidelines manual’.

These booklets are available as PDF files from the NICE website (www.nice.org.uk/guidelinesprocess). Information on the progress of the guideline will also be available from the website.

Appendix: Referral from the Department of Health

The Department of Health asked the Institute to develop a guideline:

> '… on involving patients in decisions about prescribed medicines. The guideline should cover:
>
> - approaches to achieving informed agreement between the prescriber and the patient on medicines to be taken
> - communication with patients around medicine-taking, including the provision and use of medicines information
> - dealing with poly-pharmacy and co-morbidity
> - the skills and competencies required by prescribers
> - medication review.'

Appendix B
Key Clinical Questions and Searches

General questions relating to shared decision making	
1.What do we mean/understand by patient involvement in decisions about medicines	Narrative using expert reviews
2. Does involvement in decisions about medicines influence adherence?	Narrative review
3. Is it possible to increase patient involvement in decisions about medicines?	Evidence review
4. What tools are available to help elicit patients beliefs about medicines?	Evidence review
5. What tools are available to help elicit patients information needs about medicines?	Evidence review
6. Does shared understanding of the diagnosis (need for treatment/symptoms) increase SDM?	Not treated as question following agreement of model of shared decision making to use
7. How can a practitioner detect whether a patient agrees/disagrees with recommendation to take medicines?	Evidence review
8. How can practitioners elicit patient's preferences for involvement in decisions about medicines?	Evidence review
9. What tools are available to support the patient in reaching an informed decision?	Evidence review
10a. What information about medicines should be provided for patients in order to enhance SDM in regard to medicines?	Narrative using expert reviews and GDG consensus

10b. How can information about medicines be provided for patients in order to enhance SDM in regard to medicines:	Evidence review
11. a) Which are the specific/practical barriers and facilitators for individuals to allow them to engage in shared decision making? (b) How can a HCP identify theses barriers and facilitators (c) Is there a way of doing this so intervention can be targeted?	Not treated as separate questions following agreement of model of shared decision making to use
12. Do interventions to increase patient involvement increase length of the consultation?	Evidence review
13. What 'aspects' of consultation style increase patient involvement in decision-making?	Evidence review
14. What are the skills and competencies required from HCPs to deliver interventions designed to increase SDM about medicines?	The GDG decided that recommendations on patient involvement and adherence indicate skills required and it was outside their expertise to decide on frameworks and competencies which should be agreed by professional organisations.
Questions related to adherence	
15. How common is non-adherence? What is the correlation between increasing	Narrative using expert reviews

adherence and clinical benefit? What are the main causes of non-adherence? Is adherence worse in vulnerable groups, if so which ones?	
16. What is the influence of side effects on adherence?	Answered in review of patients experience of medicines
17. a) Which are the specific/practical barriers and facilitators for individuals in medicine taking? (b) How can HCP identify theses barriers and facilitators (c) Is there a way of doing this so intervention can be targeted?	Evidence review of patient experience
18. How can HCP tailor information to specific patient groups – cognitive capacity, cultural groups	Evidence review of patient experience
19. What are the needs of carers/families in affecting adherence?	GDG consensus that carers and families needs for information are same as those of patients.
20. Is medicine taking altered by the purpose of medicine (i.e. symptomatic, preventive etc)?	Not answered as separate questions – see evidence review for 17.
21. How do patients' beliefs about medicines and HCP influence adherence?	Not answered as separate questions – see evidence review for 17.
22. How can HCP elicit patients' beliefs affecting	Not answered as separate

non-adherence?	question
23. Which interventions are effective in increasing adherence? (content of interventions, how delivered and who delivers them)	Evidence review
24. Dosing regime Does change in dosing regime affect adherence?	Evidence review
25. Practical Do prescription costs/charges affect adherence/how do patients handle cost issues?	Evidence review
26. Dosage formulation & packaging Does drug formulation/packaging affect adherence?	Evidence review
27. Side-effects Is there any evidence on interventions that aim to minimize side-effects in order to increase adherence?	Evidence review
28. Information and how delivered How does the way and amount of the information that is presented (e.g. pictorial vs. written form) affect adherence?	Evidence review
29. Financial incentives Do rewards affect adherence/what are they?	GDG considered not relevant to UK settings so omitted
30. Psychobehavioural interventions	Evidence review

Do specific forms of therapy (e.g. CBT) affect adherence?	
31. Overall treatment plans Is care planning important in affecting adherence? (i). Do patient plans affect adherence?	GDG consensus to omit
32. Contract Would a contractual agreement between HCP and patient affect adherence?	Evidence review
33. Effect of reminders Do reminders (and what types of reminders, text messaging etc) help increase adherence? Are these more important before or after a review?	Evidence review
34. Patient identification of medicine Does changing the name of medicines affect the way people take medicines?	GDG consensus to omit
35. Effect of self-monitoring of effect of medication Does being involved in self-monitoring (e.g. of own blood pressure) help adherence? Does case-management affect adherence (i.e. by one specific person)?	Evidence review
36. Does effect of intervention differ according to which HCP delivers the intervention?	GDG consensus to omit
37. What elements of the clinician-pt relationship influence adherence?	Question developed on trust in doctor-patient relationship. Answered as part of question

	13.
38. What information regarding medicines should be provided for patients and practitioners on medicines when patients are discharged from secondary care?	Narrative review and consensus
39. What is the role of the pharmacist or HCP in overcoming barriers to adherence?	GDG considered that question not relevant following agreement of concepts in guideline.
40. What would impact adherence after the prescription is issued?	GDG considered that question not relevant following agreement of concepts in guideline.
41. What is medication review?	Does medication review increase patient involvement in decisions about medicines and adherence to medicines? (question altered by GDG)
42. What should be the content of medication reviews?	
43.When/how often and by whom should medication reviews be done?	
44. Does the use of dosette boxes affect adherence to prescribed medication?	Evidence review After consultation it was brought to our attention that devices like dosette boxes may be classified under different headings and that some researchers label them as 'reminders' or as 'packaging'. We therefore re-examined the

	papers included in the packaging review and reminder reviews and extracted those relevant to dosette-type devices. These we have termed multi-compartment medicine systems although there is no agreed term in the published literature.
45. How can practitioners assess adherence?	GDG consensus
46. What are the advantages and disadvantages of self-report in assessing patient's adherence?	Evidence review
47. What information regarding medicines should be provided for patients and practitioners when patients are discharged from secondary care?	Narrative review using expert reviews

Search strategies used in this guideline

The strategies were developed for use on the Dialog DataStar web interface. The following databases were searched: Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessment Database (HTA), MEDLINE, EMBASE, CENTRAL, CINAHL and Social Sciences Citation Index. Where appropriate to the question AMED and PsycINFO were also searched.

The Economic literature was searched using an economic and quality of life filter developed by ScHARR for Medline and EMBASE. The following were searched: NHS Economic Evaluations Database (NHSEED), MEDLINE, and EMBASE.

The strategies shown are those for MEDLINE using the Dialog DataStar interface unless otherwise stated. Copies of all the search strategies are available on request from the National Collaborating Centre for Primary Care.

Where a search strategy was developed for a specific question, the question number has been included. However, many of the searches were used for a range of questions in which only the topic (rather than the question number) has been stated.

Cochrane Review update

MEDICINES CONCORDANCE COCHRANE REVIEW UPDATE MEDLINE SEARCH STRATEGY

Database: Ovid MEDLINE(R) <1950 to February Week 4 2007>
Search Strategy:

1 patient compliance/ (30688)
2 treatment refusal/ (8108)
3 (patient$ adj2 compliance).ti,ab. (6120)
4 (patient$ adj2 concordance).ti,ab. (261)
5 (patient$ adj2 adherence).ti,ab. (1362)
6 (patient$ adj2 non-compliance).ti,ab. (218)
7 (patient$ adj2 non-adherence).ti,ab. (45)
8 (treatment$ adj (compliance or adherence or non-compliance or non-adherence or refus$)).ti,ab. (1573)
9 (therap$ adj (compliance or adherence or non-compliance or non-adherence)).ti,ab. (474)
10 (regimen adj (compliance or adherence or non-compliance or non-adherence)).ti,ab. (150)
11 ((medicine$ or medication$) adj (concordance or compliance or non-compliance or adherence or non-adherence)).ti,ab. (1489)
12 (drug adj (concordance or compliance or non-compliance or adherence or non-adherence)).ti,ab. (521)
13 or/1-12 (44015)
14 randomized controlled trial.pt. (230838)
15 controlled clinical trial.pt. (74323)
16 randomized controlled trials.sh. (47283)
17 random allocation.sh. (57126)
18 double blind method.sh. (89989)
19 single blind method.sh. (10668)
20 or/14-19 (391621)
21 clinical trial.pt. (433213)
22 exp clinical trials/ (187465)
23 (clin$ adj2 trial$).ti,ab. (106314)
24 ((singl$ or doubl$ or trebl$ or tripl$) adj2 (blind$ or mask$)).ti,ab. (87077)
25 placebos.sh. (25859)
26 placebo$.ti,ab. (100472)
27 random$.ti,ab. (362469)
28 or/21-27 (788551)
29 20 or 28 (818320)
30 13 and 29 (10092)
31 (letter or comment or editorial).pt. (823569)
32 30 not 31 (9874)
33 limit 32 to humans (9821)
34 limit 33 to yr="2004 - 2007" (2382)
35 limit 34 to english language (2241)
36 from 35 keep 1-1500 (1500)

Questions relating to shared decision making and adherence

MEDICINE CONCORDANCE AND SHARED DECISION MAKING MEDLINE SYSREV SEARCH STRATEGY - Searched 15/08/07

1. (DECISION ADJ AID$2).TI,AB.
2. (DECISION ADJ MAKING).TI,AB.
3. DECISION-MAKING#.DE.
4. (DECISION ADJ SUPPORT ADJ SYSTEM$2).TI,AB.
5. DECISION-SUPPORT-SYSTEMS-CLINICAL#.DE.
6. (PATIENT ADJ INVOLVEMENT).TI,AB.
7. (PATIENT ADJ PARTICIPATION).TI,AB.
8. PATIENT-PARTICIPATION#.DE.
9. PROFESSIONAL-FAMILY-RELATIONS#.DE.
10. PROFESSIONAL-PATIENT-RELATIONS#.DE.
11. (CLINICIAN$2 OR DOCTOR$2 OR PHYSICIAN$2).TI. AND (PATIENT$2 OR PEOPLE$2).TI.
12. ATTITUDE-OF-HEALTH-PERSONNEL#.DE.
13. (DECISION ADJ AID$2).TI,AB.
14. (DECISION ADJ SUPPORT ADJ TECHNIQUE$2).TI,AB.
15. DECISION-SUPPORT-TECHNIQUES#.DE.
16. (SHARED ADJ DECISION).TI,AB.
17. (SHARING ADJ DECISION$2).TI,AB.
18. (INFORMED ADJ DECISION$2).TI,AB.
19. (INFORMED ADJ CHOICE).TI,AB.
20. (SHARE$2 OR SHARING OR INFORMED).TI,AB. AND DECISION$.TI,AB.
21. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20
22. PATIENT-COMPLIANCE.DE.
23. TREATMENT-REFUSAL.DE.
24. (PATIENT$2 NEAR COMPLIANCE).TI,AB.
25. (PATIENT$2 NEAR CONCORDANCE).TI,AB.
26. (PATIENT$2 NEAR ADHERENCE).TI,AB.
27. (PATIENT$2 NEAR (NON-COMPLIANCE OR NONCOMPLIANCE)).TI,AB.
28. (PATIENT$2 NEAR (NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
29. (TREATMENT$2 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE OR REFUS$)).TI,AB.
30. (REGIMEN ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
31. ((MEDICINE$2 OR MEDICATION$2) ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ

ADHERENCE)).TI,AB.

32. (DRUG ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
33. 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32
34. 21 AND 33
35. (SYSTEMATIC$ ADJ REVIEW$).AB.
36. REVIEW.PT.
37. META-ANALYSIS.AB.
38. META-ANALYSIS.PT.
39. META-ANALYSIS.TI.
40. 35 OR 36 OR 37 OR 38 OR 39
41. LETTER.PT.
42. COMMENT.PT.
43. EDITORIAL.PT.
44. 41 OR 42 OR 43
45. 40 NOT 44
46. 34 AND 45
47. ANIMAL=YES
48. HUMAN=YES
49. 47 NOT (47 AND 48)
50. 46 NOT 49
51. LG=EN
52. 50 AND 51

The SDM strategy was revised to AND terms 1 to 13 (shared decision making terms) with terms 15 to 21 (the patient involvement terms) to ensure that all relevant papers were picked up.

MC & SDM MEDLINE SYS REV SEARCH STRATEGY – REVISED - **Searched 11/12/07**

1. (DECISION ADJ AID$2).TI,AB.
2. (DECISION ADJ MAKING).TI,AB.
3. DECISION-MAKING#.DE.
4. (DECISION ADJ SUPPORT ADJ SYSTEM$2).TI,AB.
5. DECISION-SUPPORT-SYSTEMS-CLINICAL#.DE.
6. (DECISION ADJ AID$2).TI,AB.
7. (DECISION ADJ SUPPORT ADJ TECHNIQUE$2).TI,AB.
8. DECISION-SUPPORT-TECHNIQUES#.DE.
9. (SHARED ADJ DECISION).TI,AB.
10. (SHARING ADJ DECISION$2).TI,AB.
11. (INFORMED ADJ DECISION$2).TI,AB.
12. (INFORMED ADJ CHOICE).TI,AB.
13. (SHARE$2 OR SHARING OR INFORMED).TI,AB. AND DECISION$.TI,AB.

14. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13
15. (PATIENT ADJ INVOLVEMENT).TI,AB.
16. (PATIENT ADJ PARTICIPATION).TI,AB.
17. PATIENT-PARTICIPATION#.DE.
18. PROFESSIONAL-FAMILY-RELATIONS#.DE.
19. PROFESSIONAL-PATIENT-RELATIONS#.DE.
20. (CLINICIAN$2 OR DOCTOR$2 OR PHYSICIAN$2).TI. AND (PATIENT$2 OR PEOPLE$2).TI.
21. ATTITUDE-OF-HEALTH-PERSONNEL#.DE.
22. 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21
23. 14 AND 22
24. (SYSTEMATIC$ ADJ REVIEW$).AB.
25. REVIEW.PT.
26. META-ANALYSIS OR METAANALYSIS OR (META ADJ ANALYSIS).AB.
27. META-ANALYSIS OR METAANALYSIS OR (META ADJ ANALYSIS).PT.
28. META-ANALYSIS OR METAANALYSIS OR (META ADJ ANALYSIS).TI.
29. 24 OR 25 OR 26 OR 27 OR 28
30. LETTER.PT.
31. COMMENT.PT.
32. EDITORIAL.PT.
33. 30 OR 31 OR 32
34. 29 NOT 33
35. 23 AND 34
36. ANIMAL=YES
37. HUMAN=YES
38. 36 NOT (36 AND 37)
39. 35 NOT 38
40. LG=EN
41. 39 AND 40

MEDICINE CONCORDANCE AND FOLLOW UP MEDLINE SYS REV SEARCH STRATEGY - Searched 29/10/07

1. (FOLLOW ADJ UP OR FOLLOWUP OR FOLLOW-UP).TI,AB.
2. FOLLOW-UP-STUDIES.MJ.
3. (MEDICATION$ ADJ REVIEW$2).TI,AB.
4. 1 OR 2 OR 3
5. PATIENT-COMPLIANCE.DE.
6. TREATMENT-REFUSAL.DE.
7. (PATIENT$2 NEAR COMPLIANCE).TI,AB.
8. (PATIENT$2 NEAR CONCORDANCE).TI,AB.
9. (PATIENT$2 NEAR ADHERENCE).TI,AB.
10. (PATIENT$2 NEAR (NON-COMPLIANCE OR NONCOMPLIANCE)).TI,AB.
11. (PATIENT$2 NEAR (NON-ADHERENCE OR NONADHERENCE OR NON ADJ

ADHERENCE)).TI,AB.

12. (TREATMENT$2 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE OR REFUS$)).TI,AB.
13. (REGIMEN ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
14. ((MEDICINE$2 OR MEDICATION$2) ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
15. (DRUG ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
16. 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15
17. 4 AND 16
18. (SYSTEMATIC$ ADJ REVIEW$3).AB.
19. REVIEW.PT.
20. META-ANALYSIS.AB.
21. META-ANALYSIS.PT.
22. META-ANALYSIS.TI.
23. 18 OR 19 OR 20 OR 21 OR 22
24. LETTER.PT.
25. COMMENT.PT.
26. EDITORIAL.PT.
27. 24 OR 25 OR 26
28. 23 NOT 27
29. 17 AND 28
30. ANIMAL=YES
31. HUMAN=YES
32. 30 NOT (30 AND 31)
33. 29 NOT 32
34. LG=EN
35. 33 AND 34

MEDICINE CONCORDANCE POUND UPDATE WITH MC/SDM TERMS MEDLINE SYSREV SEARCH STRATEGY - **Searched 29/11/07**

1. PRESCRIPTIONS-DRUG#.DE.
2. PHARMACEUTICAL-PREPARATIONS-AD.DE. OR PHARMACEUTICAL-PREPARATIONS-AE.DE. OR PHARMACEUTICAL-PREPARATIONS-CT.DE. OR PHARMACEUTICAL-PREPARATIONS-DU.DE.
3. DRUGS-NON-PRESCRIPTION-AD.DE. OR DRUGS-NON-PRESCRIPTION-AE.DE. OR DRUGS-NON-PRESCRIPTION-CT.DE. OR DRUGS-NON-PRESCRIPTION-TU.DE.
4. DRUG-THERAPY-AE.DE. OR DRUG-THERAPY-NU.DE. OR DRUG-THERAPY-PX.DE. OR DRUG-THERAPY-UT.DE.
5. DRUG-UTILIZATION.DE.

6. PRESCRIB$.MP.
7. PRESCRIPTION$1.MP.
8. NON-PRESCRIPTION$1.MP.
9. (OVER NEAR COUNTER).MP.
10. OTC$1.MP.
11. DISPENS$4.MP.
12. PHARMACEUTICAL$1.MP.
13. DRUGS$1.MP.
14. MEDICIN$2.MP.
15. MEDICATION$1.MP.
16. (DRUG ADJ THERAPY).MP.
17. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16
18. (DECISION ADJ AID$2).TI,AB.
19. (DECISION ADJ MAKING).TI,AB.
20. DECISION-MAKING#.DE.
21. (DECISION ADJ SUPPORT ADJ SYSTEM$2).TI,AB.
22. DECISION-SUPPORT-SYSTEMS-CLINICAL#.DE.
23. (PATIENT ADJ INVOLVEMENT).TI,AB.
24. (PATIENT ADJ PARTICIPATION).TI,AB.
25. PATIENT-PARTICIPATION#.DE.
26. PROFESSIONAL-FAMILY-RELATIONS#.DE.
27. PROFESSIONAL-PATIENT-RELATIONS#.DE.
28. (CLINICIAN$2 OR DOCTOR$2 OR PHYSICIAN$2).TI. AND (PATIENT$2 OR PEOPLE$2).TI.
29. ATTITUDE-OF-HEALTH-PERSONNEL#.DE.
30. (DECISION ADJ AID$2).TI,AB.
31. (DECISION ADJ SUPPORT ADJ TECHNIQUE$2).TI,AB.
32. DECISION-SUPPORT-TECHNIQUES#.DE.
33. (SHARED ADJ DECISION).TI,AB.
34. (SHARING ADJ DECISION$2).TI,AB.
35. (INFORMED ADJ DECISION$2).TI,AB.
36. (INFORMED ADJ CHOICE).TI,AB.
37. (SHARE$2 OR SHARING OR INFORMED).TI,AB. AND DECISION$.TI,AB.
38. 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37
39. PATIENT-COMPLIANCE.DE.
40. TREATMENT-REFUSAL.DE.
41. (PATIENT$2 NEAR COMPLIANCE).TI,AB.
42. (PATIENT$2 NEAR CONCORDANCE).TI,AB.
43. (PATIENT$2 NEAR ADHERENCE).TI,AB.
44. (PATIENT$2 NEAR (NON-COMPLIANCE OR NONCOMPLIANCE)).TI,AB.
45. (PATIENT$2 NEAR (NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
46. (TREATMENT$2 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR

NONADHERENCE OR NON ADJ ADHERENCE OR REFUS$)).TI,AB.

47. (REGIMEN ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
48. ((MEDICINE$2 OR MEDICATION$2) ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
49. (DRUG ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
50. 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49
51. (FOCUS ADJ GROUP$1).MP.
52. INTERVIEWS.DE. OR INTERVIEW$.MP. OR RESEARCH.DE.
53. NURSING-RESEARCH-METHODOLOGY-MT.DE.
54. (PATIENT ADJ EXPERIENCE).MP.
55. (PATIENTS ADJ EXPERIENCES).MP.
56. (PATIENT ADJ PERCEPTION).MP.
57. (PATIENTS ADJ PERCEPTIONS).MP.
58. (PATIENT ADJ PERSPECTIVE).MP.
59. (PATIENTS ADJ PERSPECTIVES).MP.
60. ETHNOGRAPH$.MP.
61. (CONTENT ADJ ANALYSIS).MP.
62. (GROUNDED ADJ THEORY).MP.
63. QUALITATIVE.MP. OR (HEALTH ADJ SERVICES ADJ RESEARCH).DE. OR (RESEARCH ADJ DESIGN).DE.
64. 51 OR 52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58 OR 59 OR 60 OR 61 OR 62 OR 63
65. 17 AND 38 AND 50 AND 64
66. QUALITATIVE.MP.
67. 65 AND 66
68. (SYSTEMATIC$ ADJ REVIEW$).AB.
69. REVIEW.PT.
70. META-ANALYSIS OR META ADJ ANALYSIS OR METAANALYSIS.AB.
71. META-ANALYSIS OR META ADJ ANALYSIS OR METAANALYSIS.PT.
72. META-ANALYSIS OR META ADJ ANALYSIS OR METAANALYSIS.TI.
73. 68 OR 69 OR 70 OR 71 OR 72
74. LETTER.PT.
75. COMMENT.PT.
76. EDITORIAL.PT.
77. 74 OR 75 OR 76
78. 73 NOT 77
79. 67 AND 78
80. ANIMAL=YES
81. HUMAN=YES
82. 80 NOT (80 AND 81)
83. 79 NOT 82

84. LG=EN

85. 83 AND 84

MEDICINES CONCORDANCE POUND UPDATE SIMPLE MEDLINE SEARCH STRATEGY - Searched 03/12/07

1. Patient-Compliance-EH.DE. OR Patient-Compliance-PX.DE. OR Patient-Compliance-SN.DE. OR Patient-Compliance-QS.DE. OR Patient-Compliance-QW.DE.
2. PATIENT ADJ COMPLIANCE
3. 1 OR 2
4. ADHERENCE
5. MEDICIN$2
6. MEDICATION$2
7. QUALITATIVE$
8. 3 OR 4
9. 5 OR 6
10. 7 AND 8 AND 9
11. 10

MC POUND UPDATE MC & SDM MEDLINE SYS REV RERUN SEARCH STRATEGY - Searched 22/01/08

1. PRESCRIPTIONS-DRUG#.DE.
2. PHARMACEUTICAL-PREPARATIONS-AD.DE. OR PHARMACEUTICAL-PREPARATIONS-AE.DE. OR PHARMACEUTICAL-PREPARATIONS-CT.DE. OR PHARMACEUTICAL-PREPARATIONS-DU.DE.
3. DRUGS-NON-PRESCRIPTION-AD.DE. OR DRUGS-NON-PRESCRIPTION-AE.DE. OR DRUGS-NON-PRESCRIPTION-CT.DE. OR DRUGS-NON-PRESCRIPTION-TU.DE.
4. DRUG-THERAPY-AE.DE. OR DRUG-THERAPY-NU.DE. OR DRUG-THERAPY-PX.DE. OR DRUG-THERAPY-UT.DE.
5. DRUG-UTILIZATION.DE.
6. PRESCRIB$.MP.
7. PRESCRIPTION$1.MP.
8. NON-PRESCRIPTION$1.MP.
9. (OVER NEAR COUNTER).MP.
10. OTC$1.MP.
11. DISPENS$4.MP.
12. PHARMACEUTICAL$1.MP.
13. DRUGS$1.MP.
14. MEDICIN$2.MP.
15. MEDICATION$1.MP.
16. (DRUG ADJ THERAPY).MP.
17. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16

18. (DECISION ADJ AID$2).TI,AB.
19. (DECISION ADJ MAKING).TI,AB.
20. DECISION-MAKING#.DE.
21. (DECISION ADJ SUPPORT ADJ SYSTEM$2).TI,AB.
22. DECISION-SUPPORT-SYSTEMS-CLINICAL#.DE.
23. (PATIENT ADJ INVOLVEMENT).TI,AB.
24. (PATIENT ADJ PARTICIPATION).TI,AB.
25. PATIENT-PARTICIPATION#.DE.
26. PROFESSIONAL-FAMILY-RELATIONS#.DE.
27. PROFESSIONAL-PATIENT-RELATIONS#.DE.
28. (CLINICIAN$2 OR DOCTOR$2 OR PHYSICIAN$2).TI. AND (PATIENT$2 OR PEOPLE$2).TI.
29. ATTITUDE-OF-HEALTH-PERSONNEL#.DE.
30. (DECISION ADJ AID$2).TI,AB.
31. (DECISION ADJ SUPPORT ADJ TECHNIQUE$2).TI,AB.
32. DECISION-SUPPORT-TECHNIQUES#.DE.
33. (SHARED ADJ DECISION).TI,AB.
34. (SHARING ADJ DECISION$2).TI,AB.
35. (INFORMED ADJ DECISION$2).TI,AB.
36. (INFORMED ADJ CHOICE).TI,AB.
37. (SHARE$2 OR SHARING OR INFORMED).TI,AB. AND DECISION$.TI,AB.
38. 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37
39. PATIENT-COMPLIANCE.DE.
40. TREATMENT-REFUSAL.DE.
41. (PATIENT$2 NEAR COMPLIANCE).TI,AB.
42. (PATIENT$2 NEAR CONCORDANCE).TI,AB.
43. (PATIENT$2 NEAR ADHERENCE).TI,AB.
44. (PATIENT$2 NEAR (NON-COMPLIANCE OR NONCOMPLIANCE)).TI,AB.
45. (PATIENT$2 NEAR (NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
46. (TREATMENT$2 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE OR REFUS$)).TI,AB.
47. (REGIMEN ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
48. ((MEDICINE$2 OR MEDICATION$2) ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
49. (DRUG ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
50. BARRIER$2 NEAR (TREATMENT$2 OR MEDICINE$ OR MEDICATION$2 OR DRUG)
51. 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50
52. 17 OR 38 OR 51
53. QUALITATIVE.MP.

54. 52 AND 53
55. (SYSTEMATIC$ ADJ REVIEW$).AB.
56. META-ANALYSIS OR METAANALYSIS OR (META ADJ ANALYSIS).AB.
57. META-ANALYSIS OR METAANALYSIS OR (META ADJ ANALYSIS).PT.
58. META-ANALYSIS OR METAANALYSIS OR (META ADJ ANALYSIS).TI.
59. 55 OR 56 OR 57 OR 58
60. 54 AND 59
61. LETTER.PT.
62. COMMENT.PT.
63. EDITORIAL.PT.
64. 61 OR 62 OR 63
65. 60 NOT 64
66. ANIMAL=YES
67. HUMAN=YES
68. 66 NOT (66 AND 67)
69. 65 NOT 68
70. LG=EN
71. 69 AND 70

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Questions relating to medication reviews

MEDICINE CONCORDANCE AND MEDICATION REVIEW MEDLINE SYSREV SEARCH STRATEGY - Searched 27/09/07

1. (MEDICATION$ ADJ REVIEW$2).TI,AB.
2. PATIENT-COMPLIANCE.DE.
3. TREATMENT-REFUSAL.DE.
4. (PATIENT$2 NEAR COMPLIANCE).TI,AB.
5. (PATIENT$2 NEAR CONCORDANCE).TI,AB.
6. (PATIENT$2 NEAR ADHERENCE).TI,AB.
7. (PATIENT$2 NEAR (NON-COMPLIANCE OR NONCOMPLIANCE)).TI,AB.
8. (PATIENT$2 NEAR (NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
9. (TREATMENT$2 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE OR REFUS$)).TI,AB.
10. (REGIMEN ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
11. ((MEDICINE$2 OR MEDICATION$2) ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
12. (DRUG ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
13. 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12
14. 1 AND 13
15. (SYSTEMATIC$ ADJ REVIEW$).AB.
16. REVIEW.PT.
17. META-ANALYSIS.AB.
18. META-ANALYSIS.PT.
19. META-ANALYSIS.TI.
20. 15 OR 16 OR 17 OR 18 OR 19
21. LETTER.PT.
22. COMMENT.PT.
23. EDITORIAL.PT.
24. 21 OR 22 OR 23
25. 20 NOT 24
26. 14 AND 25
27. ANIMAL=YES
28. HUMAN=YES
29. 27 NOT (27 AND 28)
30. 26 NOT 29
31. LG=EN
32. 30 AND 31

Questions relating to equalities issues, patients with learning disabilities, and ethnic minorities

MEDICINES CONCORDANCE AND LEARNING DISABILITIES AND ETHNIC MINORITIES MEDLINE SYSREV SEARCH STRATEGY - Searched 15/10/07

1. (learning NEAR difficult$3).TI,AB.
2. (mental$4 ADJ (handicap$3 OR retard$6)).TI,AB.
3. (learning ADJ (disable$2 OR disabilit$3)).TI,AB.
4. (intellect$3 NEAR (disable$2 OR disabilit$3)).TI,AB.
5. (mental NEAR (deficien$4 OR incapacit$3)).TI,AB.
6. (intellect$3 NEAR impair$).TI,AB.
7. (down$2 ADJ syndrome).TI,AB.
8. (fragile ADJ syndrome).TI,AB.
9. (cognitiv$3 ADJ impair$).TI,AB.
10. (subnormal NEAR intellect$3).TI,AB.
11. oligophren$.TI,AB.
12. phenylketonuria.TI,AB.
13. Mental-Retardation#.DE.
14. Mentally-Disabled-Persons#.DE.
15. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14
16. Minority-Groups#.DE.
17. Ethnic-Groups#.DE.
18. Multilingualism#.W..DE.
19. Refugees#.W..DE.
20. Population-Groups#.DE.
21. Continental-Population-Groups#.DE.
22. Hispanic-Americans#.DE.
23. African-Continental-Ancestry-Group#.DE.
24. American-Native-Continental-Ancestry-Group#.DE.
25. Asian-Continental-Ancestry-Group#.DE.
26. European-Continental-Ancestry-Group#.DE.
27. Oceanic-Ancestry-Group#.DE.
28. African-Americans#.DE.
29. Arabs#.W..DE.
30. Asian-Americans#.DE.
31. Gypsies#.W..DE.
32. Mexican-Americans#.DE.
33. Inuits#.W..DE.
34. Jews#.W..DE.
35. Indians-Central-American#.DE.
36. Indians-North-American#.DE.
37. Indians-South-American#.DE.
38. Cultural-Characteristics#.DE.

39. ((underserve$2 OR disadvantage$2) NEAR (group$2 OR population$2)).TI,AB.
40. ethnic$6.TI,AB.
41. (multi-ethnic OR multi ADJ ethnic OR multiethnic).TI,AB.
42. (multi-racial OR multi ADJ racial OR multiracial).TI,AB.
43. (migrant$2 OR immigrant$2).TI,AB.
44. refugee$2.TI,AB.
45. (asylum-seekers OR asylum ADJ seekers).TI,AB.
46. (cultural ADJ diversit$4).TI,AB.
47. (multi-lingual OR multi ADJ lingual OR multilingual).TI,AB.
48. (multi-cultural OR multi ADJ cultural OR multicultural).TI,AB.
49. (cross-cultural OR cross ADJ cultural OR crosscultural).TI,AB.
50. (trans-cultural OR trans ADJ cultural OR transcultural).TI,AB.
51. Islam#.W..DE.
52. Hinduism#.W..DE.
53. Buddhism#.W..DE.
54. (minor$4 NEAR religio$3).TI,AB.
55. (islam$3 OR hindu$3 OR sikh$3 OR buddhis$2).TI,AB.
56. Judaism.W..DE.
57. 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56
58. 15 OR 57
59. PATIENT-COMPLIANCE.DE.
60. TREATMENT-REFUSAL.DE.
61. (PATIENT$2 NEAR COMPLIANCE).TI,AB.
62. (PATIENT$2 NEAR CONCORDANCE).TI,AB.
63. (PATIENT$2 NEAR ADHERENCE).TI,AB.
64. (PATIENT$2 NEAR (NON-COMPLIANCE OR NONCOMPLIANCE)).TI,AB.
65. (PATIENT$2 NEAR (NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
66. (TREATMENT$2 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE OR REFUS$)).TI,AB.
67. (REGIMEN ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
68. ((MEDICINE$2 OR MEDICATION$2) ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
69. (DRUG ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
70. 59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 OR 66 OR 67 OR 68 OR 69
71. 58 AND 70
72. (SYSTEMATIC$ ADJ REVIEW$).AB.
73. REVIEW.PT.
74. META-ANALYSIS.AB.

75. META-ANALYSIS.PT.
76. META-ANALYSIS.TI.
77. 72 OR 73 OR 74 OR 75 OR 76
78. LETTER.PT.
79. COMMENT.PT.
80. EDITORIAL.PT.
81. 78 OR 79 OR 80
82. 77 NOT 81
83. 71 AND 82
84. ANIMAL=YES
85. HUMAN=YES
86. 84 NOT (84 AND 85)
87. 83 NOT 86
88. LG=EN
89. 87 AND 88

MC & EQUALITIES ISSUES MEDLINE SEARCH - Searched 27/05/08

1. (LEARNING NEAR DIFFICULT$3).TI,AB.
2. (MENTAL$4 ADJ (HANDICAP$3 OR RETARD$6)).TI,AB.
3. (LEARNING ADJ (DISABLE$2 OR DISABILIT$3)).TI,AB.
4. (INTELLECT$5 NEAR (DISABLE$2 OR DISABILIT$3)).TI,AB.
5. (MENTAL NEAR (DEFICIEN$4 OR INCAPACIT$3)).TI,AB.
6. (INTELLECT$3 NEAR IMPAIR$).TI,AB.
7. (DOWN$2 ADJ SYNDROME).TI,AB.
8. (FRAGILE NEAR SYNDROME).TI,AB.
9. (COGNITIV$3 ADJ IMPAIR$).TI,AB.
10. (SUBNORMAL NEAR INTELLECT$3).TI,AB.
11. OLIGOPHREN$.TI,AB.
12. PHENYLKETONURIA.TI,AB.
13. MENTAL-RETARDATION#.DE.
14. MENTALLY-DISABLED-PERSONS#.DE.
15. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14
16. MINORITY-GROUPS#.DE.
17. ETHNIC-GROUPS#.DE.
18. MULTILINGUALISM#.W..DE.
19. REFUGEES#.W..DE.
20. POPULATION-GROUPS#.DE.
21. CONTINENTAL-POPULATION-GROUPS#.DE.
22. HISPANIC-AMERICANS#.DE.
23. AFRICAN-CONTINENTAL-ANCESTRY-GROUP#.DE.
24. AMERICAN-NATIVE-CONTINENTAL-ANCESTRY-GROUP#.DE.
25. ASIAN-CONTINENTAL-ANCESTRY-GROUP#.DE.

26. EUROPEAN-CONTINENTAL-ANCESTRY-GROUP#.DE.
27. OCEANIC-ANCESTRY-GROUP#.DE.
28. AFRICAN-AMERICANS#.DE.
29. ARABS#.W..DE.
30. ASIAN-AMERICANS#.DE.
31. GYPSIES#.W..DE.
32. MEXICAN-AMERICANS#.DE.
33. INUITS#.W..DE.
34. JEWS#.W..DE.
35. INDIANS-CENTRAL-AMERICAN#.DE.
36. INDIANS-NORTH-AMERICAN#.DE.
37. INDIANS-SOUTH-AMERICAN#.DE.
38. CULTURAL-CHARACTERISTICS#.DE.
39. ((UNDERSERVE$2 OR DISADVANTAGE$2) NEAR (GROUP$2 OR POPULATION$2)).TI,AB.
40. ETHNIC$6.TI,AB.
41. (MULTI-ETHNIC OR MULTI ADJ ETHNIC OR MULTIETHNIC).TI,AB.
42. (MULTI-RACIAL OR MULTI ADJ RACIAL OR MULTIRACIAL).TI,AB.
43. (MIGRANT$2 OR IMMIGRANT$2).TI,AB.
44. REFUGEE$2.TI,AB.
45. (ASYLUM-SEEKERS OR ASYLUM ADJ SEEKERS).TI,AB.
46. (CULTURAL ADJ DIVERSIT$4).TI,AB.
47. (MULTI-LINGUAL OR MULTI ADJ LINGUAL OR MULTILINGUAL).TI,AB.
48. (MULTI-CULTURAL OR MULTI ADJ CULTURAL OR MULTICULTURAL).TI,AB.
49. (CROSS-CULTURAL OR CROSS ADJ CULTURAL OR CROSSCULTURAL).TI,AB.
50. (TRANS-CULTURAL OR TRANS ADJ CULTURAL OR TRANSCULTURAL).TI,AB.
51. ISLAM#.W..DE.
52. HINDUISM#.W..DE.
53. BUDDHISM#.W..DE.
54. (MINOR$4 NEAR RELIGIO$3).TI,AB.
55. (ISLAM$3 OR HINDU$3 OR SIKH$3 OR BUDDHIS$2).TI,AB.
56. JUDAISM#.W..DE.
57. 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56
58. 15 OR 57
59. (DECISION ADJ AID$2).TI,AB.
60. (DECISION ADJ MAKING).TI,AB.
61. DECISION-MAKING#.DE.
62. (DECISION ADJ SUPPORT ADJ SYSTEM$2).TI,AB.
63. DECISION-SUPPORT-SYSTEMS-CLINICAL#.DE.
64. (DECISION ADJ SUPPORT ADJ TECHNIQUE$2).TI,AB.
65. DECISION-SUPPORT-TECHNIQUES#.DE.
66. (SHARED ADJ DECISION).TI,AB.
67. (SHARING ADJ DECISION$2).TI,AB.

68. (INFORMED ADJ DECISION$2).TI,AB.
69. (INFORMED ADJ CHOICE).TI,AB.
70. (SHARE$2 OR SHARING OR INFORMED).TI,AB. AND DECISION$.TI,AB.
71. 59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 OR 66 OR 67 OR 68 OR 69 OR 70
72. PATIENT-COMPLIANCE#.DE.
73. TREATMENT-REFUSAL#.DE.
74. (PATIENT$2 NEAR COMPLIANCE).TI,AB.
75. (PATIENT$2 NEAR CONCORDANCE).TI,AB.
76. (PATIENT$2 NEAR ADHERENCE).TI,AB.
77. (PATIENT$2 NEAR (NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE)).TI,AB.
78. (PATIENT$2 NEAR (NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
79. (TREATMENT$2 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE OR REFUS$)).TI,AB.
80. (REGIMEN$2 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
81. ((MEDICINE$2 OR MEDICATION$2) ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
82. (DRUG$2 ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
83. (THERAP$7 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE OR REFUS$)).TI,AB.
84. 72 OR 73 OR 74 OR 75 OR 76 OR 77 OR 78 OR 79 OR 80 OR 81 OR 82 OR 83
85. 71 OR 84
86. 58 AND 85
87. PT=COMMENT OR PT=CONGRESSES OR PT=EDITORIAL OR PT=LETTER
88. 86 NOT 87
89. ANIMAL=YES
90. HUMAN=YES
91. 89 NOT (89 AND 90)
92. 88 NOT 91
93. LG=EN
94. 92 AND 93
95. GREAT-BRITAIN#.DE.
96. 94 AND 95

Question 24: Dose changing

MC & DOSE CHANGING MEDLINE SYS REV SEARCH STRATEGY - Searched 25/03/08

1. (CHANGE OR CHANGING OR CHANGES).TI,AB.
2. (AFFECT OR AFFECTS OR AFFECTING).TI,AB.
3. (DOSE OR DOSES OR DOSAGE).TI,AB.
4. 1 OR 2 OR 3
5. PATIENT-COMPLIANCE.MJ.
6. TREATMENT-REFUSAL.MJ.
7. (PATIENT$2 NEXT COMPLIANCE).TI,AB.
8. (PATIENT$2 NEXT CONCORDANCE).TI,AB.
9. (PATIENT$2 NEXT ADHERENCE).TI,AB.
10. (PATIENT$2 NEXT (NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE)).TI,AB.
11. (PATIENT$2 NEXT (NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
12. (TREATMENT$2 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE OR REFUS$4)).TI,AB.
13. (THERAP$7 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE OR REFUS$4)).TI,AB.
14. (REGIMEN$2 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
15. ((MEDICINE$2 OR MEDICATION$2) ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
16. (DRUG$2 ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
17. 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16
18. 4 AND 17
19. (SYSTEMATIC$ ADJ REVIEW$).AB.
20. REVIEW.PT.
21. META-ANALYSIS OR METAANALYSIS OR (META ADJ ANALYSIS).AB.
22. META-ANALYSIS OR METAANALYSIS OR (META ADJ ANALYSIS).PT.
23. META-ANALYSIS OR METAANALYSIS OR (META ADJ ANALYSIS).TI.
24. 19 OR 20 OR 21 OR 22 OR 23
25. 18 AND 24
26. LETTER.PT.
27. COMMENT.PT.
28. EDITORIAL.PT.
29. 26 OR 27 OR 28
30. 25 NOT 29

31. ANIMAL=YES
32. HUMAN=YES
33. 31 NOT (31 AND 32)
34. 30 NOT 33
35. LG=EN
36. 34 AND 35

Question: Consultation length

MC & CONSULTATION LENGTH & SDM TERMS MEDLINE SYS REV SEARCH STRATEGY - Searched 26/03/08

1. (PATIENT ADJ INVOLVE$4 NEAR INCREAS$3).TI,AB.
2. (PATIENT ADJ INVOLVEMENT).TI,AB.
3. (INCREASE NEAR (LENGTH OR DURATION)).TI,AB.
4. CONSULTATION.TI,AB.
5. ((LENGTH OR INCREAS$3 OR EXTEN$4) NEAR CONSULTATION$2).TI,AB.
6. 1 OR 2 OR 3 OR 4 OR 5
7. (DECISION ADJ AID$2).TI,AB.
8. (DECISION ADJ MAKING).TI,AB.
9. DECISION-MAKING#.DE.
10. (DECISION ADJ SUPPORT ADJ SYSTEM$2).TI,AB.
11. DECISION-SUPPORT-SYSTEMS-CLINICAL#.DE.
12. (PATIENT ADJ INVOLVEMENT).TI,AB.
13. (PATIENT ADJ PARTICIPATION).TI,AB.
14. PATIENT-PARTICIPATION#.DE.
15. PROFESSIONAL-FAMILY-RELATIONS#.DE.
16. PROFESSIONAL-PATIENT-RELATIONS#.DE.
17. (CLINICIAN$2 OR DOCTOR$2 OR PHYSICIAN$2).TI. AND (PATIENT$2 OR PEOPLE$2).TI.
18. ATTITUDE-OF-HEALTH-PERSONNEL#.DE.
19. (DECISION ADJ AID$2).TI,AB.
20. (DECISION ADJ SUPPORT ADJ TECHNIQUE$2).TI,AB.
21. DECISION-SUPPORT-TECHNIQUES#.DE.
22. (SHARED ADJ DECISION).TI,AB.
23. (SHARING ADJ DECISION$2).TI,AB.
24. (INFORMED ADJ DECISION$2).TI,AB.
25. (INFORMED ADJ CHOICE).TI,AB.
26. (SHARE$2 OR SHARING OR INFORMED).TI,AB. AND DECISION$.TI,AB.
27. 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26
28. 6 AND 27
29. (SYSTEMATIC$ ADJ REVIEW$2).AB.
30. REVIEW.PT.
31. (META-ANALYSIS OR META ADJ ANALYSIS OR META-ANALYSIS).AB.

32. (META-ANALYSIS OR META ADJ ANALYSIS OR META-ANALYSIS).PT.
33. (META-ANALYSIS OR META ADJ ANALYSIS OR META-ANALYSIS).TI.
34. 29 OR 30 OR 31 OR 32 OR 33
35. PT=COMMENT OR PT=EDITORIAL OR PT=LETTER
36. 28 AND 34
37. 36 NOT 35
38. ANIMAL=YES
39. HUMAN=YES
40. 38 NOT (38 AND 39)
41. 37 NOT 40
42. LG=EN
43. 41 AND 42

Question 26: Dosage formulation and packaging

MC & FORMULATION & PACKAGING MEDLINE SYSREV SEARCH - Searched 13/03/08

1. DRUG-PACKAGING#.DE.
2. CHEMISTRY-PHARMACEUTICAL.DE.
3. (DRUG ADJ FORMULATION).TI,AB.
4. PACKAGING.TI,AB.
5. 1 OR 2 OR 3 OR 4
6. PATIENT-COMPLIANCE.MJ.
7. TREATMENT-REFUSAL.MJ.
8. (PATIENT$2 NEXT COMPLIANCE).TI,AB.
9. (PATIENT$2 NEXT CONCORDANCE).TI,AB.
10. (PATIENT$2 NEXT ADHERENCE).TI,AB.
11. (PATIENT$2 NEXT (NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE)).TI,AB.
12. (PATIENT$2 NEXT (NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
13. (TREATMENT$2 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE OR REFUS$4)).TI,AB.
14. (THERAP$7 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE OR REFUS$4)).TI,AB.
15. (REGIMEN$2 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
16. ((MEDICINE$2 OR MEDICATION$2) ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
17. (DRUG$2 ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE

OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.

18. 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17
19. 5 AND 18
20. (SYSTEMATIC$ ADJ REVIEW$).AB.
21. REVIEW.PT.
22. META-ANALYSIS OR METAANALYSIS OR (META ADJ ANALYSIS).AB.
23. META-ANALYSIS OR METAANALYSIS OR (META ADJ ANALYSIS).PT.
24. META-ANALYSIS OR METAANALYSIS OR (META ADJ ANALYSIS).TI.
25. 20 OR 21 OR 22 OR 23 OR 24
26. 19 AND 25
27. LETTER.PT.
28. COMMENT.PT.
29. EDITORIAL.PT.
30. 27 OR 28 OR 29
31. 26 NOT 30
32. ANIMAL=YES
33. HUMAN=YES
34. 32 NOT (32 AND 33)
35. 31 NOT 34
36. LG=EN
37. 35 AND 36

Question 25: Prescription fees

MC & PRESCRIPTION FEES MEDLINE SYSREV SEARCH - Searched 18/03/08

1. PRESCRIPTION-FEES#.DE.
2. ((COST OR COSTS) NEAR PRESCRIPTION$2).TI,AB.
3. ((COST OR COSTS) NEAR ADHERENCE).TI,AB.
4. (COST OR COSTS).TI,AB.
5. 1 OR 2 OR 3 OR 4
6. PATIENT-COMPLIANCE.MJ.
7. TREATMENT-REFUSAL.MJ.
8. (PATIENT$2 NEXT COMPLIANCE).TI,AB.
9. (PATIENT$2 NEXT CONCORDANCE).TI,AB.
10. (PATIENT$2 NEXT ADHERENCE).TI,AB.
11. (PATIENT$2 NEXT (NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE)).TI,AB.
12. (PATIENT$2 NEXT (NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
13. (TREATMENT$2 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE OR REFUS$4)).TI,AB.
14. (THERAP$7 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR

NONADHERENCE OR NON ADJ ADHERENCE OR REFUS$4)).TI,AB.

15. (REGIMEN$2 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
16. ((MEDICINE$2 OR MEDICATION$2) ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
17. (DRUG$2 ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
18. 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17
19. 5 AND 18
20. (SYSTEMATIC$ ADJ REVIEW$).AB.
21. REVIEW.PT.
22. META-ANALYSIS OR METAANALYSIS OR (META ADJ ANALYSIS).AB.
23. META-ANALYSIS OR METAANALYSIS OR (META ADJ ANALYSIS).PT.
24. META-ANALYSIS OR METAANALYSIS OR (META ADJ ANALYSIS).TI.
25. 20 OR 21 OR 22 OR 23 OR 24
26. 19 AND 25
27. LETTER.PT.
28. COMMENT.PT.
29. EDITORIAL.PT.
30. 27 OR 28 OR 29
31. 26 NOT 30
32. ANIMAL=YES
33. HUMAN=YES
34. 32 NOT (32 AND 33)
35. 31 NOT 34
36. LG=EN
37. 35 AND 36

MC & PRESCRIPTION FEES REVISED MEDLINE SEARCH STRATEGY - Searched 28/04/08

1. SEARCH: PRESCRIPTION-FEES#.DE.
2. SEARCH: FEES-AND-CHARGES#.DE.
3. SEARCH: ((COST OR COSTS) NEAR PRESCRIPTION$2).TI,AB.
4. SEARCH: ((COST OR COSTS) NEAR ADHERENCE).TI,AB.
5. SEARCH: (COST OR COSTS).TI,AB.
6. SEARCH: 1 OR 2 OR 3 OR 4 OR 5
7. SEARCH: PATIENT-COMPLIANCE.MJ.
8. SEARCH: TREATMENT-REFUSAL.MJ.
9. SEARCH: (PATIENT$2 NEXT COMPLIANCE).TI,AB.
10. SEARCH: (PATIENT$2 NEXT CONCORDANCE).TI,AB.
11. SEARCH: (PATIENT$2 NEXT ADHERENCE).TI,AB.
12. SEARCH: (PATIENT$2 NEXT (NON-COMPLIANCE OR NONCOMPLIANCE OR

NON ADJ COMPLIANCE)).TI,AB.

13. SEARCH: (PATIENT$2 NEXT (NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
14. SEARCH: (TREATMENT$2 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE OR REFUS$4)).TI,AB.
15. SEARCH: (THERAP$7 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE OR REFUS$4)).TI,AB.
16. SEARCH: (REGIMEN$2 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
17. SEARCH: ((MEDICINE$2 OR MEDICATION$2) ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
18. SEARCH: (DRUG$2 ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
19. SEARCH: 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18
20. SEARCH: 6 AND 19
21. SEARCH: LETTER.PT.
22. SEARCH: COMMENT.PT.
23. SEARCH: EDITORIAL.PT.
24. SEARCH: 21 OR 22 OR 23
25. SEARCH: 20 NOT 24
26. SEARCH: ANIMAL=YES
27. SEARCH: HUMAN=YES
28. SEARCH: 26 NOT (26 AND 27)
29. SEARCH: 25 NOT 28
30. SEARCH: LG=EN
31. SEARCH: 29 AND 30
32. SEARCH: GREAT-BRITAIN#.DE.
33. SEARCH: 31 AND 32

Questions relating to preferences for involvement, beliefs, information needs, and agreement

MC MEDICINES BELIEFS PREFERENCES FOR INVOLVEMENT & AGREEMENT
MEDLINE SEARCH STRATEGY - Searched 16/04/08

1. ((PATIENT$1 OR PUBLIC) ADJ (INFORMATION OR SATISFACTION OR PERCEPTION$1 OR PREFERENCE$1 OR BELIEF$1 OR ATTITUDE$1 OR AGREEMENT OR OPINION$1)).TI,AB.
2. (INFORMATION ADJ NEED$1).TI,AB.
3. (MEDICINE$1 ADJ INFORMATION).TI,AB.
4. 1 OR 2 OR 3
5. (MEDICINE$1 OR MEDICATION$1).TI,AB.
6. PRESCRIPTIONS-DRUG#.MJ.
7. PRESCRIPTION$1.TI,AB.
8. DECISION-MAKING#.MJ.
9. TREATMENT.TI,AB.
10. 5 OR 6 OR 7 OR 8 OR 9
11. 4 AND 10
12. QUESTIONNAIRES#.W..MJ.
13. (MEASURE OR MEASURING OR MEASUREMENT).TI,AB.
14. ASSESS$5.TI,AB.
15. QUESTIONNAIRE$1.TI,AB.
16. SCALE$1.TI,AB.
17. TOOL$1.TI,AB.
18. INSTRUMENT$1.TI,AB.
19. VALID$3.TI,AB.
20. 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19
21. 11 AND 20
22. LETTER.PT.
23. COMMENT.PT.
24. EDITORIAL.PT.
25. 22 OR 23 OR 24
26. 21 NOT 25
27. ANIMAL=YES
28. HUMAN=YES
29. 27 NOT (27 AND 28)
30. 26 NOT 29
31. LG=EN
32. 30 AND 31

Question: Compliance aids

MC & DOSETTE BOXES MEDLINE SEARCH STRATEGY - Searched 28/04/08

1. DOSETTE$1
2. (NOMAD OR MANRAX) NEAR SYSTEM$1
3. MONITORED NEAR DOS$3 NEAR SYSTEM$1
4. 1 OR 2 OR 3
5. LETTER.PT.
6. COMMENT.PT.
7. EDITORIAL.PT.
8. 5 OR 6 OR 7
9. 4 NOT 8
10. ANIMAL=YES
11. HUMAN=YES
12. 10 NOT (10 AND 11)
13. 9 NOT 12
14. LG=EN
15. 13 AND 14

The search strategy was revised to include all compliance aids.

MC AND COMPLIANCE AIDS MEDLINE SEARCH STRATEGY - Searched 01/05/08

1. DOSETTE$1
2. (NOMAD OR MANRAX) NEAR SYSTEM$1
3. MONITORED NEAR DOS$3 NEAR SYSTEM$1
4. COMPLIANCE ADJ AID$1
5. 1 OR 2 OR 3 OR 4
6. LETTER.PT.
7. COMMENT.PT.
8. EDITORIAL.PT.
9. 6 OR 7 OR 8
10. 5 NOT 9
11. ANIMAL=YES
12. HUMAN=YES
13. 11 NOT (11 AND 12)
14. 10 NOT 13
15. LG=EN
16. 14 AND 15

Question: Self-reporting of adherence

MC & SELF REPORTING MEDLINE SEARCH STRATEGY - Searched 30/04/08

1. (SELF-REPORT$3 OR SELF ADJ REPORT$3 OR SELFREPORT$3).TI,AB.
2. (PATIENT ADJ REPORT$3).TI,AB.
3. 1 OR 2
4. PATIENT-COMPLIANCE.MJ.
5. TREATMENT-REFUSAL.MJ.
6. (PATIENT$2 NEXT COMPLIANCE).TI,AB.
7. (PATIENT$2 NEXT CONCORDANCE).TI,AB.
8. (PATIENT$2 NEXT ADHERENCE).TI,AB.
9. (PATIENT$2 NEXT (NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE)).TI,AB.
10. (PATIENT$2 NEXT (NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
11. (TREATMENT$2 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE OR REFUS$4)).TI,AB.
12. (THERAP$7 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE OR REFUS$4)).TI,AB.
13. (REGIMEN$2 ADJ (COMPLIANCE OR ADHERENCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
14. ((MEDICINE$2 OR MEDICATION$2) ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
15. (DRUG$2 ADJ (CONCORDANCE OR COMPLIANCE OR NON-COMPLIANCE OR NONCOMPLIANCE OR NON ADJ COMPLIANCE OR ADHERENCE OR NON-ADHERENCE OR NONADHERENCE OR NON ADJ ADHERENCE)).TI,AB.
16. 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15
17. 3 AND 16
18. LETTER.PT.
19. COMMENT.PT.
20. EDITORIAL.PT.
21. 18 OR 19 OR 20
22. 17 NOT 21
23. ANIMAL=YES
24. HUMAN=YES
25. 23 NOT (23 AND 24)
26. 22 NOT 25
27. LG=EN
28. 26 AND 27

Evidence Extractions

Question: Is it possible to increase patient involvement in decisions about medicines?

Grading: 1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias

Lewin SA;Skea ZC;Entwistle V;Zwarenstein M;Dick J;

Interventions for providers to promote a patient-centred approach in clinical consultations

Ref ID 8713 2001

Study Type	Systematic Review	**Funding**	Health in Partnership initiative, DOH (UK); Dept for International Development (UK); Nuffield Commonwealth Programme (UK); Chief Scientist Office of the Scottish Executive Health Department (UK); Medical Research Council (South Africa).

Number of participant	RCTs; Controlled clinical trials; Controlled before and after studies; Interrupted time series studies.
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	The main conclusion is that there is 'fairly strong evidence to suggest that some interventions to promote patient-centred care in clinical consultations may lead to significant increases in the patient centredness of consultation processes'. However the evidence on patient-centred care in consultations is limited and the effects are mixed for behaviours and health status. Further research is required. 17 studies were included all of which included an element of training for HCPs. Seven studies involved multi-faceted interventions. 12/14 studies which assessed consultation processes found some improvement. 6/11 studies which looked at patient satisfaction found significant differences on one or more measures for the intervention group. It may not be completely relevant to the question as it is about improving patient-centeredness care and may not involve increasing patient involvement.
Effect due to factor in study?	

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Wetzels R;Harmsen M;van WC;Grol R;Wensing M;

Interventions for improving older patients' involvement in primary care episodes

Ref ID 5434 2007

Study Type Systematic Review **Funding** Cochrane Collaboration.

Number of participant RCT and quasi experimental

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

It is limited as it is interventions for improving older patients' involvement. Therefore this is partially the population we are looking at - would be better if whole population.

Also two of the studies were not relevant as they were not relating to consultation length.

They found some positive effects of specific methods to improve the involvement of older people in health care episodes. However there is not enough studies to conclude and recommend the use of any intervention in practice. The literature on older patients is sparse.

One study is therefore relevant to us (Cegala 2001) which had a partly open method of allocation; double blinding; 45 participants (22 intervention and 23 control) which is small; They gave a brief pre-interview questionnaire for baseline measurement.

It is strong because it is well-conducted but it did not find enough strong studies to be of a good source of evidence for a guideline.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Grading: 1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

Harrington-Jane NL;

Improving patients' communication with doctors: A systematic review of intervention studies

Ref ID 8780 2004

Study Type Systematic Review **Funding** NHS London Regional Office, Research and Development Programme.

Number of participant RCT and Quasi-experimental.

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Out of 16 studies, 10 reported a significant increase and five reported a non-significant increase in patient participation. This participation was measured by patient question asking, patient clarification, consultation length, expressed affect, doctor encouraging patient participation.

Equal numbers of studies reported significant and non-significant trends in question-asking behaviour. Four out of five studies showed significant increases in patient clarification.

Only 2 studies showed significant increases in patient satisfaction due to the interventions. However overall high levels of satisfaction were reported.

Overall, half of the interventions resulted in increased patient participation. With more significant results for bids for clarification than question asking.

This study aimed to examine the intervention studies which were designed to increase patients' participation in medical consultations and so answers the question of what tools are available to help practitioners elicit patients beliefs about medicines and information needs. Those interventions which encourage patients to gain clarification may increase patient participation and satisfaction.

The review noted any weaknesses within the review of the studies. There was a problem in that the use of different systems of reporting - audiotaped, video, made it hard to be comparable. Most of the studies were not blind to group allocation which

	could cause bias. There was little consistency in the measures used - the most frequent used was question-asking.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Little P;Dorward M;Warner G;Moore M;Stephens K;Senior J;Kendrick T;

Randomised controlled trial of effect of leaflets to empower patients in consultations in primary care

Ref ID 8864 2004

Study Type Randomised Controlled Trial **Funding** Southampton University

Number of participant	N=636 total General leaflet - 317 No general leaflet - 319 Depression leaflet - 318 No depression leaflet - 319
Inclusion/Exclusion Criteria	Aged 16-80 years, consulting at one of five general practices in the UK. Patients were excluded if they were receiving specialist psychiatric treatment, had dementia, were too unwell to consent, were receiving treatment for depression or were only collecting a prescription.
Patient Characteristics	42.5% male; 70% married and 53% in paid work
Recruitment	Patients were consulting at one of five general practices in the UK.
Setting	GP practice in the UK
Interventions/ Test/ Factor being investigated	Participants were randomised to four conditions: receipt of a general leaflet, depression leaflet, both leaflets and no leaflets (control group). The general leaflet which asked patients to list issues they wanted to raise and explained that the doctor wanted them to ask questions, talk and discuss any problems of concern to them. The depression leaflet listed symptoms of depression (without labelling as such) and asking if they had them and that the doctor would like to discuss them. The outcomes measured were patient satisfaction (the scores reflected aspects of doctor patient communication), consultation time, prescribing, referral and investigation.
Comparisons	Comparisons are made between receiving a general leaflet, a depression leaflet, both or neither
Length of Study/ Follow-up	Before and after consultation
Outcome measures studied	Self measured satisfaction and enablement scale
Results	The only significant interaction was the increase in satisfaction for those who received the general leaflet, the mean difference was 0.17 (95% CI 0.01 to 0.32, p=0.04). The general leaflet was significantly more effective when consultations were shorter (leaflet 0.64, 95% CI 0.19 to 1.08; time 0.31, 95% CI 0.0 to 0.06; interaction between both showed that consultations of 5, 8, and 10 mins increased satisfaction by 14%, 10% and 7%). The leaflet overall caused a small non-significant increase in consultation time. This was also shown for subscales of satisfaction – comfort from communication 1.02 (95% CI 0.36 to 1.68), relief of distress 0.74 (95% CI 0.0 to 1.49), intention to comply with management decisions 0.65 (95% CI 0.06 to 1.23) and rapport 0.81 (95% CI 0.16 to 1.45). The general leaflet increased the number of

	investigations by the doctor (OR 1.43, 95% CI 1.00 to 2.05), which was unlikely to be due to chance or confounders after controlling.
Safety and adverse effects	None
Does the study answer the question?	The results show an increased number of consultations and general leaflets may help to empower patients in the context of a GP consultation
Effect due to factor in study?	This is a self measured outcome and is subject to bias
Consistency of results with other studies?	Unknown
Directly applicable to guideline population?	Yes
Internal Validity	Self report

Rao JK;

Communication interventions make a difference in conversations between physicians and patients: A systematic review of the evidence

Ref ID 8777 2007

Study Type	Systematic Review	**Funding**	National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia, and ORC Macro Inc.

Number of participant	RCT
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	

Does the study answer the question?

2193+ citations found, 344 articles pulled for detailed review, 69 of which described trials of communication interventions that targeted physicians or patients and reported an objective measure of verbal communicative behaviour. Of these 30 were nonrandomised controlled trials and excluded. 36 RCTs eligible for review and abstraction. 18 were interventions for practicing physicians or residents, 15 interventions on patients and 3 intervened on both.

They rated the interventions low to high intensity. Most of the studies were moderately or highly intense.

Most of the 21 studies which included physicians found that there was significant improvement in communication behaviours of physicians/residents. Very high intensity interventions lead to more open-ended questions (4 studies) and fewer biomedically focused questions (2 studies) than the comparison physicians group. Compared to controls intervention physicians were more likely to elicit patients' previsit concerns (3 studies) and show an overall patient-centred communication style (6 studies).

Intervention physicians gave more information on specific issues (6 studies), received higher ratings for their skills (3 studies) than comparison physicians. Some findings showed no effect on communication style (2 studies).

18 studies of interventions focusing on patients, were mixed new, continuing or both types of patients. Information was the most common type of intervention, often through written instructions. Some studies included models of desirable communication behaviours such as examples of questions to ask physicians (7 studies).

Of the 18 studies 3 assessed the effects on patients information providing behaviours - results were mixed. 17 studies assessed patient involvement using different measures - the findings were mixed even the moderately intense interventions. From the 7 studies that assessed the degree that patients spoke during the visit 5 of these showed significant changes in their communication patterns. All of these included skills practice as part of the intervention, they demonstrated a greater ability to direct, or initiate conversation and obtained more information than controls. 2 studies that were of low-intensity did not have significant changes in patient involvement.

Authors Conclusions: They found that generally the interventions enhanced communication behaviours among physicians. Similar modest effects were found for the patient interventions. Intervention intensity was important in physicians' behaviours but was less pronounced with patients. Few studies assessed the effect of the interventions on information verifying behaviours (e.g checking understanding, summarising information). Many of the interventions cannot be implemented into everyday practice and so more practical interventions need to be designed.

Strengths: Low in bias as only RCTs included and quality assessed. Noted the intensity of the intervention studies. Methodology annotated well. Weaknesses: different populations and settings make comparability difficult.

Relationship to question: there are interventions available, for physicians which can improve their communication to the individuals and elicit more patient-centred dialogue. There are also interventions which can improve patients communication when visiting their physician thus gaining more information. These can both lead to more elicitation of patients beliefs about medicines and information needs.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Providing a web-based online medical record with electronic communication capabilities to patients with congestive heart failure: randomized trial.

Ref ID 1819 2004

Study Type Randomised Controlled Trial **Funding** Commonwealth Fund.

Number of participant Total sample: 107. intervention group: 54, control group: 53.

Inclusion/Exclusion Criteria Inclusion: Patients were eligible for the study if they were followed in the practice, spoke English, and were 18 years of age or older. They needed to have used a Web browser before, although they did not need to have access to the Internet at home.

Exclusion: Physicians, nurses, physician assistants, and nurse practitioners.

Patient Characteristics Mean age (years): Intervention group: 57, Control group: 55. Gender: Male: intervention group: 80%, control group: 74%. White, non-Hispanic: Intervention group: 92%, control group: 88%. No significant differences reported between treatment and control groups. External validity: participants enrolled in study had significant baseline differences in baseline characteristics from those who refused to enrol in the study but who were offered the opportunity to do so.

Recruitment Patients were approached in waiting room on hospital and asked if they wished to participate.

Setting

Interventions/ Test/ Factor being investigated The SPPARO (System Providing Access to Records Online) software consisted of a web-based electronic medical record, an educational guide, and a messaging system enabling electronic communication between the patient and staff. The medical record consists of clinical notes, laboratory reports, and test results (including reports of radiographs and echocardiograms). The educational guide is an online version of the printed materials that all patients in the heart failure practice receive at their first visit. The messaging system allowed patients to exchange secure messages with the nursing staff in the practice. Staff regularly contacted participants to encourage them to use the system.

Comparisons System Providing Access to Records Online (SPPARO) intervention v standard care. Intervention v control.

Length of Study/ Follow-up 1 year.

Outcome measures studied Surveys assessing doctor-patient communication, adherence, and health status were conducted at baseline, 6 months, and 1 year (1 year results given below). Adherence assessed by two mailed self-report questionnaires.

Results Adherence: General adherence to medical advice showed significant improvement in the intervention group compared with the control group (intervention group: 85, Control group: 78. Difference +6.4 (95% CI 1.8, 10.9), p=0.01). Adherence to medications showed a similar trend but did not reach statistical significance (intervention group: 3.6, Control group: 3.4, Difference +0.2 (95% CI -0.1, 0.6), p=0.15).

Other outcomes: At 12 months, the intervention group was not found to be superior in self-efficacy or for other measures of health status. Patient satisfaction with doctor patient-communication demonstrated a trend towards improvement in two areas: how well patients felt their problems were understood, and how well doctors explained information. While significant results were found for these two items individually, the findings did not reach statistical significance when adjusted for multiple comparisons. There was no significant improvement in the other patient satisfaction domains. The intervention group had more emergency department visits (20 vs 8, p=0.03), but these visits were not temporally related to use of the online medical record. There were no differences between the two groups in terms of the number of deaths, number of patients hospitalized, number of hospitalizations, number of patients taken to emergency rooms, number of visits to emergency rooms, number of patients in heart failure practice or number of visits to heart failure practice.

Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention was to improve patient education, engagement and empowerment. An internet-accessible medial record can offer modest benefits, with improvements in adherence, patient satisfaction with doctor-patient communication.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant outcomes relating to SDM (self-efficacy, adherence and satisfaction).
Internal Validity	

Wetzels R;Wensing M;van WC;Grol R;

A consultation leaflet to improve an older patient's involvement in general practice care: A randomized trial

Ref ID 4945 2005

Study Type	Randomised Controlled Trial	**Funding**	EU (Quality of life and management of living resources programme 1998-2002); The ageing population and disabilities; Netherlands Organisation for Health Research and Development.

Number of participant	315 pre-intervention and 263 post-intervention.
Inclusion/Exclusion Criteria	Gp patients aged 70 years or older who had consulted them recently during the period June to November 2002. Exclusion criteria: visually impaired or if gp thought not suitable for participating.
Patient Characteristics	Mean age 75 years. Mainly male.
Recruitment	Letter sent by gp.
Setting	Gp practice. Netherlands.
Interventions/ Test/ Factor being investigated	The intervention practices received a consultation leaflet by mail. This leaflet included a short motivating text on patient involvement and a mixture of open and pre-structured questions to help patients prepare for the next consultation and prioritize which problems they wanted to discuss with their gp. The questions were chosen as they would help to explore patient's ideas, fears and expectations and encourage them to address important issues. GPs received a 30 minute practice visit to motivate them to involve patients and instruct them on use of the consultation leaflet.
Comparisons	Leaflet by mail compared to usual care.
Length of Study/ Follow-up	Questionnaire sent after consultation.
Outcome measures studied	Perceived involvement in primary care was the primary outcome after use of the leaflet. Secondary outcomes were consultation length, demographic characteristics, and whether they discussed one of eight underreported health problems.

Results	Subjects were satisfied with their involvements and the GPs behaviour during the consultation, however no difference in effect as a result of the leaflet on involvement, enablement or satisfaction were found between the intervention and control groups. Estimated effect size difference of PEI -0.226 (95% CI -0.475 to 0.022, p=0.075); COMRADE 0.091 (95% CI -0.129 to 0.311, p=0.42); EUROPEP -0.171 (95% CI -0.472 to 0.131), p=0.267) and consultation length 0.411 (95% CI -2.043 to 2.866, p=0.74) when adjusted for clustering and leaflet used correctly. Intervention group leaflet users reported more psychological symptoms to their GP compared with non-users of the leaflet (p=0.034).
Safety and adverse effects	Ethical committee of the University Medical Centre Nijmegen assessed the study and gave approval.
Does the study answer the question?	Overall the main findings do not support the use of the implementation programme on improving involvement, enablement or satisfaction of older patients in their care. This relates to the question as it is tools to elicit beliefs about patient beliefs.
Effect due to factor in study?	Power of study – the necessary 30 patients per gp was not always possible to gather. To detect a medium effect (effect size 0.50 between groups required 24 gps and 10 patients per gp (power=0.80), alpha =0.05. As pre-intervention response rates were low post-intervention gps were asked to send questionnaires to the last 30 patients who visited them.
Consistency of results with other studies?	
Directly applicable to guideline population?	The population of gp patients is the population of interest, some of the patients will not be. The intervention is of interest to this guideline.
Internal Validity	Sig more females in the intervention group.

Grading: 1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias*

Loh A;Simon D;Wills CE;Kriston L;Niebling W;Hõrter M;

The effects of a shared decision-making intervention in primary care of depression: a cluster-randomized controlled trial

Ref ID 3740 2007

Study Type Randomised Controlled Trial **Funding** German Ministry of Health

Number of participant	Primary care physicians were the unit of randomisation. The sampling frame (n=148) were sent a letter, 30 accepted the invitation to take part, 20 were randomly assigned to the intervention group and 10 to the control group, after drop out 15 and 8 were left respectively. The physicians had to recruit newly diagnosed depressive patients. The intervention physicians enrolled 263 patients and the control group 142.
Inclusion/Exclusion Criteria	Age 18 and above, with new diagnosis of depression and functional language and literacy ability
Patient Characteristics	Mean age of patients ranged from 40.8-50.4; the proportion of female patients ranged from 65.3% to 77.8%.
Recruitment	Patients were recruited through their primary care physicians.
Setting	Primary care in Germany
Interventions/ Test/ Factor being investigated	The effects of a shared decision-making intervention in primary care of depression were compared to usual care on adherence, satisfaction and clinical outcomes.
Comparisons	The intervention was a multifaceted program including physician training, a decision board for use during the consultation and afterwards by the patient, and printed patient interpenetration vs. no intervention
Length of Study/ Follow-up	16 weeks total
Outcome measures studied	Patient participation, treatment adherence, patient satisfaction, consultation time and clinical outcomes.
Results	There was no difference for the control group in patient participation before and after, whereas the intervention group had significantly higher patient participation from pre to post intervention for the doctor facilitation scale (p=0.001) and there was an increase in the patient participation scale (p=0.010). There were no significant differences in treatment adherence. Patient satisfaction was significantly higher in the intervention 29.8 (sd=2.7) than the control group 27.0 (sd=3.6), p=0.014. There were no values taken for satisfaction before the intervention. There was no difference between groups for length of consultation. Neither group had a statistically significant reduction in depression severity from baseline to post-intervention.
Safety and adverse effects	No
Does the study answer the question?	Shared decision making appears to increase satisfaction but not adherence.
Effect due to factor in study?	No - validity of outcome measures should be described
Consistency of results with other studies?	Unknown

Directly applicable to guideline population?	Yes
Internal Validity	Self reported outcomes

Wilkinson CR;Williams M;

Strengthening patient-provider relationships

Ref ID 8834 2002

Study Type	Randomised Controlled Trial	**Funding**	Not mentioned.

Number of participant	278, 136 in the control arm and 141 in the intervention arm.
Inclusion/Exclusion Criteria	Not mentioned.
Patient Characteristics	Mean age approximately 60 years; 12% female; Main diagnoses: diabetes mellitus, alcohol dependency, hypertension, prolonged PTS, cardiovascular problems; chronic renal failure.
Recruitment	Questionnaires were sent from the gp.
Setting	Gp practice.
Interventions/ Test/ Factor being investigated	Participants for both groups were randomly selected and a letter asked if they would like to participate. The intervention group were mailed an appointment guidebook with instructions before their scheduled routine visits with gp. After the visit both groups were sent a short questionnaire to be posted back. The guidebook was 10 pages and title 'How to be prepared', with appointment lists, suggestions for getting ready, including writing down questions and concerns to discuss. Instructions for the day, sample phrases, suggestions for follow-up issues and health promotion, notes page. The questionnaire assessed patient perceptions relating to preparedness, self-effectiveness, and visit effectiveness. The intervention group received a questionnaire with six more questions relating to the guidebook itself, on its usefulness and that they did receive the book.
Comparisons	Intervention group versus usual care (a standard letter reminding of visit).
Length of Study/ Follow-up	The questionnaire was sent after their visit to the gp by post.
Outcome measures studied	Perceptions of preparedness, self-effectiveness, visit effectiveness and usefulness of guidebook. By questionnaire.
Results	There were no significant differences between the two groups who agreed or strongly agreed on the five questions of the questionnaire. Proportion of patients indicating agree or strongly agree for intervention and control respectively: Prepared for appointment – 0.87 vs 0.86, difference +0.26, not significant (sig. alpha 0.10); questions answered +1.52, not significant; did not leave with unresolved issues +0.72, not significant; listened to what I had to say +1.09, not significant; involved in making decisions +0.17 not significant; better than usual in meeting needs +0.96, not significant. Feedback on service provision: 82% of the comments from the control group were positive. Comments from intervention group were mainly on how to improve/or the usefulness of the guidebook. 100% read it.
Safety and adverse effects	Safety: data collection completed following human subject guidelines and study approval. Informed responses would be part of a research project and would remain confidential. They had the right to participate or to not. Giving back the questionnaire was giving consent to participate.

Does the study answer the question?	There was no significant differences in the consultation between the two groups therefore there was no effect of the guidebook on the outcomes of interest. This suggests that this tool (guidebook) did not improve the patient outcomes of preparedness, self-effectiveness significantly. This relates to the question as this tool would not be able to improve the patient participation and to help elicit beliefs and information needs any more than without this guidebook.
Effect due to factor in study?	There was no power calculation. There is no reference as to whether the drop-out rate difference between the control and intervention group was significant. The blinding and allocation concealment was not clear so can not be certain that the overall effect is due to the study intervention.
Consistency of results with other studies?	Consistent.
Directly applicable to guideline population?	Some of the population was relevant while some were not (e.g those with alcohol dependency). It does look at whether a guidebook improves shared decision-making between providers and patients.
Internal Validity	Allocation concealment, blinding.

Question: How can practitioners elicit patient's preferences for involvement in decisions about medicines?

Grading: 3	Non-analytic studies (for example, case reports, case series)

Braman AC;

Patient personality predicts preference for relationships with doctors

Ref ID 6689 2004

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

The Autonomy Preference Index (API, Ende et al 1989) and the Krantz Health Opinion survey (KHOS, Krantz et al, 1980) measured the desire for receiving comprehensive information and for decision-making power in doctor-patient interactions. Parts A and B of the API measure desire for decision-making power and part C measures preference for information. With statements such as 'Even if the news is bad, you should be well-informed.

Health locus of control was measured with Form #B of the Multidimensional Health Locus of Control Questionnaire (MHLC, Wallston eta l 1978). Items of the three scales (internal, powerful others, and chance) were rated on a 6-point likert scale form 1 (strongly disagree) to 6 (strongly agree).

Assertiveness was measured by the Assertive-Behaviour Competence Inventory for Older Adults (Northrup and Edelstein 1998), which was developed specifically for use with an older population.

The Self-efficacy scale (Sherer et al 1982) measured self-efficacy, or feelings of personal mastery. The scale consists of 17 items measuring mastery for general situations and six items measuring mastery in social situations on a scale of 1 (strongly agree) to 7 (strongly disagree).

The highest correlation was between the API part A and the KHOS Behavioral Involvement subscale ($r=0.62$, $p<0.001$). This was significant, however it indicates that less than 50% of the variance is shared between these two variables. The other correlations were lower still. The cut off was 0.50 for combining the scales so these two were combined.

Demographic variable accounted for around 20% of the variance in patient preferences and personality accounted for an additional 9-20% significant variance in preference. Specifically, assertiveness was predictive of desire for information.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Caress A;

Patient roles in decision-making

Ref ID 1155 1997

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

This cross-sectional study conducted at a regional renal unit in the north of England included 462 participants gained from a convenience sample over 12 months. 155 were pre-dialysis, 103 were dialysis patients and 147 were transplant patients.

A set of sort cards, which were developed by Degner and Russell (1988) and validated with cancer patients as acceptable was used.

The patients picked a single card which was closest to their preferred role in decision-making. The patients also picked a single card closest to their perceived role in decision-making. Paients were also asked to give their rationale for their preferred role.

The 5 sort cards:

Active options
Card A: I prefer to make the final decision about which treatment I will receive.
Card B: I prefer to make the final selection of my treatment after seriously considering my doctor's opinion.
Collaborative option
Card C: I prefer that my doctor and I share responsibility for deciding which treatment is best for me.
Passive options
Card D: I prefer that my doctor makes the final decision about which treatment will be used but seriously considers my opinion.
Card E: I prefer to leave all decisions regarding my treatment to my doctor.

The key points found from the study were that: participation preference was highly individualistic, with a lot of patients wishing to remain passive. Those who did prefer an active role were unlikely to attain this preference; trust in the HCP can influence the prference; desire for informatino is not synonymous with desire for participation.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Cox K;Britten N;Hooper R;White P;

Patients' involvement in decisions about medicines: GPs' perceptions of their preferences

Ref ID 6698 2007

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Cox (2007) adapted a questionnaire by Degner and Sloan (1992) which involved patients with cancer. Cox's study involved asking about medicines. Cox's study included 479 patients who were approached in the waiting room in general practitioner surgeries to participate and then given an interview where they completed the pre-consultation questionnaire. They were also administered a questionnaire after the consultation.

The gp was given a questionnaire before, which included their preferred role in decision making with patients and a questionnaire afterwards detailing their perceptions of the decision-making during each consultation. The doctors' assessment of patients' preference to be involved in shared decision making was correct in 32% of the consultations, overestimated in 45% of the consultations and underestimated in 23% of the consultations. The patients' preferences for decision making involved: 39% wanting the gp to share the decision, 45% wanting the gp to be main (28%) or only (17%) decision-maker and 16% wanting to be the main (14%) or only (2%) decision-maker.

The questionnaire given to the patients at pre-consultation included the following 5 statements, of which patients were asked to choose one:
•I would prefer that I make the decision about medicines I take for this problem.
•I would prefer that I make the final decision about medicines I take for this problem after seriously considering my doctor's opinion.
•I would prefer that my doctor and I share responsibility for deciding about medicines I take for this problem.
•I would prefer that my doctor makes the final decision about medicines I take for this problem, but seriously considers my opinion.
•I would prefer that my doctor makes all decisions about medicines I take for this problem.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Doherty C;Doherty W;

Patients' preferences for involvement in clinical decision-making within secondary care and the factors that influence their preferences

Ref ID 5543 2005

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Participants were given two single question questionnaires which described five choices for decision-making preferences on the autonomy preference index (API). The two questionnaires asked the same questions but one referred to the nurse while the other referred to the doctor. The participants were asked to choose which preference best described their personal preference for decision-making with each profession. Questionnaire responses were used to form the basis of the subsequent interview.

The data for the study came from audio-taped interviews using a semi-structured interview schedule. All interviews were conducted in private while the patients were in hospital. Interviews lasted between 20 and 55 minutes, the tapes then transcribed and analysed individually and compared to the whole group.

The results showed no significant differences in preferences for decision-making between men and women, different age or education levels. Of the Medical patients (opposed to surgical patients) 30% wished an active role, 40% a collaborative role and 30% a passive role. [Most of the results showed medical and surgical together].

The patients choice on the API was not always reflected in the interview.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Ende J;Kazis L;Ash A;Moskowitz MA;

Measuring patients' desire for autonomy: decision making and information-seeking preferences among medical patients

Ref ID 8863 1989

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

A survey design instrument was used to measure patients' preferences of autonomy - desire to make medical decisions and desire to be informed. This is relevant to our question as it is a survey which could be given to patients in order to elicit their preferences for decision making. It was also tested for reliability and validity.

The final instrument developed was the Autonomy Preference Index (API) which comprised an 8-item scale on information seeking and 15 items on decision-making;

Decision-making preference scale
A) General items for decision-making preference (patients respond to each item on a five-point likert scale from 'strongly disagree to strongly agree'.
1. The important medical decisions should be made by your doctor, not by you.
2. You should go along with your doctor's advice even if you disagree with it.
3. When hospitalised, you should not be making decisions about your own care.
4. You should feel free to make decisions about everyday medical problems
5. If you were sick, as your illness became worse you would want your doctor to take greater control.
6. You should decide how frequently you need a check-up.

B) Vignettes (respond on 5-point scale) response choices were: 'you feel alone', 'mostly you', 'the doctor and you equally', 'mostly the doctor' and 'the doctor alone'.

The API was checked for test-retest reliability on a sample of 50 patients who were asked to retake the questionnaire two weeks after the original one. After deleting unreliable items, the test-retest reliability score for each scale was calculated using Pearson product-moment correlations. Test-retest reliability for the scale was 0.84, and the information seeking scale was 0.83. The scales were tested further for internal consistency reliability using the Cronbach alpha formula both had a co-efficient of 0.82.

Concurrent validity of the decision-making scale was established by correlating with an empirically related global item attached to the instrument. This asked patients to show 'which statement best describes your attitude towards medical care?' by choosing one of five statements:
'The patient should take complete control'
'The patient should have more control than the doctor'
'The patient and the doctor should share control equally'
'The doctor should have more control than the patient'
'The doctor should take complete control'.
Patients responses correlated significantly with their decision making scale scores ($r=0.54$, $p<0.0001$).

Convergent validity of the decision-making scale was measured by administering it to a selected population of diabetic patients who were selected as being highly motivated at self-care and home monitoring. Comparing the mean scores of these patients with the general study population found that the selected diabetic population scored significantly higher ($p<0.01$) than the general population.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Hill SA;Laugharne R;

Decision making and information seeking preferences among psychiatric patients

Ref ID 785 2006

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

This study used the API for information seeking preferences in psychiatric patients. Therefore it was slightly altered for the population:

1. As you become more unwell you should be told more and more about your illness.
2. You should be kept informed about what is happening inside your body as a result of your illness.
3. Even if the news is bad, you should be well infromed.
4. Your psychiatrist should explain the purpose of any investigations, e.g. blood tests.
5. You should be given information only when you ask for it.
6. It is important for you to know all the side effets of your medication.
7. Information about your illness is as important to you as treatment.
8. When there is more than one way to treat a problem, you should be told about all the options.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Langewitz W;Nubling M;Weber H;

Hospital patients' preferences for involvement in decision-making: A questionnaire survey of 1040 patients from a Swiss university hospital

Ref ID 7922 2006

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

As part of their questionnaire, Langewitz (2006) adapted the API to a 4 point Likert scale: fully agree, slightly agree, slightly disagree, fully disagree. How much do you agree with the following statements:
•One should stick to the physician's advice even if one is not fully convinced of his ideas (Follow physician's advice).
•It should completely be left to physicians to decide on a patient's treatment (Physician should decide)
A question was also included which targeted patient's information needs:
•Even when the news is bad the patient must be informed (information).
They also asked the extent that patients needed help in their daily activities.

Medication: Not specific to medication-taking but decision-making.
Condition: Any.
Location: University Hospital of Basel in NW Switzerland.
Delivery: received a letter two weeks after discharge from hospital asking them to fill in an enclosed questionnaire.
Population: Patients discharged from the hospital 1040 responded (59% response rate).
Purpose: Assessing patients' preferences for involvement in decision-making and receiving information.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Neame R;Hammond A;Deighton C;

Need for information and for involvement in decision making among patients with rheumatoid arthritis: a questionnaire survey

Ref ID 4000 2005

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

self-report questionnaire was designed to collect data on 5 key topics: information-seeking and decision making preferences, knowledge of RA, disease features, DMARD experience, and sociodemographic factors.

Need for information and desire for involvement in decision making were measured using a validated tool (the Autonomy Preference Index). The decision making preference scale of the API includes 6 general items, which were used in this study. The remaining items of this scale are statements regarding management of upper respiratory tract infection.

The need for information was very high. Information seeking preference scores (median 82.5, interquartile range 80-92.5) were significantly higher P< 0.001) than decision-making preference score (mean 56.4, s.d=13.6). Need for information and for decision making were both higher in women than men, and associations with these needs differed in men and women. Younger age and greater knowledge of RA predicted greater need for decision making. There was no correlation between need for information and for involvement in treatment decisions for either sex.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Schneider A;Wensing M;Quinzler R;Bieber C;Szecsenyi J;

Higher preference for participation in treatment decisions is associated with lower medication adherence in asthma patients

Ref ID 7216 2007

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Medication: For asthmatics.
Condition: Asthma patients.
Location: Saxony-Anhalt, Heidelberg, Gerrmany.
Delivery: A series of questionnaires, which included the API. Posted to patients with chance to win three prizes if sent back.
Population: 185 patients responded from 43 practices. Asthma patients from 46 general practices.
Purpose: To investigate the inter-relations between medication adherence, self-management, preference for involvement in treatment decisions and preference for information in asthma patients in primary care.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Tortolero-Luna-Guillermo BG;

Relationship between English Language Use and Preferences for Involvement in Medical Care among Hispanic Women

Ref ID 6273 2006

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

A 211-item survey instrument was developed in English and translated into Spanish. It included questions on demographic characteristics, health status, reproductive history, menopausal status, access to healthcare, experience with HRT and hysterectomy, outcome expectations about HRT and hysterectomy, medical decision-making and social support.

To explore women's attitudes about active participation in medical decision making they used a framework consisting of two decision theories, multiattribute utility theory (Keeney 1976). And the conflict theory of decision making (Janis 1977). Women's preferences for decision making and information seeking were measured by a slightly modified version of the Autonomy Preference Index (API, developed by Ende et al). The original index consists of two scales: an 8-item informatio-seeking scale (ISS) and a 15-item decision-making (DM) scale. The latter consists of a 6-item subscale that measures decision making in general and a 9-item subscale that measures decision making using three clinical disease-specific vignettes representing increasing severity (upper respiratory infection, hypertension, and myocardial infaction). For this study, the 6-item subscale for general DM preference and the 8-item ISS were used in their original formats. However, the disease-specific DM subscale was modified to include two clinical management vignettes (hypertension and use of HRT) and two surgical vignettes. Other vignettes were added in addition to these.

Overall, they expressed a strong desire for obtaining medical information about their condition from their physician (mean score 85.7 out of 100) and for participating in

	shared medical decision making both for medical decisions in general and for the specific surgical procedures. They expressed a lower preference for participating in medical decision-making related to HRT (mean score 31) and high blood pressure management (mean score 36.9).
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Question: What tools are available to help elicit patients beliefs about medicines?

Grading: 1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

Hamilton W;Russell D;Stabb C;Seamark D;Campion-Smith C;Britten N;

The effect of patient self-completion agenda forms on prescribing and adherence in general practice: a randomized controlled trial

Ref ID 13907 2007

Study Type	Randomised Controlled Trial	**Funding**	Grants from the Medicines Partnership, East Devon and Exeter Primary Care Trusts. Also funding from a NHS Researcher Development Award.

Number of participant	1610 completed all details initially (all prescribing outcomes known) 811 were in the intervention group and 799 were in the control group.
Inclusion/Exclusion Criteria	No exclusion criteria - stated that all patients attending during normal working hours of the g.p practice were eligible.
Patient Characteristics	For those with prescribing outcomes known the median age was 56 (IQR=38,70) and the no. of males was 623(38%).
Recruitment	When arriving at gp surgery offered an envelope with a brief description of the study. If wished to proceed they opened the envelope. This was a covering letter, short form to write down contact details, pen and in half was a SCAF (see intervention).
Setting	Ten gp practices in Devon (9) and Dorset (1).
Interventions/ Test/ Factor being investigated	The intervention group received a SCAF, which was (previously piloted) a one-sided sheet with 5 questions: 1. What made you decide to come to see the doctor? Please describe the problem you have e.g. symptoms or current illness. 2. Your ideas about your illness: What do you think is wrong with you? 3. Your concerns: Have you any particular worries about your illness? 4. Your expectations: How do you think your problem should be treated? What do you hope the doctor will do? 5. Medication: Do you think you should receive a prescription for your problem? The participants (or their carers) were asked to complete this while waiting for their appointment and to give it to the doctor when they went in. The gp was allowed to use the SCAF in any way they deemed appropriate for that consultation. The SCAFS were not retained or returned to the study team. A letter was sent out to the patient within 24 hours of their consultation with 2 questionnaires: the Medical Interview Satisfaction Scale and the Satisfaction with Decision Questionnaire. They also requested consent for the researchers to look at their gp records for prescriptions issued in the consultation. Prescripiton details and re-attendances were identified from the practices' computer systems. Adherence was measured by structured telphone interviews by a researcher blinded to the intervention status at 2 weeks and 12 weeks. Up to 5 telephone calls were made. The GPs participating were offered a semi-structured telephone interview after participation with a researcher in Medicines Partnership (one of the funders) to allow criticisms to be aired. The interview focused on whether gps believed the SCAF affected the consultation and their prescribing. Also to see if change in consultation style also occurred for the control patients.
Comparisons	Intervention and usual care.
Length of Study/ Follow-up	Up to 12 weeks follow-up.

Outcome measures studied	Prescribing, reattendance and adherence data.
Results	56% of the intervention and 53% of the control group were given a prescription, p=0.10. Mean no. of items on prescription: 1.78 (SD=1.37) for intervention and 1.87 (SD=1.34) for control (p=0.32). Median cost of prescription: £5.60 (SD=£2.12, £16.05) vs £5.94 (£2.46, £18.89), p=0.30). 9.9% of the intervention and 10.4% of the control group re-attended (p=0.79). Mean satisfaction was 5.37 for intervention group and 5.40 for control gorup (p=0.64). The overall mean adherence for short-term medication: intervention group 89% and control 85%; for long-term medication at 2 weeks: intervention 93% and control 95%; No significant differences found between the groups. Only 29 out of the 53 doctors completed the telephone interview. 28% considered that the SCAF had affected their prescribing on at least one patient and 31% believed it had an effect on their consultation style, although any effect was considered 'slight' and only related to patients who had actually received a SCAF.
Safety and adverse effects	No safety issues reported. Ethical approval from North & East Devon Research Ethics Committee.
Does the study answer the question?	Yes the SCAF may be an instrument to be used to elicit patients' beliefs and concerns about their medication. The results did not support the hypothesis tested, none of the outcome measures produced any differences between the groups.
Effect due to factor in study?	Most considerations were taken into account in the methodology. However the control group may be confounded by the intervention as the same doctor is used. They used a telephone interview to see if this had occurred and 28% of the doctors said it had. However only 29 out of 53 doctors took the interview and none of them reported anything about the control group.
Consistency of results with other studies?	
Directly applicable to guideline population?	Yes.
Internal Validity	Intervention may confound control group-see below

Grading: 3	Non-analytic studies (for example, case reports, case series)

Aikens JE;Nease-Donald-E-Jr;Klinkman MS;

Explaining patients' beliefs about the necessity and harmfulness of antidepressants

Ref ID 17875 2008

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Condition: Unipolar non-psychotic major depression.
Medication: depression treatment.
Type of study: Cross-sectional design.
Purpose: To identify the demographic and clinical characteristics that account for patients' beliefs about anti-depressants.
Population: 165 patients.
Location: Michigan.
Intervention: BMQ – specific and general.
Mode of delivery: Before patients started antidepressants, interview and self-report measures were used to assess treatment beliefs, depression features, and comorbid conditions. Clinical Research Coordinators were trained and certified in implementing the procedures.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Brown C;Battista DR;Bruehlman R;Sereika SS;Thase ME;Dunbar JJ;

Beliefs about antidepressant medications in primary care patients: relationship to self-reported adherence

Ref ID 17880 2005

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Condition: depression.
Medication: antidepressant medication.
Type of study: report of a 12 month observational study.
Purpose: describe beliefs about medication in primary care patients prescribed antidepressants for depression. Secondly, to examine the factor structure of the Beliefs about Medicines Questionnaire (BMQ) and compare it with the previously reported factor structure of the BMQ in medical conditions and thirdly examine the association of medication beliefs with self-reported medication adherence.
Population: 192 family practice patients referred by their primary care physician.
Location: Pittsburgh.
Intervention: BMQ-specific and general.
Mode of delivery: Doesn't say.
Results: Factor analysis indicates that the BMQ is valid in a sample of primary care patients receiving treatment for depression and has a similar factor structure to that obtained in samples of patients with chronic medical conditions.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Clifford S;Barber N;Horne R;

Understanding different beliefs held by adherers, unintentional nonadherers, and intentional nonadherers: application of the Necessity-Concerns Framework

Ref ID 17907 2008

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question? Cross-sectional survey to assess variations in beliefs about medicines in patients for chronic condition patients. Using the Necessity-Concerns Framework.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Horne R;Cooper V;Gellaitry G;Date HL;Fisher M;

Patients' perceptions of highly active antiretroviral therapy in relation to treatment uptake and adherence: The utility of the necessity-concerns framework

Ref ID 7202 2007

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Condition: HIV+.
Medication: HAART.
Type of study: prospective longitudinal study of uptake and adherence to HAART. Followed up over time.
Population: 136 patients.
Location: HIV outpatient clinic in Brighton and not currently taking Antiretroviral medication.
Intervention: BMQ – HAART-specific version (BMQ-HAART).
Mode of delivery: Patient initially referred to a research assistant and were tracked to see who accepted/declined HAART and followed over a year. After offered treatment a standardised questionnaire was given.
Results: Uptake of HAART was associated with perceptions of personal necessity for treatment (OR 7.41, 95% CI 2.84 to 19.37) and concerns about potential adverse effects (OR 0.19, 95% CI 0.07 to 0.48). Perceived necessity and concerns about adverse effects elicited before initiating HAART predicted subsequent adherence.
Discussion: The necessity-concerns framework is a useful theoretic model for understanding patient perspectives of HAART and predicting uptake and adherence, with implications for the design of evidence-based interventions.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Horne, R., Weinman, J., Hankins, M.

The beliefs about medicines questionnaire: the development and evaluation of a new method for assessing the cognititve representation of medication.

Ref ID 17905 1999

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Chronic illness sample of 524 patients (asthmatic, diabetic and psychiatric patients) from hospital clinics and cardiac, general medical and renal (haemodiaysis) in-patients.

Inclusion: If prescribed one or more medicines for regular use in the treatment of their illness for at least two months prior to the study and if could read and understand the questionnaire and fell well enough to complete it.

It shows the development and evaluation of a tool to assess patient beliefs about their medication therefore this does help answer the question. There are two parts to the tool, the BMQ-General, which assesses beliefs about medicines in general. The other part is the BMQ-Specific which assesses beliefs specific to medicine. This is the part of interest to our question, and so this is extracted, and the BMQ-General is not. The study states that the two sections of the BMQ can be used in combination or separately.

The BMQ-Specific comprises of two 5-item factors assessing beliefs about the necessity of prescribed medicines (Specific-Necessity) and concerns about prescribed medication based on beliefs about the danger of dependence and long-term toxicity and the disruptive effects of medication (Specific-concerns).

Method: to simplify patients broad range of beliefs about specific and general medication into 'core themes' which could be evaluated as psychometric scales. The BMQ scales were derived from a pool of items representing commonly held beliefs about medication using exploratory Principal Components Analysis (PCA).

The BMQ-Specific items - Your views about medicines prescribed for you:

- We would like to ask you about your personal views about medicines prescribed for you.
- These are statements other people have made about their medicines.
- Please indicate the extent to which you agree or disagree with them by ticking the appropriate body.
- There are no right or wrong answers. We are interested in your personal views.

Rated: strongly agree, agree, uncertain, disagree, strongly disagree

My health, at present, depends on my medicines.
Having to take medicines worries me.
My life would be impossible without my medicines.
Without my medicines I would be very ill.
I sometimes worry about long-term effects of my medicines.
My medicines are a mystery to me.

My health in the future will depend on my medicines.
My medicines disrupt my life.
I sometimes worry about becoming too dependent on my medicines.
My medicines protect me from becoming worse.

Note: to elicit beliefs about individual components of the treatment regimen the reference statement should refer to the medicine by name e.g. Your views about aspirin prescribed for you. Additional items can refer to a named illness eg. Your views about medicines prescribed for your asthma.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Jenkins L;Britten N;Stevenson F;Barber N;Bradley C;

Developing and using quantitative instruments for measuring doctor- patient communication about drugs

Ref ID 7606 2003

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

This study used the BMQ. When pilot-testing the BMQ they found it useful for identifiying reasons people stopped taking their medication and areas that bothered them. However in other respects the response was poor, making it difficult to interpret whether a non-repsonse was a refusal to answer or because the question did not apply to a patient's situation. They therefore incorporated questions on adherence into the telephone interview to improve the response.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Kemp-Steven FHWC;

Psychological factors and use of antiepileptic drugs: Pilot work using an objective measure of adherence

Ref ID 11724 2007

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Condition: Epilepsy.
Medication: Lamotrigine or Lamotrigine and a low-dose Phenobarbital marker.
Type of study: qualitative.
Purpose: To determine the influence of patients' beliefs about epilepsy, beliefs about medication and a range of neuroepilepsy variables on drug adherence among a sample of epilepsy patients.
Population: 37 patients recruited from a local epilepsy outpatient clinic.
Location: Leeds?
Intervention: BMQ specific and general adapted for present sample of epilepsy patients. Hospital anxiety and depression scale.
Mode of delivery: Not mentioned.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Khanderia U;Townsend KA;Erickson SR;Vlasnik J;Prager RL;Eagle- K-A;

Medication adherence following coronary artery bypass graft surgery: Assessment of beliefs and attitudes

Ref ID 6528 2008

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Condition: following a coronary artery bypass graft surgery.
Medication: antiplatelet agents, Beta Blockers, angiotensin-converting enzyme inhibitors, and statins.
Type of study: Questionnaire.
Purpose: To evaluate the association between self-reported adherence and the beliefs patients have about cardiovascular medicines used after CABG.
Population: 132 patients discharged for 6-24 months following coronary artery bypass graft (CABG).
Location: Michigan?
Intervention: BMQ specific and general.
Mode of delivery: Patients were identified from cardiac surgery registry. Sent an explanation of the project, an informed consent letter, a survey and return envelope.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Kumar K;Gordon C;Toescu V;Buckley CD;Horne R;Nightingale PG;Raza K;

Beliefs about medicines in patients with rheumatoid arthritis and systemic lupus erythematosus: a comparison between patients of South Asian and White British origin

Ref ID 17879 2008

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Condition: Rheumatoid Arthritis and systemic lupus erythematosus.
Medication: DMARTS.
Type of study: Questionnaire.
Purpose: To assess whether patients with RA and SLE who are of South Asian origin have different beliefs about medicines in general, and about DMARDS in particular, compared with patients of White British/Irish origin.
Population: 100 patients of South Asian origin (50 RA: 50 SLE) and 100 patients of White British/Irish origin (50 RA; 50 SLE). Taking a DMARD and had done so for 3 months or over.
Location: The outpatient Rheumatology Departments of Sandwell and West Birmingham Hospitals NHS trust and the University Hospital Birmingham NHS Foundation Trust.
Intervention: BMQ specific and general. HAQ and SF-36.
Mode of delivery: A research nurse read questionnaires to all the patients. All patients recorded their responses themselves and no prompts given.
Results: NB took 20 minutes to complete all the questionnaires and provide demographic details.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Menckeberg TT;Bouvy ML;Bracke M;Kaptein AA;Leufkens HG;Raaijmakers JM;Horne R;

Beliefs about medicines predict refill adherence to inhaled corticosteroids

Ref ID 6630 2008

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Condition: Asthma.
Medication: Inhaled corticosteroids.
Type of study: Cross-sectional.
Population: 238 patients aged 18-45 years who filled at least two ICS prescriptions in 11 community pharmacies.
Location: Netherlands.
Intervention: BMQ – necessity and concerns. Specific and General.
Mode of delivery: Questionnaire posted to patient with SAO.
Conclusion: Adherence by prescription-refill records correlated with patients' beliefs about ICS (necessity and concerns). The Necessity-Concerns Framework provides an insight into not only patients' intentions to take medication but also their actual medication-taking behaviour.

It shows use of the BMQ (specific and general).

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Theunissen-Nicolet CM;

Ref ID 473 2003

Study Type	Qualitative	**Funding**	

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?	This study includes the BMQ and the illness perception questionnaire. The illness perception questionniare is too long at 80-item. This study used the 19-item BMQ questionnaire.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	

Internal Validity

Question: What tools are available to help elicit patients information needs about medicines?

Grading: 3	Non-analytic studies (for example, case reports, case series)

Agard A;Hermerun G;Herlitz J;

When is a patient with heart failure adequately informed? A study of patients' knowledge of and attitudes toward medical information

Ref ID 7585 2004

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

This qualitative analysis of semistructured interviews was conducted at Sahlgren's University Hospital, Gothenburg, Sweden on patients 60 years and over who were receiving treatment after a heart failure diagnosis.

The semi-structured qualitative interview had 4 open-ended questions as an interview guide. The questions were:
1. What is your opinion about the medical information that you have been given?
2. What kind of information is lacking?
3. What information have you been given about heart failure?
4. What is your attitude toward receiving prognostic information?

They were also encouraged to speak about the questions and to raise other issues related to them to ensure their major personal concerns really emerged.

To avoid respondents feeling ignorant or embarassed about not being able to adequately answer questions relating knowledge they were asked first about the information they had been given, rather than asking directly about their knowledge of diagnosis, treatment and prognosis.

Many patients had a limited understanding of their disease but said they were still satisfied with the information they received. Some were indifferent to, accepted or were unaware of their low level of knowledge.

They concluded that 'to inform the patient adequately, physicians and nurses should determine the patient's level of knowledge and explore why those patients who have

a limited understanding do not assimilate or request information. The information they provide should also be adapted to the patient's capacity, wishes and emotional reactions.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Astrom K;Carlsson J;Bates I;Webb DG;Duggan C;Sanghani P;McRobbie D;

Desire for information about drugs. A multi-method study in general medical inpatients

Ref ID 17897 2000

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

The purpose of this study was to refine and validate the Intrinsic Desire for Information (IDI) 12-item scale. This was done by interfacing quantitative and qualitative data and explore the relationship between the scale score and patient demographics.

The IDI consisted of 12 structured items and 5 open questions.

The 12 quantitative items were extracted from a larger 50-item questionnaire which explored patient's desires for medical information. This was completed by 501 patients. The 12 items were scored on a five step Likert scale 5=strongly agree, 4=agree, 3=uncertain, 2=disagree and 1=strongly disagree.

The open questions were derived form the project aims and questions from Lindegren (1999).

Questionnaire items (scored from strongly agree through strongly disagree on a 5-point Likert scale).
1.I always speak to my pharmacist when I want information about my medicines.
2.Sometimes I feel a little inhibited when I ask for information…they might think I should know already.
3.If there is anything I need to know, it's most convenient to ask at the surgery.
4.It's not really my place to ask for information, they have enough to do.
5.The people at the hospital can easily give me information when I go for my appointment.
6.I needs as much information about my medicines as possible.
7.Too much knowledge is a bad thing.
8.You can never know enough about these things.
9.I don't need any more knowledge about my medicines/illness.
10.I read about my medicines/illness as much as possible.
11.What you don't know (with respect to medicines/illness) doesn't hurt you.
12.I find information about my medicines/illness confusing

Open questions:
13.What kind of information about your medicines do you want? Why?
14.How do you want your information to be presented (written, oral, both, other)? Why?
15.Who would you like to give you information about your medicines? Why?
16.When would it be best to have the information about your medicine presented (at hospital, at home, at the community pharmacy, at the GP's)? Why?
17.Would you like to sit down and talk about your medicines with a pharmacist at the hospital?

They concluded that the desire for information may be more complicated and involve an emotional or behavioural component. This simple tool could be useful in predicting patients' information preferences. Further validation and testing needed in clinical settings.

It should be noted that this is about information preferences which may differ from information needs.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Braman AC;

Patient personality predicts preference for relationships with doctors

Ref ID 6689 2004

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

The Autonomy Preference Index (API, Ende et al 1989) and the Krantz Health Opinion survey (KHOS, Krantz et al, 1980) measured the desire for receiving comprehensive information and for decision-making power in doctor-patient interactions. Parts A and B of the API measure desire for decision-making power and part C measures preference for information. With statements such as 'Even if the news is bad, you should be well-informed'.

Health locus of control was measured with Form B of the Multidimensional Health Locus of Control Questionnaire (MHLC, Wallston eat l 1978). Items of the three scales (internal, powerful others, and chance) were rated on a 6-point likert scale form 1 (strongly disagree) to 6 (strongly agree).

Assertiveness was measured by the Assertive-Behaviour Competence Inventory for Older Adults (Northrup and Edelstein 1998), which was developed specifically for use with an older population.

The Self-efficacy scale (Sherer et al 1982) measured self-efficacy, or feelings of personal mastery. The scale consists of 17 items measuring mastery for general situations and six items measuring mastery in social situations on a scale of 1 (strongly agree) to 7 (strongly disagree).

The highest correlation was between the API part A and the KHOS Behavioral Involvement subscale ($r=0.62$, $p<0.001$). This was significant, however it indicates that less than 50% of the variance is shared between these two variables. The other correlations were lower still. The cut off was 0.50 for combining the scales so these two were combined.

Demographic variable accounted for around 20% of the variance in patient preferences and personality accounted for an additional 9-20% significant variance in preference. Specifically, assertiveness was predictive of desire for information.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Doherty C;Doherty W;

Patients' preferences for involvement in clinical decision-making within secondary care and the factors that influence their preferences

Ref ID 5543 2005

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Participants were given two single question questionnaires which described five choices for decision-making preferences on the autonomy preference index (API). The two questionnaires asked the same questions but one referred to the nurse while the other referred to the doctor. The participants were asked to choose which preference best described their personal preference for decision-making with each profession. Questionnaire responses were used to form the basis of the subsequent interview.

The data for the study came from audio-taped interviews using a semi-structured interview schedule. All interviews were conducted in private while the patients were in hospital. Interviews lasted between 20 and 55 minutes, the tapes then transcribed and analysed individually and compared to the whole group.

The results showed no significant differences in preferences for decision-making between men and women, different age or education levels. Of the Medical patients (opposed to surgical patients) 30% wished an active role, 40% a collaborative role and 30% a passive role. [Most of the results showed medical and surgical together].

The patients choice on the API was not always reflected in the interview.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Duggan C;Bates I;

Development and evaluation of a survey tool to explore patients' perceptions of their prescribed drugs and their need for drug information

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Duggan (2000) developed and evaluated a survey tool (intrinsic desire for information) to find out Patients' perceptions and information needs in regards to their medication. It was tested for reliability and by factor analysis and was used with 2 cohorts of patients in East London (sample of 500).

This instrument was too long - 25 item instrument.

The 12-item scale was deemed too long to meet our inclusion criteria, however some of the open questions may be of relevance.

The IDI (for reference only):
Part 1 – Demographic details.
Part 2 – Questionnaire items (scored from strongly agree through strongly disagree on a 5-point Likert scale).
1.I always speak to my pharmacist when I want information about my medicines
2.Sometimes I feel a little inhibited when I ask for information…they might think I should know already.
3.If there is anything I need to know, it's most convenient to ask at the surgery.
4.It's not really my place to ask for information, they have enough to do.
5.The people at the hospital can easily give me information when I go for my appointment.
6.I need as much information about my medicines as possible.
7.Too much knowledge is a bad thing.
8.You can never know enough about these things.
9.I don't need any more knowledge about my medicines/illness.
10.I read about my medicines/illness as much as possible.
11.What you don't know (with respect to medicines/illness) doesn't hurt you.
12.I find information about my medicines/illness confusing

Open questions:
13.What kind of information about your medicines do you want? Why?
14.How do you want your information to be presented (written, oral, both, other)? Why?
15.Who would you like to give you information about your medicines? Why?

16.When would it be best to have the information about your medicine presented (at hospital, at home, at the community pharmacy, at the GP's)? Why?
17.Would you like to sit down and talk about your medicines with a pharmacist at the hospital?

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Ende J;Kazis L;Ash A;Moskowitz MA;

Measuring patients' desire for autonomy: decision making and information-seeking preferences among medical patients

Ref ID 8863 1989

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

A survey design instrument was used to measure patients' preferences of autonomy - desire to make medical decisions and desire to be informed. This is relevant to our question as it is a survey which could be given to patients in order to elicit their preferences for decision making. It was also tested for reliability and validity.

The final instrument developed was the Autonomy Preference Index (API) which comprised an 8-item scale on information seeking and 15 items on decision-making;

Decision-making preference scale
A) General items for decision-making preference (patients respond to each item on a five-point likert scale from 'strongly disagree to strongly agree'):
1. The important medical decisions should be made by your doctor, not by you.

2. You should go along with your doctor's advice even if you disagree with it.
3. When hospitalised, you should not be making decisions about your own care.
4. You should feel free to make decisions about everyday medical problems.
5. If you were sick, as your illness became worse you would want your doctor to take greater control.
6. You should decide how frequently you need a check-up.

B) Vignettes (respond on 5-point scale) response choices were: 'you feel alone', 'mostly you', 'the doctor and you equally', 'mostly the doctor' and 'the doctor alone'.

The API was checked for test-retest reliability on a sample of 50 patients who were asked to retake the questionnaire two weeks after the original one. After deleting unreliable items, the test-retest reliability score for each scale was calculated using Pearson product-moment correlations. Test-retest reliability for the scale was 0.84, and the information seeking scale was 0.83. The scales were tested further for internal consistency reliability using the Cronbach alpha formula both had a co-efficient of 0.82.

Concurrent validity of the decision-making scale was established by correlating with an empirically related global item attached to the instrument. This asked patients to show 'which statement best describes your attitude towards medical care?' by choosing one of five statements:
'The patient should take complete control'
'The patient should have more control than the doctor'
'The patient and the doctor should share control equally'
'The doctor should have more control than the patient'
'The doctor should take complete control'.
Patients responses correlated significantly with their decision making scale scores ($r=0.54$, $p<0.0001$).

Convergent validity of the decision-making scale was measured by administering it to a selected population of diabetic patients who were selected as being highly motivated at self-care and home monitoring. Comparing the mean scores of these patients with the general study population found that the selected diabetic population scored significantly higher ($p<0.01$) than the general population.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Hill SA;Laugharne R;

Decision making and information seeking preferences among psychiatric patients

Ref ID 785 2006

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

This study used the API for information seeking preferences in psychiatric patients. Therefore it was slightly altered for the population:

1. As you become more unwell you should be told more and more about your illness.
2. You should be kept informed about what is happening inside your body as a result of your illness.
3. Even if the news is bad, you should be well informed.
4. Your psychiatrist should explain the purpose of any investigations, e.g. blood tests.
5. You should be given information only when you ask for it.
6. It is important for you to know all the side effets of your medication.
7. Information about your illness is as important to you as treatment.
8. When there is more than one way to treat a problem, you should be told about all the options.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Langewitz W;Nubling M;Weber H;

Hospital patients' preferences for involvement in decision-making: A questionnaire survey of 1040 patients from a Swiss university hospital

Ref ID 7922 2006

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

As part of their questionnaire, Langewitz (2006) adapted the API to a 4 point Likert scale: fully agree, slightly agree, slightly disagree, fully disagree. How much do you agree with the following statements:
•One should stick to the physician's advice even if one is not fully convinced of his ideas (Follow physician's advice).
•It should completely be left to physicians to decide on a patient's treatment (Physician should decide).
A question was also included which targeted patient's information needs:
•Even when the news is bad the patient must be informed (information).
They also asked the extent that patients needed help in their daily activities.

Medication: Not specific to medication-taking but decision-making.
Condition: Any.
Location: University Hospital of Basel in NW Switzerland.
Delivery: received a letter two weeks after discharge from hospital asking them to fill in an enclosed questionnaire.
Population: Patients discharged from the hospital 1040 responded (59% response rate).
Purpose: Assessing patients' preferences for involvement in decision-making and receiving information.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Neame R;Hammond A;Deighton C;

Need for information and for involvement in decision making among patients with rheumatoid arthritis: a questionnaire survey

Ref ID 4000 2005

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

A self-report questionnaire was designed to collect data on 5 key topics: information-seeking and decision making preferences, knowledge of RA, disease features, DMARD experience, and sociodemographic factors.

Need for information and desire for involvement in decision making were measured using a validated tool (the Autonomy Preference Index). The decision making preference scale of the API includes 6 general items, which were used in this study. The remaining items of this scale are statements regarding management of upper respiratory tract infection.

The need for information was very high. Information seeking preference scores (median 82.5, interquartile range 80-92.5) were significantly higher P<0.001) than decision-making preference score (mean 56.4, s.d=13.6). Need for information and for decision making were both higher in women than men, and associations with these needs differed in men and women. Younger age and greater knowledge of RA predicted greater need for decision making. There was no correlation between need for information and for involvement in treatment decisions for either sex.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Schneider A;Wensing M;Quinzler R;Bieber C;Szecsenyi J;

Higher preference for participation in treatment decisions is associated with lower medication adherence in asthma patients

Ref ID 7216 2007

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Medication: For asthmatics.
Condition: Asthma patients.
Location: Saxony-Anhalt, Heidelberg, Gerrmany.
Delivery: A series of questionnaires, which included the API. Posted to patients with chance to win three prizes if sent back.
Population: 185 patients responded from 43 practices. Asthma patients from 46 general practices.
Purpose: To investigate the inter-relations between medication adherence, self-management, preference for involvement in treatment decisions and preference for information in asthma patients in primary care.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Strydom A;Forster M;Wilkie BM;Edwards C;Hall IS;

Patient information leaflets for people with learning disabilities who take psychiatric medication

Ref ID 11273 2001

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

This partially answers the question of what tools are available to elicit patients information needs because the study, although does not elicit whether they have information needs, it elicits what knowledge they have about their medication, to see what is lacking. This was a study with people with learning disabilities who take psychiatric medication.

They used a questionnaire to ask the participants about their medication knowledge:
- Can you read the medication label? (yes no)
- What is written on the label ?(don't know/medication name/my name/chemist's name/dose/other)
- What is your medication called? (don't know/brand or generic name/approximate name/description)
- What are you taking medication for? (don't know/knew indication/approximate indication)
- Is there anything you should not do while taking this medication? (don't know/yes, plus example)
- Are there any side effects? (don't know/one/two or more)

The authors used their findings for the framework for a structure of a patient information leaflet for people with learning disabilities who take medicines for psychiatric medications.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Tortolero-Luna-Guillermo BG;

Relationship between English Language Use and Preferences for Involvement in Medical Care among Hispanic Women

Ref ID 6273 2006

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

A 211-item survey instrument was developed in English and translated into Spanish. It included questions on demographic characteristics, health status, reproductive history, menopausal status, access to healthcare, experience with HRT and hysterectomy, outcome expectations about HRT and hysterectomy, medical decision-making and social support.

To explore women's attitudes about active participation in medical decision making they used a framework consisting of two decision theories, multiattribute utility theory (Keeney 1976). And the conflict theory of decision making (Janis 1977). Women's preferences for decision making and information seeking were measured by a slightly modified version of the Autonomy Preference Index (API, developed by Ende et al). The original index consists of two scales: an 8-item information -seeking scale (ISS) and a 15-item decision-making (DM) scale. The latter consists of a 6-item subscale that measures decision making in general and a 9-item subscale that measures decision making using three clinical disease-specific vignettes representing increasing severity (upper respiratory infection, hypertension, and myocardial infection). For this study, the 6-item subscale for general DM preference and the 8-item ISS were used in their original formats. However, the disease-specific DM subscale was modified to include two clinical management vignettes (hypertension and use of HRT) and two surgical vignettes. Other vignettes were added in addition to these.

Overall, they expressed a strong desire for obtaining medical information about their condition from their physician (mean score 85.7 out of 100) and for participating in shared medical decision making both for medical decisions in general and for the specific surgical procedures. They expressed a lower preference for participating in medical decision-making related to HRT (mean score 31) and high blood pressure management (mean score 36.9).

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Zwaenepoel L;Bilo R;De BW;De VM;Reyntens J;Hoorens V;Sermeus W;Laekeman G;

Desire for information about drugs: a survey of the need for information in psychiatric in-patients

Ref ID 17874 2005

Study Type	Qualitative	**Funding**	

Number of participant	
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	Medication: Psychiatric medication. Population:179 Psychiatric in-patients. Purpose: to explore information preferences and test Dutch translated version of IDI scale. Location: Flanders, Belgium. Delivery: Standardised interviews with patients in 11 hospitals. The IDI-scale and five open questions (as detailed in Astrom, 2000). This used the IDI scale plus open questions and so relates to our question.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Question: How can information about medicines be provided for patients in order to enhance SDM in regard to medicines?

Grading: 1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

Trevena LJ;Davey HM;Barratt A;Butow P;Caldwell P;

A systematic review on communicating with patients about evidence

Ref ID 2400 2006

Study Type Systematic Review **Funding** Not mentioned.

Number of participant RCTs and Systematic Reviews.

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

The review concluded that communicating with patients about evidence does increase their understanding regardless of the tools used. The authors also found that there was a greater effect if information was structured (either written, verbal or video) or interactive (computer, touch screen, question prompts) and particularly if the information was tailored to the individual. Probabilitistic information was found to be best represented as even rates in relevant groups of people, rather than words, probabilities or summarized as effect measures such as relative risk reduction. Written information was reported to be more effective if illustrations and graphs were used.

This helps answer the question by showing which types of information, through which medium and which format information is best provided as shown by a range of systematic reviews and RCTs.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Wills CE;Holmes RM;

Patient comprehension of information for shared treatment decision making: State of the art and future directions

Ref ID 232 2003

Study Type Systematic Review **Funding** Not mentioned.

Number of participant Not reported. Assume that it is other types of study.

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

They found two studies where participants preferred presentation of medication in terms of relative risk rather than absolute risk format. They found that people simplify relative risk information into a simplified format of small or large risks and there is a tendency to seriously under or overestimate their personal risks for health outcomes. There is a need to tailor the format of risk communication to the individual's level of numeracy. In routine clinical encounters information should be presented balanced, in both positive and negative frames. Graphics can improve the understanding of numerical probability information. However some people may dislike some types of displays or misunderstand them. Consistent finding of individual differences in preferences for probability information in words, numbers of both formats implies a need for routine individualized assessments of patient preferences for format.

The review concluded that the impact of information presentation in different formats on patients' understanding and preferences was variable. Most of the studies were not clinical patients and so may not be able to generalise to a clinical setting. The goal is to give balanced, complete and parsimonious information, and take into account individual needs and preferences.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Question: What tools are available to support the patient in reaching an informed decision? How effective are these tools?

Grading: 1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias

O'Connor AM;Stacey D;Entwistle V;Llewellyn-Thomas H;Rovner D;Holmes-Rovner M;Tait V;Tetroe J;Fiset V;Barry M;Jones J;

Decision aids for people facing health treatment or screening decisions

Ref ID 8717 2003

Study Type Systematic Review

Funding Canadian Institute of Health Research (Canada); Nuffield Trust of University of Oxford (UK); Ontario Ministry of Health Career Scientist funding for AO'C (Canada); Leverhulme Trust Research Fellowship funding for VE (UK); Canada Res. Chair Program.

Number of participant RCTs.

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

35 RCT studies were included in the systematic review. 221 decision aids were identified but very few had been evaluated, with only 31 assessed in the RCTs. It was difficult to make conclusions because of the variability of decision contexts, decision aid designs, type of comparison interventions, targeted outcomes and how they were measured. This withstanding the RCTs showed that decision aids do a better job than usual care interventions in improving people's knowledge regarding options, enhancing realistic expectations about the benefits/harms of options, reducing decisional conflict, decreasing the amount of people remaining undecided, and stimulating a more active role in decision making.

Therefore this is a high quality systematic review which has shown that there are decision aids which can support the patient to reach an informed decision.

It should be noted that many of the decisions involved populations which were not included in our search. However there were trials which included HRT.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Grading: 1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

Fraenkel L;Rabidou N;Wittink D;Fried T;

Improving informed decision-making for patients with knee pain

Ref ID 3718 2007

Study Type	Randomised Controlled Trial	**Funding**	From the Veterans Affairs Connecticut Healthcare system and the Yale University School of Medicine. In part by a grant by the Claude D. Pepper Older Americans Independence Center at Yale University School of Medicine

Number of participant	87 patients. Data available for 40 in the pamphlet group and 43 in the ACA Task group.
Inclusion/Exclusion Criteria	Over the age of 60 years; self-report of pain involving one or both knees on most days of the month; the ability to read and understand English; ability to perform a choice on this task; Excluded if judged to be too ill to participate; were scheduled for an urgent visit; had a disease other than osteoarthritis that causes knee pain; had relative or absolute contraindications to one or more of the proposed treatment options. These were ascertained by self-report.
Patient Characteristics	Mean age was 74 years, Most were Caucasian 65% control and 72% intervention group;
Recruitment	A research assistant recruited participants by approaching patients waiting in the primary care waiting room area.
Setting	Veteran Affairs Connecticut Healthcare System.
Interventions/ Test/ Factor being investigated	Performed an Adaptive Conjoint Analysis (ACA). This is an interactive computer tool which could generate immediate feedback to the participant and help them construct treatment preferences by means of tradeoffs by rating tasks.
Comparisons	The intervention vs. the control group who received an Arthritis Foundation information pamphlet.
Length of Study/ Follow-up	Immediately and at 3 months.
Outcome measures studied	Primary outcome measure was decision conflict scale immediately after the consultation. Questionnaire. Secondary outcomes were anxiety, knowledge, and decision-making preferences.
Results	The computerised decision aid group had lower decision conflict immediately after the clinic (mean 0.18, 95% CI -0.34 to -0.01) and mean -0.15 (95% CI -0.37 to 0.06) at three month follow-up. Both groups had less decision conflict after the consultation but the difference between groups was significant at 5% level. Subscales suggest this was due to feeling better informed and clearer of their personal values for the risks and benefits of alternative options. The reduction in anxiety fell significantly but there was no difference between groups. Knowledge scores improved slightly after the consultation but at three months were back at baseline level. Participants in the decision aid group were less likely to start warfarin than those in the guideline arm (39/53, 73.6%) compared to guidelines (50/56, 81.7%), RR=0.82, 95% CI 0.68 to 0.99, this was however almost completely due to participants not already on warfarin, here the difference was 4/6, 25% compared to guidelines 15/16, 93.8%, RR=0.27, 95% CI 0.11 to 0.63. There was no difference in health outcomes 3

	months after the clinic.
Safety and adverse effects	None
Does the study answer the question?	Participants using this computer tool designed to increase patient awareness of choice and evaluate the tradeoffs related to available treatment options were more confident in their ability to obtain information about available treatment options, were better prepared to participate in their visit and had better arthritis related self efficacy compared to patients receiving an information pamphlet.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	Subjective outcome measure

Montgomery AA;Fahey T;Peters TJ;

A factorial randomised controlled trial of decision analysis and an information video plus leaflet for newly diagnosed hypertensive patients

Ref ID 257 2003

Study Type Randomised Controlled Trial **Funding** Unknown.

Number of participant	Patients were allocated to decision analysis only (n=52); video/leaflet only (n=55); video/leaflet and decision analysis (n=51) or usual care (n=59).
Inclusion/Exclusion Criteria	Patients aged 32 to 80 years (mean age 59 years) newly diagnosed with hypertension.
Patient Characteristics	Mean age 58.5 years; 48% female.
Recruitment	Patients were recruited in the Avon Health Authority, UK.
Setting	South west England.
Interventions/ Test/ Factor being investigated	The value of tools designed to aid decision making in patients with newly diagnosed hypertension is assessed in this study. Two tools are considered: a decision analysis and video/leaflet.
Comparisons	Comparisons are made between treatments, treatment combination and no treatment.
Length of Study/ Follow-up	3 months.
Outcome measures studied	Decisional Conflict Scale and subscales, state anxiety, knowledge about hypertension and actual treatment decision.
Results	Both interventions successfully reduced patients' total decisional conflict at follow-up. Decision analysis decreased the decisional conflict more than the video/leaflet. Total decisional conflict mean for decision analysis was 27.6 (s.d=12.1), no decision analysis 38.9 (s.d=18.3) adjusted difference -9.4 (95% CI -13.0 to -5.8) p<0.001; video/leaflet 30.3 (s.d=13.4) and no video/leaflet was 36.8 (s.d=18.8), -4.2 (95% CI -7.8 to -0.6), p=0.021. The Decisional conflict subscales showed a clear reduction in three of the five subscales - uninformed 23.7 (s.d=11.8) compared to no decision analysis 40.7 (s.d=23.1) adjusted difference -15.7 (95% CI -20.2 to -11.2), unclear values 28.4 (s.d=14.7) vs. 43.8 (s.d=24.3) adjusted difference -13.1 (95% CI -18.0 to -8.1) and unsupported 24.4 (s.d=13.4) vs. 34.8 (s.d=18.3) adjusted difference -8.7 (95% CI 12.8 to -4.7) and some evidence for reduction in uncertainty and no evidence for decision quality. The video/leaflet intervention showed no evidence in

these last two subscales and there was only clear evidence on the uninformed subscale. For the intention to start treatment when followed up the adjusted risk ration: Yes versus unsure 1.19 (95% CI 0.59 to 2.40) for decision analysis and 1.80 (95% CI 0.89 to 3.63) for the video/leaflet. No versus unsure 3.15 (95% CI 0.91 to 10.98) and 0.52 (95% CI 0.15 to 1.77) respectively. The overall p values were 0.09 and 0.17 respectively. Actual prescription of medication was not different for either intervention or controls. There was a suggestion (p=0.055) that anxiety may be reduced by decision analysis although the evidence there was weak and no evidence of this for the video/leaflet intervention. Both interventions significantly increased knowledge of hypertension. Those who received both interventions had the lowest decisional conflict (27.1 compared with 28.2 and 33.3 and 44.2 for decision analysis only, video/leaflet and control). They had a high knowledge score – the same as video/leaflet. Within the regression models there was a significant (antagonistic) interaction between decision analysis and video/leaflet, so the effect of each was reduced by the presence of the other (interaction coefficient 12.5, 95% CI 5.4 to 19.5, p=0.001 for decisional conflict and -9.1, 95% CI -16.3 to -1.9, p=0.013 for knowledge. This study was followed up in 2005 by Emmett et al, who found that there was no evidence of any difference in blood pressure, cardiovascular disease risk for either intervention or between them. There were also no effects on medication prescribing, self-reported adherence, consulting behaviour or management changes.

Safety and adverse effects None.

Does the study answer the question? Both interventions were successful in reducing patients' total decisional conflict with decision analysis resulting in a greater decrease than video/leaflet however the decision analysis took 45 minutes to an hour to complete.

Effect due to factor in study? Yes.

Consistency of results with other studies? Yes.

Directly applicable to guideline population? Yes.

Internal Validity Multiple sites

Oakley S;Walley T;

A pilot study assessing the effectiveness of a decision aid on patient adherence with oral bisphosphonate medication

Ref ID 3611 2006

Study Type Randomised Controlled Trial **Funding** Eli Lilly and Merck Sharp & Dohme.

Number of participant 33 women - 16 in intervention group and 17 in control group.

Inclusion/Exclusion Criteria Post menopausal women prescribed oral bisphosphonates with a diagnosis of osteoporosis or aged over 65 and had radiological evidence of fragility fracture. Patients prescribed oral bisphosphonates because of long term steroid use were excluded.

Patient Characteristics Average age 77 years with 'no differences between groups.'

Recruitment The women were patients in one practice in Dorset.

Setting GP practice in Dorset.

Interventions/ Test/ Factor being investigated This study was done to assess the acceptability of a decision aid and its potential impact on patient adherence with oral bisphosphonate. The aid comprised of an information booklet, an audiocassette and worksheet to be used at home by the

	patient before an appointment with a doctor.
Comparisons	The intervention group was compared to a control group receiving normal care.
Length of Study/ Follow-up	Patients were followed up for 4 months.
Outcome measures studied	Adherence was measured by monitoring repeat prescriptions. Patients views were assessed by open questions. Patient satisfaction was assessed using the Satisfaction with Information about Medicines Scale (SIMS) & Beliefs about Medicines Questionnaire.
Results	There were no statistically significant changes in adherence & satisfaction over the course of the study (p=0.47) and changes in adherence did not differ between the 2 groups (p=0.80). Patients using the decision aid valued the opportunity to discuss their treatment with the GP in a dedicated consultation.
Safety and adverse effects	None
Does the study answer the question?	Although the decision aid was appreciated for the ability to discuss their medication with the GP it did not appear to affect patient adherence to medication.
Effect due to factor in study?	Yes
Consistency of results with other studies?	
Directly applicable to guideline population?	Direct.
Internal Validity	Possible differences between groups

Weymiller AJ;Montori VM;Jones LA;Gafni A;Guyatt GH;Bryant SC;Christianson TJ;Mullan RJ;Smith SA;

Helping patients with type 2 diabetes mellitus make treatment decisions: statin choice randomized trial

Ref ID 707 2007

Study Type	Randomised Controlled Trial	**Funding**	Mayo Clinic and American Diabetes Association.

Number of participant	52 patients received the Decision Aid and 46 received usual care.
Inclusion/Exclusion Criteria	Eligible patients had type 2 diabetes, no contraindications to statins, no major visual, hearing or cognitive impairment and were willing to provide informed consent.
Patient Characteristics	Mean age in treatment group was 64 (s.d=12) and in the control group was 66 (s.d=8). There were only 16 women in the treatment group and 26 women in the control group. Six people in the treatment group had a CV risk less than 15%; there were 15 control patients in this category. 15-30% risk was assigned to 16 of the treatment group and 7 of the control group. Greater than 30% group was found in 30 treatment patients and 24 control patients.
Recruitment	Patients were referred to the metabolic clinic for a one off consultation Faculty and fellows at the clinic were randomized.
Setting	Mayo Clinic Rochester Minn.
Interventions/ Test/ Factor being investigated	Use of a Decision Aid about statin drugs versus control pamphlet and its effect on treatment decision making.
Comparisons	Comparisons are made between groups in knowledge level, decisional conflict, acceptability and adherence.

Length of Study/ Follow-up	3 months.
Outcome measures studied	Self reported adherence and a likert scale for acceptability. Knowledge testing was not described.
Results	Amount of information was significantly higher in treatment group (OR3.4 [1.7-6.7]). Helpfulness of the information and overall acceptability were also significantly higher in the treatment group (OR 2.3, s.d=1.4 to 3.8) respectively and 2.8 (s.d=1.2 to 6.9) respectively. The treatment group had less decisional conflict (difference, -10.6; 95% CI -15.4 to -5.9 on a 100 point scale) than the control group. At three months there was no significant difference in adherence to patient choice (analysis adjusted by sex, cardiovascular risk, and number of medications; OR 1.9, 95% CI 0.4 to 9.8.
Safety and adverse effects	None.
Does the study answer the question?	A decision aid may reduce decisional conflict but is does not appear to affect long term adherence. Further research is recommended.
Effect due to factor in study?	Small trial but good consistency with other studies.
Consistency of results with other studies?	Yes.
Directly applicable to guideline population?	Yes.
Internal Validity	The outcome measurement is by self report

Grading: 1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias*

Hamann J;Cohen R;Leucht S;Busch R;Kissling W;

Shared decision making and long-term outcome in schizophrenia treatment

Ref ID 3748 2007

Study Type	Randomised Controlled Trial	**Funding**	By the German Ministry of Health and Social Security within a funding project.

Number of participant	107 patients were included in the original study and agreed to be followed up.
Inclusion/Exclusion Criteria	Inclusion: All men and women aged 18-65 years who had an ICD-10 diagnosis of schizophrenia or schizophreniform disorder. Exclusion: Severe mental retardation, lack of fluency in German, refusal to give written informed consent.
Patient Characteristics	Intervention vs control group: Mean age: 38 years old (s.d=11.4); gender: 48% female; mean duration of illness: 9.2 years (s.d=8.5); mean number of hospitalisations due to schizophrenia: 5.6 (s.d=5.7).
Recruitment	Follow-up of patients from original study (Hamann, 2006) who agreed to be included. Originally recruited in the wards.
Setting	12 acute psychiatric wards of 2 German hospitals.
Interventions/ Test/ Factor being investigated	Intervention was an experimental SDM intervention. The intervention was to inform of treatment options and prepare them for a 'planning talk' with their physicians. A printed decision aid was given - a 16 page booklet covering the pros and cons of oral vs depot formulation, first vs second generation antipsychotics, psycho education, and type of socio-therapeutic intervention. Nurses were trained in assisting patients to work through the booklet. Within the booklet patients were to write down their experiences with previous antipsychotic medication and to indicate their preferences regarding the different options on each topic. The planning talk with the psychiatrist regarded further treatment according to their preferences indicated by the patient.
Comparisons	Intervention versus treatment as usual, with no further instructions for physicians and nursing staff.
Length of Study/ Follow-up	Long-term follow up of patients for 18 months after discharge.
Outcome measures studied	Outcomes (patients view): Perceived involvement in medical decisions; knowledge about disease and treatment at time of discharge; satisfaction with treatment. Outcomes (psychiatrist's view): Psychopathology scores: time spent in individual contacts;
Results	Univariate analysis found no significant differences between groups. When multivariate analysis was conducted to control for the re-hospitalisation rate it showed that there was a positive trend for the decision aid and planned talk in reducing rehospitalisation. Higher participation preferences (OR= 1.06, p=0.03) and better knowledge (OR =1.23, p=0.03) rates significantly predicted rehospitalisation. No other effects were shown. Patients showing good compliance at 6 months were 41% in the intervention and 55% in the control, p>0.05. Patients showing good compliance at 18 months was 60% vs 58%, p>0.05.
Safety and adverse effects	None mentioned but was approved by an ethics committee of the Technische Universitat, Munchen.

Does the study answer the question?	Yes the intervention is a decision aid booklet. SDM with acutely ill in-patients with schizophrenia is possible and feasible and improves important treatment patterns - increases patients perceived involvement, knowledge about disease and attitudes to treatment. The structured intervention increased participation in psycho education and socio-therapeutic interventions.
Effect due to factor in study?	There were differences in the study groups - the patients in the intervention group were hospitalised a week longer than patients in the control group (statistically significant) and the knowledge of treatment was higher in the intervention group (statistically significant). Power calculation was not used. Therefore the overall effect may not be due to the intervention.
Consistency of results with other studies?	Consultation time with the psychiatrist was increased in the intervention group 4min/week, however this was not statistically significant p>0.05.This is similar to some other studies as most do not have statistical significance and time is longer/shorter.
Directly applicable to guideline population?	This is comparable as it is a decision aid intervention to increase SDM, yet unlike the other studies is with acute psychiatric patients, which is included in our remit. Therefore it is of relevance to the guideline.
Internal Validity	Allocation concealment;

Thomson RG;Eccles MP;Steen IN;Greenaway J;Stobbart L;Murtagh MJ;May CR;

A patient decision aid to support shared decision-making on anti-thrombotic treatment of patients with atrial fibrillation: randomised controlled trial

Ref ID 8831 2007

Study Type Randomised Controlled Trial **Funding** Welcome Trust.

Number of participant	145 patients randomised - 69 to implicit tool and 67 to guidelines.
Inclusion/Exclusion Criteria	Aged 60 and had either chronic non-valvular atrial fibrillation or paroxysmal atrial fibrillation. Exclusion criteria: acute onset of AF including cardioversion; previous stroke or TIA; dementia or contraindication to warfarin.
Patient Characteristics	Mean age of 73 years and 44% female. 71.4% of guideline group and 69.8% of decision aid group were already taking warfarin. There were no significant differences between the groups.
Recruitment	Recruited from 40 GP practices in northwest England.
Setting	Research clinic.
Interventions/ Test/ Factor being investigated	This study compares an implicit computerised decision aid with evidenced based paper guidelines.
Comparisons	The primary outcome measure was the decision conflict scale measured after the clinic visit.
Length of Study/ Follow-up	3 months.
Outcome measures studied	Decision Conflict Scale (DCS) was the primary outcome. Secondary outcome measures were the State Trait Anxiety Inventory, a knowledge scale and Degner's decision making preference scale (these were not described).
Results	Post clinic participants in the decision aid arm were significantly more likely to judge that they were more important in making the decision (p=0.018) consistent with the anticipated impact of the delivery mode. Decision conflict fell in both groups post clinic compared to preclinic, the difference between groups post clinic was significant at the 5% level (p=0.036). There were no differences between groups in the DCS at three months. There was not significant difference between groups in anxiety or knowledge scores. Those not on warfarin already were significantly less likely to start warfarin than those in the paper guidelines arm: here the difference was 4/16, 25% compared to guidelines 15/16, 93.8%, RR 0.27 (95% CI 0.11 to 0.63).

Safety and adverse effects	Although this approach has a positive impact on decision conflict comparable to other studies of decision aids, it also reduced the uptake of a clinically effective treatment to prevent stroke that may have important implications for health outcomes.
Does the study answer the question?	Yes, this study raises an important point about shared decision making and potentially about the unbiased development of decision making tools.
Effect due to factor in study?	The outcome measure validation was not described.
Consistency of results with other studies?	Unknown.
Directly applicable to guideline population?	Yes.
Internal Validity	Outcome measures subjective

Question: What aspects of consultation style increase patient involvement in decision-making?

Grading: 1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias

McKinstry B;Ashcroft RE;Car J;Freeman GK;Sheikh A;

Interventions for improving patients' trust in doctors and groups of doctors

Ref ID 672 2006

Study Type Systematic Review **Funding** Cochrane Review

Number of participant RCT

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question? These studies assessed patient trust rather than patient involvement in decision making. Consultation style was not considered in two of the three included studies. One study was a trial of training interventions for doctors. One explored the impact on trust of disclosing physician incentives to patients in an HMO and another investigated the effect of induction visits on new HMO members. Only the latter study relates to consultation style but the HMO model is not applicable in the UK NHS in this instance.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Grading: 1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

Shields CG;Epstein RM;Fiscella K;Franks P;McCann R;McCormick K;Mallinger JB;

Influence of accompanied encounters on patient-centeredness with older patients

Ref ID 8827 2005

Study Type Randomised Controlled Trial **Funding** National Institute on Aging.

Number of participant	30 - 13 accompanied and 17 unaccompanied.
Inclusion/Exclusion Criteria	Patients were at least 65 years and not cognitively impaired and had a companion who could accompany them.
Patient Characteristics	There were no significant differences in demographic data between groups. Age in two groups 66.1 to 68.5; years of education 13.6 to 14.1; general health on SF-36 61.3 to 62.5.
Recruitment	Patients were recruited through a large residency-based family medicine practice and a small hospital based geriatric practice.
Setting	Rochester, New York.
Interventions/ Test/ Factor being investigated	The influence of accompanied visits on physician patient communication.
Comparisons	Accompanied versus unaccompanied.
Length of Study/ Follow-up	One gp visit only.
Outcome measures studied	Communication measures including numbers of words used and MPCC which measures 3 aspects of PCC (patient centred communication).
Results	Companions were not assigned a specific role during the session and physicians were not asked to conduct the sessions in any particular way. There were no statistically significant differences between accompanied and unaccompanied visits on the number of issues that patients raised, however patients did raise more issues in unaccompanied visits. No statistically significant differences were observed for levels of patient-centeredness, or satisfaction, even if patients who were accompanied reported being slightly more satisfied. Physicians were more likely to promote collaboration in treatment decision making with patients than with companions ($p<0.0001$). Physicians were also more responsive to issues regarding exploring the disease and illness when the issues were raised by the patient compared with the companion ($p<0.03$).
Safety and adverse effects	None.
Does the study answer the question?	Being accompanied does not appear to make a difference in physician patient interaction in this small pilot study.
Effect due to factor in study?	No - this study is a small pilot and needs to be repeated with a larger sample.
Consistency of results with other studies?	No.
Directly applicable to guideline population?	Yes.
Internal Validity	Possible Hawthorne effect

van-Dam HA;

Provider-patient interaction in diabetes care: Effects on patient self-care and outcomes A systematic review

Ref ID 5988 2003

Study Type Systematic Review **Funding** Unknown

Number of participant RCT

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question? Eight studies were included after a rigorous methodological quality assessment, and these showed different interventions on different levels of the provider-patient interaction in diabetes care. Four studies focused on provided consulting behaviour modifications (studies 1-4), and four studies focused directly on patient behaviour change (studies 5-8).
All studies were conducted in practical diabetes care, three in hospital outpatient clinics and five in general practices.
The main findings suggest that the most effective interventions are those with a direct approach to support patient participation (i.e. by assistant-guided patient preparation for visits to doctors, empowering group education, group consultations, or automated telephone management) in diabetes care and self-care behaviour, while interventions which focus on change of provider behaviour were less effective. Thus, the authors advocate a shift from the traditional medical model to a more patient centred, patient participation and empowerment paradigm of delivery of diabetes care.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Grading: 1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias*

Savage R;Armstrong D;

Effect of a general practitioner's consulting style on patients' satisfaction: a controlled study

Ref ID 1752 1990

Study Type Randomised Controlled Trial **Funding** RCGP Schering scholarship.

Number of participant	350 were invited to participate. 200 completed both assessments.
Inclusion/Exclusion Criteria	Ages 16-75 with any presenting symptom; excluded if they had a life threatening condition.
Patient Characteristics	There were no significant differences in terms of age, sex, ethnic origin, presenting problem.
Recruitment	Patients in a deprived inner city area were invited to participate.
Setting	GP surgery, London.
Interventions/ Test/ Factor being investigated	Patients were randomised to receive a directing or sharing style in the part of the consultation regarding treatment, advice and prognosis.
Comparisons	The styles were compared on measures of satisfaction with the gps perceived understanding of their problem and the explanation they received and whether they felt that they had been helped immediately after the consultation and one week later.
Length of Study/ Follow-up	1 week.
Outcome measures studied	Patient questionnaires were analysed which measured 3 areas of satisfaction.
Results	There were no significant differences in the mean length of consultations between the two experimental groups. Patients who had the directing style of consultation reported significantly higher levels of satisfaction on almost all the outcome measures, and was particularly strong for patients with physical problems (excellent explanation $p<0.02$; excellent understanding $p=0.04$). There was no significant difference in the responses to the directing and sharing styles in longer consultations, where the main treatment was advice and among patients with psychological or chronic problems. Statistical significance values were not reported.
Safety and adverse effects	None.
Does the study answer the question?	Direct consultation appeared to be more satisfactory particularly for patients with physical problems and for patients who received a prescription.
Effect due to factor in study?	No - outcome measures not validated and high dropout rate.
Consistency of results with other studies?	Unknown.
Directly applicable to guideline population?	Yes.
Internal Validity	Self report; Hawthorne effect

Question: Do interventions to increase patient involvement increase length of the consultation?

Grading: 1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias

Kinnersley P;Edwards A;Hood K;Cadbury N;Ryan R;Prout H;Owen D;Macbeth F;Butow P;Butler C;

Interventions before consultations for helping patients address their information needs

Ref ID 27 2007

Study Type Systematic Review **Funding** Cochrane Collaboration

Number of participant	RCTs only (see above)
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	This answers the question very well as many of the studies included consultation length and this study looked at the interventions before consultations to help patients address their information needs - which included interventions before consultations to encourage question asking and information gathering by the patient, which can lead to increased patient participation. The main conclusion of the review: Often the outcomes included question asking, patient participation, patient anxiety, knowledge, satisfaction and consultation length. Interventions before consultations led to a small and statistically significant increase in consultation length, whereas those implemented some time before the consultation had no effect. This study is a very strong systematic review for guideline evidence, however not all the studies were within the remit of the guideline as they included patient participation within other areas than medicine taking. This should be noted.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	

Internal Validity

Wetzels R;Harmsen M;van WC;Grol R;Wensing M;

Interventions for improving older patients' involvement in primary care episodes

Ref ID 5434 2007

Study Type Systematic Review **Funding** Cochrane Collaboration.

Number of participant RCT and quasi experimental

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

It is limited as it includes interventions for improving older patients' involvement. Therefore this is partially the population we are looking at - would be better if whole population.

Also two of the studies were not relevant as they were not relating to consultation length.

They found some positive effects of specific methods to improve the involvement of older people in health care episodes. However there are not enough studies to conclude and recommend the use of any intervention in practice. The field of older patients is sparse.

One study is therefore relevant to us (Cegala 2001) which had a partly open method of allocation; double blinding; 45 participants (22 intervention and 23 control) which is small; They gave a brief pre-interview questionnaire for baseline measurement.

It is strong because it is well-conducted but it did not find enough strong studies to be of a good source of evidence for a guideline.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Grading: 1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

Cohen D;Longo MF;Hood K;Edwards A;Elwyn G;

Resource effects of training general practitioners in risk communication skills and shared decision making competences

Ref ID 7456 2004

Study Type Randomised Controlled Trial **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Edwards A;Elwyn G;Hood K;Atwell C;Robling M;Houston H;Kinnersley P;Russell I;Study Steering Group;

Patient-based outcome results from a cluster randomized trial of shared decision making skill development and use of risk communication aids in general practice

Ref ID 236 2004

Study Type Randomised Controlled Trial **Funding** DOH.

Number of participant	20 GPs participated and 747 patients attended. 715 patients completed the exit questionnaire; 655 completed the 1 month questionnaire and 618 completed the 6 month questionnaire.
Inclusion/Exclusion Criteria	Physicians: In practice between 1-10 years; to have sufficient practice computerization for identification of relevant patients and to be audio taped in routine surgery consultations before the stud. Patients were identified from practice registers with one of four conditions: Non-valvular atrial fib; prostatism; menorrhagia; and menopause related problems.
Patient Characteristics	Physicians: 12 men and 8 women with an average of 38 years. Among patients the mean age in each condition category was as follows: prostatic symptoms 63 years, atrial fib 65 years, menorrhagia 45 years and hormone replacement therapy 56 years. There were no statistically significant differences between groups in mean ages, gender or response rates.
Recruitment	Physicians who met inclusion criteria were recruited from practices in Gwent, South Wales. Patients were identified from practice registers.
Setting	Research clinic and GP surgery.
Interventions/ Test/ Factor being investigated	The use of shared decision making skills or the use of simple rick communication aids on patient confidence in the decision, anxiety, enablement, health status, satisfaction, intention to adhere to chosen treatment and perceived support in decision.
Comparisons	The comparison is between shared decision making or risk communication.
Length of Study/ Follow-up	6 months.
Outcome measures studied	The primary outcome measure was patient confidence in the decision as measured by the COMRADE instrument, anxiety, enablement, health status, satisfaction, intention to adhere to chosen treatment and perceived support in decision.
Results	No statistically significant effects of the risk communication or shared decision intervention were seen on the whole range of patient based outcomes. Patient confidence in the decision (2.1 increase, 95% CI 0.7 to 3.5). P<0.01) and expectation to adhere to chosen treatments (0.7 increase, 95% CI 0.04 to 1.36, p<0.05) were significantly greater among patients seen in the research clinics when more time was available compared with usual surgery time.
Safety and adverse effects	None.
Does the study answer the question?	As no statistically significant effects of the risk communication or shared decision intervention were seen on the whole range of patient based outcomes this study can only conclude that there was no improvement or deterioration in patient based outcomes following skills based interventions to UK GPs regarding shared decision making and risk communication. ** Note: A further report on this study by Cohen et al provided data on the resource effects of training GPs in risk communication skills and shared decision making competences and concluded that the training cost £1218 per practitioner which increased the cost of a consultation by £2.89.
Effect due to factor in study?	Probably.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant.
Internal Validity	No control group for physicians or for patients

Harrington-Jane NL;

Improving patients' communication with doctors: A systematic review of intervention studies

Ref ID 8780 2004

Study Type Systematic Review

Funding NHS London Regional Office, Research and Development Programme.

Number of participant RCT and Quasi-experimental.

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Out of 16 studies, 10 reported a significant increase and five reported a non-significant increase in patient participation. This participation was measured by patient question asking, patient clarification, consultation length, expressed affect, doctor encouraging patient participation.

Equal numbers of studies reported significant and non-significant trends in question-asking behaviour. Four out of five studies showed significant increase in patient clarification.

Only 2 studies showed significant increases in patient satisfaction due to the interventions. However overall high levels of satisfaction were reported.

Overall, half of the interventions resulted in increased patient participation. With more significant results for bids for clarification than question asking.

This study aimed to examine the intervention studies which were designed to increase patients' participation in medical consultations and so answers the question of what tools are available to help practitioners elicit patients beliefs about medicines and information needs. Those interventions which encourage patients to gain clarification may increase patient participation and satisfaction.

The review noted any weaknesses within the review of the studies. There was a problem in that the use of different systems of reporting - audiotaped, video, made it hard to be comparable. Most of the studies were not blind to group allocation which could cause bias. There was little consistency in the measures used - the most frequent used was question-asking.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Little P;Dorward M;Warner G;Moore M;Stephens K;Senior J;Kendrick T;

Randomised controlled trial of effect of leaflets to empower patients in consultations in primary care

Ref ID 8864 2004

Study Type Randomised Controlled Trial **Funding** Southampton University.

Number of participant	N=636 total General leaflet - 317 No general leaflet - 319 Depression leaflet - 318 No depression leaflet - 319
Inclusion/Exclusion Criteria	Aged 16-80 years, consulting at one of five general practices in the UK. Patients were excluded if they were receiving specialist psychiatric treatment, had dementia, were too unwell to consent, were receiving treatment for depression or were only collecting a prescription.
Patient Characteristics	42.5% male; 70% married and 53% in paid work.
Recruitment	Patients were consulting at one of five general practices in the UK.
Setting	GP practice in the UK.
Interventions/ Test/ Factor being investigated	Participants were randomised to four conditions: receipt of a general leaflet, depression leaflet, both leaflets and no leaflets (control group). The general leaflet which asked patients to list issues they wanted to raise and explained that the doctor wanted them to ask questions, talk and discuss any problems of concern to them. The depression leaflet listed symptoms of depression (without labelling as such) and asked the patient to identify if they had these symptoms and if so that the doctor would like to discuss them. The outcomes measured were patient satisfaction (the scores reflected aspects of doctor patient communication), consultation time, prescribing, referral and investigation.
Comparisons	Comparisons are made between receiving a general leaflet, a depression leaflet, both or neither.
Length of Study/ Follow-up	Before and after consultation.
Outcome measures studied	Self measured satisfaction and enablement scale.
Results	The only significant interaction was the increase in satisfaction for those who received the general leaflet, the mean difference was 0.17 (95% CI 0.01 to 0.32, p=0.04). The general leaflet was significantly more effective when consultations were shorter (leaflet 0.64, 95% CI 0.19 to 1.08); time 0.31 (95% CI 0.0 to 0.06); interaction between both showed that consultations of 5, 8, and 10 mins increased satisfaction by 14%, 10% and 7%). The leaflet overall caused a small non-significant increase in consultation time. This was also shown for subscales of satisfaction – comfort from communication 1.02 (95% CI 0.36 to 1.68), relief of distress 0.74 (95% CI 0.0 to 1.49), intention to comply with management decisions 0.65 (95% CI 0.06 to 1.23) and rapport 0.81 (95% CI 0.16 to 1.45). The general leaflet increased the number of investigations by the doctor, OR 1.43 (95% CI 1.00 to 2.05), which was unlikely to be due to chance or confounders after controlling.
Safety and adverse effects	None.

Does the study answer the question?	The results show an increased number of consultations and general leaflets may help to empower patients in the context of a GP consultation.
Effect due to factor in study?	This is a self measured outcome and is subject to bias.
Consistency of results with other studies?	Unknown.
Directly applicable to guideline population?	Yes.
Internal Validity	Self report

Longo MF;Cohen DR;Hood K;Edwards A;Robling M;Elwyn G;Russell IT;

Involving patients in primary care consultations: assessing preferences using discrete choice experiments.[see comment]

Ref ID 7453 2006

Study Type Randomised Controlled Trial **Funding**

Number of participant	584/747 questionnaires were returned (78% returned)
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	Does the doctor listen? B=2.63, SE 0.22, p<0.001. How easy is the information to understand? B=2.30, SE 0.17, p<0.01. Who chooses your treatment? B Doctor 0, You 0.10, Ref 0.13, p=0.001. Length of consultation B=1.05, SE 0.10, p<0.001. Type of training - risk communication B 0.56,SE 0.32, p=0.08, SDM B -0.609, SE 0.33, p=0.063.
Safety and adverse effects	
Does the study answer the question?	The discrete choice experiment explores the different attributes of a consultation and which are most important to the patient. It showed that all attributes were significant, having a doctor who listens and who gives information which is easy to understand is more important than other attributes. Shows SDM and consultation length are of lesser priority than other consultation attributes. But that SDM may have greater value once the patient has experienced it.

Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	It is a discrete choice experiment derived from Edwards (2004) RCT. Therefore it is of interest alongside this study rather than standing alone. It looks at patient preferences rather than the change in time of consultation due to SDM intervention.
Internal Validity	

Middleton JF;McKinley RK;Gillies CL;

Effect of patient completed agenda forms and doctors' education about the agenda on the outcome of consultations: randomised controlled trial

Ref ID 8884 2006

Study Type	Randomised Controlled Trial	**Funding**	Scientific Foundation Board of the Royal College of General Practitioners.

Number of participant	976 in total sample size. 480 were allocated to the no education arm. 496 were allocated to the education arm. 237 were allocated to the agenda form no education arm. 242 were allocated to the no agenda form no education arm. 236 were allocated to the agenda form education arm. 240 were allocated to the no agenda form education arm.
Inclusion/Exclusion Criteria	Inclusion criteria: accepted an appointment in a study consultation with their gp. Exclusion criteria: none.
Patient Characteristics	No data given.
Recruitment	If requested an appointment at the participating practitioners, they were informed of the study by the receptionist and given the choice to be included or not.
Setting	Leicestershire and Nottinghamshire.
Interventions/ Test/ Factor being investigated	Educational workshop attended by the doctors to increase their awareness of the patient agenda model of the consultation.
Comparisons	Comparison is between intervention and no intervention. Within each arm there is another intervention and no intervention.
Length of Study/ Follow-up	No follow-up.
Outcome measures studied	Number of problems identified. Time required to manage each problem. Duration of consultations. Number of problems raised. Patient satisfaction.
Results	Duration of consultation: No education plus no agenda form: mean 7.1 (95% CI 6.5 to 7.7) Change in means (Reference group-intervention group): No education plus agenda form:0.9 (95% CI 0.3 to 1.5) Education plus no agenda form: 0.7 (95% CI -0.18 to 1.6) Education plus agenda form: 1.9 (95% CI 1.0 to 2.8) No. of problems identified: (each group as above) Mean 1.7 (95% CI 1.5 to 1.8) 0.2 (95% CI 0.1 to 0.4)

	0.3 (95% CI 0.1 to 0.6) 0.5 (95% CI 0.3 to 0.7) Time per problem (seconds) 305.7 (95% CI 276.8 to 334.5) -10.8 (95% CI -39.1 to 17.5) -26.4 (95% CI -67 to 14.1) -14.7 (95% CI -55.2 to 25.7) General satisfaction 83.6 (95% CI 81.5 to 85.8) 1.4 (95% CI -1.1 to 3.8) -0.3 (95% CI -3.2 to 2.7) 0.1 (95% CI -2.9 to 8.0) Professional care 83.7 (95% CI 81.8 to 85.6) 1.0 (95% CI -1.0 to 8.0) 1.16 (95% CI -1.4 to 3.7) 1.2 (95% CI -1.3 to 3.7) Perceived time 80.0 (95% CI 72.4 to 77.6) 1.7 (95% CI -1.4 to 4.7) -0.1 (95% CI -3.7 to 3.4) 2.5 (95% CI -1.0 to 6.p) Depth of doctor-patient relationship 74.2 (95% CI 71.7 to 76.7) 3.0 (95% CI 0.5 to 5.6) 1.7 (95% CI -1.7 to 5.0) 2.5 (95% CI -0.8 to 5.8) By the way presentations 1.00 0.7 (95% CI 0.4 to 1.0) 1.2 (95% CI 0.7 to 2.1) 0.9 (95% CI 0.5 to 1.5)
Safety and adverse effects	Study approved by Leicestershire local research ethics committee.
Does the study answer the question?	Yes. An agenda form completed by the patient before the consultation or general practioner education about the agenda from or both helped identify more problems in the consultation even though consultations were longer.
Effect due to factor in study?	The methodology is generally sound and the power of the study was 5% significance level and 80% power used.
Consistency of results with other studies?	Varied.
Directly applicable to guideline population?	Population - includes anyone attending gp therefore any patient will be included, not specific to medication-taking population, however will include a lot of patients on medication Intervention directly comparable to that of interest for guideline.
Internal Validity	Blinding; groups differ?

Grading: 1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias*

Hamann J;Langer B;Winkler V;Busch R;Cohen R;Leucht S;Kissling W;

Shared decision making for in-patients with schizophrenia

Ref ID 3119 2006

Study Type	Randomised Controlled Trial	**Funding**	By the German Ministry of Health and Social Security thorough the funding of a project.

Number of participant	107 patients. 49 in the intervention group and 58 in the control group.
Inclusion/Exclusion Criteria	Inclusion: All men and women aged 18-65 years who had an ICD-10 diagnosis of schizophrenia or schizophreniform disorder. Exclusion: Severe mental retardation, lack of fluency in German, refusal to give written informed consent.
Patient Characteristics	Intervention vs control group: Age 35.5 (s.d=11.9) vs 29.6 (s.d=10.8), p=0.06 Gender 20 (41%) vs 31 (53%), p=0.24 Education 10 or more years 21 (43%) vs 22 (38%), p=0.43 Duration of illness 8.8 (s.d=8.6) vs 9.5 (s.d=8.5), p=0.70 Number of hospitalisations 5.4 (s.d=5.0) vs 5.8 (s.d=6.6), p=0.78 PANSS total score 82.8 (s.d=22.7) p=0.07 Knowledge 12.5 (s.d=4.8) vs 10.4 (s.d=4.9), p=0.04 No. of days from admission to inclusion in the study 19.5 (s.d=19.8) vs 11.2 (s.d=12.1), p=0.01
Recruitment	Consecutively recruited in the wards.
Setting	12 acute psychiatric wards of 2 German hospitals.
Interventions/ Test/ Factor being investigated	Intervention was an experimental SDM intervention. The intervention was to inform of treatment options and prepare them for a 'planning talk' with their physicians. A printed decision aid was given - a 16 page booklet covering the pros and cons of oral vs depot formulation, first vs second generation antipsychotics, psycho education, and type of socio-therapeutic intervention. Nurses were trained in assisting patients to work through the booklet. Within the booklet patients were to write down their experiences with previous antipsychotic medication and to indicate their preferences regarding the different options on each topic. The planning talk with the psychiatrist regarded further treatment according to their preferences indicated by the patient.
Comparisons	Intervention versus treatment as usual, with no further instructions for physicians and nursing staff.
Length of Study/ Follow-up	Long-term follow up of patients for 18 months after discharge.
Outcome measures studied	Outcomes (patients view): Perceived involvement in medical decisions; knowledge about disease and treatment at time of discharge; satisfaction with treatment. Outcomes (psychiatrist's view): Psychopathology scores: time spent in individual contacts;
Results	Outcome the patients view: - Perceived involvement COMRADE* 79.5 (s.d=18.6) after the intervention vs 69.7 (s.d=20) at study entry, F=4.94, p=0.03. - COMRADE before discharge 76.8 (s.d=20.9) vs 73.5 (s.d=19.3), F=1.88, p=0.18. - Knowledge before discharge 15.0 (s.d=4.4) vs 10.9 (s.d=5.4),F=6.65, p=0.01. - Drug Attitude Inventory (DAI) before discharge 6.9 (s.d=2.8) vs 5.5 (s.d=2.9), F=3.60, p=0.06. - ZUF8 (patients satisfaction) 16.3 (s.d=3.7) vs 16.4 (s.d=3.2), F=0.66, p=0.42.

Outcome the psychiatrists view:
- Psychopathology (PANSSS score) means 58.0 vs 59.3, p>0.05.
- Co-operation means 60.6 vs 60.9, p>0.05.
- Time spent in individual contacts: means 64 vs 60 min/weeks, p>0.05.
- Estimated (by Doctor) compliance: means 1.7 vs 2.0, p>0.05.
- Psychiatrists in the intervention group were more satisfied with what had been achieved during hospitalisation means in 5 point scale overall satisfaction 3.8 vs 3.5, p=0.02.

* COMRADE: Combined Outcome Measure for Risk Communication and Treatment Decision Making Effectiveness.

Safety and adverse effects

None mentioned but was approved by an ethics committee of the Technische Universitat, Munchen.

Does the study answer the question?

Yes it shows values for the amount of time patients spent with the psychiatrists - for those in the intervention and those not.

SDM with acutely ill in-patients with schizophrenia is possible and feasible and improves important treatment patterns - increases patients perceived involvement, knowledge about disease and attitudes to treatment. The structured intervention increased participation in psycho education and socio-therapeutic interventions.

Effect due to factor in study?

There were differences in the study groups - the patients in the intervention group were hospitalised a week longer than patients in the control group (statistically significant) and the knowledge of treatment was higher in the intervention group (statistically significant). Power calculation was not used. Therefore the overall effect may not be due to the intervention.

Consistency of results with other studies?

Consultation time with the psychiatrist was increased in the intervention group 4min/week, however this was not statistically significant p>0.05.This is similar to some other studies as most do not have statistical significance and time is longer/shorter.

Directly applicable to guideline population?

This is comparable as it is an intervention to increase SDM, yet unlike the other studies is with acute psychiatric patients, which is included in our remit. Therefore it is of relevance to the guideline.

Internal Validity

Allocation concealment;

Loh A;Simon D;Wills CE;Kriston L;Niebling W;Hõrter M;

The effects of a shared decision-making intervention in primary care of depression: a cluster-randomized controlled trial

Ref ID 3740 2007

Study Type Randomised Controlled Trial **Funding** German Ministry of Health

Number of participant

Primary care physicians were the unit of randomisation. The sampling frame (n=148) were sent a letter, 30 accepted the invitation to take part, 20 were randomly assigned to the intervention group and 10 to the control group, after drop out 15 (intervention group) and 8 (control group) participants were left. The physicians had to recruit newly diagnosed depressive patients. The intervention physicians enrolled 263 patients and the control group 142.

Inclusion/Exclusion Criteria

Age 18 and above, with new diagnosis of depression and functional language and literacy ability

Patient Characteristics

Mean age of patients ranged from 40.8-50.4; the proportion of female patients ranged from 65.3% to 77.8%.

Recruitment

Patients were recruited through their primary care physicians.

Setting

Primary care in Germany

Interventions/ Test/ Factor being investigated	The effects of a shared decision-making intervention in primary care of depression were compared to usual care on adherence, satisfaction and clinical outcomes.
Comparisons	The intervention was a multifaceted program including physician training, a decision board for use during the consultation and afterwards by the patient, and printed patient interpretation vs. no intervention
Length of Study/ Follow-up	16 weeks total
Outcome measures studied	Patient participation, treatment adherence, patient satisfaction, consultation time and clinical outcomes.
Results	There was no difference for the control group in patient participation before and after, whereas the intervention group had significantly higher patient participation from pre to post intervention for the doctor facilitation scale (p=0.001) and there was an increase in the patient participation scale (p=0.010). There were no significant differences in treatment adherence. Patient satisfaction was significantly higher in the intervention 29.8 (s.d=2.7) than the control group 27.0 (s.d=3.6), p=0.14. There were no values taken for satisfaction before the intervention. There was no difference between groups for length of consultation 29.2 (s.d=10.7) vs 26.7 (s.d=12.5), p=0.14. Neither group had a statistically significant reduction in depression severity from baseline to post-intervention.
Safety and adverse effects	No
Does the study answer the question?	Shared decision making appears to increase satisfaction but not adherence.
Effect due to factor in study?	Unsure - validity of outcome measures should be described.
Consistency of results with other studies?	Unknown
Directly applicable to guideline population?	Yes
Internal Validity	Self reported outcomes

McLean M;Armstrong D;

Eliciting patients' concerns: a randomised controlled trial of different approaches by the doctor

Ref ID 723 2004

Study Type	Randomised Controlled Trial	**Funding**	Study derived from an MSc at Guys Kings and St Thomas' School of Medicine. No funding mentioned.

Number of participant	56 in the intervention group and 54 in the control group.
Inclusion/Exclusion Criteria	Inclusion: Self-limiting illness. Exclusion: If were to be referred to hospital or given a prescription other than for symptom control or if spontaneously expressed a clear concern about their illness.
Patient Characteristics	No details mentioned apart from disease status: Musculoskeletal 23%, cough 20%, upper respiratory tract infection 18%, Virus 17%, Ear infection 6%, other 16%.
Recruitment	They were recruited by asking them when they presented in the surgery if they wished to be part of a study.

Setting	Four training general practices in SE of UK
Interventions/ Test/ Factor being investigated	The intervention is a written prompt to elicit patients concerns: -May I ask if you have any concerns about this…(illness/pain) you have come about today? Followed by - Anything in particular about the…? And, if still unforthcoming - What is it about the… that concerns you?
Comparisons	Comparison between the above written prompt and no written prompt (usual care). - This could be difficult to separate as both spoken by same doctor.
Length of Study/ Follow-up	Questionnaire given after consultation while still in the surgery. No further follow-up.
Outcome measures studied	'Professional care' score General satisfaction Depth of relationship Perceived time Enablement Anxiety
Results	Length of consultations: 11 minutes vs 10 minutes - not statistically significant When entered into a multiple regression to assess their ability to predict satisfaction with professional care - consultation length coefficient=0.21 ($p<0.05$) contributed less than the intervention status 0.29 ($p<0.005$) but was still a major predictive factor. CSQ scores: Professional care: intervention group 80.9 (s.d=16.1) control group 88.2 (s.d=11.8), Mean diff 7.3 (95% CI 2.0 to 12.6). General satisfaction: 81.2 (s.d=19.9) vs 80.3 (s.d=19.5), -0.9 (95% CI -8.4 to 6.5). Depth of relationship: 61.3 (s.d=21.4) vs 66.1 (s.d=19.1), 4.8 (95% CI -2.8 to 12.5). Perceived time 71.9 (s.d=27.1) vs 72.8 (s.d=26.5), 0.9 (95% CI -9.2 to 11.1). Enablement 37.0 (s.d=24.7) vs 39.0 (s.d=30.9), 2.0 (95% CI -8.6 to 12.6). Anxiety 35.4 (s.d=9.9) vs 32.9 (s.d=10.8), -2.5 (95% CI -6.4 to 1.5).
Safety and adverse effects	None mentioned. Ethical approval obtained from 3 relevant local research ethics committees.
Does the study answer the question?	It helps in answering the question as it is an intervention aimed to increase patient participation and it looks at consultation length. They found a small but significant increase in the professional care score of the consultation satisfaction questionnaire but no other benefits detected. Patients with acute self-limiting illness are more satisfied when GPs are prompted to ask them about their concerns. There was only a 10% increase in consultation time (which itself seemed responsible for some of the benefit). The benefit is meagre, a larger study might change these measures.
Effect due to factor in study?	The power was flawed, as mentioned in the limitations of the study (from erroneous published data) so the study did not have the power to detect smaller differences, and therefore a larger sample size would be needed. There could have been bias from the randomisation and the allocation concealment and the two groups may not have got a different treatment due to the methodology.
Consistency of results with other studies?	The result that consultation length was increased but not significant is consistent with the majority of other studies in the field.
Directly applicable to guideline population?	This is directly comparable to the population and one of the interventions relevant to this guideline.
Internal Validity	Allocation concealment,randomisation.

Question: What are the barriers and facilitators for individuals in medicine-taking?

Grading: 1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias

Pound P;Britten N;Morgan M;Yardley L;Pope C;Daker-White G;Campbell R;

Resisting medicines: a synthesis of qualitative studies of medicine taking

Ref ID 2447 2005

Study Type Systematic Review **Funding** Not reported.

Number of participant qualitative evidence

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

The synthesis revealed widespread caution about taking medicines and highlighted the lay practice of testing medicines, mainly for adverse effects. Some concerns about medicines cannot be resolved by lay evaluation, however, including worries about dependence, tolerance and addiction, the potential harm from taking medicines on a long-term basis and the possibility of medicines masking other symptoms.
Additionally, in some cases medicines had a significant impact on identity, presenting problems of disclosure and stigma. People were found to accept their medicines either passively or actively, or to reject them. Some were coerced into taking medicines. Active accepters might modify their regimens by taking medicines symptomatically or strategically, or by adjusting doses to minimise unwanted consequences, or to make the regimen more acceptable. Many modifications appeared to reflect a desire to minimise the intake of medicines and this was echoed in some peoples' use of non-pharmacological treatments to either supplant or supplement their medicines. Few discussed regimen changes with their doctors. We conclude that the main reason why people do not take their medicines as prescribed is not because of failings in patients, doctors or systems, but because of concerns about the medicines themselves. On the whole, the findings point to considerable reluctance to take medicine and a preference to take as little as possible. We argue that peoples' resistance to medicine taking needs to be recognised and that the focus should be on developing ways of making medicines safe, as well as identifying and evaluating the treatments that people often choose in preference to medicines

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Grading: 1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

Mills EJ;Nachega JB;Bangsberg DR;Singh S;Rachlis B;Wu P;Wilson K;Buchan I;Gill CJ;Cooper C;

Adherence to HAART: a systematic review of developed and developing nation patient-reported barriers and facilitators

Ref ID 8844 2006

Study Type Systematic Review **Funding** Ontario HIV treatment network

Number of participant This analysis includes 37 qualitative studies and 47 surveys using structured questionnaires or structured interviews.

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question? Barriers identified in both economic settings (developed and developing world) included: fear of disclosure, concomitant substance abuse, forgetfulness, suspicions of treatment, regimens that are too complicated, number of pills required, decreased quality of life, work and family responsibilities, falling asleep and access to medication. Important facilitators reported by patients in developed nation settings included having a sense of self work, seeing positive effects of antiretrovirals, accepting their seropositivity, understanding the need for strict adherence, making use of reminder tools, and having a simple regimen.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Munro SA;Lewin SA;Smith HJ;Engel ME;Fretheim A;Volmink J;

Patient adherence to tuberculosis treatment: a systematic review of qualitative research

Ref ID 8845 2007

Study Type Systematic Review **Funding** Unknown

Number of participant Qualitative

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Eight primary themes arose. 1. Organisation of treatment and care including access to care, treatment requirements and relationship with the provider 2. Interpretation of illness and wellness 3. Financial burden including impact on work, cost of treatment, general poverty 4. Knowledge attitudes and beliefs about treatment 5. Law and immigration 6. Personal characteristics and adherence behaviour including substance abuse, gender, religion, motivation 7. Side effects 8. Family, community and household influence.

The majority of the studies in this review were conducted in developing countries but the conclusions are similar in many ways to the Pound study.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Grading: 3	Non-analytic studies (for example, case reports, case series)

Adam BD;Maticka TE;Cohen JJ;

Adherence practices among people living with HIV

Ref ID 360 2003

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Adherence practices among people living with HIV

Sample:
35 participants, 31 men and 4 women taking HAART. Most were in their thirties (21) or forties (10).

Data collection:
Interviews.

Setting:
Recruited from nurses at HIV Care Programme in Windsor, Ontario, Canada or by mail out to local AIDS service organizations.

Theoretical approach (if any):
Inductive

Categories of respondent:
Patients.

Concepts:
Work demands affect medication schedule.

Disrupted routines – remember through habit, but if routine is disrupted then can forget.

Dose adjusting – (difficult lunchtime dose) to simplify schedule to life.

Reworking food rules – taking without food/limited food due to scheduling demands.

Side effects – Some said they adhered despite side effects for others this was a powerful discincentive.

Depression.
Effectiveness – adherence influenced by belief in efficacy of medication.

Social support and other memory aids – methods that help them remember dosing schedules.

US border crossing.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Alfonso V;Bermbach N;Geller J;Montaner JG;

Individual variability in barriers affecting people's decision to take HAART: A qualitative study identifying barriers to being on HAART

Ref ID 7586 2006

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Patients prescribed HAART.

Sample:
15 consecutive patients who were diagnosed with HIV ; not currently taking ART and not being on ART for prior 3 months with CD4 cell counts below 200/mm3 and or a prior AIDS-defining illness; able to give informed consent and communicate in English; free of excessive alcohol and illicit drug use. Thirteen males and two females. 67% Caucasian, 67% had some college or university training. , 67% were unemployed.

Data collection:
Interviews.

Setting:
Outpatient HIV clinic in downtown area of a large Canadian City.

Theoretical approach (if any):
Critical incident technique.

Categories of respondent:
Patients.

Concepts:
Medication factor concerns – e.g side effects, fear of side effects, scheduling, complexity of regimen, dietary requirements were main reasons they decided not to take HAART even though they acknowledged the benefits.

Many had been on HAART or seen friends/family and so knew of the problems in the regimen.

Mood: existing mood states e.g depression, anxiety and anger discouraged them taking their medications. Also the potential the medications could worsen mood.

Many had been at enough medical appointments and felt uncomfortable and vulnerable sitting in the waiting room of a HIV clinic and preferred less specialized services to keep HIV status confidential.

Lack of support: the threat of medication to social relationships – stigma, side effects would lead others to know they were HIV+ and judge and reject them.

Narrow focus of treatment providers exacerbated disempowerment.

Outcome expectancies: treatment seemed more hazardous than not taking.

Different barrier categories varied per person.

Interpretation:
Although many were aware of the benefits and ability to take it they did not feel it was the right choice for them at the present time. Many were suffering from depressive symptoms.
Weigh up pros and cons and view discomfort and disruption not worth it.

Many care providers may assume the decision is a lack of concern about health but is often based on a broader evaluation of physical, emotional and social health or well-being.
Most thought if decided to start medication they would be able to take it successfully.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Aronson B;

Medication management behaviors of adherent short-term antibiotic users

Ref ID 317 2005

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context
Short-term antibiotic users for acute infectious illness. Nearly perfect adherence, few instances of skipped/delayed dose but all completed regimens.

Sample
Over 18s able to read and understand English, prescribed oral, self-administered short-term antibiotic regimen of more than 2 days but fewer than 15 days. 11 patients at start, 7 completed interviews.

Data collection
Semi-structured interviews.

Setting
Outpatient clinics in major urban teaching hospital and suburban outpatient managed care in the north-east (USA).

Theoretical approach (if any)
Qualitative content analysis.

Categories of respondent
Patient.

Concepts
Knew how to take medications prescribed.
Were comfortable with dose-taking schedule – could describe how they adapted their medication dosing based on own personal schedule. Although adherent overall patients took at times convenient for them.
Several incidences of a delayed dose because of forgetfulness, change in schedule, or not being home. Dose taken when remembered, usually 1-2 hours.
Developed own mechanisms to remember to take antibiotics.

Sought remedies to resolve any adverse effects to the antibiotics.
A change in provider would not have influenced their medication taking behaviours although a few said certain provider characteristics important to them.
Concurrent use of other medications did not alter their antibiotic taking.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Attebring MF;Herlitz J;Ekman I;

Intrusion and confusion--the impact of medication and health professionals after acute myocardial infarction

Ref ID 77 2005

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Secondary prevention.

Sample:
Patients who had undergone a first time myocardial infarction and who visited the cardiac preventive nurse during march to September 2002. excluded were those who were not able to communicate due to stroke or dementia or not being able to speak Swedish. Patients who had undergone by-pass surgery were also excluded.
20 patients were included in the study.

Data collection:
Interviews.

Setting:
Outpatient clinic at University hospital in Sweden.

Theoretical approach (if any):
Hermeneutic approach. The authors pre-understanding guided the interpretation of the interviews.

Categories of respondent:
Patients who had had a first myocardial infarction.

Concepts:
Findings related to impact of medication and impact of health care professional. The impact of medication was related to dealing with symptoms related to medication, feeling the medication took control and intruded on their lives and feeling of security provided by medications that they would not have another heart attack. The impact of health care professions was related to receiving conflicting advice, wanting reassurance from physicians and difficulties in the time after discharge relating to concerns and anxieties about health, medication.

Interpretation:
Higher level of interpretation of findings lead to use of concepts of intrusion and confusion.

Author's interpretation is that of issues related to the patients medications and HCPs had a significant impact on their life after discharge.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Badger F;Nolan P;

Concordance with antidepressant medication in primary care

Ref ID 41 2006

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Concordance with antidepressant medication in primary care.

Sample:
60 patients who had recent episode of depression (treated in past 12 months). 23 men and 37 women (proportions reflecting gender differences in depression).

Data collection:
Semi-structured questionnaire.

Setting:
Four primary care centres.

Theoretical approach (if any):
Framework analysis to identify recurrent themes.

Categories of respondent:
Patients.

Concepts:
The role of and relationship with health practitioners – perceptions of consultations especially the first one affected concordance e.g time spent.

Factors related to the depressive illness – severity and length of depressive illness affected initial concordance.

Beliefs about and experiences of medication for depression – personal or family experience of antidepressants.

The wider context of depression – public opinion of depression and treatment, counseling favoured over antidepressants. Will power sufficient for recovery.

Interpretation:
Practitioners must identify depressed patients' attitudes to medications and offer evidence-based information.

Patients expect practitioners to ask about their medication, as it is interpreted as caring.

Equal partnership is recommended however some participants said they were far too ill, especially at the start to engage in discussions about treatment preferences so trust practitioners to make decisions in their best interests.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Bajcar J;

Task analysis of patients' medication-taking practice and the role of making sense: a grounded theory study

Ref ID 21 2006

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Medication taking of patients on long-term medications from the patients perspective.

Sample:
11 participants aged between 41 and 64 years, with 1-7 chronic illnesses varying from 1 to 40 years, taking between 1 and 30 medications. College or university education.

Data collection:
Semi-structured interviews.

Setting:
Toronto, Ontario, Canada.

Theoretical approach (if any):
Grounded theory.

Task analysis used to assess needs to patients on long term medications.

Categories of respondent:
Educated, non-retired patients with chronic illness.

Concepts:
Core category was 'Making sense of medication taking' patients which directly influences and was in turn influenced by 'medication taking acts; medication taking self-assessment and context.

Making sense of medication refers to patients attempts to rationalise what is happening to them and their bodies and to understand their medications in the contexts of their illness, their bodies and their daily lives. This was both cognitive and emotional. 3 modes of 'making sense' are described non-problematic occurred when 2 conditions were present – patient had access to information needed to understand situation and all the pieces of information received were consistent; problematic mode – missing information about situation or contradictory information with what expected or own experience; stunned mode – not able to make sense, felt paralyzed or stunned e.g when learned of illness or major change in medications or illness progressed/deteriorated.

Medication taking acts: deciding on approach to taking medicine, organizing daily schedule, determining how to remember to take medication, administering the medication.

Medication self-assessment appears to have 4 components: assessment of medications' effectiveness, assessment of medication's undesirable effects, assessment of the status of illness and evaluating the outcomes of strategies initiated by the patient.

Context of medication taking – influence on making sense. Key factors:
Trust in health care system, trust in health care provider and the relationship, knowledge of situation and interpretation of literature, acceptance of illness and medications, emotional status, moral outlook (values, beliefs, myths).

Interpretation:
Making sense of medications is not easy. While struggling to make sense of medications the patient shifts to a stunned mode, where unable to understand information. This state typically can gordo be observed by others. Health care providers need to recognise the importance of this mode.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Bane C;Hughes CM;Cupples ME;McElnay JC;

The journey to concordance for patients with hypertension: a qualitative study in primary care

Ref ID 7587 2007

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Perspectives of patients with hypertension in regard to concordance.

Sample:
27 participated in focus groups and 2 in individual interviews.
Inclusion criteria was that people had no cognitive impairment and had been prescribed anti-hypertensive medication for at least one year.

Exclusion criteria: patients currently prescribed more than one other cardiovascular medication or medication for any other condition.

Data collection:
Focus group discussions that took place in each patients local surgery. Moderated by one researcher. Due to low response rate in one practice, patients were invited to participate in semi-structured interviews.

Setting:
General Practice in Northern Ireland.

Theoretical approach (if any):
No theoretical approach - method of constant comparison with an iterative approach.

Categories of respondent:
Patients.

Concepts:
Findings related to patient experience of consultation and role in consultation, information needs and attitudes to medicines and lifestyle advise.

Interpretation:
Authors' views are that participants demonstrated willingness to be involved in concordance but require support from HCP to address their concerns and confusion about the nature of hypertension.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Bollini P;Tibaldi G;Testa C;Munizza C;

Understanding treatment adherence in affective disorders: a qualitative study

Ref ID 7589 2004

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context
Understanding treatment adherence in affective disorders

Sample
22 participants with a diagnosis of major unipolar depression or bipolar disorder who were in contact with the community health centres.

Data collection
Focus groups.

Setting
Three community health centres, two in Turin and one in a small industrial town near Turin.
Theoretical approach (if any)
Thematic analysis.

Categories of respondent
Patients, family members, mental health professionals.

Concepts
The role of medication and other treatments: all but four patients thought medications were an important part of treatment. Unlike the thinking of family members which was more negative towards medication. One who gave their partner less dosing than prescribed.

The causes of non-adherence: The experience with drugs is not all positive. Difficulty accepting diagnosis and therefore psychotropic drug treatment; Stop treatment as they feel better and test to see whether they need treatment; Mild adverse reactions, which were tolerable as they had been informed about them and they could contact CMHC for reassurance or to adjust does;

What interventions would help increase adherence? Getting more information and being put at ease; easier accessibility to centres when in need; less turnover of staff so don't have to repeat details to various people; less stigma of disease within society, although 2/3 who mentioned this related the fear of stigmatization to non-adherence.

Interpretation
The study of patients, family/friends and professionals should be compared in studies as hold different views.

The denial of diagnosis and testing medication to see if still needed were barriers to adherence. Adverse reactions if managed adequately did not contribute to non-adherence. Whereas mental health profs thought this was the main reason.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Campero L;Herrera C;Kendall T;Caballero M;

Bridging the gap between antiretroviral access and adherence in Mexico

Ref ID 7590 2007

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
HIV antiretroviral access and adherence.

Sample:
40 participants with HIV, under half were medically insured, half were unemployed. Ranging in age from 26 to 57 years old. Most women were widowed or divorced and lived with their children. 6 of the 40 were not taking antiretrovirals.

Data collection:
Interviews.

Setting:
HIV clinics in urban areas in four Mexican States.

Theoretical approach (if any):
Grounded theory.

Categories of respondent:
Patients, Support persons (family/friends), support group leaders (from hospital-based HIV/AIDS clinics).

Concepts:
Late diagnosis and inopportune initiation of treatment: Many got very little or no information about the disease and how to care for themselves, lacked information to make decisions about medications.

Seeking and accessing antiretrovirals: some had limited access to treatment e.g time-limited or waiting lists for medication. Mainly due to insurance - [n.b not applicable to the UK]. Circumstances on when to star or postpone treatment varied, physician choice, negative experiences of friends, the perception of health and illness – unless physically deteriorating was obvious there is minimization of importance by patients and family members.

Relationships with health care providers and treatment adherence: Many had been discriminated or their human rights violated by service providers and poor quality care. Physicians with specialised training are able to provide better HIV management but not all who have such patients receive this training. Deficiencies in physician-patient communication were constant across a range of circumstances such as not having time. Patients then do not have adequate knowledge relying on preexisting beliefs. Often they change their dosing schedule themselves without worrying about poor adherence as they think their schedule is flexible.

Adverse effects one of the most frequent motivations for abandoning treatment or modifying doses.

The role of support groups and family members in ART adherence: more information gained on treatment and also of the quality of care they should be receiving.

Most identified family members as important source of support but not as providers of information about ART treatment. Although they can inadvertently promote or reinforce poor adherence, due to lack of information on consequences of interrupting the treatment regimen.

Interpretation:
Lack an adequate evidence base to make informed choices about ART and have little access to social support or other strategies to improve adherence.

Physicians are often paternalistic in their relationship with the patient, as children who should obey rather than adults who should make informed decisions.

Physicians do not explain the reasons behind the therapeutic decisions or what happens to the body with HAART. This can lead to patients making decisions of changing medication and decreasing adherence on their own.

More doctors and health care personnel need specialised training.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Carrick R;Mitchell A;Powell RA;Lloyd K;

The quest for well-being: a qualitative study of the experience of taking antipsychotic medication

Ref ID 88 2004

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	Context: The experience of taking antipsychotic medication Sample: 25 adults taking antipsychotic medication, aged 18 to 65, fluent English speaking. Data collection: Semi-structured interviews, focus groups. Setting: Exeter, South West England. Theoretical approach (if any): Grounded theory. Categories of respondent: Patients. Concepts: Wellbeing: tried to maximise well-being by reducing distressing symptoms and side effects. Managing treatment: Whether active in treatment decisions or out of their control. In positively-viewed doctor-patient relationships phrases like 'we decided' are used. In other situations they found that doctors might have a different goal in mind, more with reducing symptoms than improving life. Many believed that if not adhering they would be sectioned and felt it wasn't a free choice or decisions made had a sense of mystery. Understanding situation: The persons understanding of their situation alters the nature of their personal goals which effects how they manage and evaluate their situation. Evaluating treatment: evaluated a drug as 'good' or 'bad' through positive or negative experiences of illness and negative and positive points to treatment. (pros and cons). Interpretation: Patients' objectives were to maximize well-being but their understanding of their situation alters their goals, and how to manage and evaluate their situation. Side effects and symptoms were possible barriers to maximizing well-being. Patients' trade off whether medication is worth it over all.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Chen CH;Wu JR;Yen M;Chen ZC;

A model of medication-taking behavior in elderly individuals with chronic disease

Ref ID 7592 2007

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Elderly individuals with Chronic disease.

Sample:
19 elderly (65 years or older) cardiac patients.

Data collection:
Interviews.

Setting:
Cardiovascular disease clinics in Tainan, Taiwan.

Theoretical approach (if any):
Grounded theory.

Categories of respondent:
Patients.

Concepts:
The findings are organized around the main theme of readiness to adhere.
When visiting physicians to relieve physical signs or symptoms no one was prepared to question the treatment regimen, to adhere was always the first thought . To convert perceptions into actions, 2 influencing factors – facilitating and inhibiting factors, played pivotal roles.

Perceived effectiveness of treatment; perceived partnership (trust with healthcare team); perceived reality (perception of the purpose of their medications and the reality that it will be long-term); interpersonal influences (information sharing with relative/friends) influenced adherence. Inhibiting factors were memory, complex dosage schedules etc; facilitating factors in terms of support, compliance devices and simple regimes.

Interpretation:
Adherence to medication is a dynamic process that may be influenced by a variety of factors.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Cooper V;Buick D;Horne R;Lambert N;Gellaitry G;Leake H;Fisher M;

Perceptions of HAART among gay men who declined a treatment offer: preliminary results from an interview-based study

Ref ID 113 2002

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Perceptions of HAART among gay men who declined treatment.

Sample:
26 gay men. Patients not taking HAART who had just declined treatment.

Data collection:
Semi-structured interviews.

Setting:
Referred by physicians at the Royal Sussex County Hospital, Brighton.

Theoretical approach (if any):
Thematic analysis.

Categories of respondent:
Patients.

Concepts:
Doubts about personal necessity for HAART – lack of HIV related symptoms, interpretation of blood test results (perceptions of CD4 count and viral load differed from doctors), long-term diagnosis of HIV (had maintained good health), preference for non-pharmacological methods of controlling HIV (e.g complementary medicine), let HIV take its course.

Concerns about potential adverse effects of taking HAART – psychological consequences, perceived negative effect on quality of life, perceived negative effect on self identity, concerns about future treatment options (resistant/immune), previous negative experience (self/others), negative attitudes to medicines in general.

Satisfaction with the amount of personal control over the decision – until felt totally at ease with decision they would not accept the treatment, wanted control over what happens to them and not let medical profession take control.

Interpretation:
In interpreting data must consider the possible effects of cognitive dissonance and self-perception on participants' beliefs about HAART, as interviews were after they had made their decision not to have treatment.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Deegan PE;

The importance of personal medicine: A qualitative study of resilience in people with psychiatric disabilities

Ref ID 7593 2005

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	Context Resilience in people with psychiatric disabilities Sample 29 participants who were enrolled in community support programs for those with severe and persistent mental illness. Aged 20-69, with various disorders. Data collection Semi-structured interviews Setting Kansas, USA. Theoretical approach (if any) Phenomenological method Categories of respondent Patient. Concepts Personal medicine (non-pharmaceutical activities or strategies to decrease symptoms and other undesirable outcomes). Non-adherence to prescribed medication occurred when pharmaceuticals interfered with personal medicine resulting in diminished quality of life. Personal medicine as meaning and purpose in life – e.g valued social roles and activities that gave their lives meaning. Personal medicine as self-care strategies – strategies to increase wellness and decrease psychiatric symptoms and unwanted outcomes. Disclosure of personal medicine to healthcare providers – some did not tell their gp for e.g disapproval. Non-adherence – some reported that sometimes psychiatric medications interfered with things that gave their life meaning and purpose, when interfered too much they stopped taking them. Interpretation Significance of personal medicine for healthcare patients – the members of the focus group found the concept useful. Focus group members said that recovery was not simply swallowing pills but about changing their lives. Patients were not asked by their healthcare service about their personal medicine and did not volunteer this information. If clinicians inquired about personal medicine prior to prescribing and worked with the patient to the goal of pharmaceuticals supporting or enhancing personal medicine then drug adherence might increase.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Elliott RA;Ross DD;Adams AS;Safran DG;Soumerai SB;

Strategies for coping in a complex world: adherence behavior among older adults with chronic illness

Ref ID 29 2007

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Adherence behaviour among older adults with chronic illness

Sample:
20 elderly people with health insurance, aged 67-90 with several medicines.

Data collection:
Semi-structured interviews.

Setting:
Eastern Massachusetts

Theoretical approach (if any):
Grounded theory.

Categories of respondent:
Patients aged 67-90 on multiple medications with co-morbidities.

Concepts:
People make choices between medicines: all participants had now or previously chosen to adjust dosing, swapping or stopping a medicine.

What influences people's choices: symptom control, side effects, fear of future risk of the disease, medication cost, negative health experience, illness beliefs and acceptability (administration route and palatability). Specific concerns or beliefs about a medicine or illness dominated over other factors such as influence of family, friends or media, health care providers, or income. These had a moderating effect.

Complexity and cost of regimens: complexity was not considered a problem. Unintentional nonadherence was reported infrequently. Nearly all had written memory aids or dosette boxes.

One factor dominates: when making choices there is influence by one dominant factor much more so than using multiple factors.

Interpretation:
In real life interviewees use different factors about medicines than they would choose when predicting future adherence factors. Mostly external factors are factors for the historical choices. Without previous experience of an illness people imagine the loss of health caused by the illness rather than life with the illness.

Usually side effects, high perceived cost or lack of effectiveness dominated the decision process, such that people did not consider anything else, but used 1 of these factors as a shortcut to help them make a choice.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Enriquez M;Lackey NR;Connor MC;McKinsey DS;

Successful adherence after multiple HIV treatment failures

Ref ID 352 2004

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Patients with HIV.

Sample:
Thirteen patients with HIC who had adhered to treatment for one year following periods of non-adherence.

Data collection:
Interview.

Setting:
Receiving treat in US clinic setting.

Theoretical approach (if any):
Giorgi method of analysis.

Categories of respondent:
Patients.

Concepts:
Themes of (1) cycles of nonadherence–related to diagnosis, coming to terms with diagnosis, denial, abusive behaviours such as use of alcohol and drugs, nihilistic about future (2) occurrence of trigger events that changed view of disease and prognosis and wanting to live (3) conscious choice to think differently about medicine, find right health care provider and right regime, creating a support system, getting control of life and having goals.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Erwin J;Peters B;

Treatment issues for HIV+ Africans in London

Ref ID 17910 1999

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	Context Black Africans who are HIV positive. Sample 44 black African patients from Uganda, Zambia, Ethiopia, Nigeria, Kenya, Zimbabwe and Tanzania Data collection Focus Groups Setting Community setting Theoretical approach (if any) Not stated Categories of respondent Patients Concepts Strongly held belief that physiology of black and white people different and drugs more appropriate for white people than black. Patients experience medical services differently, some wanting a very medical centered type of treatment. Most important source of information for treatment was word of mouth. Alternative treatments specific to Black African population were used by interviewees- traditional drugs and newer drugs sold specifically as cure for HIV/Aids. This was generally not disclosed to medical professionals. Patients received support from the churches who could advise patients not to take drugs. Patients reported distrust of doctors and hospitals as wishing to hasten death of black African patients. Patients immigration status had implications for their eligibility for treatment and their willingness to present themselves for treatment. Focus group with women indicated particular issues for them about access and confidentiality.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Field K;Ziebland S;McPherson A;Lehman R;

'Can I come off the tablets now?' A qualitative analysis of heart failure patients' understanding of their medication

Ref ID 7596 2006

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Heart failure patients understanding of medication.

Sample:
37 participants (men and women) with heart failure. Aged 35 to 85 years. 86% were white British. At all stages of heart failure.

Data collection:
Open-ended narrative interviews (part of DiPex).

Setting:
UK 2003, recruited through GPs, cardiologists, specialist nurses and patient support groups.

Theoretical approach (if any):
Thematic analysis.

Categories of respondent:
Patients.

Concepts:
Three levels of patient awareness of medication was described:

Level 1 Doing what I'm told – not knowledgeable of their condition or medication.
Level 2 Leaving it up to your GP: knew names of medication but did not know what pills for.
Level 3 Candidates for concordance – more knowledgeable about medication. But these people were not typical of heart failure patients – e.g. a retired GP, retired nurse.

Interpretation

Current levels of understanding suggest few understand the side effects or their changing symptoms of the condition. Few understand what medicines are for. Medication reviews may present opportunity to monitor their understanding of their medicine.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Fraenkel, L.M.S;

Participation in medical decision making: The patients' perspective

Ref ID 413 2007

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
The essential elements to enable patient participation in medical decision making.

Sample:
25 women and 1 man from community dwelling subjects undergoing bone density measurements. Mean age 61 (range 49 to 76). All were Caucasian, 69% married, 50% had a graduate degree and 23% were retired.

Data collection:
Semi-structured interviews.

Setting:
Participants were from a larger study examining preference for treatment for

osteoporosis from 6 centers in the greater New Haven, Connecticut area.

Theoretical approach (if any):
Grounded theory.

Categories of respondent:
Patients.

Concepts:
Patient knowledge.

Explicit encouragement of patient participation by physicians.

Appreciation of the patient's responsibility/rights to play an active role in decision making.

Awareness of choice.

Time.

Interpretation:
Several needs must be met before patients can become active participants in decisions related to their health care. This includes ensuring patients know that there is uncertainty in medicine and the importance of active patient participation in decisions related to their health care. Also to understand the trade-offs related to available options and to be able to discuss options with their gps and arrive at a decision concordant with their values.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Garcia-Popa-Lisseanu MG;Greisinger A;Richardson M;Malley KJ;Janssen NM;Marcus DM;Tagore J;Suarez-Almazor ME;

Determinants of treatment adherence in ethnically diverse, economically disadvantaged patients with rheumatic disease

Ref ID 7599 2005

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Patients with RA and SLE.

Sample:
40 participants. Economically disadvantaged and ethnically diverse sample. Aged between 18 and 80 with disease duration of less than 15 years, currently treated with steroids, antirheumatic drugs or biologic agents.

Data collection:
Focus groups.

Setting:
Recruited from outpatient Rheumatology Clinic of general hospital (providing medical care for economically disadvantaged patients) in Houston, Texas, USA.

Theoretical approach (if any):
Grounded theory.

Categories of respondent:
Patients.

Concepts:
Barriers to drug treatment adherence:

Forgot/chose to discontinue – often due to large amount of medication they had to take.

4 major barriers to treatment regimen: fear of side effects (most commonly mentioned), perceived lack of efficacy of therapies, financial costs of drug therapy and problems with the health system environment and logistics.
Language barriers, difficulties with scheduling system, lack of transportation, symptom severity – missed appointments.

Interpretation:
In all focus groups, regardless of disease or ethnicity most reported occasions when forgot or voluntarily stopped treatment.
Patients were informed of possible side effects, by reading or from physician, although not clear understanding of ratio between possible benefits and toxicity.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Gascon JJ;Sßnchez OM;Llor B;Skidmore D;Saturno PJ;

Why hypertensive patients do not comply with the treatment: results from a qualitative study

Ref ID 89 2004

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Hypertensive patients who do not comply with the treatment.

Sample:
44 Hypertensive patients aged 18 to 80 years treated with hypertension medication for over 3 months, non-compliant and having good physical and mental health to participate.

Data collection:
Focus groups.

Setting:
Two primary health care centres in Murcia, Spain.

Theoretical approach (if any):
Grounded theory.

Categories of respondent:
Patients.

Concepts:
Beliefs and attitudes toward antihypertensive drugs: fears of long-term use, damaging the body. Thought it safe not to take from time to time. Experimented with the medicines to see how felt without them. Wish to find out about alternatives. More confidence in herbal remedies.

Beliefs and attitudes toward hypertension – gained from magazines, tv and others.

Little time in consultation, most of time used to get the prescription and note-taking by physician, little eye-contact, lack explanation.

Interpretation:
Negative feelings toward medication, dissatisfaction with clinical encounters as barriers with regard to following treatment advice.

Can have lay knowledge and beliefs on medication that can reduce compliance and must be addressed by the physician and given adequate information.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

George M;Freedman TG;Norfleet AL;Feldman H;Apter AJ;

Qualitative research-enhanced understanding of patients' beliefs: results of focus groups with low-income, urban, African American adults with asthma

Ref ID 7600 2003

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Focus groups on beliefs of low-income, urban, African American adults with asthma.

Sample:
15 low-income, urban, African American adults with persistent asthma.

Data collection:
Three focus groups.

Setting:
A primary or asthma specialty care practice of the University of Pennsylvania Health System.

Theoretical approach (if any):
Thematic analysis.

Categories of respondent:

Patients.

Concepts:
The main medication use explored was the use of inhaled corticosteroids (ICS). Patients perceptions related to their own assessment of their asthma – that they did not need inhaler every day, problems in accessing medication, forgetting to take the medicine by getting distracted, not knowing what to do if forgot to take, worries about the medication.

Strategies to promote ICS adherence suggested by patients were– fewer doses, less frequently (combination therapy), getting into routine, letting them know of some side effects.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Givens JL;Datto CJ;Ruckdeschel K;Knott K;Zubritsky C;Oslin DW;Nyshadham S;Vanguri P;Barg FK;

Older patients' aversion to antidepressants: A qualitative study

Ref ID 7601 2006

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Older patients' aversion to antidepressants.

Sample:
42 Primary care patients, 60 years and over, whom expressed reluctance or refusal

to use antidepressant medication.

Data collection:
Semi-structured interviews.

Setting:
Primary care practices of the University of Pennsylvania Health System and the Philadelphia Department of Veterans Affairs.

Theoretical approach (if any):
Constant comparative method (Grounded Theory).

Categories of respondent:
Patient.

Concepts:
Fear of addiction.

Resistance to viewing depression as a medical illness.

Concern that antidepressants will prevent feelings of natural sadness.

Prior negative experiences with medications for depression.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Gordon K;Smith F;Dhillon S;

Effective chronic disease management: Patients' perspectives on medication-related problems

Ref ID 137 2007

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Chronic disease management – medication related problems.

Sample:
98 participants, 42% male and 58% female, mean age 67 (range 32-89 years). 83% were white and 17% black. 42% lived alone. Identified with a medication-related problem at the screening interview. Prescribed medication for cardiovascular disease.

Data collection:
Interviews.

Setting:
Recruited in five general medical surgeries and four community pharmacies in Lambeth, Southwark and Lewisham HA areas in South London.

Theoretical approach (if any):
Inductive.

Categories of respondent:
Patients.

Concepts:
5 categories of medication-related problem emerged:

Perceptions and fear of side-effects and their methods of coping with them.

Views and actions regarding the use of medicines.

Cognitive, physical and sensory problems affecting the use of their medicines.

Lack of information and/or understanding about the use of medicines.

Problems attributed to access to, and organization of, services.

Interpretation:
All categories of problem had potential implications for the success of therapy in that they created barriers to adherence, access to medication or informed decision-making. The study demonstrated how patients actively engage in decision-making about their medicines in the home, if not in the consultation.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Gray J;

Becoming adherent: experiences of persons living with HIV/AIDS

Ref ID 47 2006

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	Context: Patients with HIV. Sample: 11 patients with HIV judged to be adherent to medication. Data collection: Interview. Setting: US sample. Theoretical approach (if any): Grounded theory. Categories of respondent: Patients. Concepts: The study described how patients approached the taking of HIV medication and the processes undertaken by patients in achieving adherence. Despite the label of being adherent the patients did report missing doses. (1)Choosing life - decision on need for treatment and the options available (2)Riding it out – adjusting to side effects (3)Figuring it out - developing a routine (4)Sticking to it – overcoming internal resistance to the routine (5)Realizing the benefits – patients saw improved clinical outcomes
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Hayes RP;Bowman L;Monahan PO;Marrero DG;McHorney CA;

Understanding diabetes medications from the perspective of patients with type 2 diabetes: prerequisite to medication concordance

Ref ID 7605 2006

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Patients with type 2 diabetes recruited through newspaper adverts and letters.

Sample:
138 socioeconomically diverse individuals with type 2 diabetes (68% female, 74% over 50 years old, 61% non-Hispanic Caucasian). On a variety of diabetes medication regimens.

Data collection:
18 focus groups.

Setting:
Veteran Affairs facility in Indianapolis, Indiana.

Theoretical approach (if any):
Content analysis.

Categories of respondent:
Patients with type 2 diabetes.

Concepts:
The inconvenience and inflexibility of the timing and frequency of taking diabetes treatments on their lives- this included being somewhere where it was possible to use medication.

Wish to avoid injections and/or insulin therapy.

The physical and emotional side effects of the medications – patients often could not differentiate between health status and effects of medicines.

Currently felt had no opportunity to express their treatment preference to their health care provider.

Interpretation:
Need to support patients in articulating and incorporating their needs and preferences into the treatment decision-making process.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Kikkert MJ;Schene AH;Koeter-Maarten WJ;Robson D;Born A;Helm H;Nose M;Goss C;Thornicroft G;Gray RJ;

Medication adherence in schizophrenia: exploring patients', carers' and professionals' views

Ref ID 7607 2006

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Medication adherence in Schizophrenia.

Sample:
27 purposely-selected patients with schizophrenia.

Data collection:
Focus groups.

Setting:
England, Germany, Italy and the Netherlands. Part of the quality of life following

adherence therapy for people disabled by schizophrenia and their carers study.

Theoretical approach (if any):
Concept mapping.

Categories of respondent:
Patients, carers and professionals. Inclusion criteria for patients were that they had to have episodes of non-adherence and this was based on hospital admissions, instability, changes in medication.

Concepts:
Factors considered important in adherence:

Professional and non-professional support, information and involvement, efficacy of medication, side effect self management, social effects of side effects (extra-pyramidal), negative expectations, insight, positive medication attitudes and expectations, negative medication attitudes, side effects.

Limitations:
Interpretation
The findings provide a comprehensive overview of all relevant issues and how they relate to one another.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Lawton J;Ahmad N;Hallowell N;Hanna L;Douglas M;

Perceptions and experiences of taking oral hypoglycaemic agents among people of Pakistani and Indian origin: Qualitative study

Ref ID 17918 2005

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
People of Pakistani and Indian origin with type 2 diabets.

Sample:
32 patients of Pakistani or Indian origin.

Data collection:
Focus Groups.

Setting:
Primary and community care in Edinburgh, Scotland.

Theoretical approach (if any):
Grounded theory.

Categories of respondent:
Patients.

Concepts:
Drugs were perceived to be more effective and better quality than those available on the subcontinent. Prescribers in UK were also considered more trustworthy as NHS did not gain from drugs prescribed.

Patients sought to reduce their intake of medication where possible, and aimed primarily to relive symptoms. Patients altered medicines when fasting, if skipping meals. Patients took care to eat foods they perceived as 'strengthening' such as chapattis and curries.

Patients altered drug intake by self-monitoring blood glucose and reducing food intake.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Lewis MP;Colbert A;Erlen J;Meyers M;

A qualitative study of persons who are 100% adherent to antiretroviral therapy

Ref ID 184 2006

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	Context: Persons who are 100% adherent to antiretroviral therapy. Sample: 13 HIV positive individuals taking antiretroviral therapy who were 100% adherence to treatment. Aged from 28 to 54 years, mean 42 years. The majority (9) were male, white (10), disabled (9), more than 84% had at least a high school education, 9 months to 12 years on treatment. Data collection: Interviews. Setting: Recruited from 3 primary care clinics and an HIV/AIDS community support organization in western Pennsylvania from 1999 to 2003. Theoretical approach (if any): Strauss and Corbin. Grounded Theory. Categories of respondent: Patients. Concepts: Managing the regimen – tailoring to fit lifestyle, accepting trade-offs and limitations, acknowledging and granting medications' role in avoiding illness and death. Managing self – owning problems and solutions (personal accountability to take control over lives), investing in self, adopting a realistic future outlook. Managing the environment – recognizing positive and negative sources of support, identifying and creating individualized tools for managing adherence, actively participating in a partnership with the health care provider.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Lukoschek P;

African Americans' beliefs and attitudes regarding hypertension and its treatment: a qualitative study

Ref ID 7609 2003

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
African Americans' beliefs and attitudes regarding hypertension and its treatment.

Sample:
92 Clinically diagnosed with hypertension for minimum of two years, prescribed antihypertensive medications, identifying selves as African American, black or Black American, 67% female.

Data collection:
Focus Groups.

Setting:
Medical clinic in a large urban municipal hospital serving mostly uninsured or Medicaid–insured. USA.

Theoretical approach (if any):
Qualitative content analysis.

Categories of respondent:
Patients.

Concepts:
Specific exploration of patients understanding of hypertension and high blood pressure – felt by some to be different, others to be the same. Patients health beliefs of problem and its causes influenced approach to treatment, including diet and lifestyle. A variety of symptoms were attributed to hypertension/high blood pressure.

Adherent patients used positive terms to affirm the multiple benefits of medication, nonadherent denigrated medication, perceiving it to be inadequate and they more likely to rely on alternative therapies.
Both types of participants referred to side effects of medication.
Beliefs of benefits versus negatives.
Patient-physician relationship.

Interpretation:
Adaptation and preservation of health beliefs: Some health beliefs change over time due to diverse societal influences, while others seem to persist.

Hypertension often goes without symptoms until comorbidities develop and then symptomatic disease following. Adherent group reported longer duration of hypertension so had experienced more symptoms.

Distrust, stress and perception of racial prejudice – expressed belief that medications were chosen to advance science rather than benefit patients. Racially specific medication was viewed with suspicion.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Morgan-Myfanwy F;

Barriers to Uptake and Adherence with Malaria Prophylaxis by the African Community in London, England: Focus Group Study

Ref ID 1875 2005

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Patients experience of anti-malarial treatments.

Sample:
44 volunteers of African origin.

Data collection:
Focus Groups.

Setting:
South London.

Theoretical approach:
Framework .

Categories of respondent:
Recruited through church and community groups.

Concepts- Malaria understood as 2 possible illnesses –one serious, the other a relatively common experience dangerous only to young or old. Patients reported they had been 'vaccinated' against malaria or had developed immunity. Some patient took risks in not treating malaria, others considered it possibly debilitating and would take drugs to avoid it.
Patients reported general dislike of anti-malarial drugs because of side effects, and doubts about effectiveness of drugs. The regime was also burdensome if only going abroad for a short period.
Patients reported forgetting to take drugs, having difficulty in recongising whether symptoms related to drugs or climate, diet etc. Patients did not understand rationale for continuing drugs once they had left the anti-malarial area and some wished to leave drugs for family in Africa where drugs are more expensive.
Accessing appointments and cost of medication was an issue.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Mutchler JE;Bacigalupe G;Coppin A;Gottlieb A;

Language barriers surrounding medication use among older Latinos

Ref ID 7612 2007

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Language barriers surrounding medication use among older Latinos.

Sample:
Latino, community-residing individuals aged 50 and over.

Data collection:
Focus Groups.

Setting:
Eastern Massachusetts.

Theoretical approach (if any):
Theoretical sampling frame (grounded theory).

Categories of respondent:
Patients.

Concepts:
Language is a barrier in dealing with medications.

Language barriers were related to perceptions of discrimination.

Despite obstacles, older Latinos are actively involved in their health choices.

Involvement in own health care is often linked to their understanding of medicines taken and relationships with physicians.

Friends and family were sources of assistance with medical concerns and as interpreters. Also for translating the directions on the label.

The physician did not need to be Latino himself, speaking a little of Spanish led to feeling understood. Formal interpreters were often experienced as not realying accurately patients words.

Trust important for decision making, and trust is related to language.

Interpretation:
Language barriers can have implications for medication choices and adherence.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Nair KM;Levine-Mitchel AH;Lohfeld LH;Gerstein HC;

I take what I think works for me: a qualitative study to explore patient perception of diabetes treatment benefits and risks

Ref ID 7613 2007

Study Type Qualitative **Funding**

Number of participant	
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	Context: Diabetes treatment. Sample: People who were not able to speak English, had gestational diabetes, or had a cognitive deficit were excluded. Data collection: Individual in-depth interviews, conducted by principal investigator. A focus group was held near the end of the analysis process as a way of “member checking” the interpretation of the data. Setting: Interviewees recruited using newsletters, diabetes clinic and a university website. The study took place in Hamilton Canada. Theoretical approach (if any): Grounded theory approach for data collection and analysis. Categories of respondent: 18 patients with a mean age of 60 years. Concepts: “ I take what I think works for me” Patient’s perception of the value of a treatment was the prevailing factor that influenced treatment decision-making. Patients had varying levels of understanding about the benefits and risk of treatment of diabetes. Most seemed to be knowledgeable about the benefits that the treatment could bring. Also, that people who were more recently diagnosed did not comprehend the potential benefits and risks of treatment as those who had experience with their disease. Medication costs and number of medications perceived as risks when starting a treatment, as the potential for no benefit to health. Some patients stopped medication as they started to feel improvements, whilst others had tried alternative medicines. Past experiences with adverse effects due to medication were also important in the assessment of benefits and risks of a treatment. Other was willing to cope with the side effects if they were able to see that the treatment was working. For major side

effects people stopped their medication on their own and then called the doctor for guidance.
Patients expressed the view that treatment decision-making was a life-long process. Patients cited having adequate information about a prescribed or recommended treatment as a key factor in their treatment benefit and risk assessment. Other sources of information were sought.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Ogedegbe G;Harrison M;Robbins L;Mancuso CA;Allegrante JP;

Barriers and facilitators of medication adherence in hypertensive African Americans: a qualitative study

Ref ID 90 2004

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Barriers and faciltators of medication adherence in hypertensive African Americans.

Sample:
106 hypertensive African American patients. 58% women, mean age 56 years.

Data collection:
Open-ended interviews.

Setting:
2 urban primary care practices.

Theoretical approach (if any):
Grounded theory.

Categories of respondent:
Patients.

Concepts:
Emphasis on problems in taking medication. Barriers were described as being patient-specific, medication specific, disease specific and logistical.
Patient barriers included - forgetfulness, beliefs about medicines, attitudes to diagnosis.

Medication-specific included side effects, number to be taken, taste, frequency and cost.

Disease-specific barriers were patients perception of hypertension and long term complications, in particular the absence of symptoms.

Logistic Barriers – inconvenience to patients in taking medication, getting prescriptions filled, re-ordering and requiring multiple reviews.

Facilitators were: reminders – circumstances that prompted patients to take medication, knowledge, doctor-patient communication, routine and social support networks.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Pyne JM;McSweeney J;Kane HS;Harvey S;Bragg L;Fischer E;

Agreement between patients with schizophrenia and providers on factors of antipsychotic medication adherence

Ref ID 275 2006

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Agreement between patients with schizophrenia and providers on adherence.

Sample:
26 out patients diagnosed with schizophrenia or schizoaffective disorder. Aged 20-70 years.

Data collection:
Interviews.

Setting:
Recruited from an outpatient and intensive case management setting. USA.

Theoretical approach (if any):
Inductive approach, content analysis and constant comparison.

Categories of respondent:
Patient. Mental health providers.

Concepts:
The study explored explanatory models held by professionals and patients about their illness under a series of headings – name of illness, cause of illness, problems associated with illness, signs that illness getting worse, factors that worsen illness, activities that maintain health and signs of health. Patients were more likely to identify stress as a cause of illness and factor that worsens illness, considered functioning a better indicator of health than symptoms and less likely to see medication as an important factor in controlling symptoms and maintaining health.

Barriers, facilitators and motivators for medication adherence from patient perception:

Eight domains were described – environment , side effects, relationship between provider and family, insight and knowledge, symptoms and outcomes , substance abuse, stigma and dosing. All eight were included as barriers, four domains – environment, provider –family relationships, insight and knowledge and dosing were also facilitators and 3 domains – environment, symptoms and outcomes and provider-family relationships were also described as motivators.

Interpretation:
Found substantial disagreement between patients and their providers with regard to their explanatory models for schizophrenia and limited provider understanding of the barriers, facilitators and motivators affecting individual patients' medication adherence decisions.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Reid M;Clark A;Murdoch DL;Morrison C;Capewell S;McMurray J;

Patients strategies for managing medication for chronic heart failure

Ref ID 7615 2006

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Patients with heart failure.

Sample:
50 patients with heart failure.

Data collection:
Interview.

Setting:
Outpatient UK clinic.

Theoretical approach (if any):
Constant comparative approach.

Categories of respondent:
Patients.

Concepts:
Descriptive analysis of patients knowledge of their illness and medication taking behaviour. Most patients were on multiple treatments with many medications throughout the day and the regimes were complex. To take medication patients tired to develop and maintain a routine. Patients reported being strategic in their use of frusemide tablets and might change timing of dose depending on activities; they also forgot to take medicines.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Ring L;Kettis LA;Kjellgren K;Kindell Y;Maroti M;Serup J;

Living with skin diseases and topical treatment: patients' and providers' perspectives and priorities

Ref ID 7616 2007

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Patients with skin diseases taking topical treatments.

Sample:
Patients who mainly had psoriasis and atopic eczema and providers of dermatological care and treatment.

Data collection:
Focus Groups.

Setting:
Swedish dermatology clinics at a university and county hospitals which had a specialist outpatient treatment unit.

Theoretical approach (if any):
Consensual Qualitative Research method (Hill et al).

Categories of respondent:
Patients, doctors, nurses, pharmacists.

Concepts:
Living with treatment was difficult and burdensome.

Treatment was time-consuming, tiresome and had different practical problems.

Creams were in large packages and hard to carry and conspicuous.

Interpretation:
Smaller packaging of topical medicine to allow patients to trials of treatment and to carry around .

Many patients were anxious about the side effects of cortisone.

Some patients were looked upon as disgusting by health-care staff. Improving physicians interpersonal skills can increase patient satisfaction, so more likely to have a positive effect on adherence.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Scotto CJ;

The lived experience of adherence for patients with heart failure

Ref ID 7617 2005

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
What is the lived experience of adherence in patients with heart failure.

Sample:
14 patients attending an outpatient heart failure clinic after hospital readmission for exacerbation of heart failure symptoms. Attempting to adhere to a prescribed

regimen of care. Aged 42 to 84 years.

Data collection:
Interviews.

Setting:
Outpatient heart failure clinic USA.

Theoretical approach (if any):
Hermeneutic approach.

Categories of respondent:
Patients.

Concepts:
Concepts of daily influence on adherence:
Personal beliefs and values may support or bring about deviations from the adherent behaviours.

The support or lack of support from healthcare providers and significant others can affect adherence.

Difficulty with adherence to appropriate behaviours also occurred when unusual circumstances arose or when temptation overcame motivation.
Acceptance of changed health status and new self-image.
Integration – of self care behaviours into routine of life.
Unusual circumstances can make patients non-adherent.

Interpretation:
Acknowledging personal beliefs and values will help promote a feeling of support from healthcare professionals. Much nonadherent behaviour occurs at times when the individual intends to be adherent.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Sidat M;Fairley C;Grierson J;

Experiences and perceptions of patients with 100% adherence to highly active antiretroviral therapy: a qualitative study

Ref ID 7618 2007

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	Context: Experiences and perceptions of patients with 100% Adherence to HAART. Sample: 10 participants (7 men and 3 women) with 100% adherence to HAART for 6 months or more previous to interviews. Purposely selected participants. Data collection: Interviews. Setting: HIV Clinic in Melbourne Sexual Health Centre, Australia. Theoretical approach (if any): Phenomenological analysis approach. Categories of respondent: Patients. Concepts: Decisions to go on HAART: the decision to start HAART was referred by the participants as shared between them and their clinicians which undoubtedly affected their choice of taking their medication as 'agreed'. Importance of client-patient relationship. Managing HAART on daily basis: all participants reported that their current HAART regimens were well suited to their lifestyles and this was a mutual decision they made with their health care providers. Each participant had a different but individually suitable strategy for their particular regimen and lifestyle. Well-established routines. Commonly used reminders – sms from clinic, mobile alarm, pill boxes. Intense side effects can discourage adherence. A good knowledge of the type, duration and severity of the expected side effects important. All reported optimal relationships and felt very well supported by all the staff at the clinic. Interpretation: When decide to go on HAART, after considering their beliefs/perceptions, it is more likely to result in positive outcomes than when a prescriptive approach is implemented. Needs a collaborative decision between doctor and patient.
Effect due to factor in study?	
Consistency of results with other studies?	

Directly applicable to guideline population?

Internal Validity

Taylor SA;Galbraith SM;Mills RP;

Causes of non-compliance with drug regimens in glaucoma patients: a qualitative study

Ref ID 110 2002

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Patients with glaucoma.

Sample:
28 patients with glaucoma.

Data collection:
Two focus groups and 11 in depth interviews.

Setting:
Receiving treat in US clinic setting.

Theoretical approach (if any):
Not stated, basic descriptive analysis.

Categories of respondent:
Patients.

Concepts:
Findings relate to patient experience of eye drops and their encounters with medical professionals:
Patients do not know how to use their drops, the most common reason for not taking medication was forgetting, side effects were commonly mentioned but not as cause of not taking drops, patients would like easier regimens, patients wanted information on glaucoma research, patients liked doctors who tried new treatments, cost was not

a factor reported as a reason for not taking drops, many patients would not report to health care professionals if they did not take use their drops.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Vermeire E;Van RP;Coenen S;Wens J;Denekens J;

The adherence of type 2 diabetes patients to their therapeutic regimens: A qualitative study from the patient's perspective

Ref ID 229 2003

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Adherence of type 2 diabetes patients to medication.

Sample:
46 patients from primary care with type 2 diabetes.

Data collection:
Focus groups.

Setting:
Flanders, Belgium.

Theoretical approach (if any):
Thematic analysis.

Categories of respondent:
Patients.

Concepts:
Health beliefs, the quality of doctor/patient communication and the quality of the information patients receive are important factors for patient adherence to treatment.

Possible explanatory models for adherence emerged, relating to knowledge of the illness, body awareness and the doctor/patient relationship.

Adherence: if no discomfort from disease it was hard to decide to adhere to treatment. Not only expect information about disease but needed encouragement and understanding of the difficulties in managing their diabetes.
Many found introduction of insulin a major crisis, as a result of losing complete control of their body. Others like it as gave more control over body.

Interpretation:
Goal was to explore and gain deeper understanding of patients perspective.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Vinter RN;Petricek G;Katic M;

Obstacles which patients with type 2 diabetes meet while adhering to the therapeutic regimen in everyday life: Qualitative study

Ref ID 203 2004

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Context:
Obstacles to Type 2 diabetes patients' adherence to medication.

Sample:
49 patients with type 2 diabetes, aged 44 to 83 years old.

Data collection:
Focus groups.

Setting:
GP/family practitioners in Zagreb.

Theoretical approach (if any):
Thematic analysis.

Categories of respondent:
Patients.

Concepts:
Confronting the diagnosis, illness-related change, treatment of illness, social context, relation to the health professionals, self-control, knowledge about the illness, expectations.

Treatment of illness: most preferred taking pills as it is simpler than eating and activity changing.

Some held the belief that insulin is connected with a more severe form of the disease and therefore had anxiety and did not take insulin. Those taking it were satisfied with it and the control it gave them over their lives. [SEVERITY OF DISEASE]

There were two extremes in relation to changing the dosage prescribed by the physician - some never changed and others did from time to time, depending on food quantity they consumed and physical activity they undertook. [STRATEGIC]

Social context – absence of support can create difficulties. Felt uncomfortable in from of colleagues and worry of job loss. [STIGMA]

Relation to health professionals – often were patronized and resulted in a negative response. The majority felt support and closeness with GP.
Knowledge of illness: some patients thought it so common in older age they saw no need to treat it. [MISINFORMATION]

Interpretation:
Insufficient knowledge of disease, especially e.g the metabolic changes that occur, different treatment options.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Wilson HS;Hutchinson SA;Holzemer WL;

Reconciling incompatibilities: a grounded theory of HIV medication adherence and symptom management

Ref ID 7624 2002

Study Type Qualitative **Funding**

Number of participant	
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	Context HIV medication adherence and symptom management. Sample 66 patients with HIV, purposive sample, 50% caucasian, 27.3% black, 10.6% hispanic, 4.5% native american, 1.5% filipino. 10% female, aged 28 to 60 years old. Data collection: Semi-structured interviews. Setting: San Francisco Bay area. Theoretical approach (if any): Grounded theory. Categories of respondent: Patients. Concepts: Contextual factors – attributional uncertainty – eg where unclear whether the interacting symptom clusters were due to their illness or medication side effects. Silent virus – for a time felt symptom free despite viral load indicators. Or Perceived Fickle Medical Markers - where t-cell counts and viral loads failed to fit their personal experience of living with their condition. Conditions to be reconciled and influence adherence choices were numerous – self-identity, illness ideology, concurrent treatment regimens, personal meaning of time and QOL, medication regimen burden and side effects and the impact on their lifestyle. Hard work to consistently adhere to regimen of treatment: Complying subprocesses - accepting, embracing and routinising. Noncomplying subprocesses – disregarding, gambling, rejecting, surrendering to their disease. They neglected and ignored their disease. Self-tailoring – reported adherent as followed regimen yet they adapted their

prescribed routine. Subprocesses – body listening, gauging, negotiating.

Interpretation:
Providers could help clients differentiate side effects from the disease. Assess a client's self-identity through a complete health history including social factors.

The decision to adhere is made each day, dose by dose. The challenge and complexity of adherence when making models to guide adherence interventions.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Question: What are the advantages and disadvantages of self-report?

Grading: 3	Non-analytic studies (for example, case reports, case series)

Bender B;Milgrom H;Rand C;

Nonadherence in asthmatic patients: is there a solution to the problem?

Ref ID 1145 1997

Study Type Review **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Conducted a literature review to assess non-adherence in asthmatic patients. A search of Medline was made from 1990 to 1997 of all pertinent articles, preferably controlled studies. Self-report measures can be collected by interview, diaries and questionnaires but no validated adherence-specific questionnaire is commonly used as they are often too specific. Self-report measures are simple, inexpensive and usually brief and so they are commonly used to measure adherence. Especially in the clinical setting they are the best measure for collecting information of beliefs, attitudes and experiences with medication regimes. Accuracy with other measures is highly variable. Spector (1986), Coutts (1992) and Gibson (1995) compared asthmatics self-reporting of inhaler usage with electronic medication monitoring devices and they showed that asthma diaries usually overestimate adherence. Demands of the setting can influence the usefulness and reliability of the information gained from self-reporting. These can be a desire to please on the part of the patient and HCP skill and sensitivity in eliciting self-reports. When collected well it can give good insight into patients' problems with adherence. And as there is unlikely to identify themselves as nonadherers, this helps identify the nonadherers (Coutts, 1992; Spector, 1986; Dolce, 1991; Morisky, 1990).
In summary, self-report measures are simple, inexpensive, brief and the best way of collecting information in the clinical setting. However diaries overestimate adherence and the demands of the setting can influence the usefulness and reliability of the measure.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Bennett Johnson SB;

Methodological issues in diabetes research. Measuring adherence

Ref ID 1279 1992

Study Type Review **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Conducted a narrative literature review of adherence measurement in diabetes management. No search or inclusion criteria was given.
They point out that self-report of regimen adherence are often mistrusted. Patients may say one thing but do something completely different, often because of what they think the doctor wants to hear. However non-compliance self-reporting appears more valid than self-reporting of compliance (Diehl, 1987). Asking about specific behaviours can lead to better adherence data (Cerkoney, 1980; Cox, 1984; Shlenk, 1984; Brownlee-Duffeck, 1987; Hanson, 1987; Hanson, 1987; Hanson, 1987; Hanson, 1988; Hanson, 1990). There have only been a few that have looked at the reliability of these reports (Hanson, 1987 and Hanson, 1988). If asked to report their specific behaviours over a certain time period, the data can be good quality (Glasgow et al, 1987; Johnson et al 1986). Multiple interviews are recommended to ensure representation of adherence behaviours.
One disadvantage with self-reporting is problems of memory recall. Where possible a significant other should additionally be interviewed regarding the patient's behaviour.
The advantages of self-report are numerous, as reliable information can be obtained; interviews can be done over the telephone making them accessible; the patient does not have to do very much apart from give their time for an interview. They however do need trained interviewers, or with multiple interviews and multiple patients the process can take a lot of time and effort. No references were made for these

assertions.
In summary, self-reporting of non-compliance is likely to be more valid, whereas compliance reporting is not valid. They can ask about specific behaviours and find out about what leads to non-compliance. It is easy for the patients to do and interviews can be done by phonecall. However there are biases with recall and people may say one thing but do another and there can be errors in reporting eg self-observation skills.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Farmer KC;

Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice

Ref ID 1064 1999

Study Type Review **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Conducted a review of methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice. They searched Medline for the years 1990 to 1999 and retrieved 2630 articles regarding patient compliance. They found that forms of self-report included questioning/interrogation and the use of diaries and survey instruments. They tabulated the various methods for assessing adherence and their advantages and disadvantages. Patient interviews are easy to use and inexpensive but the patient can be influenced by question construction and interviewer's skill. Adherence questionnaires are easy to administer (on site, mail, telephone), can be validated and may explain patient behaviour. However there is a lack of continuous data and the accuracy is instrument dependent.

Patient interviews are considered the most unreliable for assessing adherence (Grymonpre, 1998; Matsui, 1994; Craig, 1985; Straka, 1997; Park, 1964; Inui, 1981; Gordis, 1969). Those who report non-adherence are usually correct, whereas those who say they are adherent may not be (Cramer, 1991). However it can depend on the method used and how it is used. Assessing self-reporting is difficult mainly because there are so many methods. The interviewer's skill and the construction of the questions can affect the accuracy and validity of self-report. The relationship and communication between the HCP and patient have shown to significantly affect compliance (Davis, 1969). Highest compliance was found with those who joked, laughed and sought suggestions from their g.p. The wording of questions can affect the response, and implications of blame can encourage biased responses (Ross, 1991). Some answers are socially desirable and concealed their real behaviour (Sherbourne, 1992). It is hard to assess studies of interviews as the way they are asked could bias the result. Stewart (1987) looked at 2 compliance questions in an interview to assess medication-taking behaviour. Comparing the results to pill counts, the questions had a specificity of 69.8% and sensitivity of 80%, therefore an overall 74.5% accuracy. The time frame used for recall can differ, some researchers do not specify, others are 7-10 days and some are a month (Grymonpre, 1998; Dirks, 1982; Straka, 1997). To correct these problems some researchers have tried to construct a standardised questionnaire for measuring adherence. For example Morisky (1986) developed a 4-item questionnaire specific to medication regimen adherence. It was assessed on unidimensionality and reliability and concurrent validity with blood pressure control. The instrument's sensitivity was 81% and specificity 44%. It was not found to be efficient at predicting poor adherence (Morisky, 1986).
In summary, a few methods of self-report were looked at. Interviews are simple and inexpensive, but can depend on the interviewer. Questionnaires can be administered in a variety of methods, but are considered the most unreliable. Those who say they are non-adherent are usually correct but many who say they were adherent may not be.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Gagne-Camille GG;

Improving self-report measures of non-adherence to HIV medications

Ref ID 3529 2005

Study Type Review **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	Reported on how to improve self-report measures for non-adherence to HIV medications, with particular attention to techniques that can be applied with questionnaires administered in clinical practice. Questionnaires are inexpensive and convenient and can be conducted in clinical and research settings. But can vary in terms of accuracy. According to many authors, forgetfulness (Brooks, 1994; Hayes & DiMatteo, 1987; Holzemer, 1999; Rand, 2000; Svarstad, 1999) and social desirability (Felkey, 1995; Gordis, 1969; Gray, 1998; Rand, 2000; Svarstad, 1999) are main factors leading to inaccurate self-reporting of non-adherence. Social desirable answers can depends on how much the patient perceives the desirability of the behaviour to be. Those behaviours perceived as undesirable are under-reported and behaviours perceived as desirable can be over-reported (Cannell 1979; Fowler, 1995). There are techniques suggested for minimising forgetfulness and social desirability (Cannell, 1979; Fowler, 1995; Sudman & Bradburn, 1974; Sudman & Bradburn, 1982) although methods to reduce these are not well-documented, are often derived from clinical practice than controlled experimental studies and their reported effectiveness is inconsistent. Suggestions were made to reduce socially desirable answers: •Assuring confidentiality and that information will not be available to HCPs (Eldred, 1998; Gordillo, 1999). •Explaining that there are no right or wrong answers (Des Jarlais, 1999; Chesney, 1990). •How the question is asked (Ickovics, in Eldred, 1998; Chesney, 1999; Svarstad, 1999). •Wording the question to increase the likelihood of gaining certain desired answers, such as non-adherence (loading the question) (Sudman, 1982; Bradburn, 1982; Allaire, 1988). •Open-ended questions can avoid the pitfalls of response categories (Schwarz, 1985; Sudman, 1982). Open-ended questions have been used in studies of HIV (e.g Chesney, 1990) and for measuring adherence/non-adherence (e.g Svarstad, 1999). Open-ended answers have shown to be less affected by social desirability than close-ended answers (Sudman, 1974). Sudman (1974) also found that open-ended questions were less affected by forgetfulness and remembering it happening more than it actually did. Recall can be aided by: •Item wording, using familiar words and words that have only one meaning and one idea (Sudman, 1982); •Words should not have blame implications (Averitt, in Eldred, 1998). •Aided-recall techniques such as memory cues may be useful (Sudman, 1982). •Specifying a reference time period, especially a recent and short time frame can aid forgetfulness (Brooks, 1994; Chesney, 1999; Holzemer, 1999; Sudman, 1982). However there is the problem of the time period being too short and not accurately representing the adherence level, as adherence varies over time (Chesney, 1997b; Gray, 1998; Kastrissios, 1998). This could be solved by using a short period of time and administering the questionnaire a number of times over the period. However, this could lead to less motivation and could be costly. Shorter periods of reference could be used when administering the questionnaire only once. According to episodic and semantic memory it may be best to ask more precise information about the past few days and less specific information from a longer time period. In summary, self-reporting by questionnaire can have biases such as social desirable responses and recall bias. These biases can be minimised using certain techniques.
Effect due to factor in study?	

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

George J;Kong-David CM;Stewart K;

Adherence to disease management programs in patients with COPD

Ref ID 17930 2007

Study Type Review **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Conducted a literature review to assess adherence of COPD patients with disease management programs. They searched OVID and International Pharmaceutical Abstracts. They did not report the inclusion/exclusion criteria or how many studies were retrieved.
They found that self-reporting of missed doses (by questionnaire) underestimated non-adherence compared to more objective measures eg capsule count (Dompeling, 1992), inhaler weights (Rand, 1995) and electronic monitoring (Rand, 1992; Braunstein, 1996; Simmons, 2000). Self-report was shown to have moderate reliability compared to objective measures such as canister weight (Rand, 1995) and electronic monitoring (Gong, 1988; Nides, 1993; Bosley,1995).
Self-reporting of non-adherence of medication for COPD has shown satisfactory reliability, when compared to objective measures (Dolce, 1991; Nides, 1993; Rand, 1995). Self-report is commonly criticised for overestimating adherence and poor reliability yet those who report non-adherence are likely to be telling the truth (Haynes, 1980; Inui, 1981; Choo, 1999; Erickson, 2001).
In summary, self-reporting questionnaires underestimate non-adherence but have shown reliability and are usually correct for those who say they are non-adherent.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Hawkshead J;Krousel-Wood MA;

Techniques for measuring medication adherence in hypertensive patients in outpatient settings: Advantages and limitations

Ref ID 1781 2007

Study Type Review **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Hawkshead (2007) {1781} presented a narrative review of the advantages and limitations of methods for measuring adherence in hypertensive patients. No mention is given to how they searched for these studies or decided to include/exclude. They state that self reporting is the simplest method for assessing medication adherence and can include patient diaries, interviews during office visits and adherence-specific questionnaires. 'Several multi-item questionnaires have been developed and tested in outpatient settings with the explicit aim of ascertaining valid and reliable estimates of adherence to antihypertensive medications', of which many have reported high measures of validity and reliability (Morisky, 1986; Kim, 2000; Shea, 1992; Hyre, 2007). There are three previously validated self-reported medication-adherence instruments – the Medication Adherence Survey (MAS), the Brief Medication Questionnaire (BMQ) and the Medical Outcomes Study (MOS). Validated self-report measures can feasibly be used in clinical settings and help to identify those who are non-adherent, and intervene to increase this (Harmon, 2006). The advantages they state are that self-report is simple and economical; it can also gather social, situational, and behavioural factors which can impact on adherence. The disadvantages are the possibility that there could be recall bias, over-estimation of compliance and responses which are socially acceptable. Validity can also depend on the skills of the interviewer as well as the question construction and timeframe (Farmer, 1999 and Wang, 2004). It is suggested that self-report could be

combined with objective information, e.g prescription-fill data, to improve adherence measurement.
In summary, some self-reporting questionnaires have been validated and can be simple and feasible to use in clinical settings and identify non-adherers. However they can have biases and overestimate adherence.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Hecht FM;

Measuring HIV treatment adherence in clinical practice

Ref ID 17931 1998

Study Type Review **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Reported briefly with a narrative review on measures for HIV adherence in clinical practice. Sackett et al (1975) compared self-report to pill counts. Of those that reported having less than 80% adherence, 95% were found non-adherent by pill count. Those reporting that they were adherent over 80% of the time, 34% were shown to be non-adherent by pill count. Gilbert and Sackett's studies, suggest that self-report is more accurate than physician assessment. Thus if HCPs want to know if patients are taking ART, they need to ask them rather than relying on their judgement. When they say they are missing medication, believe them, as this is mostly the truth. Patient self-report tends to overestimate adherence. Those who report missing doses infrequently may have a significant problem of non-adherence. Hecht (1998) says that what matters is how HCPs ask the questions. Stating it should be in a specific, non-judgmental way and one that allows them to disclose

non-adherence. Therefore, questions should not imply that they are wrong if they do not take their medication the way they are 'supposed to'. A time period must also be specified. No references given for these conjectures.
Self-report is more accurate than physician's judgement alone. It tends to overestimate adherence. It depends on how the questions are asked and a time period must be specified.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

LaFleur,J;

Methods to Measure Patient Compliance with Medication Regimens

Ref ID 3353 2004

Study Type Review **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Conducted a brief narrative review of methods to measure compliance with medication regimens. No search or inclusion/exclusion criteria were given. They state that self-report is the most popular method for assessing compliance as it is inexpensive but is often unreliable (Myers, 1998). Self-report can include patient interviews or self-report surveys. When compared to objective measures e.g. electronic monitoring devices or drug level monitoring of compliance self-reporting has shown to over-report compliance over 50% of the time (Spector, 1986; Gordis, 1969; Waterhouse, 1993; Straka, 1997). It is also often inaccurate for those reporting non-compliance with medication-taking. In Kwon (2003) a comparison of self-reporting of antidepressant use with prescription claims showed a 20% difference in those reporting non-adherence to antidepressants. The reasons for any

discrepancies with other measures could be that patients do not understand regimens, know indications for their medicine, or not report behaviours perceived as not socially-acceptable, or forgetting of non-compliance. No references were given for these assertions.
In summary, self-report by interviews or surveys can be inexpensive but can be unreliable and over-report compliance. Those who report non-compliance can also be inaccurate. There could be biases such as social desirability, recall and not understanding medication regimes.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Miller LG;Hays RD;

Measuring adherence to antiretroviral medications in clinical trials

Ref ID 928 2000

Study Type Review **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Reviewed current literature on measuring adherence to Antiretroviral Medications in clinical trials. They report that the simplest method of measuring adherence is self-report. But there is no standardised instrument. Self-reported surveys are quick and avoid sophisticated methodology or equipment and are inexpensive compared to other methods of measurement. They have limitations, such as significantly exceeding adherence measured by other objective methods (Bond, 1991; Stratka, 1997; Cramer, 1991). HIV studies also confirm this (Golin, 1999; Arnsten, 2000; Paterson, 1999; Bangsberg, 1999). Interviews and surveys often promote socially acceptable responses (DiMatteo, 1982). Less adherent patients report higher

adherence than they actually had (Bond, 1991). Memory can also affect the accuracy of reporting adherence. Most surveys use broad response categories to report the proportion of pills taken, thus small degrees of nonadherence is hard to distinguish with self-report. The information is useful, but accuracy is limited and biased towards higher adherence.
However, self-reported non-adherence has been associated with worse virologic outcomes (Demasi, 1999; Bangsberg, 1999; Duong, 1999; Murri, 1999; Le Moing, 1999) and as an independent predictor of clinical response to HAART when controlling objective virologic and immunologic markers (Montaner, 1999). Therefore it can provide information that explains variation in clinical response to antiretroviral therapy which is not explained by other clinical factors.
In summary, self-report surveys are simple and inexpensive but can overestimate adherence. Interviews and surveys can have social desirability and recall biases. Also as categories are large, small degrees of non-adherence are hard to detect. There is no standardised instrument. However it can explain variation in clinical responses to ART.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Paterson DL;Potoski B;Capitano B;

Measurement of adherence to antiretroviral medications

Ref ID 817 2002

Study Type Review **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Conducted a brief narrative review to ascertain how adherence to antiretroviral medicine should be measured. The methods reported were electronic monitoring, pill counts, pill recognition, review of pharmacy records, patient self-report, biological parameters, therapeutic drug monitoring and provider prediction of adherence. They noted that how a question is asked can influence self-report of adherence (i.e. in face-to face inquiry or patient-completed questionnaires). A non-judgemental stance can help and this can be achieved by a preamble before the questions to show that they are not being judged and are looking for honest answers (Turner, 2001).
Another disadvantage of self-report (face-to-face interview) is that periods shorter than 7 days are not long enough to determine the percentage of adherence likely, however some patients may not correctly report adherence for 7 day periods. They state that additional questions may be necessary to counteract this e.g about adherence at the weekend.
One method to counteract problems with gaining honest answers is computer-assisted self-interviewing (Bangsberg, 2001) or diary. Diaries hold advantage as they can be inexpensive and accurate. Their disadvantage is that some may complete them retrospectively or not at all.
Paterson (2002) asserts that self-report is 'likely to be the simplest means of assessing adherence' and so the reliability is important to assess. Adherence was found to be 'considerably higher' than that measured by electronic monitoring or pill count (Liu et al, 2001). Self-report overestimates adherence. It is most useful in those who admit to being poor adherers (Murri 2000). They conclude that electronic monitoring devices are the closest to a gold standard in adherence measurement.
In summary, various self-reporting measures were reported and interviews may be too late for recall or may be too early to gain useful adherence information. Diaries are inexpensive and can be more accurate as there is no recall bias however they may not be completed or completed retrospectively. Self-report can overestimate adherence but can identify those who report non-adherence.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Rand CS;Wise RA;

Measuring adherence to asthma medication regimens

Ref ID 1254 1994

Study Type Review **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	Reported in a narrative review on measuring adherence to asthma medication regimens. They did not state search or inclusion criteria. They state that self-report is the most inexpensive and quick way of measuring adherence (Soutter, 1974). The possible advantage of diary cards is that they can measure adherence across time and can reveal patterns between the disease exacerbation and compliance with the medication. As there are many drugs used within asthma prescribing, it can help to see the adherence of certain drugs rather than just overall. It can also specifically assess overuse, inappropriate use or erratic use of medications as well as triggering events for the need for medication e.g. in Kesten (1991). Asthma diaries may share commonalities but there is no standardised diary as such in research. A disadvantage of asthma diaries can be they may be complex and time-consuming. Also criteria of acceptable adherence may differ from patient to patient. One way to evaluate the level of adherence is to use trained, masked, medical personnel to score the compliance. It is preferable to develop standardised compliance criteria for all raters and train them by a standardised protocol and make sure there is interrater reliability. Many studies have used questionnaires to collect clinic or follow-up data of patient adherence (Bailey, 1987; Kinsman, 1980; Dolce, 1991), mainly designed for a particular research project. Many have adherence questions within a larger questionnaire, such as the 76-item Revised Asthma Problem Behaviour Checklist for adults. Rand (1994) points out that both asthma diaries and self-report are the most common for assessing asthma medication adherence but that these instruments, because they are not standardised or not published so they rarely have validity and reliability assessed. Except for the Medication Adherence Scale and Inhaler Adherence Scale (Kinsman, 1980; Dolce, 1991; Bailey, 1990), which are six-item scales based on Morisky's work (1990). This instrument was found to have a Chronbach's alpha of 0.76 and 0.69 and was concordant with outcome measures in the UAB adult asthma study. The limitations of self-report have been mentioned by many authors (Masur, 1981; Mawhinney, 1991; Cramer, 1989; Rand, 1992). When compared to objective measures it varies highly on the degree of accuracy (Gordis, 1966; Mattar, 1974). Diary self-reports were compared to electronic medication monitoring device to measure adherence to asthmatic medication by Spector (1986). The findings were that all patients self-reported using the inhaler on certain days, whereas the measured medication suggested just over half did so. Adding a diary can add more complexity to the patient regime than there all ready is. It has been shown that the greater the complexity of a regime the lower the compliance (Masur, 1981). Some participants alter their records of medication use to appear compliant (Mawhinney, 1991; Rand, 1992). This can be improved if they also have reporting by the family/partner of the patient (Paulson, 1977). Self-reporting can also depend on the individual patient or practitioner. For example elderly patients may have memory impairment, especially when taking many medications and not report accurately. Long-term usage may be forgotten but able to recall recent usage. The skill and sensitivity of the HCP can also play a role in how much information is given and the reliability of it. When collected carefully it could be very god insight into the problems of a patient's adherence. Also it is unlikely that patients will represent themselves as non-adherers (Gordis, 1976) so it will identify non-adherers correctly. In summary, self-report is inexpensive and quick and diaries can measure adherence across time and reveal any patterns and assess overuse of medication. However there is no standardised diary and it can be complex and time consuming. If there is no standardised questionnaire of diary then no validity or reliability are assessed. Therefore there is variation on accuracy, depends on the individual or practitioner.
Effect due to factor in study?	

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Turner BJ;

Adherence to antiretroviral therapy by human immunodeficiency virus- infected patients

Ref ID 879 2002

Study Type Review **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Reviewed literature to compare various measures of adherence to Antiretroviral Therapy. This was a narrative review with no details of search/inclusion criteria. They state that self-reports are less complex but that there can be problems with recall over long time periods. Many studies use self-report over the past 4 days but additional questions may be needed, e.g. about weekends, as this tends to be a difficult time for adherence.

All types of self-reporting overestimate adherence compared to other measures (Arnsten, 2001; Golin, 1999; Melbourne, 1999). Even those who report missing doses tend to overestimate adherence compared to other measures (Wagner, 2000). Social desirability biases can contribute. Those who report problems with adherence usually have poorer adherence with other measures (Haynes, 1980). Those who report non-adherence appear responsive to interventions, and are important to identify (Haynes, 1980).

The validity can be increased with a preamble before questions about adherence in order to reassure patients that information will not be held against them and that non-adherence is common. Audio computer-assisted self-interviewing is suggested for more sensitive topics (Metzger, 2000; Gribble, 2000).

In summary, all types of self-report overestimate adherence, even with those who report non-adherence and biases such as social desirability can occur. Certain techniques could be used to minimise these biases.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Question: Does change in dosing regime affect adherence?

Grading: 1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

Molina JM;Podsadecki TJ;Johnson MA;Wilkin A;Domingo P;Myers R;Hairrell JM;Rode RA;King MS;Hanna GJ;

A lopinavir/ritonavir-based once-daily regimen results in better compliance and is non-inferior to a twice-daily regimen through 96 weeks

Ref ID 17958 2007

Study Type	Randomised Controlled Trial	**Funding**	Supported by Abbott Laboratories.

Number of participant	196 patients met the eligibility criteria. Subjects were randomized (3:2) to LPV/r soft gelatin capsules 800/200 mg QD (n = 115) or 400/100 mg BID (n = 75). Subjects received TDF 300 mg and FTC 200 mg QD.
Inclusion/Exclusion Criteria	
Patient Characteristics	QD group 81% were male, whilst in the BID group there were 75%. Mean age was 39.2 (11.1) for the QD group and 37.7 (9.0) in the BID group.
Recruitment	Not reported.
Setting	French Clinics.
Interventions/ Test/ Factor being investigated	LLPV/r soft gelatin capsules 800/200 mg QD (once-daily regimen) (n = 115) or 400/100 mg BID (twice daily regimen) (n = 75). All Subjects received TDF 300 mg and FTC 200 mg QD.
Comparisons	Between treatments.
Length of Study/ Follow-up	Up to 96 weeks.
Outcome measures studied	Adherence, antiviral, immunologic changes, viral drug resistance.
Results	A total of 190 antiretroviral-naive subjects with plasma HIV-1 RNA above 1000 copies/ml and any CD4(+) T cell count were enrolled. Adherence to LPV/r through 96 weeks was measured using MEMS((R)) monitors. Median baseline VL and CD4(+) T cell count were 4.8 log(10) copies/ml and 216 cells/mm(3), respectively. Prior to week 96, 37% (QD) and 39% (BID) of subjects discontinued, primarily due either to adverse events (17% QD, 9% BID) or to loss to follow-up or nonadherence (12% QD, 17% BID). The proportion of subjects with VL <50 copies/ml (57% QD, 53% BID; p = 0.582 (ITT NC = F)), change in CD4 count (244 cells/mm(3) QD, 264 cells/mm(3) BID; p = 0.513), and evolution of resistance did not differ between groups through 96 weeks. Diarrhea (17% QD, 5% BID, p = 0.014) was the most common moderate or severe, study drug-related adverse event.
Safety and adverse effects	11% of the QD patients discontinued and 3% in the BID due to gastrointestinal adverse events.
Does the study answer the question?	Adherence to LPV/r was higher for the QD group than the BID group and declined over time in both groups. Time to loss of virologic response was significantly associated with adherence to LPV /r in both groups. LPV/r QD resulted in virologic response similar to LPV/r BID through 96 weeks in antiretroviral-naive subjects. Adherence was significantly higher in the QD group
Effect due to factor in study?	
Consistency of results with other studies?	

Directly applicable to guideline population?

Internal Validity

Portsmouth SD;Osorio J;McCormick K;Gazzard BG;Moyle GJ;

Better maintained adherence on switching from twice-daily to once-daily therapy for HIV: a 24-week randomized trial of treatment simplification using stavudine prolonged-release capsules

Ref ID 1216 2005

Study Type Randomised Controlled Trial

Funding The study was sponsored by Bristol-Myers Squibb (USA).

Number of participant	43 patients, 22 once daily (intervention) group, 21 in twice daily (control) group.
Inclusion/Exclusion Criteria	Inclusion: Participants were included in the study if they were over 18 years of age and weighed over 40 kg. In women of childbearing potential, pregnancy was excluded and consent was obtained to ensure that they were willing to use two effective forms of contraception (including barrier contraception). Exclusion: Subjects were excluded if they had proven or suspected hepatitis, an active AIDS-defining disease, a history of bilateral peripheral neuropathy or signs of bilateral peripheral neuropathy of grade 2 or higher.
Patient Characteristics	Twice daily (control group): Male:18, female:, 3, Median age (years) (range): 45 (31–62), Number on d4T: 19, Number on Combivir: 2, Time on current regimen at baseline (months) (range): 24 (4–55), Baseline median CD4 count (cells/mL) (range): 457 (94–983), Viral load at screening (HIV-1 RNA copies/mL): All undetectable (< 50). Once daily (intervention group): Male: 21, female: 1, Median age (years) (range): 40 (23–56), Number on d4T: 18, Number on Combivir: 4, Time on current regimen at baseline (months) (range): 17 (5–53), Baseline median CD4 count (cells/mL) (range): 403 (111–1083), Viral load at screening (HIV-1 RNA copies/mL): All undetectable (<50). All participants had a viral load currently suppressed below the level of assay detection (o50 HIV-1 RNAcopies/mL; bDNA Chiron; Chiron Corporation, Emeryville, CA, USA). All participants had been receiving one of the following regimens for a minimum of 16 weeks: d4T IR bid13TC 150 mg bid1EFV 600 mg qd or ZDV 300 mg bid13TC (as Combivirs; Glaxo, Uxbridge, UK) 150 mg bid1EFV 600 mg qd.
Recruitment	Participants were recruited from a large central London clinic cohort.
Setting	Single center study.
Interventions/ Test/ Factor being investigated	Once daily group (intervention): the prolonged release capsule group (PRC) were assigned to take d4T PRC/3TC/EFV all once-daily (24 h apart). Twice daily (control group): participants in the control group were assigned to continue either d4T IR/3TC/EFV or Combivirs/EFV as per their screening regimen. Note: participant weighing less than 60 kg were prescribed either 30 mg of d4T IR or 75 mg of d4T PRC.
Comparisons	Intervention treatment v Control treatment.
Length of Study/ Follow-up	28 weeks (screened 4 weeks prior to randomization).
Outcome measures studied	Adherence: Measured via MEMS Cap. Information from MEMSs was downloaded at baseline, week 12 and week 24 visits. Quality of Life (measured at baseline, week 12, 24). Also measured: general clinical examination, viral load, full blood counts, SR.

Results	ADHERENCE: At baseline, adherence observed in the study population was high at 98.5% (range 96.3–100%). After randomization, patients allocated to the PRC (intervention) maintained this high adherence, while those allocated to IR (control) showed a significantly reduced adherence in 'taking compliance' (P=0.0237) (percentage of prescribed number of doses taken), 'correct dosing compliance' (P=0.0104) (percentage of days with correct number of doses taken) and 'timing compliance' (P=0.028) (percentage of doses taken within 3 hours of the prescribed dosing intervals) at both weeks 12 and 24. QOL: No significant differences between groups from basdeline to week 24. Both groups showed improvement in cognitive function at week 12 and 24 (P<0.001). In the intevention group at week 24, 90.4% of patients had viral loads of <50 copies compared with 86.4% of those in the control group; 100% in both groups has viral loads of <50 copies on the observed analysis. No patients on the intervention virological rebound during the course of follow-up. There were no significant changes in CD4 counts (cells/mL) during 24 weeks of follow-up. There were no significant differences in total cholesterol, LDL, amylase, g-GT or serum lactate measurements during the study. No patients had signs or symptoms of peripheral neuropathy at baseline and no patient developed neuropathy over 24 weeks of follow-up.
Safety and adverse effects	One patient in the control group opted to switch to an alternative NRTI because of a loss of subcutaneous fat. One patient in the control group left the study to switch therapy, and one patient experienced dizziness on switching to d4T PRC (intervention treatment) and opted to switch back to d4T IR (control treatment). There were no significant changes in CD4 counts (cells/mL) during 24 weeks of follow-up. There were no significant differences in total cholesterol, LDL, amylase, g-GT or serum lactate measurements during the study. No patients had signs or symptoms of peripheral neuropathy at baseline and no patient developed neuropathy over 24 weeks of follow-up.
Does the study answer the question?	Yes. Subjects switching from twice-daily therapy to once-daily therapy demonstrate less of a decline in adherence over 24 weeks. The once-daily regimen is as effective and tolerable as a regimen containing the twice-daily formulation.
Effect due to factor in study?	Fairly confident, however, as concealment and blinding issues are not mentioned in study these may have potentially been a source of bias.
Consistency of results with other studies?	
Directly applicable to guideline population?	Direct relevance.
Internal Validity	Concealment and blinding are not addressed.

Schroeder K;Fahey T;Ebrahim S;

How Can We Improve Adherence to Blood Pressure-Lowering Medication in Ambulatory Care? Systematic Review of Randomized Controlled Trials

Ref ID 1479 2004

Study Type Systematic Review **Funding** NHS R&D fund, Bristol.

Number of participant RCT.

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Simplifying dosing regimens improved adherence in 7 of 9 studies with relative improvement in adherence increasing by 8% to 19.6%. All of the studies that used objective outcome measurement (Medication Event Monitoring System) showed an improvement in adherence through the use of once daily instead of twice daily dosing regimens, although 4 of these compared 2 different drugs. Only 1 study showed an increase in adherence (90% vs 82%; $p<0.01$) together with a reduction in systolic blood pressure of 6 mm Hg ($p<0.01$).

Methodological quality of the studies reviewed was problematic in this review.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Shi, L., Hudges, M., Yurgin, N., Boye, K.S.

Impact of dose frequency on compliance and health outcomes: a literature review (1966-2006)

Ref ID 8865 2007

Study Type Systematic Review **Funding** Eli Lilly and Company.

Number of participant RCT and prospective observational studies.

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	Looked at the impact of dose frequency on compliance and health outcomes, particularly for injectables. Of the 21 studies that measured compliance, 17 reported a positive impact of reducing dose frequency on compliance, whilst inconclusive results were seen in four. Details of the dose frequency reductions contained in the studies were not provided by the review. Articles not measuring compliance as the main outcome looked at efficacy and other outcomes of extended-release medications in comparison to the immediate-release forms. The studies also supported the general benefits of reducing dosing frequency on improved quality of life or patients satisfaction (6 studies), greater control over side effects (5 studies) and improved economic outcomes using extended-release formulation (2 studies).
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Grading: 1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias*

Claxton AJ;Cramer J;Pierce C;

A systematic review of the associations between dose regimens and medication compliance

Ref ID 1542 2001

Study Type Systematic Review **Funding** Eli Lilly.

Number of participant Study types were not described.

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question? This review of 76 studies that used gold-standard electronic monitoring devices demonstrated that patients take about 51% to 79% of doses daily as prescribed across a wide range of therapeutic areas. Compliance was inversely related to the number of doses per day. Mean dose taking compliance was 71% (34% to 97% range), and declined as the number of daily doses increased: 1 dose = 79% (s.d=14%), 2 doses=69% (s.d=15%), 3 doses = 65% (s.d=16%), 4 doses = 51% (s.d=20%). Compliance was significantly higher for once-daily versus 3 times daily (p=0.008), once daily versus 4 times daily (p=0.001) and twice daily versus 4 times daily regimens (p=0.001). However there were no significant differences in compliance between once daily and twice daily regimens or between twice daily and three times daily regimens. In the subset of 14 studies that reported dose timing results, mean dose timing compliance was 59% (s.d=24%); more frequent dosing was associated with lower compliance rates.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Iskedjian M;Einarson TR;MacKeigan LD;Shear N;Addis A;Mittmann- N;Ilersich AL;

Relationship between daily dose frequency and adherence to antihypertensive pharmacotherapy: Evidence from a meta-analysis

Ref ID 1530 2002

Study Type Systematic Review **Funding** No external funding

Number of participant Prospective trials (RCTs and cohort studies), retrospective chart reviews and database analyses.

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question? Eight studies involving a total of 11,465 observations were included (1830 for daily [QD] dosing, 4405 for twice a day dosing [BID] and 4147 for dosing >2 times daily [>BID] and 9655 for multiple daily dose [MDD]). The primary objective was to assess adherence. The average adherence rate for QD dosing (91.4%, s.d=2.2%) was significantly higher than for MDD (83.2%, s.d=3.5%; p<0.001). This rate was also significantly higher than for BID dosing (p=0.026); 92.7% [s.d=2.3%] vs 87.1% [s.d=2.9%]). The difference in adherence rates between BID dosing (90.8%, s.d=4.7%) and >BID dosing (86.3%, s.d=6.7%) was not significant (p=0.069).

All these figures must be reviewed with caution due to flaws in the methodology of the meta analysis.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Parienti JJ;Massari V;Reliquet V;Chaillot F;Le MG;Arvieux C;Vabret A;Verdon R;

Effect of twice-daily nevirapine on adherence in HIV-1-infected patients: a randomized controlled study

Ref ID 378 2007

Study Type Randomised Controlled Trial **Funding** Academic grant.

Number of participant	Nevirapine 400 mg once-daily (n=31) or continue nevirapine 200 mg twice-a-day (n=31).
Inclusion/Exclusion Criteria	Patients with chronically HIV-1 infection, receiving nevirapine-based antiretroviral therapy with RNA-HIV levels less than 400 copies/ml for more than 6 months and without liver enzyme abnormality.
Patient Characteristics	Patients with chronically HIV-1 infection, receiving nevirapine-based antiretroviral therapy with RNA-HIV levels less than 400 copies/ml for more than 6 months and without liver enzyme abnormality. Patients were aged 24-76 years (mean 48.1)
Recruitment	Sixty-two patients were recruited.
Setting	Four french academic medical centres
Interventions/ Test/ Factor being investigated	Adherence was measured using electronic monitoring devices and validated by sequential plasma drug levels. Participants were randomly assigned to switch to nevirapine 400 mg once-daily (n=31) or continue nevirapine 200 mg twice-a-day (n=31). After the randomised phase, participants had an opportunity to choose their antiretroviral dosage. Primary outcome was the mean percentage of adherence
Comparisons	Between treatments.
Length of Study/ Follow-up	follow-up period of 12 months. A first 3 month observational, 4 month randomized, 5 month interventional.
Outcome measures studied	Adherence and viral supression.
Results	Fifty-two patients qualified for electronic data analysis. During the randomized phase, the mean adherence rate was non-significantly superior by 0.5% in once-daily versus twice-a-day dosing (p=0.68), adjusting for previous twice-a-day adherence rate (p<0.0001). Once-daily group increased days without dose, OR 1.7 (95% CI 1.0 to 2.8) p=0.04), adjusting for previous drug interruptions (p<0.0001). In the longitudinal analysis, once-daily dosing was significantly associated with at least two consecutive days without dose OR 4.4 (95% CI 1.9 to 10.3) p<0.001.
Safety and adverse effects	ten serious adverse events including one death were reported in seven patients. None were drug related.
Does the study answer the question?	Changing from twice daily to once daily nevirapine does not improve adherence.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Question: Effect of prescription charges on adherence to prescribed medicine.

Grading: 3	Non-analytic studies (for example, case reports, case series)

Atella V;Schafheutle E;Noyce P;Hassell K;

Affordability of medicines and patients' cost-reducing behaviour: empirical evidence based on SUR estimates from Italy and the UK

Ref ID 17902 2005

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

This study aimed to explore how and to what extent costs incurred by patients influence their decision-making behavior in accessing medicines, both in the UK and in Italy.
Based on findings from focus groups, a questionnaire was designed to assess medication cost issues. As such, several hypotheses were tested regarding patients' decision-making behaviour and how it was influenced by health and sociodemographic status and the novel concept of a self-rated affordability measure. Patients were eligible if they had either dyspepsia or mild hypertension. They were sampled as successive patients who visited 51 physicians in Italy and 21 community pharmacists in the UK. Samples were drawn from the areas of Manchester and Rome. Of the 550 dyspepsia and 600 hypertension questionnaires distributed, 122 and 153 were returned- a response rate of 22.2% and 25.5%, respectively. In the UK, 296 dyspepsia and 277 hypertension questionnaires were distributed, targeting dyspepsia patients who bought OTC medicines, and dyspepsia and hypertension patients who had to pay prescription charges; 110 dyspepsia and 134 hypertension questionnaires were returned, giving a response rates of 37.5% and 48.4%. In both countries the majority of the respondents were not exempt.
The self-rated affordability measure showed that 70.3 per cent of the UK sample and 66.5 percent of the Italian sample had to think about the cost of medicines at least sometimes. Also, 24.3 per cent and 16.3 per cent, respectively said they always have to think about how much money they have available to spend when they obtain medicines. According to the results, the patient initiated strategy most commonly used by UK respondents with affordability problems is (1) to delay the dispensing of drugs until they get paid, (2) not visiting the GP to avoid incurring the cost of prescribed medication and (3) reducing the dose below that prescribed to extend the

course of medication.
Affordability issues were also strong when examining the use of self-medication strategies. The UK respondents were particularly cost conscious when considering the price of an OTC product before buying it, or they would ask for something cheaper if they could not afford a particular OTC product.
The authors point out that affordability seemed to play a more important role in the UK sample than in the Italian, however they do point out that Italian patients with dyspepsia were sampled only through GPs and may be those more severely affected and/or less likely to be disposed towards self medication. Also, OTC products are much more expensive in relation to the prescription charge that they are in the UK where the prescription charge is high.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Hirth RA;Greer SL;Albert JM;Young EW;Piette JD;

Out-of-pocket spending and medication adherence among dialysis patients in twelve countries

Ref ID 17901 2008

Study Type Qualitative **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

They examined out of pocket medication spending and cost-related medication nonadherence among dialysis patients in twelve countries including the UK.
Data were gathered from 2002 to 2004 as part of the dialysis outcomes and practice patterns study (DOPPS), an observational study of hemodialysis practices and outcomes in twelve countries- Australia, New Zealand, Belgium, Canada, France, Germany, Italy, Spain, Sweden, United Kingdom, Japan, and the United States. A

random sample of patients was selected, totaling N=7.766. Of the selected 83 per cent who agreed to enroll and have their medical records abstracted, 85 per cent of these enrolled patients also completed the patient questionnaire. A total of 70 per cent of patients provided both medical and questionnaire data. Local currencies were converted to US Dollars.
Questionnaires and medical record abstraction techniques were standardised across countries and languages. Patient questionnaires were administered soon after recruitment. They were asked about the total out-of-pocket spending for prescription and over the counter (OTC) medications in the previous month. They were also asked “Do you sometimes decide not to purchase medications because of cost?” and to report their out-of-pocket spending for hemodialysis treatments.
Whilst the United States reported 86 per cent of out-of-pocket spending for medications, only patients in Australia/New Zealand, Belgium, and Sweden were significantly more likely to face out-of-pocket spending, while those in France, Japan, Spain and the UK were significantly less likely to do so.
Mean monthly spending for prescription and OTC medications ranged from $8 in the UK to $114 to the United States. Among patients with medication spending, only 10 per cent faced monthly costs greater than $30 in the United Kingdom, whereas 10 per cent incurred costs greater than $310 in the United States.
Observed cost-related nonadherence, indicated by the proportion of patients who reported that they sometimes did not purchase medications because of cost, was significantly less than expected in France, Japan, Spain, Sweden and the UK. Nonadherence was associated with the percentage of patients reporting any out-of-pocket spending and the average out-of-pocket cost. Although the US had high out-of-pocket spending burdens, their nonadherence was still clearly higher than would be expected on the basis of the percentage facing any costs or the mean cost burden. On the other hand, Sweden and Belgium had lower levels of nonadherence than would be expected given either measure of out-of-pocket spending burden. The lowest nonadherence rates existing in France, Japan, Spain and the UK were correlated with low out-of-pocket spending.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Question: Does medicine packaging affect adherence?

Grading: 1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias

Orton L;Barnish G;

Unit-dose packaged drugs for treating malaria. [Review] [40 refs]

Ref ID 1251 2005

Study Type Systematic Review **Funding** Cochrane review

Number of participant 3 quasi RCTs and one cluster RCT

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

A meta analysis of two trials (596 participants) showed that participant reported treatment adherence was higher with blister packed tablets compared with tablets in paper envelopes RR 1.18 (95% CI 1.12 to 1.25). Two trials using tablets in sectioned polythene bags as the intervention also noted an increase in participant reported treatment adherence. The cluster RCT (6 clusters) compared it with tablets in paper envelopes and the other trial compared it with syrup in bottles, RR 2.15 (95% CI 1.76 to 2.61), 299 participants.

The authors stated that there was insufficient evidence to determine the effect of unit dose packaged antimalarial drugs on treatment failure. Unit dose packaging supported by prescriber training and patient information appears to improve participant reported treatment adherence, but these data come from trials with methodological limitations.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Grading: 1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

Connor J;Rafter N;Rodgers A;

Do fixed-dose combination pills or unit-of-use packaging improve adherence? A systematic review. [Review] [26 refs]

Ref ID 1501 2004

Study Type Systematic Review **Funding** Unknown

Number of participant	Randomized or quasi-randomized controlled trials
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	15 trials met inclusion criteria: fixed dose combination pills were investigated in three of these while unit-of-use packaging was studied in 12 trials. The results of the trials suggested that there were trends towards improved adherence which reached statistical significance in seven out of thirteen trials reporting medication adherence. Measures of adherence were however heterogeneous and interpretation was further limited by methodological issues, particularly small sample size, short duration and loss to follow up. Uncertainty remains about the size of the benefits of drug formulation and packaging.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Lee JK;Grace KA;Taylor AJ;

Effect of a pharmacy care program on medication adherence and persistence, blood pressure, and low-density

lipoprotein cholesterol: a randomized controlled trial.[see comment]

Ref ID 190 2006

Study Type	Randomised Controlled Trial	**Funding**	This study was partially funded by a competitive junior investigator grant award from the American Society of Health-System Pharmacists Research and Education Foundation, managed under the auspices of the TRUE Research Foundation.

Number of participant	Total 200. 159 after randomization for 2nd stage of study: 83 in follow up group, 76 in return to usual care group.
Inclusion/Exclusion Criteria	Inclusion: aged 65 years or over, taking 4 or more chronic medications daily. Exclusion: Patients were excluded if they did not live independently (assisted living or nursing home residents were excluded) or in the presence of any serious medical condition for which 1-year survival was expected to be unlikely.
Patient Characteristics	Age, mean (s.d), y: Usual Care (UC) Group: 78 (s.d=6.2); Intervention group: 77 (s.d=10.5). Men: UC group: 56 (s.d=73.7), Intervention group: 62 (s.d=74.7). Race: White: Intervention group: 51 (s.d=61.4) , UC group: 43 (s.d=56.6); Black: Intervention group: 29 (s.d=34.9), UC group: 29 (s.d=34.9). No. of chronic medications, mean: intervention group: 9.1 (s.d=3.2), UC group: 8.3 (s.d=2.8). Significant differences between groups prior to randomisation in antidepressant usage, using medication or chart listing and the number of participants taking ACE inhibitors and niacin. These differences are addressed by using multi-variable analysis.
Recruitment	
Setting	Walter Reed Army Medical Center.
Interventions/ Test/ Factor being investigated	Months 3-8 received by all patients: The comprehensive pharmacy care program consisted of 3 elements, including individualised medication education (using standardised scripts), medications dispensed using an adherence aid (blister packs) and regular follow-up with clinical pharmacists every 2 months. Individualized educational interventions were performed to teach participants their drug names, indications, strengths, adverse effects, and usage instructions during each visit. Patients in intervention group continued to receive intervention for study months 9-14. Patients in control group returned to usual care for this period.
Comparisons	Intervention for months 3-8 vs intervention for months 3-14.
Length of Study/ Follow-up	14 months.
Outcome measures studied	Adherence was assessed at baseline via pill counts and expressed as amount of medication taken compared to what should have been taken. Measured again at 1, 2, 4, 6, 8, 10, 12 and 14 months. Also measured: changes in blood pressure and LDL-C.
Results	Adherence: 1-8 months: Mean baseline medication adherence at completion of run-in phase was 61.2% (s.d=13.5%). After initiation of the 6-month pharmacy care program, there was improvement in medication adherence noted at the 4-month pharmacy visit. At 4, 6, and 8 months, medication adherence was 96% or higher. At the conclusion of phase 1 (8 months), the primary end point was met with a mean medication adherence of 96.9% (s.d=5.2%), representing an absolute change in adherence of 35.5% (95% CI 31.2% to 38.5%) p<0.001). Adherence 8-14 months: For the primary end point of the randomised clinical trial, the continued pharmacy care group showed sustained mean medication adherence 95.5% (s.d=7.7%), whereas medication adherence declined in the usual care group 69.1% (s.d=16.4%) p<.001. However, medication adherence at the conclusion of phase 2 for the usual care group was modestly higher than at study entry (run-in phase, 66.5% (s.d=14.0%) vs 61.1% (s.d=14.1%) p=0.02). At the end of the study, those elderly patients assigned to usual care had a similar frequency (compared with their baseline method of medication administration) of receiving help with their medications (11.6%

	vs 15.9%; p=0.58) and using a pillbox (62.3% vs 49.3%; p=.09), but were more likely to use a medication chart (65.2% vs 13.0%; p<0.001). Multiple linear regression analysis controlling for baseline differences (p<0.20) in the study groups showed that the assignment to usual care (B=0.81; p<0.001) and taking medications for psychiatric or memory problems (B=0.15; p=0.007) were independently related to the change in medication adherence during phase 2. Other outcomes: 1-8 months: Improved adherence was associated with improvements in both secondary end points (BP and LDL-C). Among patients with drug-treated hypertension (n=184), mean systolic BP was reduced from 133.2 (s.d=14.9) mm Hg to 129.9 (s.d=16.0) mm Hg (p=0.02). Diastolic BP was not significantly reduced. There was no change in the number of antihypertensive agents taken from baseline to the end of phase 1. Among patients with drug-treated hyperlipidemia (n=162), mean (s.d) LDL-C decreased from 91.7 (s.d=26.1) mg/dL 2.38 (s.d=0.68) mmol/L) to 86.8 (s.d=23.4) mg/dL 2.25 (s.d=0.61) mmol/L) p=0.001. Other outcomes months 8-14: A pre-specified analysis of the associated changes in BP and lipid levels in the continued pharmacy care group showed significant reductions in systolic BP ?6.9mmHg (95% CI ?10.7 to ?3.1mmHg) p=.04 vs usual care) and diastolic BP ?2.5mmHg (95% CI ?4.9 to ?0.2 mm Hg) p=0.39 vs usual care. The mean number of antihypertensive agents used was similar between treatment groups. The LDL-C was not further reduced from 9 to 14 months in the continued pharmacy care group and was not different between study groups.
Safety and adverse effects	None.
Does the study answer the question?	Yes. Continued care in intervention group led to them keeping their improved adherence compared to control group.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Direct.
Internal Validity	

Grading: 1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias*

Schneider PJ;Murphy JE;Pedersen CA;

Impact of medication packaging on adherence and treatment outcomes in older ambulatory patients

Ref ID 17942 2008

Study Type	Randomised Controlled Trial	**Funding**	Centers for Medicare and Medicaid Services. Medications provided by Merck (Whitehouse Station, N.J) Packaging by PCI services, Philadelphia.

Number of participant	85 participants. 47 in the intervention group and 38 in the control group.
Inclusion/Exclusion Criteria	Inclusion: Patients taking or just starting lisinopril for hypertension. 65 years or over. Exclusion: If assessed by physician as having cognitive impairment e.g psychoses or Alzeimers disease, visual impairment or severe asthma.
Patient Characteristics	Mean age 72 years Mean no medications 5 26 men in the intervention group and 16 ment in the control group
Recruitment	Not reported.
Setting	3 health centres/hospital clinics, USA.
Interventions/ Test/ Factor being investigated	Randomised to receive daily-dose blister packaged medication (pill calendar) as the intervention compared to traditional bottles of loose tablets as the control group. Patients returned for refills every 28 days during a 12 month period where the pharmacist would record the time between prescription refills for the medication and any study-related problems. At 6 and 12 months after enrolling the patients visited the physician to find out blood pressure management; the occurrence of morbidity in the past 6 months e.g. angina, myocardial infarction and stroke; and any medical services they had required in the past 6 months e.g. hospitalisations or emergency department visits. Medical charts were reviewed by two pharmacists to gather this information.
Comparisons	The intervention group compared to usual care.
Length of Study/ Follow-up	12 months.
Outcome measures studied	% of prescriptions refilled on time. Medication possession ration (MPR -the sum of the day's supply for all prescriptions received during the study divided by the number of days between the first and last prescription dispensed. Blood pressure.
Results	The percentage of times prescriptions were refilled on time (within 5 days before or after due date) were significantly higher 80.4% (s.d=21.2) for the intervention group than the control group, 66.1% (s.d=28), p=0.012. The Medication possession rate was also significantly higher for the intervention group, 0.93 (s.d=11.4) and 0.87 (s.d=14.2) for the control group, p=0.039. No differences were found between the groups for systolic blood pressure and diastolic blood pressure measures at 6 and 12 months.
Safety and adverse effects	None reported. Approval for study obtained from the human subjects committee at each centre and written informed consent obtained before enrollment from each participant.

Does the study answer the question?	Two different ways of packaging medication, one which shows the day each dose is intended to be taken and provides information on how to take properly can improve the treatment regimen adherence and treatment outcomes in elderly patients.
Effect due to factor in study?	Possibly.
Consistency of results with other studies?	Yes as the intervention is simpler than most of the other interventions in the area which are multi-component.
Directly applicable to guideline population?	The population is relevant as they are taking medications.
Internal Validity	Possible selection bias.

Question: Does medicine formulation affect adherence?

Grading: 1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias*

Bangalore S;Kamalakkannan G;Parkar S;Messerli FH;

Fixed-dose combinations improve medication compliance: a meta- analysis

Ref ID 1682 2007

Study Type Meta-analysis **Funding** Unknown

Number of participant	RCTs and retrospective reviews of data bases
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	A total of 11,925 patients on fixed dose combination were compared against 8317 patients on free drug component regimen. Fixed dose combination resulted in a 26% decrease in the risk of non compliance compared with free drug component regimen (pooled RR 0.74, CI 0.69 to 0.80, p<0.0001). There was no evidence of heterogeneity in this analysis (p=0.07). A subgroup analysis of the four studies on hypertension showed that fixed dose combination (pooled RR 0.76 (CI 0.71-0.81, p<0.0001); decreased the risk of medication non-compliance by 24% compared with free drug combination regimens. The results of this study should be viewed with caution due to methodological issues noted above.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Question: Do reminders (and what types of reminders, text messaging etc) increase adherence to prescribed medicine?

Grading: 1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias

Beaucage K;Lachance-Demers H;Ngo TT;Vachon C;Lamarre D;Guevin JF;Martineau A;Desroches D;Brassard J;Lalonde L;

Telephone follow-up of patients receiving antibiotic prescriptions from community pharmacies

Ref ID 582 2006

Study Type Randomised Controlled Trial **Funding** Pro Coc Ltee.

Number of participant	Total sample: 255. Intervention group: 126, Control group: 129.
Inclusion/Exclusion Criteria	Inclusion: 1. have an expected duration of antibiotic treatment, 2. speak English or French, 3. be able to converse over the telephone, 4. be available for a telephone call during and at the expected end of antibiotic treatment and for up to 48 hours after. Exclusion: 1/ were initiating prophylactic antibiotic treatment 2/ did not self-manage their medication 3/ were already participating in another clinical trial 4/ in the opinion of the pharmacist, required intense clinical follow up or 5/ would benefit from more intense clinical follow up in a special medical hospital clinic.
Patient Characteristics	Age (mean): Intervention group: 47, s.d=20, control group: 49 s.d=20. Sex: women: Intervention group: 55%, control group: 60%.
Recruitment	
Setting	Six community pharmacies.
Interventions/ Test/ Factor being investigated	Pharmacist telephone follow up intervention (PTFI): A telephone call was made to patients in the intervention group by a pharmacist 3 days into treatment. The pharmacist asked about the patient's general condition, on the presence of adverse effects, the participants understanding of dosing. The pharmacist emphasized the importance of adherence and offered motivation for the patient. The patients were offered an opportunity to ask questions and were given the pharmacists contact details in case they wanted to make contacted there pharmacist at a later time. Usual pharmacist intervention (UPI): Given pharmacists contact details. No follow up calls.
Comparisons	Pharmacist telephone follow up intervention (PTFI) vs usual pharmacist intervention (UPI). Intervention vs control.
Length of Study/ Follow-up	Length of antibiotic treatment.
Outcome measures studied	Adherence: measured on the expected last day of antibiotic treatment. Patients reported the number of tablets they had left.
Results	Note: adherence defined as the percentage of tablets consumed of total number tablets provided. Adherence: Mean adherence to treatment was 94% (s.d=9%) and 94% (s.d=12%) in the intervention and control groups respectively (p=0.803). The proportion of patients with less than 80% adherence was similar in the two groups (Intervention group: 8%, control group: 9%). Number of infectious symptoms and infection severity: There were no significant differences between the groups on these two variables. Other outcomes: drug related problems were identified in 53% of intervention group patients and 8% of control patients (p<0.001). Oral recommendations were made more often for intervention group patients (52%) than control patients (6%) (p<0.001). Recognized pharmaceutical advise was given to 10% of intervention patients and 2% of control patients (p=0.015). Study-specific advice was given to 5% of intervention patients and 1% of control patients (p=0.064, non-significant).

Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention had no effect on participants' adherence.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Yes.
Internal Validity	

Grading: 1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

De Geest; Schafer-Keller P;Denhaerynck K;Thannberger N;Kofer S;Bock A;Surber C;Steiger J;

Supporting medication adherence in renal transplantation (SMART): a pilot RCT to improve adherence to immunosuppressive regimens

Ref ID 354 2006

Study Type Randomised Controlled Trial **Funding** No details given.

Number of participant	Total sample: 18. Intervention group: 6, control group: 12.
Inclusion/Exclusion Criteria	Inclusion: the patient had to be non-adherent to their immunosuppressive regimen (defined as <98% taking adherence and/or one or more drug holidays: No medication intake >36 h for a twice daily dosing regimen or >60 h for a once daily dosing regimen), at least 18 yr old; to be in follow-up at the University Hospital Basel, Switzerland, or at the Cantonal Hospital, Aarau, Switzerland; to speak German or French; to be literate; to have undergone kidney transplant surgery at least one year prior to the study; to be able to self-administer immunosuppressive drugs; to reside within a 180 km radius of Basel; and to provide written informed consent to participate in the RCT. Exclusion: Patients were excluded if they lacked mental clarity based on clinician's appraisal, could not read forms or EM printouts with at least corrective lens, or had no telephone service at home.
Patient Characteristics	Total sample: age: 45.6 (s.d=1.2 yrs); 78.6% male. Baseline characteristics not given in detail (may be reported in a different study).
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	Intervention group (IG): The IG received one home visit and three telephone interviews, one at the end of the month for three consecutive months (from) a nurse. The intervention was aimed at increasing patients' self-efficacy in taking their medication. During the home visit EM printouts were discussed with patient for problem detection, and adherences goals were made. All patients received self-efficacy interventions consisting of four elements: developing mastery experiences in taking medications correctly (2) participating in role modelling (3) verbally persuading by the intervention nurse and (4) addressing negative effects of physiological arousal. Nurses also implemented additional educational (refreshment course on adherence), behavioral (e.g. the use of reminders) and/or social support interventions (e.g. asking family members to fill in prescriptions) if they felt this would help the patient. Telephone calls served to discuss adherence in previous month (using EM data, checking on health status, and discussing (and changing if appropriate) adherence interventions.
Comparisons	Intervention and usual care vs usual care. Intervention vs control.
Length of Study/ Follow-up	9 months.
Outcome measures studied	Adherence: assessed through electronic monitoring (EM) of medication intake during a nine-month period (three months intervention, six months follow-up). Time and date of each bottle opening was recorded.
Results	Adherence: Non-adherence declined remarkably in both groups during the first three months of the study (Intervention group: p=0.04; Control group: p=0.06). Although the intervention group patients' chance of being non-adherent during the first three months decreased more than the control groups patients' chance this group difference did not reach statistical significance (p=0.31). This was also the case at nine months (p=0.58). Note of interest: Authors suggest results indicate an inclusion effect (inclusion in the study results in more adherence). They also note that although the intervention appeared to add further benefit in medication compliance, a lack of

	statistical power may have prevented a strong statistical statement.
Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention did not significantly improve adherence relative to the improvement in the control group.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Direct.
Internal Validity	

Hamet P;Campbell N;Curnew G;Eastwood C;Pradhan A;

Avapromise: a randomized clinical trial for increasing adherence through behavioural modification in essential hypertension.

Ref ID 2526 2003

Study Type Randomised Controlled Trial **Funding** Not reported.

Number of participant	N=2402 to the intervention group; n=2462 to the control group.
Inclusion/Exclusion Criteria	Inclusion criteria: History of diastolic blood pressure higher than 90mmHg and/or systolic blood pressure higher than 140 mmHg; and untreated or current hypertension treatment requiring alteration in the opinion of the physician aged 18 to 79 years and if female; unable to become pregnant and willingness to give informed consent. Exclusion criteria: pregnant; breastfeeding or women with childbearing potential; taking any investigational drug given within 30 days of initiation of therapy, and participation in other clinical studies while enrolled in the protocol; undergoing peritoneal dialysis; presence of certain cardiovascular disorders and allergies/hypersensitivities; requiring active treatment for substance abuse within the past two years; mentally or legally incapacitated; any other condition that might pose a risk to the patient of interfere with the study objectives.
Patient Characteristics	The mean age of patients was 58 years (range 16 to 89 years), 51% of those enrolled were female. Eighty-four percent of patients had chronic hypertension. The mean baseline systolic blood pressure was 160 mmHg and the mean diastolic blood pressure was 95mmHg.
Recruitment	From the GP practices.
Setting	GP practice. Canada.
Interventions/ Test/ Factor being investigated	Patients were assigned to receive a once daily dose of irbesartan 150mg that could be increased to 300mg, with our without the intervention avapromise. The avapromise intervention was created to modify behaviour by medication adherence through reinforcement and lifestyle modification. It is made up of two elements that are delivered in unison. The first element attempts to reinforce medication behaviours by using medication reminder letters, blood pressure diaries and telephone nurse counselling sessions. The second element addresses lifestyle management through educational brochures dealing with topics such as healthy living, nutrition, physical fitness and stress management. Patients assigned to the intervention group were mailed the material at one, two, three, four, six and 12 months. Patients in the control group received usual care educational materials in their physician’s offices.
Comparisons	Between treatments.

Length of Study/ Follow-up	Up to 12 months.
Outcome measures studied	Patient's discontinuation with their irbesartan treatment regimens. Patient compliance was assessed by comparing the rate and time to discontinuation between the 2 groups.
Results	A total of 25% of patients discontinued their treatment from the intervention group and 25.5% from the control group (p=0.94). There was no statistically significant difference in the duration of irbesartan compliance between the treatment groups. Overall the average duration of irbesartan compliance 267 days (s.d=127) and was similar between treatment groups (267 days for the intervention group and 269 days for the control group).
Safety and adverse effects	Nineteen percent of the patients prematurely terminated the study due to serious adverse drug reactions. Five deaths were reported. Fifty-four per cent of patients who discontinued reported side effects.
Does the study answer the question?	The intervention did not yield an increase in the rates of adherence in patients with essential hypertension.
Effect due to factor in study?	Relative certainty.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant study.
Internal Validity	

Mannheimer SB;Morse E;Matts JP;Andrews L;Child C;Schmetter B;Friedland GH;

Sustained benefit from a long-term antiretroviral adherence intervention: Results of a large randomized clinical trial

Ref ID 2766 2006

Study Type Randomised Controlled Trial **Funding** Not reported.

Number of participant	A total of 928 FIRST study participants (98% of target) were eligible for enrollment into the CPCRA Adherence Study, and data from these participants were used in the main ITT analyses. Participants were distributed into study groups by cluster randomization as follows: 10 clusters (256 patients) in the MM arm, 10 clusters (254 patients) in the ALR arm, 9 clusters (196 patients) in the MM + ALR arm, and 9 clusters (222 patients) in the control (usual care) arm.
Inclusion/Exclusion Criteria	Not reported.
Patient Characteristics	Age (y), mean 38 ± 10; Gender: female 22%, male 78%
Recruitment	Not reported.
Setting	Clinical research centres, Canada.
Interventions/ Test/ Factor being investigated	Medication manager (MM), A little reminder (ALR), MM + ALR, or neither (control). MM participants received individualized, structured, long-term adherence support from trained MMs. ALR participants received individually programmed ALR alarms for use throughout the study. The medication manager (MM) intervention involved a trained research staff member who worked individually with study participants to provide tailored adherence support over time in a standardized protocol-guided manner, identifying and addressing each participant's information, motivation, and skills for ARV adherence using detailed questionnaires. This multifaceted intervention was based on health behavioral theory, including the information, motivation, and behavioral skills model of behavior change.

	The second intervention was the electronic medication reminder system. The study used a small portable alarm (A Little Reminder [ALR]; individually programmed to sound and flash at times of all ARV doses. The ALR addressed the most common reason for missed ARV doses reported at the time the study was developed, forgetfulness.
Comparisons	Between treatments.
Length of Study/ Follow-up	A median of 30 months.
Outcome measures studied	Virologic failure was the primary outcome. Secondary outcomes were: plasma HIV RNA level, CD4 cell count, adherence, ARV regimen changes, ARV resistance, grade 4 adverse events, and quality of life.
Results	The 928 participants, followed a median of 30 months, included 22% women and 75% nonwhites; the median baseline CD4 count was 155 cells/mm. First virologic failure was 13% lower in all MM versus no-MM groups (P=0.13) and 28% lower in MM versus no-MM subgroups randomized to 2-class ARV arms in the parent ARV study (p=0.01). MM (vs. no-MM) participants had significantly better CD4 cells count (p=0.01) and adherence (p<0.001) outcomes. Participants randomized to the MM intervention had a higher rate of reporting 100% adherence over time compared with participants randomized to a no-MM intervention (OR=1.42; p<0.001). No significant differences were seen between the ALR and no-ALR groups for any long-term secondary endpoint, including proportion over time with an HIV RNA level, 50 copies/mL, log HIV RNA level over time, CD4 change over time, adherence, changes in ARV drugs, grade 4 adverse events, and quality of life.
Safety and adverse effects	None reported.
Does the study answer the question?	This large randomized clinical trial demonstrated that interpersonal structured adherence support was associated with improved long-term medication adherence and virologic and immunologic HIV outcomes.
Effect due to factor in study?	Yes
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant.
Internal Validity	

Urien AM;Guillen VF;Beltran DO;Pinzotas CL;Perez ER;Arocena MO;Sanchez JM;

Telephonic back-up improves antibiotic compliance in acute tonsillitis/pharyngitis

Ref ID 2084 2004

Study Type Randomised Controlled Trial **Funding** Not stated.

Number of participant	64 patients in each group (intervention and control).
Inclusion/Exclusion Criteria	To be over 18 years, diagnosed as having tonsilitis/pharyngitis of possible bacterial aetiology, antibiotic treatment required according to medical criteria, to be on the phone and to have patient's oral agreement. Exclusion criteria: to have mental illness, to have started antibiotic treatment before consulting a doctor, refusal of treatment, pregnancy or breast feeding, allergy to the antibiotic chosen for the protocol, living with patients who had already taken part in the study and belonging to any group that according to the doctors opinion would make monitoring difficult.
Patient Characteristics	No significant differences for any variable.

Recruitment	By consecutive sampling via on-demand visits to the Health Centre.
Setting	Health Care Centre. Spain.
Interventions/ Test/ Factor being investigated	Intervention group was given mixed strategy and the control group only had thorough educational advice by detailed and appropriate verbal instructions to make diagnosis and prognosis understood. The control group was taught how to comply with treatment: duration, and frequency and time of dosage to avoid the risk of relapse, complications or bacterial resistance. The telephone call was undertaken on the 4th day after the start of treatment, when the first box of antibiotic should be finished. The patient was advised to continue the treatment according to the dosage and number of days that had been prescribed. The patient was also reminded that although he or she may feel better or even cured, the treatment was to be continued for 10 days. The criterion for evaluating the compliance was to count the tablets in a spot check at the patient's house. A tablet count of 80–110% defined good compliance.
Comparisons	Between treatments.
Length of Study/ Follow-up	Not clear but seems to be up to 10 days after beginning treatment.
Outcome measures studied	Adherence, clinical improvement.
Results	A good compliance percentage was 66.1% (57.7 to 74.5%) and was significantly higher in the intervention group (78.3%) than in the control group (54.1%) (P=0.005). Most frequent reasons for discontinuation alleged were clinical improvement (33.3%), oversight (24.2%) and side effects (18.2). Patients from both groups gave similar reactions (p= 0.304). Seventeen non-compliant patients who did not recognise any reason for their non-compliance were found. There were no differences between the two groups in terms of clinical improvement (p=0.567).
Safety and adverse effects	None reported.
Does the study answer the question?	In conclusion telephonic back-up significantly improved the compliance obtained by educational strategy only. It should be used in clinical practice.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	Consistent.
Directly applicable to guideline population?	Relevant study.
Internal Validity	Single-blinded study.

Grading: 1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias*

Guthrie RM;

The effects of postal and telephone reminders on compliance with pravastatin therapy in a national registry: results of the first myocardial infarction risk reduction program

Ref ID 76 2001

Study Type Randomised Controlled Trial **Funding** Bristol Myers Squibb Co. Princeton, New Jersey.

Number of participant	13,100 in total. Intervention group n=10,335; Control group n=2765.
Inclusion/Exclusion Criteria	Inclusions: High risk for MI (determined by the First Heart Attack Risk Test). Those with risk scores of 4 or over on a scale of -1 to +16 for men and -1 and +17 for women were considered at increased risk for a first MI and suitable for enrolment. Exclusions: previous MI, current therapy with a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (statin); Membership in a federally funded health care program (except Medicare or plans for federal employees); Women of childbearing potential.
Patient Characteristics	Mean age 58 years. Sex 51% Female; 49% Male. Ethnicity 80% White; 9% Black; 6% Hispanic; 3% Asian, 2% other. Primary-care patients at increased risk of a first Myocardial Infarction (MI). Elevated total cholesterol level; Community-based.
Recruitment	By physicians who were enrolled in the study.
Setting	Community-based gps, USA.
Interventions/ Test/ Factor being investigated	Postal and telephone reminders given to the intervention group to comply with Pravastatin Therapy. Patients at enrolment are given a 2-week supply of pravastatin at no charge. They also received prescriptions from their physicians for additional prevastatin treatment and were given recommendations about modifying lifestyle and complying with medication regimens to limit the risk for a first MI. The intervention group received telephone reminders at weeks 2 and 8, as well as reminder postcards at week 4. These communications stressed the importance of following the physician's instructions and to take medications as prescribed. Reminder postcards were sent to both groups at 4 and 5 months after enrolment. Physicians completed follow-up evaluation forms after patient visits scheduled according to their normal practices.
Comparisons	The intervention group versus usual care.
Length of Study/ Follow-up	At 3 months then at 6 months (or study discontinuation).
Outcome measures studied	Compliance.
Results	No significant effect in compliance between the groups: 80% in the intervention group reported they were taking pravastatin as prescribed, compared to 77% in the usual care group. 64% in the intervention and 62% of the usual care group reported they missed no doses in the previous 7 days. Reported medication adherence was significantly ($p<0.05$) associated with the adoption of other coronary risk-reducing behaviours according. Of those reporting to take pravastatin 97% reported visiting their physicians as scheduled compared to 82% of those who were not compliant with pravastatin regimens ($p<0.01$). 62% of the compliant group modified eating habits compared to 51% in the noncompliant group ($p<0.01$); 39% reported losing weight compared to 35% in the noncompliant group ($p<0.01$) and 41% increased physical activity compared to 31% of those reporting non-compliance at 6 months ($p<0.01$).

Safety and adverse effects	Not reported.
Does the study answer the question?	Yes. There was no significant results for the use of telephone and postcard reminders (or baseline characteristics) on compliance or with recommended coronary risk-reducing behaviours. Therefore this relates to the question that it does not support reminders increasing adherence to medications.
Effect due to factor in study?	No power calculation, but a large sample was included. And the effect was non-significant.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant.
Internal Validity	No allocation concealment or blinding- selection

Stewart A;Noakes T;Eales C;Shepard K;Becker P;Veriawa Y;

Adherence to cardiovascular risk factor modification in patients with hypertension

Ref ID 1176 2005

Study Type Randomised Controlled Trial **Funding** Information not given.

Number of participant	Total sample: 83 patients. Intervention group: 41, control group: 42 patients.
Inclusion/Exclusion Criteria	Inclusion: Attendance at a hypertension clinic in one geographical area and providing informed consent.
Patient Characteristics	Stated that groups did not differ significantly at baseline. Age, sex and ethnicity of sample not stated.
Recruitment	
Setting	Hypertension clinics in one geographical area.
Interventions/ Test/ Factor being investigated	5 (pairs) of telephone calls (to patient and family member) made once monthly over 24 weeks. Delivered by a physiotherapist. During calls patients (or family member) were asked about their exercise program and reminded about there diet and medication.
Comparisons	Four once monthly educational sessions, the prescription of a home based walking program + once monthly phone calls (intervention) vs four once monthly educational sessions the prescription of a home based walking program (serving as control group).
Length of Study/ Follow-up	36 weeks.
Outcome measures studied	Self-report measurement of adherence (not adequately described). Participants presumably simply asked if they were taking medication correctly.
Results	Adherence: At week 24 significantly more patients in the intervention group (65%) were taking there medications as prescribed than in the control group (44.7%, p=0.05), however, there was no difference between the groups at week 36 (82.4% vs 86.7%). Other outcomes: The adherence of 62.8% (s.d=34.5) of the intervention group to the given health behaviour modification program was significantly higher than the 39.3% (s.d=42.8%) of the control group (p=0.007). There were no significant changes between the two groups in any blood pressure measurements. The intervention groups improvement in knowledge score from baseline to week 24 (48%, s.d=14 to 72% s.d=20) was significantly greater than that in the control group (47% s.d=15 to 62% s.d= 21, p=0.04) although there was not a significant difference

between the groups from week 24 to 36. There were no significant differences in the distance walked between the two groups at anytime point. The weight lose in the intervention group at week 24 (1 kg, s.d=4) was significantly greater than that in the control group (0 kg, s.d=4, p=0.03) although there was not a significant difference between the groups from week 24 to 36. There was a significant difference between the two groups at weeks 24 in terms of the number of patients reporting feeling tired (p=0.05, mean and s.d not given for groups) but not week 36. At week 24 significantly more patients in the intervention group (65%) were controlling their salt intake than in the control group (39.5%, p=0.02), however, there was no difference between the groups at week 36. At week 24 significantly more patients in the intervention group (67.5%) reported being able to control their stress than patients in the control group (47.4%, p=0.05) a difference that remained significant at week 36 (76.5% vs 38.5% p=0.04). There was no difference between the groups at week 24 or 36 in self reported smoking and alcoholic intake.

Safety and adverse effects None.

Does the study answer the question? Yes. The intervention appeared to increase adherence at week 24 but not at week 36.

Effect due to factor in study? Potential confounding factors.

Consistency of results with other studies?

Directly applicable to guideline population? Relevant.

Internal Validity

Vrijens B;Belmans A;Matthys K;de K;Lesaffre E;

Effect of intervention through a pharmaceutical care program on patient adherence with prescribed once-daily atorvastatin

Ref ID 2554 2006

Study Type Randomised Controlled Trial **Funding** Pfizer Belgium.

Number of participant 392 patients total. Intervention group: 194, control group: 198.

Inclusion/Exclusion Criteria Inclusion/exclusion: aged 18 years or above, who had been taking atorvastatin for at least 3 months, and who had no contraindications to continuation of the treatment, could be included in the study provided they usually got their medication in one of the pharmacies participating in the study. Three months of administration of atorvastatin was necessary to preclude recruiting newly diagnosed patients.

Patient Characteristics Male n (%): Intervention group: 106 (55%), control group: 91 (46%). Age (yrs): Mean (std): Intervention group: 61.9 (9.9), control group: 60.4 (10.2). Significant differences between groups at baseline in terms of age and HDL (addressed in analysis).

Recruitment Patients who usually visited one of the participating pharmacies were asked to enrol in the study.

Setting 35 pharmacies in Belgium.

Interventions/ Test/ Factor being investigated The supportive intervention program consisted of review by the patients' pharmacist, jointly with the patient, of the electronically compiled dosing history, a 'beep-card' that reminds patient of the dosing time, and educational reminders. In the intervention group, the pharmacist delivered an educational message at each follow-up visit, updated the 'compliance passport' and analyzed, together with the patient, the electronically compiled dosing history of the past month/3 months. The pharmacist was trained on how to communicate with, and teach the patient to read the MEMS graphics.

Comparisons	Support intervention program vs usual care. Intervention v control.
Length of Study/ Follow-up	12 months.
Outcome measures studied	Adherence: Medication Electronic Monitoring System (mems). The primary outcome parameter is 'post-baseline adherence' to prescribed therapy defined as the proportion of days during which the MEMS record showed that the patient had opened the container.
Results	Adherence: The average duration of the baseline and post baseline periods were respectively 90 and 215 days. Baseline adherence in the intervention group showed a small but statistically significantly higher value than that observed in the non-intervention group ($p<0.003$). Post-baseline adherence results were 6.5% higher for the intervention group than for the non-intervention group. Results were similar for both language regions. A Wilcoxon test stratified for language region and baseline adherence shows that post-baseline adherence is significantly different for both groups ($p<0.001$), indicating that for similar levels of baseline adherence, intervention had a beneficial effect on post-baseline adherence. In the intervention group, 25 (13%) subjects discontinued medication prior to 300 days, in contrast to 51 (26%) subjects in the non-intervention group. After 300 days, persistence was significantly ($p<0.002$) higher in the intervention group (87%) compared to the non-intervention group (74%).
Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention led to a significant increase in adherence and medication persistence.
Effect due to factor in study?	Fairly although some concerns.
Consistency of results with other studies?	
Directly applicable to guideline population?	Yes.
Internal Validity	

Question: Is there any evidence on interventions that aim to minimise side effects in order to increase adherence?

Grading: 1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

Adler DA;Bungay KM;Wilson IB;Pei Y;Supran S;Peckham E;Cynn DJ;Rogers WH;

The impact of a pharmacist intervention on 6-month outcomes in depressed primary care patients

Ref ID 1974 2004

Study Type	Randomised Controlled Trial	**Funding**	Grant from the National Institute of Mental Health.

Number of participant	N= 258 intervention, and n= 249 control.
Inclusion/Exclusion Criteria	Inclusion criteria: 1) received care from a PCP in any site; 2) met DSM-IV criteria for major depressive disorder (MDD) and/or dysthymia; 3) were 18 years of age or older; 4) could read and understand English; 5) had no acute life threatening condition with a terminal prognosis of <6 months; 6) were not pregnant (or had not given birth within the last 6 months). Exclusion criteria: patients with current alcoholism (defined as more than one positive response on the CAGE, plus one item assessing current usage), bipolar disorder, and/or psychotic disorders. Patients with life-time alcoholism, long-term/chronic depression (those with >=4 MDD episodes in their lifetime plus their first diagnosis >10 years ago), anxiety disorders, likely personality disorders (as indicated by NEO scores >=17), or comorbid medical conditions were not excluded.
Patient Characteristics	The sociodemographic characteristics of the patients were: 42.3 years, mean age; 71.8% female; 72.4% White; 29.7% married; 60.9% employed 20 or more hours per week; and 17.6% mean household income <10 K. Overall, 37.1% of patients had seen a psychiatrist or mental health provider in the last 3 months. There were 40% who met the criteria for MDD, 24% for dysthymia, and 36% for DD. There were no differences in these characteristics in any of the intent to treat analyses.
Recruitment	Recruited from 9 primary care practices (PCP) in metropolitan Boston.
Setting	Primary Care Practices (PCP). USA.
Interventions/ Test/ Factor being investigated	The intervention was based on the use of a protocol based on clinical pharmacy principles and AHCPR guidelines, and did not involve prescribing a specific AD medication. The protocol emphasized: 1) obtaining a thorough medication history, 2) assessing a patient's medication regimen for drug-related problems (such as side effects or drug interactions), 3) monitoring drug efficacy and toxicity, especially for the symptoms of depression, 4) educating patients about depression and antidepressants, 5) encouraging patients to start and maintain AD therapy, and 6) facilitating communication with a patient's PCP. Pharmacists contacted the patients initially by telephone to set up an appointment. After the initial appointment they informed the patient's PCP and provided the PCP with a thorough medication history (including adherence to prescribed medications and drug-related problems) and whatever recommendations the pharmacist may have suggested to improve the regimen. In addition to the pharmacist activities, pharmacists fulfilled some basic patient needs, such as that of general social support and overcoming system inadequacies. Control group: The PCPs who saw the control patients received the results of the depression screener indicating a DSM-IV diagnosis of major depressive disorder (MDD) and/or dysthymia. Other than that, control patients received usual care.
Comparisons	Between Treatments.
Length of Study/ Follow-up	Up to 6 months.
Outcome measures studied	Anti-Depressant (AD) use rates at 6 months and changes in severity of depression as assessed by a modification of the Beck Depression Inventory (BDI).
Results	The intervention group had more patients on ADs at 3 and 6 months than the control group (3 months, 60.6% vs 48.9%, p=0.024; 6 months, 57.5% vs. 46.2% adjusted, p=0.025).

Outcomes (mBDI scores) at 6 months favoured the intervention group, but the trend did not reach statistical significance (17.7 for intervention vs 19.4 for control, adjusted, p=0.16, based on 384 patients who completed both initial and 6 month questionnaire. Results at 3 months were similar. Adjusted results at 6 months for the MHI were similar in direction (51.9 vs 49.0, p=0.15) and MCS (40.4 vs 38.6, p=0.19), but were not statistically significant. Furthermore, there were no differences in 6-month outcomes for PCS (42.9 in both groups).

For patients not on ADs at study entry (n=234), rates of AD use were higher in the intervention group at both 3 months (29.2% vs 11.0%, p=0.005) and 6 months (32.3% vs 10.9% adjusted p=0.001). For patients using ADs at study entry (n=227), there were no significant differences in AD use between intervention and control groups either at 3 (90.7% vs 87.2, p=0.50) or 6 months (83.4% vs 78.4%, p=0.33).

For patients not on ADs at enrolment, mental health outcomes for the intervention patients were no different than control patients, including mBDI (18.1 vs 19.9, p=0.32).

Rates of AD use at 6 months were higher in intervention than control patients who had chronic depression (42.7% vs 13.9%, p=0.05), dysthymia (47.8% vs 15.6%, p=0.06), and potential personality disorder (37.1% vs 13.4%, p=0.01).

Safety and adverse effects None reported.

Does the study answer the question? Pharmacists significantly improved rates of AD use in PC patients, especially for those not on ADs at enrolment, but outcome differences were too small to be statistically significant. Difficult-to-treat subgroups may benefit from pharmacists' care.

Effect due to factor in study? Yes.

Consistency of results with other studies?

Directly applicable to guideline population? Relevant study.

Internal Validity Not blinded study. Self-reported outcomes.

Collier AC;Ribaudo H;Mukherjee AL;Feinberg J;Fischl MA;Chesney M;Adult AIDS;

A randomized study of serial telephone call support to increase adherence and thereby improve virologic outcome in persons initiating antiretroviral therapy

Ref ID 966 2005

Study Type Randomised Controlled Trial

Funding National Institute of Allergy and Infectious Disease, National Institutes of Health; National HIV/AIDS Research Programme.

Number of participant Total sample: 282. Intervention group: 142, control group: 140.

Inclusion/Exclusion Criteria Inclusion/exclusion: All participants had < 200 CD4 T cells/mm3 or >80000 HIVE RNA copies/ML of plasma at screening, no or limited previous antiretroviral therapy (no previous use of lamivudine, nonnucleoside reverse transcriptase inhibitors, or protase inhibitors), hemoglobin > 9.1 g/DL (for men) or > 8.9 g/dL (for women) > 850 neutrophils/mm3, > 65000 platelets/mm3, hepatic aminotranferase levels <5 times the upper limit of reference values and amylase <1.5 times the upper limit of reference values and they could not be pregnant or breast feeding.

Patient Characteristics Sex: male: control group: 84%, intervention group: 76%. Age (mean): control group: 38.2 (s.d=8.7), intervention group: 39.8 (s.d=9.7). Race: white: control group: 44, intervention group: 51. Black: control group: 34, intervention group: 23, Hispanic: control group: 18, intervention group: 21.

Recruitment

Setting	30 centres.
Interventions/ Test/ Factor being investigated	Intervention: Scripted phone calls (16 over 96 weeks) plus usual care: The calls focused on the participants' medication-related behaviour and barriers to adherence were identified and discussed. Targets/strategies to improving adherence were developed and calls also offered social support and advice around side effects.
Comparisons	Scripted phone calls + usual care v usual care. Intervention v control.
Length of Study/ Follow-up	96 weeks.
Outcome measures studied	Self report questionnaire. Subjects who reported having missed <1 dose during the previous 4 days were considered >95% adherent. Given in weeks 8, 16, 24, 48, 72, 96.
Results	Adherence: Self reported adherence was high in both groups, with 72% of participants in each group reporting >95% adherence (OR, 0.86, 95% CI 0.57 to 1.29; p=0.46) (data for means across time points given in graph, impossible to figure out exact means from this). Virologic failure: The two groups did not differ significantly in time to virologic failure.
Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention did not increase adherence relative to usual care.
Effect due to factor in study?	Fairly. Possible confounding factors (see above).
Consistency of results with other studies?	
Directly applicable to guideline population?	Yes.

Internal Validity

Rathbun RC;Farmer KC;Stephens JR;Lockhart SM;

Impact of an adherence clinic on behavioral outcomes and virologic response in treatment of HIV infection: a prospective, randomized, controlled pilot study

Ref ID 1289 2005

Study Type Randomised Controlled Trial

Funding The study was funded by a research grant from the Society of Infectious Diseases Pharmacists.

Number of participant	43 total sample. Intervention group: 22, standard care: 21.
Inclusion/Exclusion Criteria	Inclusion/exclusion criteria: Patients with or without prior antiretroviral therapy exposure were eligible to participate. Antiretroviral therapy selection was made by the patient's primary care provider and consisted of >3 antiretroviral agents. Medication recycling of 1 to 2 nucleoside reverse-transcriptase inhibitors (NRTIs) in the new regimen was allowed, provided no evidence of resistance was present by genotypic or phenotypic testing or suspected based on treatment history. Patients receiving a QD drug regimen, a medication regimen containing 3 NRTIs, or a salvage regimen (defined as presence of resistance to >2 agents in the regimen), or who were currently participating in a pharmaceutical company-sponsored clinical trial, were excluded. Patients actively being followed in the adherence clinic were also not eligible.

Patient Characteristics	Age, median, y: Intervention group: 38.0, Control group: 38.0. Female: Intervention group: 4 (25%), Control group: 1 (6%). White: Intervention group: 12 (75%), Control group: 11 (65%), Black: Intervention group: 2 (13%), Control group: 5 (29%). Hispanic: Intervention group: 2 (13%), Control group: 1 (6%). Patients assigned to the adherence clinic group had higher CD4 counts (median) 296 (s.d=278) vs 104 (s.d=103) cells4~L in the standard care group; p=0.008. No other significant differences between groups reported.
Recruitment	
Setting	An early intervention service HIV clinic.
Interventions/ Test/ Factor being investigated	Provided by a clinical pharmacist. The adherence intervention for the adherence clinic group consisted of education about appropriate HAART administration, food restrictions, and adverse-event management strategies, and also included monitoring of patient progress after therapy initiation. Information provided to patients was tailored to the individual. Visual aids developed by the pharmaceutical industry and reminder devices were used to reinforce optimal administration timing. Patients were seen for a 1.0- to 1.5-hour visit at the initiation of HAART and a 30-minute follow-up visit after 2 weeks to assess adverse events and medication scheduling. Phone follow-up was typically conducted within 1 week of the baseline visit to identify early problems. Additional visits and phone follow-up were conducted through week 12 for patients who required more assistance. The adherence intervention in the standard care group consisted of education provided during the patients' office visits with their primary care providers.
Comparisons	Adherence clinic group v standard care group. Intervention v control.
Length of Study/ Follow-up	28 weeks.
Outcome measures studied	Adherence: Assessed via 2 means: Electronic monitoring with the eDEM Monitor in System was used to measure adherence to one antiretroviral agent in the regimen and a self report measure given at weeks 4, 16, 28.
Results	Adherence: Mean adherence at weeks 4, 16, and 28 was 86% (s.d=27%), 77% (s.d=28%), and 74% (s.d=31%) in the adherence clinic group versus 73% (s.d=32%), 56% (s.d=39%), and 51% (s.d=41%) in the standard care group (week-16 difference, 21% (90% CI 1% to 42%); week-28 difference 23% (90% CI 1%-44%). The proportions of patients with adherence >90% and >95% at week 4 were 81% and 62% in the adherence clinic group and 47% and 41%, respectively, in the standard care group, but the differences did not reach statistical significance. The mean decline in adherence between weeks 4 and 28 for the adherence clinic group was 12% (p=0.15), whereas the mean decline in the standard care group was 22% (p=0.002). Sixty-nine percent of patients in the adherence clinic group took their medication on schedule versus 42% in the standard care group (p=0.025); mean decline in adherence from weeks 4 to 28 was 12% in the adherence clinic group (p=0.15) versus 22% in the standard care group (p=0.002). This difference was also observed after 28 weeks, when the mean dose precision was 53% versus 31% in the adherence clinic and standard care groups, respectively (p=0.046). SELF REPORT: Patients overestimated their adherence when compared with electronic monitoring results (91% by self-report vs 76% by electronic monitoring). No difference in the rate of adherence between the 2 groups was observed (94% vs 89% for the adherence clinic and standard care groups, respectively; p=0.51). OTHER OUTCOMES: HIV-1 RNA levels were <400 copies/mL at weeks 4, 16, and 28 in 63%, 100%, and 94% of the adherence clinic group and 29% (p=non-significant), 71% (p=0.04), and 65% (p=non-significant) of the standard care group. The proportion of patients with HIV-1 RNA <50 copies/mL was not significantly different between the two groups. The change in CD4 count was similar in both groups
Safety and adverse effects	None.
Does the study answer the question?	Yes. Participants in the intervention group were more adherent than those in control group, although this difference was not significant (but see small sample size).
Effect due to factor in study?	Yes.

Consistency of results with other studies?

Directly applicable to guideline population? Relevant.

Internal Validity

Rickles NM;Svarstad BL;Statz-Paynter JL;Taylor LV;Kobak KA;

Pharmacist telemonitoring of antidepressant use: effects on pharmacist-patient collaboration

Ref ID 1097 2005

Study Type	Randomised Controlled Trial	**Funding**	Sonderegger Research Center. National Service Research Service Award from Nation Institute of Mental Health.

Number of participant	Total sample: 63 patients. Intervention group: 31, Control group: 32.
Inclusion/Exclusion Criteria	Inclusion: patients were eligible if they had no antidepressant use in the past 4 months, were 18 or over, were willing to pick up their antidepressant from a study pharmacy during the next 4 months, had no hearing impairment and planned to be in the local area for the next 4 months. Exclusion: patients were excluded if they had a score below 16 on Beck Depression Inventory 2, required a translator, were pregnant or nursing, were receiving medication for psychotic or bi-polar disorder, and/or had physical conditions requiring additional caution with their anti-depressant.
Patient Characteristics	Gender: Male: Intervention group: 19.4% , Control group: 12.5%. Age (m, SD): Intervention group: 37.8 +/-10.7 , Control group: 37.5 +/- 13.4. Race: white: Intervention group: 87.1% Control group: 96.9%. other: Intervention group: 12.9% , Control group: 3.1%. Intervention group were more likely at baseline to have a history of psychotropic medication ($p < 0.05$.)
Recruitment	Patients presenting new antidepressant prescriptions in their community pharmacies were approached.
Setting	8 community pharmacies.
Interventions/ Test/ Factor being investigated	Intervention (PGEM) group. Received 3 monthly calls from the study pharmacist. 1st call: patients knowledge of medication and beliefs, adverse events, concerns, treatment goals were assessed as well as how patients had been using the medication up to the call. Pharmacists made recommendations about adverse events, ways to decrease non-adherence etc. Follow-up calls: adherence issues, adverse events and concerns addressed as well if patient felt they had been progressing towards treatment goals. New recommendations were made
Comparisons	Pharmacist guided education and monitoring (PGEM) (intervention) vs usual care. Intervention vs control.
Length of Study/ Follow-up	6 months.
Outcome measures studied	Adherence: Pharmacy records assessed at 3 and 6 months. Validated by comparing to patients prescription insurance claims and self-reported adherence (high correlations so only pharmacy refill data given).
Results	Adherence: There was not a significant difference between the study groups in terms of missed doses over the first three months of the study (intervention group: 18.1%, s.d=23.5, control group: 18.7%, s.d=22.1, p=non-significant). There was, however, a significant difference at six months with the rate of missed doses significantly lower in the intervention group (30.3%, s.d=36.4 vs 48.6%, s.d=39.2, p=<0.05). Patient feedback to pharmacist (FPFP) scale: the mean total was significantly higher

	on this scale for the intervention group (22.7, s.d=4.83) than the control group (10.9, s.d=4.32) (p<0.001). Cognitive outcomes: The intervention group scored higher on three cognitive outcomes: antidepressant knowledge (mean: 2.54, s.d=0.74 vs 2.06, s.d=0.93, p<0.05), antidepressant belief scale (15.7, s.d=2.84 vs 14, s.d=2.32, p<0.001) and orientation towards treatment progress (12.4, s.d=2.50 vs 9.37, s.d=3.22, p<0.001). Clinical outcomes: The two groups did not differ significantly in terms of depressive symptoms. Both groups showed improvements over the first three month period (p<0.001).
Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention group were not significantly more adherent at three months but were at six months.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Yes.
Internal Validity	

Grading: 1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias*

Chisholm MA;Mulloy LL;Jagadeesan M;DiPiro JT;

Impact of clinical pharmacy services on renal transplant patients' compliance with immunosuppressive medications

Ref ID 61 2001

Study Type	Randomised Controlled Trial	**Funding**	Supported by a grant from the Carlos and Marguerite Mason Trust Fund.

Number of participant	24 total sample. Intervention group: 12, control group: 12.
Inclusion/Exclusion Criteria	Inclusion: patients must have been between the ages of 18 and 60 yrs, received only one kidney transplant, received follow-up care at MCG for at least 1 yr post-transplantation, prescribed the same immunosuppressant medication for at least 1 yr post-transplantation, and received their immunosuppressant medications from the MCG Outpatient Pharmacy for the entire first year post-transplantation.
Patient Characteristics	Separate group analysis not given. The mean age in years of the patients was 49.2 (s.d=10.2). The patient population consisted of 18 males (75%), 6 females (25%), 14 Caucasians (58.3%), 9 African–Americans (37.5%), and 1 Hispanic (4.2%).
Recruitment	
Setting	A tertiary care teaching facility.
Interventions/ Test/ Factor being investigated	Clinical pharmacy services (CPS) Intervention: Delivered by clinical pharmacists. Included the pharmacist taking medication histories and reviewing (at least once monthly) patients' medications with an emphasis on optimizing medication therapy to achieve compliance outcomes while minimizing adverse events related to medication. The clinical pharmacist also provided recommendations to the nephrologists with the goal of achieving desired outcomes. Counselling involved discussions of patients concerns around their medication therapy and instructing them how to properly take their medications. Counselling was both verbal and/or in writing emphasizing the importance of compliance, when and how to take medications, and the correct dose/number of tablets. Participants could contact the pharmacist via phone if necessary.
Comparisons	Clinical Pharmacy Services (CPS) + routine care vs routine care. Intervention v control.
Length of Study/ Follow-up	12 months.
Outcome measures studied	Compliance was estimated by comparing patients' monthly pharmacy refill records to the prescribed regimen documented in the patients' medical records. Immunosuppressive serum concentrations were measured to confirm compliance.
Results	A Compliance rate (CR) of 80% was used as a minimum threshold for a patient to be classed as compliant. Adherence: At the end of 1 yr post-transplant, the mean CR of 96.1 (s.d=4.7%) for patients who had clinical pharmacist intervention was statistically higher than the mean CR of 81.6 (s.d=11.5%) for patients who did not have clinical pharmacist involvement (p=0.001). For 6 of the 12 months post-transplant (months 6–8 and 10–12 post-transplant) there were differences between CRs between the intervention and control groups, with higher rates in the intervention group (p=0.05). There was a significant difference in the duration of compliance between the groups (p<0.05). At 12 months post transplant, 75% of the intervention patients remained compliant each month since transplant, whereas 33.3% (n=4) of the control patients remained compliant. The mean time to the first non-compliant month was 11 months for the intervention group, with a 95% confidence interval of 10–12 months. The mean time to the first non-compliant month was 9 months for the control group, with a 95% CI of 7–11 months.

	Other outcomes: Intervention patients (64% of levels classed as being in 'target' range) had a greater achievement of ‘target’ serum concentrations than control patients (48%) (p=0.05).
Safety and adverse effects	None.
Does the study answer the question?	Yes. The Clinical pharmacy services (CPS) Intervention significantly improved adherence.
Effect due to factor in study?	Study has potential problems with internal validity which may have effected outcome.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant.
Internal Validity	

Finley PR;Rens HR;Pont JT;Gess SL;Louie C;Bull SA;Lee JY;Bero LA

Impact of a collaborative care model on depression in a primary care setting: a randomized controlled trial

Ref ID 2521 2003

Study Type Randomised Controlled Trial **Funding** Not reported.

Number of participant	N=75 patients, intervention group and usual care group n=50 patients. Mean age in control group: 54.1 (s.d=17.3) and in intervention group: 54.4 (s.d=14.1).
Inclusion/Exclusion Criteria	All patients were members of the health maintenance organization (HMO) who were receiving primary care services and who had started antidepressant therapy. Exclusion criteria: evidence that subjects had received an antidepressant during the preceding 6 months; concurrent psychiatric or psychological treatment; current symptoms of mania or bipolar disorder; psychotic symptoms; eminent suicidal tendencies; and active substance abuse or dependence.
Patient Characteristics	Mainly female patients (85% intervention, 84% control groups)
Recruitment	Through the HMO.
Setting	Primary care setting. USA.
Interventions/ Test/ Factor being investigated	Subjects who returned study surveys were mailed a $20 cheque as reimbursement for participation. Intervention group: An intake interview that lasted 30 minutes was conducted after randomization, in which care managers assessed the severity of psychopathology, identified potential stressors and other predisposing factors. Medical, psychiatric and drug histories were recorded. Symptoms, aetiology, and prognosis of depression were discussed, and a detailed explanation of the role of antidepressants was presented (including potential therapeutic effects and adverse effects). Patients were also advised of other treatment options and resources available at the centre. Care managers were permitted to titrate antidepressant drugs in a fashion consistent with the HMOs clinical guidelines and current recommended practices. After the initial interview, the intervention group were scheduled for frequent follow-up phone calls and clinic appointments. Phone calls lasted 5-10 minutes and during these calls, pharmacists followed a standardized set of questions that assessed drugs adherence, therapeutic effects, adverse effects, and other social or medical factors. Documentation of all patient contacts was entered into the official medical record in the form of a detailed progress note. Adherence was determined from the HMO's computerized prescription refill records. Measurement of drug adherence was expressed as a medication possession ratio (MPR). The MPR was defined as the number of day’s supply of drug that the patient received during the 6 month study period, including the quantity and strength of drug

	as well as prescribing directions. Usual care: subjects received brief counselling on the prescribed drug, therapeutic end points, and side effects in a manner consistent with patient education routinely delivered to members receiving prescriptions from the HMO's outpatient pharmacy.
Comparisons	Between treatments.
Length of Study/ Follow-up	Up to 6 months.
Outcome measures studied	Adherence; severity of symptoms; patient satisfaction; resource utilization.
Results	From the intervention group, 79% returned the mailed surveys, compared to 50% from the control group. After 6 months, the intervention group demonstrated a significantly higher drug adherence rate than that of the control group (67% vs 48%, p=0.038). The MPR was higher for the intervention group than for the control group at both 3 and 6 months, but the difference was not significant. Patient satisfaction was significantly greater among members randomly assigned to pharmacists' services than among controls (p<0.05), and provider satisfaction surveys revealed high approval rates as well. Changes in resource utilization were favourable for the intervention group, but differences from the control group did not achieve statistical significance. Clinical improvement was noted in both groups, but the difference was not significant.
Safety and adverse effects	None reported.
Does the study answer the question?	Clinical pharmacists had a favourable effect on multiple aspects of patient care. Future studies of this model in other health care settings appear warranted.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	Consistent.
Directly applicable to guideline population?	Relevant study.
Internal Validity	Patients not blinded to study.

Katon W;Russo J;Von KM;Lin E;Simon G;Bush T;Ludman E;Walker E;

Long-term effects of a collaborative care intervention in persistently depressed primary care patients

Ref ID 33 2002

Study Type	Randomised Controlled Trial	**Funding**	Supported with grants from the National Institute of Mental Health Services.

Number of participant	N= 114 for both intervention and control groups.
Inclusion/Exclusion Criteria	Inclusion criteria: Patients between the ages of 18 and 80 from 1 of the 4 primary care clinics who received a new antidepressant prescription (no prescriptions within the last 120 days) from a primary care physician for the diagnosis of depression or anxiety. Exclusion criteria: if patients had a screening score of 2 or more on the CAGE alcohol screening questionnaire, 13 were pregnant or currently nursing, planned to disenroll from the Group Health insurance plan within the next 12 months, were currently seeing a psychiatrist, had limited command of English, or had recently used lithium or antipsychotic medication.

Patient Characteristics	There were no significant differences between the 114 intervention and 114 usual-care patients on the following demographic variables, including age (I, 47.2 ± 14.0 years vs UC, 46.7 ± 13.4 years), percent employed full- or part-time (I, 72.6% vs UC, 64.9%), and percent Caucasian (I, 79.8% vs UC, 80.7%). There was a significant difference between intervention and control patients in the percent of female subjects (p=0.02).
Recruitment	Using GHC automated registration, pharmacy, and visit data.
Setting	4 Large primary care clinics. USA.
Interventions/ Test/ Factor being investigated	Usual care group: provided by GHC family physicians and involved prescription of an antidepressant medication, 2 or 3 visits over the first 6 months of treatment, and an option to refer to GHC mental health services. Both intervention and usual-care patients could also self-refer to a GHC mental health provider. GHC usually scores at about the seventy-fifth percentile on National Committee for Quality Assurance/Health Plan Employer Data and Information Set measures of quality of depression care. Intervention group: a multifaceted intervention was developed that targeted patients, physicians, and process of care. Each patient received a book and companion videotape developed by the study team, which reviewed the biopsychosocial model of depression, how medications and psychotherapy help depression, and how to become involved as an active partner with their physician in the care of their depressive illness. After the baseline interview and randomization, the research assistant scheduled 2 sessions for intervention patients with a psychiatrist (one 50-minute initial session and one 25-minute follow-up session) in the primary care clinic. Visits were usually spaced 2 weeks apart, with a brief telephone call to review progress between the first and second visits and, if necessary, between the third and fourth visits. The psychiatrist reviewed the course of the current depressive episode and the patient's biopsychosocial history. When severe side effects or inadequate response to treatment occurred, the psychiatrist helped the patient and primary care physician alter the dosage or choose an alternative medication.
Comparisons	Between treatments.
Length of Study/ Follow-up	Up to 28 months.
Outcome measures studied	Adherence to antidepressant medication, severity of depressive symptoms, and functional impairment.
Results	In the high strata during the first 6 months, 72% (n=24) of the intervention patients and 40% (n=14) of the controls were adherent to an adequate dosage of medication (p<0.01). This trend was also seen in the second 6-month period: 70% (n=23) of the intervention patients and 37% (n=13) of the controls were adherent to an adequate dosage of medication (p<0.05). For the moderate-severity strata, intervention patients were only more likely to adhere to 90 days or more of adequate dosage of antidepressants during the first 6-month block of time (76% of the intervention patients versus 46% of the controls, p<0.05) Similar, but non-significant, trends were observed for the second 6-month block. For the other three 6-month periods, the percentages were very similar for the treatment groups in both strata. The intervention group was associated with continued improvement in depressive symptoms at 28 months in patients in the moderate-severity group (p=0.004), but not in patients in the high-severity group (p=0.88). There were no significant differences in total ambulatory costs between intervention and control patients over the 28-month period (p=0.40).
Safety and adverse effects	None reported.
Does the study answer the question?	The intervention group showed improvement in depressive outcomes without additional health care costs in approximately two thirds of primary care patients with persistent depressive symptoms.
Effect due to factor in study?	Some methodological limitations.

Consistency of results with other studies?	Consistent.
Directly applicable to guideline population?	Relevant study.
Internal Validity	Not blinded study.

Vivian EM;

Improving blood pressure control in a pharmacist-managed hypertension clinic

Ref ID 2538 2002

Study Type	Randomised Controlled Trial	**Funding**	Supported by the Christian R and Mary F Lindback Foundation.

Number of participant	Total sample: 56. Intervention group: 27, control group: 29.
Inclusion/Exclusion Criteria	Inclusion: age older than 18 years, confirmed diagnosis of hypertension (defined as systolic blood pressure > 140 mm Hg or diastolic > 90mm Hg), receiving antihypertensive drug therapy (and blood pressure >140/90mm Hg), receiving all drugs from the pharmacy participating in study, and not receiving care at the pharmacist managed clinic (until the study began). Exclusion: a secondary cause of hypertension, such as chronic renal disease, renovascular disease, pheochromocytoma, Cushing's syndrome, and primary aldosteronism; had missed more than three appointments in the last year; or were in hypertensive crisis (defined as systolic blood pressure > 210 mm Hg or diastolic > 110 mm Hg). Patients were also excluded if they had a diagnosis of New York heart Association class 3 or 4 chronic heart failure, end stage renal disease, a psychiatric disorder, severe hepatic dysfunction defined as transaminase levels greater than 3 times the upper normal limit, or terminal cancer or other condition that limited life expectancy to less than one year.
Patient Characteristics	All participants in study were male. Race: Afro-American: intervention group: 22 , control group: 19, Caucasian: intervention group: 3, control group: 7. other: intervention group: 1, control group: 1. Age (mean, sd): intervention group: 64 (s.d=10.9), control group: 65.5 (s.d=7.8). Significant difference in diastolic blood pressure between groups at baseline.
Recruitment	
Setting	A medical center.
Interventions/ Test/ Factor being investigated	Pharmacist-managed hypertension clinic care (intervention): Patients in intervention group saw a clinical pharmacist once/month at a pharmacist-managed hypertension clinic. The pharmacist could make changes in the prescribed drugs and dosages and provided medication counselling centred around the discussion of side effects, recommending lifestyle changes and an assessment of compliance at each visit.
Comparisons	Pharmacist-managed hypertension clinic care (intervention) vs traditional PCP care (control). Intervention vs control.
Length of Study/ Follow-up	6 months.
Outcome measures studied	Adherence: 1/ self report questionnaire (monthly measured in intervention group, at baseline and 6 months for control group) 2/ drug refill information from pharmacy.
Results	Note: None compliance: defined as missing more than 3 doses of drug in 1 week or having pharmacy records indicate failure to refill drugs within 2 weeks after the scheduled refill date. Adherence: There were no significant differences in compliance (from the self report measure) between (p>0.25, mean, sds not given for adherence) or within (p>0.07)

	the two groups at baseline or the end of the study. 68% of patients in the intervention group admitted forgetting to taking there drug at least once a week vs 48% in the control group (p=0.253). 92% of patients in both the intervention group and control group took there drugs as directed by their healthcare professional and did not take more than prescribed (p=1.00). Pharmacy records indicated the 85% of patients in the intervention group received their refills within 2 weeks of the next refill date vs 93% of patients in the control group (p>0.42). Blood pressure control: 81% of patients in the intervention group obtained a blood pressure below 140/90 mm Hg at the end of the study vs 30% of patients in the control group (p=0.001). Mean changes in systolic blood pressure for the intervention and control groups were -18.4 (95% CI -26.3 to 10.5) and 3.98 (95% CI -11.8 to 3.79) respectively (=0.001). Mean changes in diastolic blood pressure for the intervention and control groups were -12.38 (95% CI -16.49 to -8.28) and 2.54 (95% CI -1.49 to 6.57) respectively (p=0.001). Of the eleven patients in the diabetes group in the intervention group 91% attained the goal blood pressure of below 130/80 mm Hg versus only 12% of 16 patients with diabetes in the control group (p=0.001). Patient satisfaction and quality of life: no statistically significant differences noted between groups.
Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention did not significantly increase adherence.
Effect due to factor in study?	Unsure, potential problems.
Consistency of results with other studies?	
Directly applicable to guideline population?	Yes.
Internal Validity	

Question: How does the way the information is presented (e.g pictorial vs written) affect adherence?

Grading: 1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias

Raynor DK;Blenkinsopp A;Knapp P;Grime J;Nicolson DJ;Pollock K;Dorer G;Gilbody S;Dickinson D;Maule AJ;Spoor P;

A system review of quantitative and qualitative research on the role and effectiveness of written information available to patients about individual medicines

Ref ID 8723 2007

Study Type Systematic Review **Funding** HTA study.

Number of participant RCTs; controlled clinical trials; controlled before and after studies; interrupted time series; before and after cohort studies; other uncontrolled designs.

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Key findings of the report show that:
•the majority of people do not value the written information they receive, and
•no robust evidence was found that the information had any effect on patient satisfaction or compliance.
The review showed that patients did not value the PILS supplied due to deficiencies in the content (e.g. complexity of language) and layout (e.g. print size). However, it did show that patients valued written information that contained condition-based details along with the medicines information, in addition to alternative treatments for the condition.
Most patients did not value the current package insert patient information leaflets (PILS) and did not consider information written by medicine manufacturers to be sufficiently independent.
In addition, the qualitative evidence included in the report did not show that patients perceive improvement of compliance as a function of PILs. This can be explained by how an informed decision not to take medication is a legitimate and acceptable outcome. In contrast, some health care professionals viewed that the increase of compliance was one of the main PIL uses.
The key points for improvement of written medicines information outlined by the review were:
•The need to involve patients in all stages of the process, as to reflect better their needs.
•To incorporate the findings from the review to improve future information design and

content.
•To present risk information numerically instead of verbal descriptions.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Raynor DK;Blenkinsopp A;Knapp P;Grime J;Nicolson DJ;Pollock K;Dorer G;Gilbody S;Dickinson D;Maule AJ;Spoor P;

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Ref ID 8723 2007

Study Type Systematic Review **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

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•To incorporate the findings from the review to improve future information design and content
•To present risk information numerically instead of verbal descriptions.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Grading: 1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

Atherton-Naji A;Hamilton R;Riddle W;Naji S;

Improving adherence to antidepressant drug treatment in primary care: A feasibility study for a randomized controlled trial of education intervention.

Ref ID 2507 2001

Study Type Randomised Controlled Trial **Funding** Grampian Primary Care Trust.

Number of participant	Total sample 45. Intervention group: 23, control group: 21.
Inclusion/Exclusion Criteria	Inclusion/exclusion: 1. Patients aged over 16 years. 2. Clinically depressed patients. 3. First consultation of a patient for depression or new episode of depression. 4. Antidepressant prescribed for patients' depression (i.e. not for other conditions). 5. Patients not suffering from dementia.
Patient Characteristics	No separate break down by group. Total sample: 88.9% were female. Age: 84.4%: 21- 60 years, 6.7%) < 21 years, 8.9% > 60 years.
Recruitment	
Setting	Five large general practices.
Interventions/ Test/ Factor being investigated	Intervention: Patients in the intervention groups received simple tailored information (mailed leaflets with written and pictorial information) 1, 6 and 16 weeks after the initial prescription (in order to reflect acknowledged 'critical periods' for non-compliance during a course of antidepressant treatment) which was personalized for each patient and specific drug and generated by a specially constructed computer programme. Leaflets contained basic information about condition, treatment and general problems people may have with adherence.
Comparisons	Intervention v usual care. Intervention vs control.
Length of Study/ Follow-up	6 months.
Outcome measures studied	Adherence: Data assessed by collection of prescriptions over 6 months. Other measurements also taken.
Results	Adherence: only 16 (35.6%) participants collected prescriptions in all 6 months, with no significant difference between the intervention and control groups (37.5 versus 33.3%) (p=0.085 and 95% CI –23.9 to 32.1). Overall, prescription collection declined from 97.7% in month 1 to 55.6% in month 6. Other outcomes: There were no significant differences in the numbers of consultations, referrals and admissions between the two groups. The participants in the intervention group had significantly lower Hospital Anxiety and Depression Scale (HADS) score on subscale and total scores than the participants in the control group. The intervention group experienced significantly less depression (median (interquartile range): Intervention group: 4.0 (1–7), control group: 8.0 (4–10), (95% CI –7 to 0) p = 0.034), anxiety (Anxiety – median (interquartile range): intervention group: 7.0 (4–11), control group: 11.0 (8–14), (95% CI –7 to –1) p = 0.022) and total scores (Total – median (interquartile range): intervention group: 11.0 (6–20), control group: 18.0 (15–24), (95% CI –13 to –1), p = 0.021) than the control group. There was no significant difference between the groups in total treatment satisfaction scores.
Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention did not increase adherence.

Effect due to factor in study?	Fairly.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant.
Internal Validity	

Segador J;Gil-Guillen VF;Orozco D;Quirce F;Carratala MC;Fernandez-Parker A;Merino J;

The effect of written information on adherence to antibiotic treatment in acute sore throat

Ref ID 1104 2005

Study Type Randomised Controlled Trial **Funding** None reported.

Number of participant	Intervention group n=79; control group n=79.
Inclusion/Exclusion Criteria	Inclusion criteria: over 18 years of age; presenting to the gp because of sore throat for less than 7 days and at least three of the four centre criteria (history of fever, absence of cough, swollen tender anterior cervical nodes and tonsillar exudates); ability to read and write correctly; ability to understand the verbal instructions given; and on the panel of a GP taking part in the research. Exclusion criteria: refusal of treatment; mental or social problems that could prevent the patient from complying with treatment; illiteracy or cognitive deficiency; allergy to the drugs prescribed in the protocol; refusal to take part in the research; pregnancy, breastfeeding or any illness that may affect short-term prognosis; and not fulfilling any of the inclusion criteria.
Patient Characteristics	Both groups were similar in age, sex (39.3% male in the intervention group vs. 49.3% in the control group, (p=0.2) and antibiotic treatment, penicillin or erythromycin (p=1).
Recruitment	From gp practice.
Setting	Gp practice, Spain.
Interventions/ Test/ Factor being investigated	To give written information at the time of the first visit. The written information emphasised the importance of completing the antibiotic treatment, of respecting intervals between doses and the drawbacks of an early drop-out, and was given only at the time of initial consultation. The control group was given verbal information only.
Comparisons	Between treatments.
Length of Study/ Follow-up	9-12 days after first GP visit.
Outcome measures studied	Adherence.
Results	The pill count average was 87.4 (s.d=25.2%) and it was higher in the intervention group 93.7 (s.d=24.5%) than in the control group 81.1 (s.d=24.5%) (p<0.05). Absolute risk reduction was 14% (95% CI -3.77 to 26.56); relative risk reduction was 24.9% (95% CI -11.04 to 58.28). Drop out rate was higher in the control group (p= 0.0001) due to improvements or resolution of symptoms.
Safety and adverse effects	None reported.
Does the study answer the question?	Written instructions, in addition to verbal ones, significantly improve compliance with antibiotic treatment in tonsillitis of acute sore throat in comparison with verbal instructions only.
Effect due to factor in study?	Yes.

Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant study.
Internal Validity	Not blinded study.

Question: Do specific forms of therapy (eg CBT) affect adherence?

Grading: 1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias

Lam DH;Watkins ER;Hayward P;Bright J;Wright K;Kerr N;Parr-Davis G;Sham P;

A randomized controlled study of cognitive therapy for relapse prevention for bipolar affective disorder: outcome of the first year

Ref ID 23 2003

Study Type	Randomised Controlled Trial	**Funding**	No information given regarding funding.

Number of participant	103 in total sample. CT group: 59; Control group: 60.
Inclusion/Exclusion Criteria	Inclusion criteria: (1) bipolar 1 disorder according to the DSM-IV18; (2) prescribed prophylactic medication at an adequate dose according to the British National Formulary 19; (3) aged 18 to 70 years; (4) at least 2 episodes in the last 2 years or 3 episodes in the last 5 years (to identify a subgroup vulnerable to relapses); (5) currently not fulfilling criteria for a bipolar episode; (6) Beck Depression Inventory 20 (BDI) score lower than 30; and (7) Bech-Rafaelsen Mania Rating Scale 21 (MRS) score lower than 9. Patients in an acute episode or with high residual symptoms were excluded because the focus of this study was relapse prevention and we did not want to use most therapy sessions for the treatment of an acute episode. Exclusion criteria: being actively suicidal (BDI suicide item score of 3) and currently fulfilling the criteria for substance use disorders.
Patient Characteristics	Age y: CT group 46.4 (s.d=12.1), control group 41.5 (s.d=10.8). Female sex (no. of patients): CT group: 28, control group 30. Age at onset, y: CT group 28.2 (s.d=11.4), control group: 26.2 (s.d=9.5). No significant baseline differences between groups.
Recruitment	Participants were either referred by their psychiatrists or contacted directly via a list of patients who had had blood drawn in the last 12 months to evaluate the serum level with mood stabilizers.
Setting	Not given.
Interventions/ Test/ Factor being investigated	Traditional cognitive therapy for depression with new elements highlighting the need for combined psychological and drug treatment, to help monitor mood and prevent relapse and to highlight the importance of sleep and routine and the therapy also addressed illness beliefs. Delivered by clinical psychologists. Consisted of 12 to 18 individual sessions within the first 6 months and 2 booster sessions in the second 6 months.
Comparisons	Cognitive therapy and minimal psychiatric care v minimal psychiatric care alone. So, intervention + usual care v usual care alone.
Length of Study/ Follow-up	12 months.
Outcome measures studied	Adherence: Monthly questionnaires returned by the patients (and every 6 months by key workers) to the psychiatric service who had the most contact with the patient. Broad scales were used to report if the patient had been fully adherent to non adherent.
Results	Adherence: 93.1% (27/29) of patients with available serum levels (after 6 months) in the CT group compared with 78.3% (18/23) of the control group had adequate serum levels (p=0.06). There was significant agreement between patients' own compliance reports and serum levels: at month 6, a significantly greater proportion of patients in the CT group 88.4% (38/43) than in the control group 66.7% (26/39) reported good compliance (i.e. missing their medication <3 times in a month). After co-varying for the compliance rating at baseline, this remained significant (p=0.02). There was a significant correlation between key workers' and patients' reports (r=0.75; n=64; p=<.001). Other outcomes: The hazard ratio for relapse in the CT group relative to the controls was 0.40 (95% CI 0.21 to 0.74; p=0.004) after medication compliance was controlled

for. When both medication compliance and the previous number of episodes were controlled for, significantly fewer patients in the CT group experienced a bipolar episode during the 12 months than in the control group (P=0.008). After medication compliance and the number of previous episodes were controlled for, patients in the CT group still had significantly fewer days in bipolar episodes than the control group (p=0.008). The CT group had significantly fewer days in the hospital for bipolar episodes as a whole and significantly fewer hospital days for depression.

Over the 12 months, the CT group showed significantly higher social functioning, less mood symptoms on the monthly mood questionnaires and significantly less fluctuation in manic symptoms compared to control group. The CT group also coped better with manic prodromes at 12 months. There were no differences between the groups in number of psychiatric appointments or prescriptions changes.

Safety and adverse effects None

Does the study answer the question? Yes

Effect due to factor in study? Fairly certain.

Consistency of results with other studies?

Directly applicable to guideline population? Relevant.

Internal Validity Measurement of adherence.

Miklowitz DJ;George EL;Richards JA;Simoneau TL;Suddath RL;

A randomized study of family-focused psychoeducation and pharmacotherapy in the outpatient management of bipolar disorder

Ref ID 2474 2003

Study Type Randomised Controlled Trial

Funding Grants: National Institute of Mental Health; a Distinguished Investigator Award; grant from the John D. and Catherine T. MacAuthor Foundation Network on the Psychobiology of Depression.

Number of participant Total sample: 101 participants. Intervention group: 31, control group: 70.

Inclusion/Exclusion Criteria Inclusion: DSM-3-R criteria for bipolar disorder (manic, mixed, or depressed episode) within the past 3 months, aged 18 to 65 years, No evidence of developmental disability or neurological disorder, no alcohol other substance use disorders in previous 6 months, living with or in regular contact (at least 4 hours a week) with a care-giving family member, English speaking, willingness to take mood stabilizing medications or antipsychotic agents, willingness and ability of all relatives and patients to give written informed consent to participate

Patient Characteristics Age: intervention group: 35.7 (s.d=9.2) control group: 35.6 (s.d=10.6). Sex: female: intervention group: 58%, control group: 66%. Ethnic minority: intervention group: 10% control group: 14%. No significant baseline differences between groups.

Recruitment

Setting

Interventions/ Test/ Factor being investigated	Family-focused therapy (intervention) (9 months length): Early sessions assessed the patient and the families coping styles. Following sessions in three modules 1/ psycho education (7 sessions): teaching about the disorder, its aetiology, signs, symptoms, how to prevent relapse 2/ Communication training (7-10 sessions): participants through role play etc skills of listening, offering feedback, and requesting changes in behaviour 3/ problem solving skills (4-5 sessions): participants identify potential problems, come up with and evaluate various solutions. Involved 21 one hour sessions. All of family involved. Conducted at patient or parents home. Crisis management (9 month length): Early sessions assessed patient and the families coping styles. 2 one hour psycho education sessions (for content see above). Then crisis intervention sessions offered as needed for 9 months. Conducted at patient or parents home. Pharmacotherapy (2 year length): study physician could adjust the frequency of a patient's clinical visits, drugs and dosage as required.
Comparisons	Family- focused therapy and pharmacotherapy (intervention) vs crisis management and amd pharmacotherapy (serves as control). Intervention vs control.
Length of Study/ Follow-up	2 years.
Outcome measures studied	Adherence: patient self-report validated by physician and family ratings.
Results	Adherence: Patients in the intervention group had higher mean drug adherence scores (1-3 scale) during follow up (2.77 s.d=0.43) than patients in the control group (2.56, s.d=0.48, p=0.04). Pharmacotherapy regimens: The 2 groups could not be distinguished on drug treatment intensity scores at any point during follow-up. The groups were also equivalent at all points in time on frequency of psychiatric visits, the use of lithium carbonate vs anticonvulsants, or the use of adjunctive anti depressants or anti-psychotics. Relapse and survival time: Of the 70 intervention patients, 54% experienced disease relapse during the two year follow-up, 17% survived without disease relapse, 6% were unchanged, and 23% terminated prematurely. Of the 31 control patients, 35% experienced disease relapse during the two year follow-up, 52% survived without disease relapse, 3% were unchanged, and 10% terminated prematurely. The group differences in relapse and non-relapse rates were significant ($p<0.005$). Patients in the intervention group remained remitted or partially remitted for longer periods than control patients (p=0.003, hazard ratio, 0.38, 95% CI 0.20 to 0.75). On average intervention group patients survived 73.5 (s.d=28.8) weeks whereas control patients survived 53.2 (s.d=39.6 weeks). Symptom type and severity: intervention group patients had a similar affective symptom scores to control patients for the first 6 months of follow up but then stabilized at the lower levels of symptom severity (p=0.007).
Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention significantly improved adherence.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Yes.
Internal Validity	

Grading: 1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

Bechdolf A;Kohn D;Knost B;Pukrop R;Klosterkotter J;

A randomized comparison of group cognitive-behavioural therapy and group psychoeducation in acute patients with schizophrenia: Outcome at 24 months

Ref ID 4504 2005

Study Type Randomised Controlled Trial

Funding This work was supported by grant from the Koln Fortune Program, Faculty of Medicine, University of Cologne, Germany.

Number of participant

88 total sample. CBT group: 40, PE group: 48.

Inclusion/Exclusion Criteria

Inclusion: Participants were aged 18–64 years and met criteria for an episode of a schizophrenic or related disorder (ICD-10: F 20, F 23, F 25).

Exclusion: Participants with a primary diagnosis of drug or alcohol dependence, organic brain disease, learning disability or hearing impairment was excluded from the study. Non-speakers of German were also excluded.

Patient Characteristics

At baseline: Age, years (mean SD): CBT group: 32.2 (s.d=9.9), PE group: 31.4 (s.d=10.6). Gender [n (%)] Female: CBT group: 22 (55.0%), PE group: 26 (54.2%). Time since diagnosis, months (mean): CBT group: 56.7 (s.d=65.4), PE group: 50.0 (58.7). Number of admissions (mean): CBT group: 2.6 (s.d=3.8), PE group: 2.4 (s.d=3.2). No significant differences between groups.

At 24 months follow-up: Age, years (mean): CBT group: 35.35 (s.d=10.54), PE group: 33.15 (s.d=10.76); Gender (n %) Female: CBT group: 8 (50.0%), PE group: 15 (55.6%). Time since diagnosis, months (mean): CBT group: 70.63 (s.d=84.4), PE group: 52.00 (s.d=60.41). no. of admissions (mean): CBT group: 4.00 (s.d=4.8), PE group: 2.59 (s.d=3.8). No significant differences between groups.

Recruitment

Participants recruited from consecutive acute admissions to the in-patient unit of the Department of Psychiatry and Psychotherapy at the University of Cologne.

Setting

Interventions/ Test/ Factor being investigated

Group CBT: 16 sessions in 8 weeks by psychiatrist or clinical psychologist focused on assessment and engagement (sharing information about voices and delusions, models of psychosis), improving self-esteem, formulation of key-problems, interventions directed at reducing the severity and the occurrence of key problems, relapse prevention/keeping well and enhancing medication compliance. A specific focus on the component "improving self-esteem" to foster feelings of hope and engagement with therapy.

Group PE: used as comparison and involved 8 sessions in eight weeks delivered by psychiatrist or clinical psychologist and focused on symptoms of psychosis, models of psychosis, effects and side-effects of medication, maintenance medication, early symptoms of relapse, relapse prevention.

Comparisons

Group Cognitive Behavioral Therapy (CBT) vs group psycho-education (PE). Intervention vs Intervention.

Length of Study/ Follow-up

24 months.

Outcome measures studied

Compliance was measured by a 4-point rating scale based on corroboration from as many sources as possible including patient, relatives, psychiatric nurse and psychiatrist-in-charge (m *2 sources).

Results	Adherence: Compliance with medication was high in both groups at intake CBT: 3.9 (0.3), PE: 3.8 (0.5). This high compliance level was maintained during the intervention period and declined during follow-up. On a descriptive level, the CBT group showed higher compliance ratings at post-treatment CBT: 3.9 (s.d=0.3), PE 3.7 (s.d=0.7) and at 24 month follow-up CBT: 3.4 (s.d=0.7), PE: 2.9 (s.d=1.1). However, there were no significant differences between the two interventions at any assessment point (post treatment: p = 0.10, 24 month follow-up, p = 0.26). Other outcomes: There was not a significant difference between the groups in terms of re-hospitalization rates or the overall length of hospital stays (part time and full time). When scores at 24-month follow-up were controlled for pre-treatment scores by ANCOVA no significant differences emerged between CBT and PE in any psychopathological syndrome at 24-month follow-up. No significant differences between treatment groups were observed when calculating individuals with clinical significant change. No significant differences emerged between treatment groups at pre-, post-treatment or 24-month follow-up.
Safety and adverse effects	None.
Does the study answer the question?	Yes. CBT does not significantly improve medication compliance compared to PE.
Effect due to factor in study?	Probably. Problem that 16 sessions of CBT were given compared to only 8 PE sessions.
Consistency of results with other studies?	
Directly applicable to guideline population?	Direct.
Internal Validity	

Gray R;Leese M;Bindman J;Becker T;Burti L;David A;Gournay K;Kikkert M;Koeter M;Puschner B;Schene A;Thornicroft G;Tansella M;

Adherence therapy for people with schizophrenia: European multicentre randomised controlled trial

Ref ID 2704 2006

Study Type	Randomised Controlled Trial	**Funding**	Quality of Life and Management of Living Resources of the European Union.

Number of participant	Total Sample: 409, AT Group: 204, HE Group: 205.
Inclusion/Exclusion Criteria	Inclusion: A clinical diagnosis of schizophrenia using ICD-10 criteria, patients would need continuing antipsychotic medication for a year after baseline assessment in the judgement of a senior psychiatrist, there needed to be evidence of clinical instability in the year before baseline, defined by one or more of the following: at least one admission to a hospital on mental health grounds, a change in type or dose of antipsychotic medication, planned or actual increased frequency of contact with mental health services, and indications of clinical instability reported by friends, carers or clinical team. Exclusion: presence of moderate or severe mental handicap (learning disability), organic brain disorders, current treatment by forensic psychiatric services, alcohol or drug dependence, inability to speak the language of the host country to a sufficient standard to receive the intervention, or assessment by the treating clinician as lacking capacity to give valid consent to participate.
Patient Characteristics	Age: AT group: 40.9 (s.d=11.7), HE Group: 42.1 (s.d=11.4). Male: AT group: 122 (60%), HE Group: 123 (60%). White European: AT group: 151 (74%), HE Group: 159 (78%). No significant differences at baseline between groups.

Recruitment

Setting	Regular psychiatric care services. 4 study sites.
Interventions/ Test/ Factor being investigated	Experimental intervention: Adherence therapy: a brief, individual CBT approach. A collaborative, patient centred phased approach to promoting treatment adherence. There are 6 elements that form the core of therapy: assessment, medication problem solving, a medication time line, exploring ambivalence, discussing beliefs and concerns about medication and using medication in the future. Key therapy skills that the therapists use include exchanging information, developing discrepancies between participants thoughts and behaviours about medications and working with resistance to discussing psychiatric medication and treatment. The overall aim of process is to achieve a joint decision about the medication. Control intervention: Health education: didactic health education package focused on the presentation of health related topics such as diet and healthy lifestyle. Delivery of both interventions: Both delivered in addition to standard care: Participants offered a maximum of 8 sessions lasting 30-50 minutes over a 5 month period. Delivered by 9 therapists (four psychologists, three psychiatrists and 2 mental health nurses).
Comparisons	Adherence therapy (AT) vs Health education (HE). Intervention (experimental) vs Intervention (control).
Length of Study/ Follow-up	52 weeks.
Outcome measures studied	Adherence: All measures after 12 months: Two measures; a key worker rating of adherence (SAIC) and a self report questionnaire MAQ. Also measured: Q of L and assessment of psychopathology.
Results	Adherence: There were no significant differences between the groups in terms of adherence at follow up using either the MAQ measure (AT group: 3.20 (1.07), HE group: 3.33 (1.02)) or SACI-C measure (At group: 5.22 (1.57), HE group: 5.03 (1.55)) at 12 month follow up. Q of L: There were no significant differences between the two groups in terms of Q of L. Psychopathology: there were no significant differences between the groups in terms of psychopathology.
Safety and adverse effects	
Does the study answer the question?	Yes. There was no difference between the adherence therapy group and health education group in terms of adherence.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant.

Internal Validity

Ruskin PE;Silver-Aylaian M;Kling MA;Reed SA;Bradham DD;Hebel JR;Barrett D;Knowles F;Hauser P;

Treatment outcomes in depression: comparison of remote treatment through telepsychiatry to in-person treatment

Ref ID 1778 2004

Study Type Randomised Controlled Trial **Funding** Not reported.

Number of participant	N=59 in the remote group, and n=60 in the in-person group.
Inclusion/Exclusion Criteria	Inclusion criteria: if patients scored 16 or higher on the Hamilton depression scale and met the DSM-IV (SCID) criteria for one of the following five diagnoses: major depressive disorder, dysthymic disorder, adjustment disorder with depressed mood, mood disorder due to a general medical condition, or depressive disorder not otherwise specified. Exclusion criteria: if patients met the criteria for bipolar disorder or schizophrenia at any point in their lifetime or met the criteria for substance abuse or dependence within the past year. They were also excluded if they required hospitalization or if they had been receiving pharmacological treatment for depression for more than a month immediately before the initial visit.
Patient Characteristics	The mean age of the participants was 49.7 years (s.d=12.8). Thirty-six percent were African American, 61% were Caucasian, and 3% were Hispanic or Asian. Fifty percent had more than 12 years of education, 33% were high school graduates, and 17% had less than 12 years of education. Thirty-nine percent were employed full-time, 19% were employed part-time, 13% were unemployed, and 30% were retired or receiving disability.
Recruitment	By being referred to any of three mental health clinics within the Department of Veteran Affairs.
Setting	Mental Health Clinic. USA.
Interventions/ Test/ Factor being investigated	To compare patients being seen by a psychiatrist either in person or by means of telepsychiatry ("remote treatment"). Treatment consisted of eight sessions with a psychiatrist over a 6-month period. The first session occurred immediately after the initial assessment by the research assistant. At this session, the psychiatrist conducted his or her own clinical evaluation. Treatment sessions lasted approximately 20 minutes and consisted of antidepressant medication management, psycho-education, and brief supportive counselling. At each visit, the patient also had a separate meeting with a research assistant during which the patient participated in an interview and completed the self-report measures described in the next section. Subjects were paid $5 per visit for their participation.
Comparisons	Between treatments.
Length of Study/ Follow-up	Up to 6 months.
Outcome measures studied	Treatment response, treatment adherence, patient satisfaction, psychiatrist satisfaction, and resource consumption or "cost effects."
Results	Medication adherence data were available for 73 subjects. Patients were excluded from this analysis if they had fewer than three visits with complete medication counts. Patients who took at least 70% of the pills they were expected to take were considered adherent, and the others were considered non-adherent. There was no difference in the percentage of adherent patients between the two treatment groups (non-significant). There was no difference in patient satisfaction between the remote and in-person groups at visit 4 (non-significant), visit 6 (non-significant), or visit 8 (non-significant). Patients' depressive symptoms, as measured by the 24-item Hamilton depression scale, significantly improved over the treatment period ($p<0.001$), and improvement did not differ by treatment group (non-significant).
Safety and adverse effects	None reported.
Does the study answer the question?	Remote treatment of depression by means of telepsychiatry and in-person treatment of depression have comparable outcomes and equivalent levels of patient adherence, patient satisfaction, and health care cost.
Effect due to factor in study?	Relative certainty.
Consistency of results with other studies?	Unknown.

Directly applicable to guideline population?	Relevant study
Internal Validity	Not blinded study.

Weber R;Christen L;Christen S;Tschopp S;Znoj H;Schneider C;Schmitt J;Opravil M;Gunthard HF;Ledergerber B;Swiss HIVC;

Effect of individual cognitive behaviour intervention on adherence to antiretroviral therapy: prospective randomized trial

Ref ID 2064 2004

Study Type	Randomised Controlled Trial	**Funding**	Swiss National Science Foundation. Equipment usage supported by a grant from GlaxoSmithKline, Switzerland.

Number of participant	60 patients total. CBT group = 32, Control group = 28.
Inclusion/Exclusion Criteria	Inclusion: therapy containing a combination of at least three antiviral drugs of at least two different drug classes, viral load below 50 copies/ml documented within the previous 3 months at a screening visit, participation in the Swiss HIV cohort study, no intravenous drug use or on stable methadone maintenance in the case of drug addiction.
Patient Characteristics	Number of female: CBT group: 25%, Control 7.1%. Median age: CBT group: 41.5 (24-71), Control group: 40.2 (25-65). No significant differences between groups on any demographic, disease status, treatment or psychosocial measurements.
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	Individual CBT: Delivered by 10 different licensed psychotherapists in private practice trained in CBT and who had attended a lecture on antiretroviral therapy. No fixed number of sessions but a minimum of 3 and max of 25 over a 1 year period. Individuals were told the focus of sessions would be focused on adherence rather than on any psychological problems. Psychotherapists where told to define with the client at least two goals for future interventions, at least one of which had to address medication adherence, although the therapists/participants could also define other goals (details of intervention poorly defined).
Comparisons	Individual cognitive behavioral therapy (CBT) plus standard care versus standard care alone. Intervention v control.
Length of Study/ Follow-up	1 year.
Outcome measures studied	Adherence: Assessed using the electronic medication exposure monitoring system. Measurements of 1st month used as baseline values. Adherence also assessed through a 10 point self report measure. Clinical, psychosocial assessments also taken.
Results	Adherence: (Note S.D's not given). Adherence at baseline (1 month) was not different between the study arms using either MEM's or self report. During the trial mean medication adherence as assessed by MEMs remained stable in the CBT group (month 1, 94.3% v month 10-12, 92.8%, with average individual slopes of -3% per year (p = 0.14). During the trial mean medication adherence as assessed by MEMs remained decreased in the control group (month 1, 94.3% v month 10-12, 88.9%, with average individual slopes of -8.7% per year (p=0.006). There was no significant difference between the slopes of the two groups however (p=0.15). The difference between the proportion of patients with -/+ 95% adherence at month 10-12 was 70.8% for CBT group and 50 % in control group (p=0.014). For self reported adherence the intervention arm were significantly more adherent than the control arm at follow-up (9.93 v 9.80, p=0.012). Other outcomes: Psychosocial measures: The coping with disease scale, the health

	locus of control scale and the self-reported symptom inventory showed no differences between groups at any period in the study. There were significant differences between groups in participants perceptions of their mental state and behaviour with the CBT group showing more prominent perceptions. VIROLOGICAL AND IMMUNOLOGICAL OUTCOMES: Only 3 patients had a viral load of 50 copies ml at month 12, one in CBT group 2 in control group. In both groups nine patients had intermittently a viral load of 50 copies/ml, which mostly returned to normal levels at the next measurement. The probability of developing a viral rebound after the trial was similar in both groups.
Safety and adverse effects	
Does the study answer the question?	Yes. CBT helps to increase adherence compared to usual treatment in patients with HIV when adherence is defined as above or equal to 95% adherence (the level of adherence estimated if antiretroviral medication is to be effacious).
Effect due to factor in study?	Fairly. No mention of blinding, no intention to treat analysis performed.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant.
Internal Validity	

Wyatt GE;Longshore D;Chin D;Carmona JV;Loeb TB;Myers HF;Warda U;Liu H;Rivkin I;

The efficacy of an integrated risk reduction intervention for HIV-positive women with child sexual abuse histories

Ref ID 1486 2004

Study Type	Randomised Controlled Trial	**Funding**	National Institute of Mental Health, Office on AIDS.

Number of participant	147. 80 to the attention control condition and 67 to the enhanced sexual health intervention (ESHI).
Inclusion/Exclusion Criteria	Inclusion: female, 18 or older, HIV+, sexually active in the past year, history of childhood sexual abuse, self-identified as African American, Latina, or European American.
Patient Characteristics	Average age 41*, all female, 79 African American, 9 European American and 59 Latinas. On average had been living with HIV for 7 years, and 13% were diagnosed with AIDS. Community and hospital based. Discrepancy reported for mean age 39/41?.
Recruitment	From county and community-based clinics, county hospitals, ethnic and AIDS-specific organisations and drug rehabilitation centers.
Setting	Los Angeles.
Interventions/ Test/ Factor being investigated	The Enhanced Sexual Health Intervention, a cognitive-behavioural approach to risk reduction with cultural and gender specific concepts.
Comparisons	Comparison between ESHI intervention and the attention control condition, which was a one-time group meeting where they received HIV prevention and child sexual abuse information and pamphlets.
Length of Study/ Follow-up	They were post tested at the end of the 11-week intervention and followed up at 3 and 6 months. End of follow-up with death or drop-out.

Outcome measures studied	Primary outcome was sexual risk reduction. Secondary outcome was HIV treatment adherence.
Results	Sexual risk reduction: Higher in the ESHI group (63.6%) than in the attention control group (56.8%), ESHI: OR=2.96, p=0.039, one-tailed. When adjusted for covariates ESHI group risk reduction was 74.5% compared to 50.4% in attention control group. Medication adherence: Adherence was roughly equal between the groups (75.6% in intervention and 73.3% of controls). No evidence of effect of ESHI: OR=1.13, p=0.41, one-tailed. There was a significant effect for adherence for those who were high attendees in the ESHI group: OR=4.09, p=0.044, one-tailed. Medication adherence was higher in those who attended at least eight sessions (91.3%) compared to seven or fewer (49.7%). High attendees in the ESHI group 74.7% compared to the control group 91.3%.
Safety and adverse effects	Wait list for control subjects to receive the intervention at after the trial for ethical considerations for those with mental health, HIV and trauma-related symptoms.
Does the study answer the question?	Yes the study does assess whether this intervention had an impact on adherence rates, which it did not unless they were high attendees of the intervention. So possible dose-effect relationship.
Effect due to factor in study?	Yes. But is suggested that study should be increased in sample size and for diversity of ethnicity.
Consistency of results with other studies?	
Directly applicable to guideline population?	Intervention very specific - enhanced sexual health intervention, but is based on the cognitive-behavioural approach. Population women only.
Internal Validity	Self-reporting; concealment; blinding;

Grading: 1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias*

van Servellen ;Nyamathi A;Carpio F;Pearce D;Garcia-Teague L;Herrera G;Lombardi E;

Effects of a treatment adherence enhancement program on health literacy, patient-provider relationships, and adherence to HAART among low-income HIV-positive Spanish-speaking Latinos

Ref ID 838 2005

Study Type	Randomised Controlled Trial	**Funding**	University-wide Aids research programme. State Office of Aids.

Number of participant	Total sample: 85 participants, 42 in intervention group, 43 in control group.
Inclusion/Exclusion Criteria	Inclusion: (HIV infected patients) 18 year or older and had problems with medication adherence as noted in the patients medical records, Spanish speaking, detectable viral load and taking antiretroviral medications for at least 3 months.
Patient Characteristics	Age: control group: 39.5 (s.d=9.3), intervention group: 41.8 (s.d=8.3). Gender: male: control group: 92.9% , intervention group: 88.4%. Those in the comparison group were diagnosed more recently 4.8 years versus 7.6 years (p=0.01) and to have spent less time on antiretroviral therapy, 44.7 versus 61.4 months (p=0.04) at baseline. 45% of participants in the control group had viral loads less than 400 copies per millilitre versus 67% of those in the intervention group (p=0.04) at baseline. Using CD4 count, there were statistically significant differences between the groups on absolute CD4 count (control group: 377 and intervention group: 212, p=0.01) at baseline.
Recruitment	
Setting	2 clinics.
Interventions/ Test/ Factor being investigated	Enhanced adherence intervention: Consisted of two parts. 1/ modular instruction: aimed at increasing patients HIV knowledge and ability to communicate with medical staff. Delivered over 5 sessions (over 6 weeks from baseline data collection) by health educators and nurse practitioners and followed up with 2/ face to face and phone call case management sessions (over 6 months from baseline data collection) by a nurse. These case management sessions concentrated on addressing patient' potential or actual risks for non adherence using motivational interviewing techniques. Content involved going over things misunderstood in stage 1, identifying barriers to adherence and finding strategies to challenge these and helping to find community, treatment and social support/referrals to help address adherence barriers.
Comparisons	Enhanced adherence intervention vs standard clinical care. Intervention vs control.
Length of Study/ Follow-up	6 months.
Outcome measures studied	Adherence: Collected at baseline, 6 weeks, 6 months via self report (collected via interview).
Results	Note adherence was calculated 3 ways: 1/ as a percentage of those missing 2 or more doses in the last 24 hours and the last 4 days, 2/ on the basis the average proportion of doses missed per day 3/ participants who had missed more then 5% and more than 10% of their doses over the last four days. Adherence: There where no significant differences between the group at 6 months in: Self efficacy of adherence management (control group, -0.06, s.d=0.59 intervention group, 0.12, s.d=0.95) 2+ doses missed in last 4 days (control group, 6.79% intervention group, -5.69%); 2+ doses missed pasted 24 hours (control group, 18.21% intervention group, -32%); average doses missed in last 4 days (control group, 0.04, s.d=0.13 intervention group, 0.02, s.d=0.14); proportion >95% adherent in last four days (control group, -4.85% intervention group, 1.71%); proportion > 90% adherent in last four days (control group, -11.47% intervention group, -0.49%); follow

medication special instructions for 4 days (control group, 0.06, s.d=0.34, intervention group, -0.07, s.d=0.36) and following medication schedule (control group, -0.09, s.d=1.60 intervention group, 0.33, s.d=1.58). These findings are reflected in the results at 6 weeks.

Health literacy: There were no significant differences between the groups in: global HIV disease treatment knowledge or HIV treatment related knowledge or knowledge risk of getting sicker. There were significant difference between the groups in recognition of HIV terms at 6 weeks (control group: 1.13, s.d=4.24; intervention group: 4.23, s.d=5.02, p <0.001) and six months (control group: 1.34, s.d=3.76 intervention group: 4.66, s.d=4.80, p < .001). There were significant difference between the groups in understanding HIV terms at 6 weeks (control group: 1.30, s.d=4.94, intervention group: 5,49, s.d=5.63, p <0.001) and six months (control group: 1.91, s.d=3.60, intervention group: 6.16, 7.97, p<0.001).

Relationship/communications: there were significant differences between the groups in relationship/communications with HIV physician at 6 week (control group, 0.58, s.d=6.70, intervention group: 3.59, 6.32, p<0.05) and 6 months (control group -1.17, s.d=6.85 vs intervention group: 7.09, s.d=8.04, p < 0.001) and in relationship/communications with medical staff at 6 months (control group: 1.11, s.d=5.97, 5.28, s.d=5.28, p <0.001).

Health Outcomes: There were significantly more individuals in the intervention group who had a drop in viral log load greater or equal to one with viral loads at 6 months (control group: 11.43%, intervention group 37.14%, p<0.01). No other significant differences reported between the groups in terms of viral load, CD4 counts or general health status.

Safety and adverse effects None.

Does the study answer the question? Yes. The intervention did not improve adherence.

Effect due to factor in study? I am unsure.

Consistency of results with other studies?

Directly applicable to guideline population? Yes.

Internal Validity

Wagner GJ;Kanouse DE;Golinelli D;Miller LG;Daar ES;Witt MD;Diamond C;Tilles JG;Kemper CA;Larsen R;Goicoechea M;Haubrich RH;

Cognitive-behavioral intervention to enhance adherence to antiretroviral therapy: a randomized controlled trial (CCTG 578)

Ref ID 371 2006

Study Type Randomised Controlled Trial **Funding** National Institute of Mental Health; University wide AIDS Research Program of the University of California.

Number of participant 230 Total sample - 199 started ART (enhanced 75; cognitive-behavioural 79; control, 76).

Inclusion/Exclusion Criteria Inclusion: Eligible patients were adults (age >/-18 years) in stable health (no active opportunistic infection) and planning to begin, restart, or switch to a new ART regimen containing a protease inhibitor (PI) or non-nucleotide reverse transcriptise inhibitor (NNRTI). ART-experienced patients had to report either having had problems with adherence or a belief that they could benefit from the intervention. Other eligibility criteria included HIV-1 RNA >/- 3000 copies/ml, no active substance

	abuse, and English or Spanish speaking.
Patient Characteristics	Mean age 39 (range 21-70). Female 20%; 30% Caucasian, 14% African American, 49% Latino, 2% Asian-Pacific Islander. Patients who were planning to begin, restart or switch to a new ART regimen.
Recruitment	Not mentioned.
Setting	5 HIV primary care clinics. California.
Interventions/ Test/ Factor being investigated	Five-session adherence interventions to increase adherence to antiretroviral treatment, given as: cognitive-behavioural alone or enhanced with two weeks practice trial, and thirdly no intervention at all but usual clinical care.
Comparisons	Group 1: Cognitive behavioral (CB) Practice Trial group v Group 2: CB No practice Trial group v Group three: Usual care group. Further within group randomization (2.1 ratio) to therapeutic drug monitoring or standard care (these groupings not addressed).
Length of Study/ Follow-up	Interviewer and self-administered questionnaires administered at screening (week -4), weeks 4, 12, 24 and 48; Blood drawn at -4, -2, 0, 1, 2, 4, 6, 12, 18, 24, 32, 40 and 48 weeks. Control group received follow-up visits every 3 months (or more).
Outcome measures studied	Adherence was the primary outcome and week 4 the primary test point; virologic response was the secondary outcome.
Results	No difference in adherence between the enhanced and cognitive-behavioural groups up to week 24. Adherence increased for the enhanced group at week 48, but declined for the cognitive behavioural group, although there was a lot of drop out in all groups by the end. The difference between interventions and the control group for % with 90% of prescribed doses taken was significant in week 4 with more adherence in the intervention group (82% vs 65%, p=0.01). This reduced to 66% for the intervention and 55% of the control by week 24 (p=0.28) but by week 48 the control group adhered more than the intervention groups (65% versus 57%, p=0.52).
Safety and adverse effects	None reported.
Does the study answer the question?	The effects of the interventions on adherence were modest and short-term and no effects with virologic and immunologic outcomes. There is need for ongoing adherence monitoring and maintenance training. This does help answer the question as it suggests that cognitive interventions do not drastically increase adherence.
Effect due to factor in study?	Yes
Consistency of results with other studies?	Yes
Directly applicable to guideline population?	Relevant as it is aimed to find out whether the intervention will increase adherence, and also uses a practice trial condition to see if this helps adherence. Only cognitive-behavioural intervention used. Population is people with HIV to start ART.
Internal Validity	Concealment bias; no blinding;

Question: Would a contractual agreement between HCP and patient affect adherence?

Grading: 1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias

Bosch-Capblanch X;Abba K;Prictor M;Garner P;

Contracts between patients and healthcare practitioners for improving patients' adherence to treatment, prevention and health promotion activities

Ref ID 667 2007

Study Type Systematic Review **Funding** Cochrane Review.

Number of participant RCTs.

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question? Overall, the conclusions from the Cochrane authors state that there is limited evidence that contracts can have a positive effect in improving adherence. In addition they argue that there is insufficient evidence from large, good quality studies to routinely recommend contracts for improving adherence to treatment or preventive health regimen.

This is a high quality study which is very relevant to the question of whether contracts improve adherence.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Question: Does being involved in self-monitoring (e.g own blood pressure) increase adherence to prescribed medicine?

Grading: 1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias*

Sadik A;Yousif M;McElnay JC;

Pharmaceutical care of patients with heart failure

Ref ID 1052 2005

Study Type Randomised Controlled Trial **Funding** Not reported.

Number of participant	Total of 221 HF patients (109 intervention; 112 control) were recruited into the study
Inclusion/Exclusion Criteria	Inclusion criteria: confirmed diagnosis of HF (by a hospital consultant), cognitive status [score > 6 as assessed by the Clifton Assessments Procedures for the Elderly (CAPE) survey] and hospital consultant consent to patient entering trial. Exclusion criteria: significant airways disease, e.g. chronic obstructive airways disease and severe mobility problems due to other causes, e.g. osteoarthritis [since both these parameters would influence forced vital capacity (FVC) and walk tests used as outcome measures in the study].
Patient Characteristics	Baseline details not given - only how measurements and assessments were performed. Nonetheless, authors state that an attempt was made to match groups as closely possible, especially for severity of HF, renal function or other concomitant illness and cognitive status.
Recruitment	Patients were recruited from the general medical wards and from cardiology and medical outpatient clinics.
Setting	Hospital. United Arab Emirates.
Interventions/ Test/ Factor being investigated	Medication knowledge was scored as a percentage value relating to the number of correct answers given to questions on name of prescribed medications, daily dosage, strength, purpose of each medication and significant side effects. A score of <50% was considered poor knowledge. In relation to compliance with prescribed medications, patient self-report on missing doses or taking extra doses of their medication, without medical advice to do so, was considered non-compliance. Intervention group: the research pharmacist discussed with their physicians if rationalization of drug therapy or simplification of dosage regimens were considered appropriate. Intervention patients were also educated (in a structured fashion) on HF, their prescribed medication and the management of HF symptoms by the research pharmacist. A printed booklet developed for this type of education programme was used and each patient was given a copy to take home. The booklet contained information on HF, its symptoms, the aims of treatment, the types of medication used and their possible side-effects, diet and lifestyle changes, advice to stick to one brand of digoxin (it having a narrow therapeutic index) and information on the action to take if doses of medication were missed. Intervention group patients were also instructed on a self-monitoring programme (signs and symptoms of HF; compliance with prescribed medication) in which they were asked to become involved; a monitoring diary card (covering 1 month) was used. Patients were asked to complete their monitoring diary cards at home and to show them to their physicians when attending an appointment. The patients were asked to return their completed diary cards to the research pharmacist for review when they visited the hospital to receive medication refills. Reinforcement of the educational message was carried out by the pharmacist as deemed necessary. Control group: patients received traditional management, i.e. excluding counselling and education by the research pharmacist, self-monitoring, pharmacist liaison with physicians, etc. Both groups of patients were asked to return to a hospital outpatient clinic at their scheduled appointment intervals followed by the hospital (3-month intervals).
Comparisons	Between treatments.
Length of Study/ Follow-up	Up to 12 months.

Outcome measures studied	Two minute walk test, forced vital capacity, blood pressure and pulse, quality of life questionnaires, HF symptoms, questionnaire outcome measures on medication knowledge and self-reported compliance with medications and lifestyle advice.
Results	The number of intervention group patients vs. control patients who exhibited self-reported compliance with the prescribed medicines (85 vs 35) and lifestyle adjustment (75 vs 29) was higher than in control group patients at 12 months ($p<0.05$). The baseline scores for these parameters were 33 vs. 32 and 22 vs. 23 respectively ($p>0.05$). At baseline the number of patients in the intervention group and the control group, respectively, whose medication knowledge was deemed poor was approximately the same (80 vs 82); it was not statistically different ($p>0.05$). There was a significant improvement in the intervention group patients after 12 months (20 vs. 84; $p<0.05$). Over the study period, intervention patients showed significant ($p<0.05$) improvements in a range of summary outcome measures [AUC (95% CI confidence limits)] including exercise tolerance [2-min walk test: 1607.2 (95% CI 474.9 to 1739.5) 1 month in intervention patients vs. 1403.3 (95% CI 1256.5 to 1549.8) in control patients], forced vital capacity [31.6 (95% CI 30.8 to 32.4) 1 month in the intervention patients vs. 27.8 (95% CI 26.8 to 28.9) in control patients], health-related quality of life, as measured by the Minnesota living with heart failure questionnaire [463.5 (95% CI 433.2 to 493.9) unit month in intervention patients vs 637.5 (95% CI 597.2 to 677.7) in control patients; a lower score in this measure indicates better health-related quality of life].
Safety and adverse effects	None reported.
Does the study answer the question?	The research provides clear evidence that the delivery of pharmaceutical care to patients with HF can lead to significant clinical and humanistic benefits.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant study.
Internal Validity	Participants not blinded. No ITT performed.

Question: Does medicine review increase shared decision-making or adherence?

Grading: 1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

Begley S;Livingstone C;Hodges N;Williamson V;

Impact of domiciliary pharmacy visits on medication management in an elderly population

Ref ID 7555 1997

Study Type Randomised Controlled Trial **Funding** Not reported.

Number of participant	Intervention group n=61; control group (V) n=63; and control group (NV) n=66.
Inclusion/Exclusion Criteria	Inclusions criteria: to be aged 75 years or older; prescribed three or more different drugs; at least a twice daily dosage for one or more of the drugs; under the care of a participating consultant; consented to participate in the study; and was returning to their home (not further institutional care).
Patient Characteristics	Majority of the patients were female (61% in the intervention group; 65% in the V group and 56% in the NV group). The median ages were 84 years (range 75 to 94) for the intervention group, 81 years (range 75 to 96) for the V group, and 82 years (range 76 to 92) for the NV group.
Recruitment	Through discharge prescriptions were presented in the hospital pharmacy (provided they met the inclusion criteria). These were three hospitals from the Crawley and Worthing district health authorities.
Setting	Hospital pharmacies.
Interventions/ Test/ Factor being investigated	Group A receiving home visits and counselling, group B which was the control and received visits only (called V group), and group C was the control group that received traditional pharmaceutical services with no visits except for the beginning and the end of the study (NV group). Structured patient interviews were conducted during the domiciliary visits and consisted of six sections: patient information; drug knowledge; patient dexterity; abbreviated mental test; medication management; and compliance with medication regimen. Patients were seen during 12 months. Other strategies were employed for improving patient compliance: emphasising the importance of compliance; giving clear instruction on the exact treatment regimen, in writing if necessary; arranging dosing times to fit into the patients daily routine; recognising the patients effort to comply at each visit; and simplification of the regimen if necessary.
Comparisons	Between treatments.
Length of Study/ Follow-up	Up to 12 months.
Outcome measures studied	No. of drugs prescribed and purchased; drug knowledge scores; patient dexterity scores; abbreviated mental test scores; medication management; compliance with medication regimen; contact with gp and health workers.
Results	At each visit there were significant differences between the groups in terms of distribution of patients at the various levels of compliance ($p<0.001$).Compliance was higher at 3 months and 12 months for the intervention group compared to the other control groups ($p<0.001$), despite the low compliance value for the intervention group at the 12 month visit. Patients in the intervention group who increased their compliance rates between visits also increased their drug knowledge scores ($p<0.005$). Mean scores for drug knowledge did not differ significantly between the groups at any of the visits, although the mean score for the intervention group increased significantly between the initial and the two weeks visits ($p=0.001$). There were no changes for patient dexterity scores between groups at any point of the study. The intervention group did not report any significant changes in abbreviated mental test score, but control V group showed a 0.2 fall and control group NV a 0.4 rise in score, both statistically significant at $p=0.05$. Contacts with GP and health workers was lower for the intervention group than for the

control (V) in each of the four time periods (p<0.01).

There was a significant decrease in in the number of patients in the intervention group storing their drugs inappropriately (p<0.01); no statistically significant decrease was seen in any of the control groups.

The proportion of patients in the intervention group hoarding drugs significantly decreased from 61% to 0 at the two weeks and one month visits (p<0.001).

Safety and adverse effects None reported.

Does the study answer the question? Patients in the intervention group had better compliance, better drug storage practices and a reduced tendency to hoard drugs, and required fewer GP consultations than patients in the control groups.

Effect due to factor in study? Yes.

Consistency of results with other studies?

Directly applicable to guideline population? Relevant.

Internal Validity

Bernsten C;Bjorkman I;Caramona M;Crealey G;Frokjaer B;Grundberger E;Gustafsson T;Henman M;Herborg H;Hughes C;McElnay J;Magner M;van Mil F;Schaeffer M;Silva S;Sondegaard B;Sturgess I;Tromp D;Vivero L;Winterstein A;

Improving the well-being of elderly patients via community pharmacy-based provision of pharmaceutical care

Ref ID 17983 2008

Study Type Randomised Controlled Trial **Funding** European Commission funding.

Number of participant A total of 1290 intervention patients and 1164 control patients were recruited.

Inclusion/Exclusion Criteria Patients were 65 years or older, taking 4 or more prescribed medications and oriented with respect to self, time and place. They were community dwelling and regular visitors to a recruited community pharmacy.
Patients were excluded if they were housebound or resident in a nursing/residential home. Identification of patients was performed via a personal approach by the pharmacy.

Patient Characteristics Median age was 74 (s.d=8) for the intervention and control group. 42.1% were male and 57.9% were female in the intervention group. 42.7% were male and 57.3% were female for the control group.

Recruitment Study sites were selected using the responses of community pharmacists who expressed interest in participating in the research, following publicity via mailshots, advertisments in pharmaceutical publications and at professional meetings.

Setting Community pharmacies.

Interventions/ Test/ Factor being investigated Pharmaceutical care program by the trained pharmacists compared to usual care which was normal services provided to the recruited patients.
Pharmacy interventions included: 1) educating the patient about their drug regimen and their condition; 2) implementing compliance-improving interventions such as drug reminder charts; 3) rationalising and simplifying drug regimens in collaboration with the patients GP. This was a continuous process throughout the 18 months of the study.

Comparisons Between treatments.

Length of Study/ Follow-up	Up to 18 months.
Outcome measures studied	Hospitalisations, quality of life, satisfaction with service provided, clinical signs and symptom control, knowledge of medicines, contact with GPs, prescription and nonprescription drug use.
Results	Seven countries were involved: Denmark, Germany, The Netherlands, Northern Ireland, Portugal, Republic of Ireland, and Sweden. Drop-outs were higher in some countries that others, however most withdrew in the first 6 months. Those who withdrew from the study were significantly older ($p<0.05$) and reported poorer quality of life at baseline ($p<0.05$). Generally, the programme had some positive effects on humanistic health outcomes such as satisfaction with treatment, and sign and symptom control, and on economic outcomes, but had less impact than anticipated on drug therapy, drug knowledge and compliance with medication. An analysis of changes in compliance during the study indicated that at 18 months a significantly higher proportion of the intervention patients changed from being noncompliant to compliant compared with the control groups ($p=0.028$). Intervention patients rated the services provided higher that the control at 6 and 18 months ($p<0.05$). There was a small statistically significant increase in satisfaction in the intervention group over time (baseline vs 12 months $p=0.039$).
Safety and adverse effects	None.
Does the study answer the question?	It is a large-scale multicentre study that assessed the effects of a pharmaceutical care programme by community pharmacists to elderly. Intervention patients reported better control of their conditions. The new service was well accepted by the intervention patients and patient satisfaction with the services improved during the study.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant.
Internal Validity	

Hanlon JT;Weinberger M;Samsa GP;Schmader KE;Uttech KM;Lewis IK;Cowper PA;Landsman PB;Cohen HJ;Feussner JR;

A randomized, controlled trial of a clinical pharmacist intervention to improve inappropriate prescribing in elderly outpatients with polypharmacy

Ref ID 5012 1996

Study Type	Randomised Controlled Trial	**Funding**	Grant from the National Institute on Aging; An Academic Award from the National Institute on Aging; The Claude D. Pepper Older Americans Independence Center.

Number of participant	208 in total were randomised, 105 to the intervention group and 103 in the control group.
Inclusion/Exclusion Criteria	Inclusion: 65 years or over, evidence of polypharmacy (5+ medicines prescribed), received primary care in the GMC. Exclusion: Residents of a nursing home, cognitively impaired (mental status questionnaire) were excluded unless a caregiver was available for involvement in

	intervention.
Patient Characteristics	Mean values: Mostly male 99%, white 77%, 70 years old, married (65.7% intervention, 85.4% control), compliance rates of 73.5%, medication knowledge 80.5%, 10 years of education, 9 chronic medical conditions, 8 prescribed medications, 3 medications recommended.
Recruitment	Those with regular scheduled medications by a Veterans Affairs physician receiving primary care in a General Medicine Clinic; computerized and manual chart audits identified participants.
Setting	The Durham Veterans Affairs Medical Centre GMC.
Interventions/ Test/ Factor being investigated	Usual care plus pharmacist intervention. Before the patients visit to the GMC the clinical pharmacist monitored their drug therapy outcomes by reviewing their medical records and medication lists and ascertaining their current medication use, drug-related problems and evaluating their needs by applying the Medication Appropriateness Index. This was then reported to the physician. After the visit to the physician the pharmacist educated the patient on the drug-related problems and encouraged compliance with strategies such as medication reminder packages or calendars and written patient materials. Reviewed principles of safe medicine use and the importance of discussing medications with their physicians.
Comparisons	Pharmacist intervention versus usual care (which included a clinical nurse reviewing patients current medications before their visit, the physician visit and then the nurse reviewing and medication modifications).
Length of Study/ Follow-up	Followed up for one year (Last telephone interview between 11.5 to 13 months after randomisation).
Outcome measures studied	Prescribing appropriateness; Health-related quality of life; Potential adverse drug events that had occurred during the past year; Patient compliance and knowledge; Patient satisfaction at end of year.
Results	Compliance was assessed by patient self-report. There were no significant differences between the groups at the end of the follow-up period with regard to medication compliance (77.4% of intervention group and 76.1% of control group complied, p=0.88) knowledge, number of medications or patient health care satisfaction. More control patients experienced adverse drug events than the intervention group (40% vs 30.2%, p=0.19). Written recommendations were enacted more (by physicians) in the intervention group than the control group (55.1% vs 19.8%, p<0.001).
Safety and adverse effects	None reported.
Does the study answer the question?	It does partially, however it should be noted that the pharmacist intervention involves not only medication review but medication education and compliance strategies. The study did not find that these increased compliance to medication, therefore this suggests that an intervention which included pharmacist medication review did not have an effect on compliance to medication.
Effect due to factor in study?	Yes
Consistency of results with other studies?	
Directly applicable to guideline population?	Patient population is of interest for this guideline the intervention is partially comparable to the intervention of interest.
Internal Validity	Subjects not blinded to treatment.

Nazareth I;Burton A;Shulman S;Smith P;Haines A;Timberal H;

A pharmacy discharge plan for hospitalized elderly patients-a randomized controlled trial

Study Type	Randomised Controlled Trial	**Funding**	The National Health Service research and development programme.

Number of participant	362 patients, 181 to the intervention and control group.
Inclusion/Exclusion Criteria	Inclusion: over 75 years and taking four or more medicines at discharge and living in the hospitals catchment area. Exclusion: not speaking English or too ill.
Patient Characteristics	Mean age of participants 84 years in both intervention and control group (s.d=5.2 and 5.4 respectively). 62% of intervention and 66% of control group were women. 97% were white. Each patient had a mean of three chronic medical conditions and on mean 6 drugs (s.d=2).
Recruitment	Patients discharged from three acute general and one long-stay hospital in a health authority in central London.
Setting	Community pharmacists visited at home.
Interventions/ Test/ Factor being investigated	Pharmacist check for discrepancies with the medicine taken and those prescribed. Assessing understanding and adherence to the medication regimen and intervened when appropriate. Counselling patients/carers on correct dosage, disposing of excess medicines and liaising with gps.
Comparisons	Intervention vs control group - who were discharged with standard procedures - a discharge letter to the gp indicating the diagnosis, investigations and current medications, no pharmacist review of medication or follow-up.
Length of Study/ Follow-up	At 3 and 6 months.
Outcome measures studied	Primary outcomes: re-admission to hospital in follow-up period. Secondary outcomes: number of deaths, attendances at hospital outpatient clinics and gps. well-being, satisfaction with service, adherence to and knowledge of medication, hoarding of meds.
Results	There was no significant differences in any of the outcome scores except patient knowledge. There was no significant difference in the mean adherence scores of those re-admitted to hospital and the rest of the subjects at 3 and 6 months. At 3 months: adherence to medicines: 79 (52%) mean 0.75 (s.d=0.3) in the intervention group and 72 (48%) mean 0.75 (s.d=0.28) for the control group. 95% CI 0. At 6 months: adherence to medicines: 60 (45%) mean 0.78 (s.d=0.3) in the intervention group and 58 (43%) mean 0.78 (s.d-0.3) in the control group. 95% CI 0.
Safety and adverse effects	None.
Does the study answer the question?	Yes. Adherence to medication did not increase from a pharmacy discharge intervention with elderly patients.
Effect due to factor in study?	The methodology was adequately addressed apart from blinding was not reported and they did not recruit to the statistical power they required. Therefore it is unsure that the effect is due to the intervention.
Consistency of results with other studies?	
Directly applicable to guideline population?	Yes.
Internal Validity	Blinding

Sturgess IK;McElnay JC;Hughes CM;Crealey G;

Community pharmacy based provision of pharmaceutical care to older patients

Ref ID 2488 2003

Study Type	Randomised Controlled Trial	**Funding**	Supported by (no details of type of support given) Northern Pharmacies Trust, Northern Ireland and European Commission under the BIOMED 2 programme.

Number of participant	Total sample: 191 patients. Intervention group: 110, Control group: 81.
Inclusion/Exclusion Criteria	Inclusion: elderly patients (? 65 years) who were community dwelling, taking four or more prescribed medications, regular visitors to the participating community pharmacy and orientated to self, time and place were eligible. Exclusion: Patients were excluded if they were housebound or living in a nursing/residential home.
Patient Characteristics	Age (years): intervention group: 73.1 (s.d=5), control group: 74.2 (s.d=6.3). Gender (% male/% females): intervention group: 36.4/63.6, control group: 39.0/61.0. There were some differences between the two groups at baseline in mean number of prescribed medications (higher in control group, p=0.05) and SF-36 domains of mental health (intervention group higher score, p=0.05), physical functioning (intervention group higher score, p=0.05) and vitality (intervention group higher score, p=0.05).
Recruitment	
Setting	10 pharmacies in Northern Ireland.
Interventions/ Test/ Factor being investigated	Note: Only half of the sites saw the project through to completion (3 intervention (from five randomised to deliver intervention) and 2 control (also from 5 original)). Delivered by community pharmacists. Intervention pharmacists assessed patients to identify drug-related problems. A number of information sources were used by intervention pharmacists during this assessment procedure including: the patient (via informal questioning), the patient's gp, study questionnaires and computerised medication records. During the assessment, pharmacists were asked to document any identified drug-related problems and to form with the patient an intervention and monitoring plan e.g. education, implementation of adherence improving strategies. Pharmacists visited patients at home to assess storage of medicines where problems were identified.
Comparisons	Pharmaceutical care programme (PCP) (intervention) v usual care. Intervention vs Control.
Length of Study/ Follow-up	18 months.
Outcome measures studied	Precise Items used to measure adherence not given (given in a separate publication) although self report scale and refill compliance rates are reported in the analysis. All measurements taken at 6, 12 and 18 months.
Results	Adherence: Self reported compliance: between-group analysis at each assessment point indicated that a significantly higher proportion of intervention patients were compliant with their medicine at 12 (intervention group: 40.4%, control group: 24.4%) and 18 (intervention group: 47.3%, control group: 14.7%) months compared to control patients ($p<0.05$) (6 months: intervention group: 34.5%, control group: 29.4%). Analysis of change in compliance during the study (change in compliance status compared to that reported at baseline) showed that a significantly higher proportion of intervention patients changed from non-compliant to compliant compared to control patients (intervention 13.4% vs control 9.1%) and a significantly higher proportion of control patients changed from compliant to non-compliant

compared to intervention patients at 18 months (control 36.4% vs intervention 4.5%). Refill compliance results: between-group analysis at each assessment point indicated that a significantly higher proportion of intervention patients were compliant with their medicines at six months (intervention group: 46.2%, control group: 19.1%) compared to control patients (p = 0.02) (results 12 months: intervention group: 40.4%, control group: 25.0%. 18 months: intervention group: 40.0%, control group: 40.6%). Analysis of change in compliance during the study (change in compliance status compared to that reported at baseline) showed no differences between control and intervention patients.

Other outcomes: Health related quality of life: During the study there was a trend for intervention patients' quality of life to decline over the 18 months whilst that of control patients appeared to significantly improve in some of the SF-36 dimensions (physical functioning: intervention group change: ?6.83, control group: +7.14 and vitality, intervention group change: ?2.26, control group: +7.24, p<0.05), however, these findings were largely driven by patients attending one control site pharmacy who showed marked improvements in SF-36 scores over time. There was no significant difference between the two groups in terms of the number of hospitalizations, the extent of prescription drug use (after baseline) and knowledge about medications. Longitudinal analysis indicated that intervention patients were taking significantly more prescribed medicines at 6 (6.13, s.d=2.32), 12 (6.63, s.d=2.72) and 18 months (6.20, s.d=2.32) compared to baseline (5.87, s.d=1.86; p<0.05), whilst that of control patients remained constant. Problems with medications: There were no significant differences between control and intervention patients during the first 12 months of the study, however, during the last 6 months, intervention patients (0.90, s.d=1.27) reported significantly fewer problems with their medicines compared to control patients (2.09, s.d=2.38) (p<0.05). There were no differences between the two groups in their reported contact with nurses, however, there were differences in GP contacts and contact with a specialist during the study. Intervention patients reported higher numbers of contacts with their GP during the first (0–6) (2.89, s.d=4.44) and second (7–12) (2.97, s.d=2.56) six month periods than control patients (0-6: 1.88, s.d=2.55. 6-12: 1.97, s.d=4.25) (p<0.05). In addition, intervention patients reported more contact with a specialist during the second (7–12) (0.89, s.d=1.25) and third (13–18) (0.87, s.d=2.60) six-monthly periods compared to control patients (7-12: 0.16, 0.50. 13-18: 0.10, s.d=0.31) (p<0.05).

Safety and adverse effects None.

Does the study answer the question? Yes. The intervention helped to increase adherence according to the majority of analysis undertaken.

Effect due to factor in study? Fairly. Baseline differences between groups a potential confounding factor.

Consistency of results with other studies?

Directly applicable to guideline population? Relevant.

Internal Validity

Zermansky AG;Petty DR;Raynor DK;Lowe CJ;Freemantle N;Vail A;

Clinical medication review by a pharmacist of patients on repeat prescriptions in general practice: A randomised controlled trial

Ref ID 7544 2002

Study Type Randomised Controlled Trial **Funding** Health Technology Assessment Programme.

Number of participant 1188 in total. 608 in the intervention group, 590 in the control group.

Inclusion/Exclusion Criteria	Inclusion: 65 years or older on repeat medication. Exclusion: in a clinical trial, a residential or nursing home or having a terminal illness.
Patient Characteristics	Data not found for ethnicity but the study was mainly a Caucasian population born in the UK.
Recruitment	A note was attached to their last prescription before their due date. This said to book an appointment with the practice receptionist.
Setting	Leeds gp practices with 4 or more partners.
Interventions/ Test/ Factor being investigated	Pharmacist medication review to make recommendations on medication changes.
Comparisons	Between intervention and control group.
Length of Study/ Follow-up	12 months.
Outcome measures studied	Primary outcome - number of repeat medication changes for each patient. Secondary outcomes - effect on the medication costs; whether medication review taken place (intervention group vs control group).
Results	The mean number of individual medication changes per patient were 2.2 intervention group vs 1.9 in control group (0.31, 95% CI 0.06 to 0.57, p=0.02. The number of repeat items rose in both groups but was significantly less for intervention group (0.2 mean, SD 1.55), control (0.4, s.d=1.53, difference -0.2, 95% CI -0.4 to -0.1). Medication costs rose in both groups but the rise was significantly less in the intervention group £1.80 mean compared to £6.53 mean for control group, difference was £4.75 per 28-day month. Saving of £61.75 per patient per year. 97% of intervention group had medication reviews compared with 44% of the control group. The most common recommendation was to stop the medicine or removal of a redundant item from a list.
Safety and adverse effects	None.
Does the study answer the question?	It helps answer about the effectiveness of medication review but adherence is not a main outcome measured. Therefore it will be included in the introduction for medication review but not as an evidence narrative on medication review increasing adherence.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Intervention very relevant for guideline but not adherence outcomes.
Internal Validity	No blinding

Grading: 1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias*

Chisholm MA;Mulloy LL;Jagadeesan M;DiPiro JT;

Impact of clinical pharmacy services on renal transplant patients' compliance with immunosuppressive medications

Ref ID 61 2001

Study Type	Randomised Controlled Trial	**Funding**	Grant from the Carlose and Marguerite Mason Trust Fund.

Number of participant	24 in total. 12 in the intervention group and 12 in the control group.
Inclusion/Exclusion Criteria	Inclusion criteria: Aged 18 to 60 years; had only one kidney transplant; received follow-up care at MCG for at least one year after transplant; prescribed same immunosuppressant for at least one years since transplant; received immunosuppressant from MCG Outpatient Pharmacy for whole year.
Patient Characteristics	75% were male, and 58.3% Caucasian, 37.5% African-American and 1 Hispanic. 33% had living-related donor kidneys, 67% had cadaveric kidneys. The mean age was 49 (s.d=10.2). Twenty one of patients prescribed cyclosporine and the other 3 had tacrolimus.
Recruitment	All patients who had a renal transplant at MCG from February 1997 to January 1999.
Setting	Medical College of Georgia Hospital and Clinics.
Interventions/ Test/ Factor being investigated	In addition to usual care, patients received direct patient care clinical services from a clinical pharmacist. They obtained medication histories and reviewed medications with emphasis on optimising medication therapy to achieve desired outcomes and to minimse adverse events. They also made recommendations to the nephrologists to get the desired outcomes. The pharmacists counselled patients on ther medication and instructed how to take correctly (verbally and/or in writing). The patients were encouraged to call the pharmacist with any questions or concerns. The patients understanding of their medication was assessed. The medication reviews and histories were conducted monthly for the intervention group. Compliance enhancement principles were used at visits or by phone.
Comparisons	Between the intervention group and the control group who received usual care but had no clinical pharmacist interaction.
Length of Study/ Follow-up	12 months.
Outcome measures studied	Compliance rate, directly observed by immunosuppressive serum concentrations.
Results	At end of 12 months the mean compliance rate was 96.1% (s.d=4.7%) for the intervention group and 81.6% (s.d=11.5%) for control group, $p<0.001$ statistically significant. For 6 of the 12 months 6-8 and 10-12) there were differences in compliance rates (64-100% for control group and 89 to 100% for intervention group) always with the intervention group higher rates ($p<0.05$). Duration of compliance differed also, with the intervention group remaining 75% compliant each month whereas only 33.3% of the control group remained compliant ($p<0.05$). Intervention patients had a greater achievement of 'target' serum concentrations than control patients ($p<0.05$).
Safety and adverse effects	Not mentioned.

Does the study answer the question?	Yes. Patients who received clinical pharmacy services along with routine traditional patient care services had better immunosuppressive compliance than patients who only received traditional patient care services. The mean compliance rate for intervention was higher than the mean for the control group. Those in the intervention achieved higher achievement of the target immunosuppressive serum concentrations than the control group. The pharmacist intervention is beneficial for enhancing medication compliance in post-transplant patients.
Effect due to factor in study?	The study was very small, with only 24 participants and the methodology was not very strong so it can not be certain that the effect is due to the study intervention. Although all measurements were consistently higher for the intervention than the control group.
Consistency of results with other studies?	
Directly applicable to guideline population?	Not only medication review but includes counselling, compliance-enhancing techniques. Not generic medication review.
Internal Validity	Selection bias; performance bias; small sample;

Grymonpre RE;Williamson DA;Montgomery PR;

Impact of a pharmaceutical care model for non-institutionalised elderly: Results of a randomised, controlled trial

Ref ID 2175 2001

Study Type	Randomised Controlled Trial	**Funding**	Not mentioned. Authors are from a University and one was a pharmacy consultant.

Number of participant	135 in total, 69 in the intervention group and 66 in the control group.
Inclusion/Exclusion Criteria	Inclusion criteria: 65 years or over, non-institutionalised, taking two or more prescribed or non-prescribed medications, and providing signed consent form.
Patient Characteristics	Mostly female (75% intervention vs 83% control, p=0.254); aged 76.9 (s.d=8.4) and 77.2 (s.d=8.8), p=0.786. All were Caucasian, Most lived alone 61% vs 77%, p=0.018)
Recruitment	Clients who presented at a clinic or were referred by Home Care programme.
Setting	A community-based health clinic.
Interventions/ Test/ Factor being investigated	Volunteers and staff were trained to conduct a comprehensive medication review and this is given to the pharmacist to identify and document potential and actual drug-related issues and to address the issues with the patient and their physician. This included their use of prescribed and non-prescribed medicines, social drugs, home remedies, their regime, their adherence and their communication with g.ps, any problems or side effects with drugs. The recommendations were given in a letter to physicians and were reviewed for appropriateness by a consultant geriatrician before given to the physician. The clients were followed up by the pharmacist when required to monitor therapeutic endpoints and sort out any problems that had arisen. The issues identified by the pharmacist were tested individually by a pharmacist and nurse to see if resolved. Physicians gave their opinion of the pharmacist's letter through a survey.
Comparisons	Between intervention group and control group. The control group received a detailed home medication history but were reviewed by a different pharmacist who referred clients to their usual pharmacist and answered any queries.
Length of Study/ Follow-up	No data given.

Outcome measures studied	Number of drugs taken, drug knowledge, adherence to drug therapy, cost of prescribed medicines, number of symptoms reported from home medication history, response of physicians' survey.
Results	The mean number of mediations adhered to at follow-up was 87 (+/-46) for the intervention and 85 (+/-41) for the control group, p=0.895, showing no significant difference in adherence.
Safety and adverse effects	If the pharmacist thought the clients were at risk of 'life-threatening' drug-related problems in the control group they were withdrawn from the study.
Does the study answer the question?	Yes. A medication review and recommendations given by the pharmacist to physicians did not change adherence or drug knowledge between the intervention and control group.
Effect due to factor in study?	The methodology is lacking in that the two groups may have been treated similarly and so a difference between the two groups would not be evident.
Consistency of results with other studies?	
Directly applicable to guideline population?	The intervention is comparable to the intervention and population of interest as it is medication review and measures adherence. However the medication history collection is conducted by a lay person rather than the pharmacist (who conducts the review).
Internal Validity	Attrition bias; Not blinded; group contamination.

Lipton HL;Bird JA;

The impact of clinical pharmacists' consultations on geriatric patients' compliance and medical care use: a randomized controlled trial

Ref ID 1627 1994

Study Type Randomised Controlled Trial **Funding** John A Hartford Foundation in New York City.

Number of participant	1,383 eligible patients approached, 10% refused, 37% discharged before deciding whether or not to enrol. 52% of patients who were eligible and approachable were enrolled. After attrition (6.5%) 706 patients remained in the trial.
Inclusion/Exclusion Criteria	Inclusion: aged 65 years or over; covered by Medicare; admitted to a non-psychiatric ward; resided within 35 miles; English speaking (or proxy); mental competent (or proxy); access to telephone; 3/4 medications prescribed for a chronic condition; Exclusion: those discharged to a nursing home or hospice;
Patient Characteristics	Intervention vs control groups: Mean age: 74 both groups MediCal recipients: 9% both groups More than 12 years education: 52% vs 44% (p=0.03) All patients were discharged from hospitals. No mention of sex, ethnicity, comorbidity, disease status given.
Recruitment	Daily hospital records were looked at for eligible patients. At least one attempt was made to approach every patient meeting the eligibility criteria.
Setting	Community hospital in San Francisco Bay, USA.
Interventions/ Test/ Factor being investigated	Two clinical pharmacists' provided a drug consultation service for geriatric patients and their physicians. Intervention: Pharmacists' reviews of the hospital records and drug regimens of the experimental, and consultations with the patients and their physicians. Both control group and experimental group patients were given booklets when discharging from hospital, to record medication information eg drug purpose, dosage and schedule. After review of the records to determine the patient's (in intervention group) clinical condition and to assess appropriateness of prescribing, the pharmacist conducted a face-to-face consultation with the intervention patients to

	discuss the purpose and use of their medications and any potential drug-related problems. Follow-up was about 15 minutes in duration. 85% of the postdischarge meetings were by telephone and the rest were in the pharmacists' office or patient's home. If significant problems were detected the patients were provided with a consultation with their physician. The pharmacists promoted the use of fewer medications and simplified regimens where appropriate – by telephoning physician to recommend discontinuation of a prescribed product or by recommending directly to the patient discontinuation of a non-prescribed product. Patient compliance was assessed by structured telephone interviews with a subsample of experimental and control patients at 6-8 weeks postdischarge and again at 12-14 weeks postdischarge.
Comparisons	Intervention vs usual care.
Length of Study/ Follow-up	Follow-up consultations were given at 1 week, 2-4 weeks, 2 months and 3 months after discharge from hospital. 6 months.
Outcome measures studied	Medical care utilisation; Patient compliance; Knowledge, regularity, frequency, dosage, missed doses; polypharmacy.
Results	T-test results showed that the intervention did not have an impact on subsequent medical care utilisation and expenditures. No significant differences found for the mean number of drugs taken and the complexity of the regime at 6-8 weeks but there was a significant change at 12-14 weeks. Intervention group were taking significantly fewer medications than controls (5.16 vs 6.75, p<0.001). The intervention also had an impact on the second measure of regimen complexity, average daily doses per drug (p=0.02). Compliance results: 274 patients were selected for this sub-study. No significant demographic differences between this sample and the overall sample were found. 233 (124 intervention and 109 control) were interviewed for the first assessment and 206 (108; 98) for the second assessment. During the first assessment (6-8 weeks) intervention group had significantly higher mean compliance 94.4 (s.d=9.4) vs 91.4 (s.d=11.6) (p=0.035). This became non-significant (p=0.334) when knowledge was removed from the analysis. At 2nd assessment the interventions impact on knowledge was stronger (p=0.001). By this time the intervention had an effect on patients' drug use 96.3 (s.d=10.2) vs 91.2 (s.d=9.6) (p<0.001). With 92% of intervention vs 77% of control patients not missing any dose of their medications (p<0.001). This was still significant whether or not knowledge of the purpose of the medication was included.
Safety and adverse effects	None reported.
Does the study answer the question?	Clinical pharmacist's consultations can improve geriatric patients' drug regimens and compliance. The need for replication among large cohorts of patients at high risk. Shows the value of sustaining the clinical pharmacist intervention for some time.
Effect due to factor in study?	No.
Consistency of results with other studies?	
Directly applicable to guideline population?	Yes
Internal Validity	Allocation concealment. Difference in the group.

Lowe CJ;Raynor DK;Purvis J;Farrin A;Hudson J;

Effects of a medicine review and education programme for older people in general practice

Ref ID 7537 2000

Study Type Randomised Controlled Trial **Funding** Grant from the Department

	of Health under the Pharmacy Practice Research Enterprise Scheme.
Number of participant	161 patients in total: 77 in the intervention group and 84 in the control group.
Inclusion/Exclusion Criteria	Inclusion criteria: 65 years or older; taking 3 or more drugs. Exclusion criteria: lived in nursing or residential care; dependent on another to administer medicine; terminal illness with life expectancy less than one year.
Patient Characteristics	Intervention group: mean age 77.5 (65-96), mainly female 67%, living with spouse or relative 55% and 4 mean medicines scheduled (2-8). Control group: mean age 75 (65-88), 67% female, 57% living with spouse or relative, 4% mean (1-10) medicines scheduled.
Recruitment	They were recruited sequentially from a list of patients in the practice 65 or over.
Setting	General practice in suburbs of Leeds.
Interventions/ Test/ Factor being investigated	An investigator visited intervention and control participants and filled in a structured questionnaire regarding their medicines, medicines taken and understanding of their purpose. The investigator assessed the intervention group participants' ability to take their medications, then reported the findings to doctors where there was need to reduce dosage and discontinue medication. They also liaised with pharmacist for modifications to medicine containers. At the second visit they gave 1 months supply of medication and removed any other prescribed medications. They discussed the regimen and explained the right way to take medications and purpose and made a reminder chart. At 3 weeks follow-up another months supply was given and the patients were asked to describe the medicines they took and their purpose, and the medications left over from the last visit were counted.
Comparisons	Comparison made between intervention group and control group - who did not receive the intervention of medication review, education and discussing medication and problems.
Length of Study/ Follow-up	Followed up after one month, then after 3 weeks.
Outcome measures studied	Knowledge of medicines, compliance with medicines - through a structured questionnaire and tablet count and patient report.
Results	The mean compliance score was 91.3% for intervention group (95% CI 89% to 94%) and 79.5% for the control group (95% CI 75% to 84%), p<0.0001. At first visit 58% of intervention group correctly described the purpose of medication, compared to 67% of control these numbers were 88% of intervention and 70% of control group by the third visit, between groups the difference was significant (p=0.0001). 47% of patients had a fall in the mean number of medicines to take from 4.1 (95% CI 3.8-4.5) to 3.9 (95% CI 3.5 to 4.2) the mean difference was -0.26 (95% CI p=0.003).
Safety and adverse effects	Approval given by Local Research Ethics Committee and informed consent from patients.
Does the study answer the question?	Yes this does answer the key question. The use of a medicine review and education increased compliance for the intervention group compared to the control group.
Effect due to factor in study?	Uncertain as to whether there may have been bias introduced into the study. The statistical power of the study was high. The overall effect is possibly due to the study intervention.
Consistency of results with other studies?	

Directly applicable to guideline population?	Intervention is under 6 months so is not exactly the requirement for the guideline but the intervention involves medication review as the intervention and compliance as an outcome so this is of direct interest to guideline.
Internal Validity	Selection bias, performance bias

Sookaneknun P;Richards RM;Sanguansermsri J;Teerasut C;

Pharmacist involvement in primary care improves hypertensive patient clinical outcomes

Ref ID 1592 2004

Study Type	Randomised Controlled Trial	**Funding**	Research grand from Chiang Mai University, Thailand.

Number of participant	235 total patients: 118 in treatment group, 117 in control group.
Inclusion/Exclusion Criteria	Inclusion: over 18 years; newly diagnosed during the pre-test period with hypertension; average DBP over or equal to 90 mm Hg; or average SBP over or equal to 140 mm Hg Exclusion: secondary causes of hypertension; unable/unwilling to return for appointments; planned to move/family member in study; SBP over 210 mmHg or DBP over 115mg Hg; severe complicating disease.
Patient Characteristics	76 women and 42 men in the treatment group; 84 women and 33 men in the control group p value 0.224; aged 63 (s.d=9), p=0.982; hypertension 57 vs 54; Hypertension with diabetes 39 vs 45; hypertension with target organ damage 13 vs 7; hypertension with diabetes and target organ damage 9 vs 11; p=0.474.
Recruitment	Databases from hospital and 2 PCUs screened for patients diagnosed as hypertensive. Or from medical records.
Setting	Mahasarakham Uni community pharmacy, Thailand
Interventions/ Test/ Factor being investigated	Pharmaceutical intervention: 30-50 minute face to face interview - assessed understanding of medications, counselled on use of medications, assessed adherence and lifestyle habits, reviewed for adverse events due to DRPs; identified, resolved and prevented DRPs; Pharmacist recommendations for regimen changes made to physicians and on medical record; also looked at lifestyle eg exercise; education leaflets and diary to record lifestyle presented.
Comparisons	Pharmacist intervention versus usual care (no pharmacist involvement).
Length of Study/ Follow-up	6 months.
Outcome measures studied	Primary outcomes: Blood pressure control, blood pressure difference. Secondary outcomes: adherence.
Results	Primary outcomes: significant reduction in both systolic and diastolic BP compared with the control group (p=0.037, 0.027, respectively). Proportion of patients whose BP stabilised was higher in the treatment group (p=0.017). Secondary outcome: the treatment group showed significantly better adherence 70% with good adherence in the treatment group compared to 60% of the control group and 40% showing poor adherence in intervention compared to 48% of control group (p=0.014) at the end of the study.
Safety and adverse effects	None mentioned
Does the study answer the question?	Yes. Adherence was increased with the pharmacists involvement.

Effect due to factor in study?	The study power was 90%, the target size of the study sample was 95 patients, with 30% added to allow for drop-outs. Yes the effect is likely to be due to the study intervention.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant as secondary outcome was change in adherence, from pharmacist involvement, which included medication review.
Internal Validity	Randomisation, concealment allocation.

Taylor CT;Byrd DC;Krueger K;

Improving primary care in rural Alabama with a pharmacy initiative

Ref ID 46 2003

Study Type	Randomised Controlled Trial	**Funding**	Supported by the ASHP Research and Education Foundation.

Number of participant	69 in total, 33 in the intervention arm and 36 in the control arm.
Inclusion/Exclusion Criteria	Adults (over 18s) receiving care within the clinics. Those who were at high risk of medication-related adverse events (five or more medications prescribed, 12 or more doses per day, four or more medication changes in the last year, three or more concurrent diseases, previous medication compliance, drugs that require therapeutic monitoring). Exclusion criteria: significant cognitive impairment, history of missing office visits, scheduling conflicts or life expectancy under a year.
Patient Characteristics	Most patients were female 63.6% in the intervention group and 72.2% in the control group (p=0.445), Most were white 60.6% vs 61.1% (p=0.966), and mean age was 64.4 and 66.7 years respectively (p=0.467) and the majority were married 75.8% vs 72.2 (p=0.935) with 12 years mean education in both groups. They were attending community-based practices. Taking on average six medications each.
Recruitment	Identified by pharmacist evaluation of clinic medical records (manual and computer) from physician's offices, of the three community-based family medicine clinics.
Setting	GP offices, Alabama, USA.
Interventions/ Test/ Factor being investigated	Four pharmacists joined the clinics to give medication reviews. The intervention group received usual medical care, as did the control group but additionally received pharmaco-therapeutic interventions from a pharmacist during office visits. The pharmacists purpose was to prevent or identify and resolve problems with drug therapy. They evaluated a drug therapy's indication, effectiveness, and dosage as well as the correctness and practicality of directions, drug-drug interactions, drug-disease interactions, therapeutic duplication, the duration of treatment, untreated indications, and expense. They reviewed medial records for medication-related problems, documented problems accurately and examined medication history to determine compliance and complications with medication and gave individualised patient education reviewing the disease, lifestyle modifications and basic drug information. Therapeutic recommendations were made to the physicians and they made follow-up visits and gave more information or answered questions. Monitoring patients' responses to drugs and consolidating medication regimens, reducing dosage frequency, devising medication reminders and teaching techniques for using certain devices eg inhalers.
Comparisons	Between intervention and no intervention.
Length of Study/ Follow-up	12 months follow-up.

Outcome measures studied	Clinical outcomes: Hospitalisations and emergency department visits, hypertension, diabetes mellitus, dysipidemia, anticoagulation, quality of life. Prescribing appropriateness and medication misadventures: edication compliance and medication knowledge.
Results	The intervention group's percentage of patients with medication compliance scores of 80-100% increased by 15%, but there was no change for the control group. However there was no significant difference at 12 months between the groups (100% of patients in the intervention group versus 88.9 (s.d=6.3) of the control group had compliance scores of 80-100% at 12 months, p=0.115). At baseline this was 84.9% (s.d=6.7) and 88.9 (s.d=5.8) p=0.728 respectively. The most frequently cited reasons were: forgetting to take the medications (n=10), having too many to take (n=9), finding it hard to read or understand the directions (n=4) and too much trouble (n=4). Hospitalisations and Emergency Department visits decreased for the intervention group by 92% and 78% respectively, whereas the control group stayed constant. NB there was a much higher number of hospitalisations and ED visits in the intervention group than the control group at baseline 11 versus 24 hospitalisations and 6 versus 18 ED visits.
Safety and adverse effects	Not mentioned.
Does the study answer the question?	Yes There was increased compliance in the group who received the pharmacists' review of medications compared to the control group who received usual care. However this was not a significant difference in compliance at 12 months.
Effect due to factor in study?	It is unclear as there is no time period or statistical power given for the result that there was increased compliance in the intervention group, but there is for twelve months, which was non-significant. There was no concealment allocation so there may have been selection bias for the intervention group, although baseline scores were similar except for hospitalisation and ED admission which was higher in the intervention group, but then decreased significantly while the control group was constant.
Consistency of results with other studies?	
Directly applicable to guideline population?	Yes this intervention and population is directly comparable to those of interest for the guideline.
Internal Validity	Selection bias; self-reporting bias;

Health Economics Extraction for Question

Which interventions are effective in increasing adherence to prescribed medication?

No 1518 **Cost effectiveness of an adherence-improving programme in hypertensive patients**

Author: Brunenberg-Danielle EM;Wetzels-Gwenn EC;Nelemans PJ;Dirksen CD;Severens JL;Sto 2007
Henri EH;Schouten-Jan SG;Prins MH;de-Leeuw PW;Joore MA;

Relevance

Intervention: Medication events monitoring system (MEMS) plus adherence training

Comparison: usual care alone

Population: 164 hypertensive patients in the MEMS arm and 89 in usual care group with systolic BP >160mm Hg and/or diastolic >95mm Hg despite use of antihypertensive drug eligible. Adherence was defined as intake minimum 85% of days as prescribed.

Perspective: health care and societal

Study type: CUA

Methods: RCT

Health valuations: TTO

Cost components Healthcare utilization (intervention, drug, consultation etc) and patient borne medical costs (Health care perspective) as non-medical costs (societal perspective).

Currency: EURO

Cost year: 2002

Time horizon: 5 months

Discount rate: not applicable

Results-cost MEMS cost EUR26 per patient, but led to a saving of drug costs of EUR40. Reduction in drug costs is mainly due to percentage of patients with drug additions or dose escalations in the MEMS arm. The mean total health care costs p amounted to EUR827 in the experimental group and 927 in the usual care arm. This is a non significant negative diff of EUR100 (95%CI -415 to 189).

Results-effectiveness At 5 months, 53.7% of MEMS patients had NBP compared to 50.6% in usual care (diff +3.1% 95CI -9.7 to 15.8). An incremental 0.003 QALYs were generated (95CI -0.005 to 0.01) in the experimental arm.

Results-ICER: From the healthcare perspective, electronic monitoring led to a cost saving of EUR100 and an additional 3.1% patie achieved NBP than in the usual care arm and was therefore dominating. From a societal perspective, and when usi as outcome measure, the incremental costs for the 5month programme of EUR47 resulted in an ICER of EUR15 667 QALY gained.

Result-Uncertainty: Univariate SA revealed considerable uncertainty. From a healthcare perspective, the probability that MEMS is cost e is estimated to be at maximum 77%. This dropped to 69% in sensitivity analysis. The effect sizes were small and not statistically significant, and results varied depending on what perspective and outcome measure was chosen. From t perspectives, the CEA bootstrap replicates on the CE plane covered the origin. The CEAC from the societal perspec suggests the very high uncertainty by ranging from 45% to 51% in the base case analysis, which did not improve in sensitivity analysis.

Source Funding: Public

Comments: The probability that this AEI in hypertensive patients is cost effective is at best moderate as there is considerable unc around the ICER. However, if in the UK the costs for electronic monitoring do not exceed those of a potential drug co saving, even a moderate increase in adherence would be cost effective. It appears uncertain as to whether certain e conclusions can be drawn from this analysis.

No 1514 **Cost effectiveness of long-acting risperidone injection versus alternative antipsychotic agents in with schizophrenia in the USA**

Author: Edwards NC;Locklear JC;Rupnow MF;Diamond RJ; 2005

Relevance

Intervention:	Long acting risperidone
Comparison:	Oral atypical antipsychotic agents (oral risperidone, olanzapine, quetiapine, ziprasidone, aripiprazole) and depot halo injections
Population:	Patients with schizophrenia in community dwelling who have previously suffered relapse requiring hospitalisation.
Perspective:	NHS (health care)
Study type:	CEA
Methods:	DECISION ANALYSIS
Health valuations:	NOT APPLICABLE
Cost components	Health care resource utilization estimates from literature and expert opinion. Pricing with published unit costs to deriv annd indirect medical costs.
Currency:	US$
Cost year:	2003
Time horizon:	One year
Discount rate:	Not applicable
Results-cost	Using long acting risperidone rather than an oral atypical antipsychotic agent is predicted to result in US$161 of heal savings per patient per year compared with oral risperdone and higher costs savings when compared with other age seems largely attributable to a reduction in relapse rates on the basis that compliance was imputed in the model as tripled with long acting risperidone.
Results-effectivenes	The model predicts that patients receiving long acting risperidone will have the best clinical outcomes in terms of the frequency and duration of relapses over the one year duration. For example, on long acting risperidone 26% of patie experience relapse requiring hospitalisation and 24% relapse not requiring hospitalisation. On haloperidol nearly two patients are predicted to have relapses requiring hospitalisation and over 60% not requiring hospitalisation.
Results-ICER:	This analysis predicts dominance of long acting risperidone over the comparators, with providing a health outcome improvement in terms of days of relapse averted whilst costing less over the time horizon of one year.
Result-Uncertainty:	Univariate sensitivity analysis was reported to have been robust. However, at the upper bound of the 95%CI for relap requiring hospitalisation there was an incremental cost for long acting risperidone with an ICER of US$821per days

hospitalisation averted compared to oral risperidone. The model seems also sensitive to the cost of hospitalisation as frequency rates of relapse.

Source Funding: Private

Comments: Compliance was assumed to be improved by long acting formula. It was estimated that a 20% point difference in cor would predict a 3.1 point improvement in the PANSS (Positive and Negative Syndrome Scale for Schizophrenia). Su improvement in turn stabilised patients so that a further 6.1 point in PANSS was achieved by further improved medic taking behaviour, and aversion of relapse.

The analysis seems of interest, but there are issues with its robustness. Values used in the SA seem relatively cons The short time horizon could be an issue and has not been thoroughly discussed. Quantifying treatment effect and q life losses in one measurement such as the QALY could considerably help interpret the findings from the analysis.

No 1513 **Clinical and economic outcomes of nonadherence to highly active antiretroviral therapy in patier human immunodeficiency virus**

Author: Munakata J;Benner JS;Becker S;Dezii CM;Hazard EH;Tierce JC;Munakata J;Benner JS;Becker S;Dezii CM;Hazard EH;Tierce JC; 2006

Relevance

Intervention: HAART, ideal adherence (based on RCT data)

Comparison: HAART, typical adherence (based on observational data)

Population: HIV positive, mean age 33 (20-60) with assumed portion of drugs consumed of 0.98 (0.95-1.0) if adherent and 0.55 (if nonadherent. Proportion of patients adherent patients in the typcial comparator arm 0.52 (0.3-0.88).

Perspective: SOCIETAL

Study type: CUA

Methods: DECISION ANALYSIS

Health valuations: n/a

Cost components Drug costs, annual costs per HIV and AIDS event, AIDS related end of life event, costs of treatment failure.

Currency: US$

Cost year: 2002

Time horizon: Lifetime horizon

Discount rate: 3% for costs and outcomes, varied between 0 to 5%.

Results-cost Lifetime discounted costs in the typical and ideal scenarios were $308 000 and $341 000, respectively. This gives ar incremental cost of $33 000.

Results-effectivenes People in the ideal scenario generated 10.2 QALYs per patient compared to 9.0 QALYs per patient in the typical sce This gives an incremental effect of 1.2 QALYs.

Results-ICER: The iCER resulted in $29 400 per QALY. This means that there is scope for an AEI. The authors calculated a wTP c value for an intervention to increase adherence. They conclude that $1 600 could be spent per patient to increase ac ideal levels, giving 15-33% reductions in treatment failure.

Result-Uncertainty: Univariate sensitivity analysis for all parameters, as well as multivariate SA for selected values. The analysis was de robust in SA.

Source Funding: Private

Comments: In severe diseases where adherence and related comorbidities are a big issue, adherence improving interventions m effective. Given that there are interventions that are effective in increasing adherence, this analysis found that $1 60(patient could be spent.

No 1512 **The economic implications of non-adherence after renal transplantation**

Author: Cleemput I;Kesteloot K;Vanrenterghem Y;De GS; 2004

Relevance

Intervention:	Renal transplantation
Comparison:	Haemodialysis
Population:	126 Patients with chronic renal failure, aged > 18 and varying adherence levels. Of these, 23 received renal transpla electronic event monitoring (EEM), 5 were defined nonadherent with medication which account for 21%.
Perspective:	SOCIETAL
Study type:	CUA
Methods:	DECISION ANALYSIS on the basis of a prospective study
Health valuations:	EQ-5D based TTO
Cost components	Direct costs of treatment and hospitalisation, costs of follow up, indirect costs and patient travel expenses. Productivi were considered but not included as only few patients were working.
Currency:	EURO
Cost year:	2000
Time horizon:	1 year follow up
Discount rate:	3% for costs and outcomes. Tested in SA.
Results-cost	Lifetime costs after transplantation in the adherent patient group are higher than lifetime costs in the non adherent gr mainly because adherent patients live longer after transplantation.
Results-effectivenes	Compared with dialysis, renal transplantation offers better outcome in both adherent and nonadherent patients.
Results-ICER:	Transplant dominated haemodialysis on all adherence levels and was therefore found to be more cost effective. Whe adherence is assumed, transplant generates a cost saving relative of dialysis and 5.19 additional QALYs. In a heterc group of adherent and nonadherent patients, the saving was greater but fewer QALYs were generated (5.06). This w due to a reduced life expectancy. Among transplant patients, adherence with immunosuppressants after transplantat associated with a QALY gain, albeit at a higher cost which was mainly due to a longer overall life span. Mean costs QALY in adherent patients relative to nonadherent patients after transplantation was EUR 35 021 (95%CI 26 959 - 4 This leaves scope for an adherence enhancing intervention, assuming a willingness to pay of £20 000 per QALY or of 2004.

Result-Uncertainty: First and second order MonteCarlo simulations and non parametric bootstrapping revealed that the model results are robust against changes in values. The 95% confidence interval did not exceed the upper bound of the WTP threshol that were not based on published evidence (discount factors, QALY loss) were specifically subjected to sensitivity an but not found to have a decision rule changing impact. Recent papers on rates of graft loss may indicate that the IcE between adherent and nonadherent patients is lower as adherent patients may benefit more from better prognosis.

Source Funding: Public

Comments: This study illustrates the effect nonadherence can have on the findings of an economic evaluation. Assuming full or g adherence, which seems common in RCTs, has the tendency to overestimate cost effectiveness by producing more fewer costs in a scenario like this study.

This study could not measure long term comorbidities of nonadherence. Had their costs in terms of treatment and Q been factored in, this would have resulted in a higher potential WTP for an AEI.

Does change in dosing regime affect adherence?

No 1517 **Cost effectiveness of a pharmacy-based coaching programme to improve adherence to antidepr**

Author: Bosmans JE;Brook OH;Van-Hout HJ;De-Bruijne MC;Nieuwenhuyse- H;Bouter LM;Stalm 2007
WB;Van-Tulder MW;

Relevance

Intervention: Pharmacist led education and coaching intervention (3 personal contacts, 1 take home video) plus standard care

Comparison: Usual care including standard oral and written information

Population: Adults in urban and rural areas with 'new episode (not used antidepressant in previous six month period)' prescriptio tricyclic antidepressant from GP for depressive complaints.

Perspective: SOCIETAL

Study type:	CEA
Methods:	RCT
Health valuations:	NOT APPLICABLE
Cost components	Direct medical (not hospitalisation!), treatment and intervention costs as well as productivity losses due to work abse
Currency:	EURO
Cost year:	2002
Time horizon:	Six months
Discount rate:	Not applicable
Results-cost	In both groups, the main contributor to costs were productivity costs. Mean total costs were EUR3275 in the interven group and EUR2961 in the control group. This resulted in an insignificant cost difference between intervention and c groups of EUR315 (95% CI -1922, 2416).
Results-effectiveness	Adherence was measured using an electronic pill container (eDEM) and was primary outcome, with the Hopkins dep 13 item subscale (SCL) used as secondary outcome for depressive symptoms. Mean adherence did not differe signi between the intervention group (88%) and the control group (86%) at six months (mean difference 2.1%, 95% CI -5.(In respect to SCL subscale, there was no statsitically significant difference between the groups either despite a slight improvement in the pharmacist intervention group (-0.15, 95% CI -0.54, 0.23).
Results-ICER:	The ICER for coaching and education by pharmacists compared with usual care was EUR149 per 1% improvement i adherence and EUR2550 per point improvement in the SCL depression mean item score.
Result-Uncertainty:	Uncertainty was considerable, reflected by insignificance of mean differences. Pairs of costs and effects were distribu four quadrants of the cost effectiveness plane. The CEAC for adherence was extremely uncertain, guiding decision r have little belief that coaching and education by pharmacists is cost effective as a means of increasing adherence to antidepressants compared with usual care. Changes in Sensitivity analysis (per protocol analysis, univariate parame changes) had little impact on results.
Source Funding:	Public

Comments: Patients with higher levels of education had higher completion rates of follow up assessments, which in turn had a si association with compliance levels. Further limitations include the use of the eDEM, which is described as the gold st for adherence measurement,however, its use itself could have increased adherence. Withdrawal rates were found to relatively high which the authors attempted to account for by additional analysis. Also there may be an issue with effe however, the authors state that more data from participants was unlikely to make the intervention appear favourable.

Guideline Development Group Declaration of Interests

Medicines Concordance

John Benson

University Lecturer in General Practice

1. Personal specific pecuniary or personal family interest:	19/09/07 Grant for research into Patient preference about risk communication - £181,268 awarded 2006. 28/02/07 Non Specific pecuniary interest Shares in GSK, tesco, Unilever 5th GDG meeting Research into Patient preferences about risk communication - £181,268 awarded 2006.
2. Personal family interest:	
3. Non-personal pecuniary interest	11/07/07 Appointed Non Executive Director, Weast Suffolk Hospital Acute Trust
4. Personal non-pecuniary interest:	

Jim Blair

Senior Lecturer Learning Disabilities

1. Personal specific pecuniary or personal family interest:	Nothing to declare 11/07/07 Invited to be a trustee by signalong
2. Personal family interest:	
3. Non-personal pecuniary interest	Nothing to declare
4. Personal non-pecuniary interest:	

Alison Bowser

Chief Executive Officer Acne Support Group

1. Personal specific pecuniary or personal family interest:	

2. Personal family interest:

3. Non-personal pecuniary interest Donations to the acne support group, which I am chief executive to. There are unconditional general fund donations and I do not receive any direct payment from any company. (Valeant Pharma; Galderma UK; Steifel Labs)

4. Personal non-pecuniary interest:

Wendy Clyne

Assistant Director, Medicines Partnership Programm

1. Personal specific pecuniary or personal family interest:

09/04/08
1. Author's fee for article in 'The Pharmacist' about concordance.
2. Author's fee for article in 'Prescriber' about concordance.
3. Fee for workshop on concordance for pre-registration pharmacists for the NPA.
4. In negotiation phase with European Commission 7th Framework Programme as a co-applicant for a EUR 2.1 million research grant on patient compliance.

09/05/07
Paid speeches

11/07/07
Involved in a GSK ran concordance programme

2. Personal family interest:

3. Non-personal pecuniary interest

22-01-09
NPC Plus has been commissioned to deliver adherence workshops from several PCTs – Lincolnshire, Solihull and Nottingham County.
NPC Plus has been commissioned by Stoke-on-Trent PCT to develop a community pharmacy long term condition adherence support service

Participation in advisory board for patient compliance support programme - LUNDBECK

General Non - Current interests
Next 12 months, commission to train practitioners in concordance consulatation skills

With GSK, Sanofi-Aventis, Shering Plough

4. Personal non-pecuniary interest:

Peter Crome

Professor of Geriatic medicine

1. Personal specific pecuniary or personal family interest:

09/04/08
1. I am attending the Brazillian Congress of Gerontology in June. My travel and hotel costs are being provided by Novartis Brazil with whom I have no connection.
2. I am hoping to undertake a clinical trial of a putative anti-dementia drug manufactured by Lilly. This contract is not yet signed.

28/02/07
Joint share ownership with Prof. L Crome - GSK

Chaired symposium in Oct 2006
subject - Pain control in older people
Organisation - NAPP

11/07/07
Have a personal pecuniary interest in that I have shares in GSK but as far as I know no GSK product was discussed

I also have a non pecuniary interest in that I have published on concordance, compliance etc.

2. Personal family interest:

3. Non-personal pecuniary interest

28/02/07
Research group - Dementia Drug trials - Ongoing
Organisation - Stive, Eisai,

4. Personal non-pecuniary interest:

28/02/07
I also have a non pecuniary interest in that I have published on concordance, compliance.

Peter Haddad

Consultant Psychiatrist and Honorary Senior Lecturer in Psychiatry

1. Personal specific pecuniary or personal family interest:

21/11/08
Lecture fees paid by Janssen
Consultancy fee from Janssen

10/10/08
1) Lecture fees (Astra-Zeneca, Janssen, lilly, Valeant).

2) Fees for consultancy (e.g. advisory boards) Eli Lilly (Advisory board on antipsychotic) Janssen (Advisory board on non-clinical education).

28/02/07

1. Lecturer fees - Astra Zeneca, Eli Lilly, Janssen-Cilag

2. Fees for consultancy: Eli Lilly, Janssen- Cilag

n.b the above list summarises my involvement with the pharmaceutical industry in the last 12 months. Please note that, with one exception, I doubt that the above fees have any relevance to this guideline as the lecturing and consultancy were not related to compliance but rather dealt with specific psychiatric illnesses (depression, schizophrenia, bipolar disorder) or treatments (antidepressants, antipsychotics). The one exception is that my work with Janssen-Cilag has related to the use of long acting injections of antipsychotic which can improve compliance in some patients with schizophrenia and other psychoses

2. Personal family interest:

10/10/08
None

3. Non-personal pecuniary interest	10/10/08 None 28/02/07 Co-Investigator in an on-going investigator-led study of quetiapine as an augmenting agent in treatment-resistant depression. The grant for this study came from Astra-Zeneca and is held by the principal investigator, not myself, at Manchester University. I received no payment for contributing to this study. I do not believe that this grant has any relevance to this guideline (the study has nothing to do with adherence) but I have mentioned it for the sake of completeness. 02/07/08 A hospital administrator contacted me to inform me that on reviewing the research contract some money from the above study was actually payable to my research fund at the Trust and this payment has subsequently been made into my Trust research fund. I have not taken any private payment. The sum of money paid into my Trust research fund was less than £3000. Payment from my research fund for work as a Co-Investigator in an on-going investigator-led study of quetiapine as an augmenting agent in treatment-resistant depression. The grant for this study came from Astra-Zeneca.
4. Personal non-pecuniary interest:	10/10/08 1. I am a co-investigator in an industry sponsored (Lilly) observational study that investigates predictors and consequences of antipsychotic non-adherence in schizophrenia. (Lilly). 2. I am a co-author of a review of conventional antipsychotic depots that will appear in a peer-reviewed supplement sponsored by industry (Lilly). 01/07 I hold the view and have expressed it in writing, that long acting antipsychotic injections may improve adherence, compared to oral antipsychotics, in some patients with schizophrenia. This view is consistent with the evidence, existing NICE guidance (e.g. 2002 schizophrenia guidance) and the views of many psychiatrists. This view could be regarded as favouring companies that manufacture long acting antipsychotic injections e.g Janssen-Cilag. 02/07/08 Since joining the GDG in Feb ’07 I have attended several medical conferences (all on a range of psychiatric subjects and organized by independent bodies) with my associated expenses being paid by various drug companies. 26/02/08 1. Lecture Fees (Bristol-Myers-Squibb: Lecture on antipsychotic side-effects) 2. Fees for consultancy (i.e. advisory boards) Eli Lilly (re: antipsychotics), Servier (re: antidepressants). NB: The above list summarises my involvement with the pharmaceutical industry since the last NICE Meeting in Jan '0816/01/08 1. Lecture Fees (Eli Lilly Janssen-Cilag) 2. Fees for Consultancy (Astra-Zeneca, Eli Lilly, Janssen-Cilag, Bristol Myers Squibb) NB: The above list summarises my involvement with the pharmaceutical industry since my last declaration of interest. My work with Janssen-Cilag relates to the use of long acting

injections of antipsychotics which can improve compliance in some patients with schizophrenia and other psychoses. Other than this the above fees do not appear to have any relevance to this guideline as the lecturing and consultancy were not related to adherence but rather dealt with specific psychiatric illnesses (schizophrenia, bipolar disorder) or treatments (antidepressants, antipsychotics).

19/09/07
1. Lecture fees (Eli Lilly ,Janssen-Cilag)
NB: The above list summarises my involvement with the pharmaceutical industry since the third NICE Meeting in July. My Work with Janssen-Cilag relates to the use of long acting injections of antipsychotics which can improve compliance in some patients with schizophrenia and other psychoses. The lectures for Eli Lilly do not appear to have any relevance to this guideline as they were not related to adherence but rather dealt with other areas including research methodology and observational studies.

Steven Hemingway

Senior Lecturer in Mental Health

1. Personal specific pecuniary or personal family interest:

07/03/07
1. Honorarium for speaking at an educational event. South London April 2007
2. Honorarium for speaking at an educational event. Leeds December 2007. Both for Pharmaceutical Janssen-Cilag LTD

02/07/08
Funding to attend ECE conference in Berlin by EISAI.

2. Personal family interest:

3. Non-personal pecuniary interest

11/07/07
£500 Educational Grant form Janssen-Cilaag Ltd to partially support me attending the Australian College of Mental Health Nurses Conference in Cairns Australia October 2007.

4. Personal non-pecuniary interest:

Robert Horne

Professor of Behavioural medicine

1. Personal specific pecuniary or personal family interest:

22/01/09
Paid consultancy and lectures to Proctor and Gamble, Shire Pharmaceuticals and Astellas.

02/07/08
June 08 Grand Round at Merck Outcomes USA-paid
Talk on adherence in HIV for BMS on 4th July 2008- paid
Consultancy on adherence research to shire pharmaceutials
Consultancy on adherence to GSK
Consultancy on adherence in IBD to Procter and Gamble

28/02/07
1. Paid consultancy work advising on research and audit programmes to monitor patient perspectives of illness and treatment and adherence to medication.
2. Speaking engagements at national and international conferences and advisory boards

presenting academic data adherence to medication across chronic illness

Activities 1. and 2. for the following companies; GlaxoSmithKline, Pfizer, Boeringher Ingelhiem, AstraZeneca, Abbott, Gilead, Novartis, ALTANA Pharma,Shire, Roche, Servier, Aventis, MSD, Proctor and Gamble, Schering Plough. Hamell

3. The above consultancy work is promulgated through a limited company with my wife Carol Elizabeth Kirkman-Horne

4. In addition,I am director of a new company Optimum Patient Care Ltd developing research-base programmes to facilitate the assessment of patient perspectives of illness and treatment in the review of chronic illness in primary care.

2. Personal family interest:

3. Non-personal pecuniary interest

22/01/09
Received unrestricted educational grants to the School of Pharmacy, University of London from Proctor and Gamble, Shire Pharmaceuticals, National Institute of Health Research (NIHR) for research into patient benefit and adherence to medication.

02/07/08
Awarded unrestricted educational grant to University of London to conduct research into patient perspectives and adherence to phosphate reduction treatments in renal disease for Shire pharmaceuticals £100k 2008-2009.

28/02/07
I have received unrestricted educational and research grants to my university- based research programme from a range of pharmaceutical companies.

- GlaxoSmithKline, Pfizer, Boeringher Ingelhiem, AstraZeneca, Abbott Gilead, Novartis, Shire, Roche, MSD

30/01/07 have received unrestricted educational and research grants to my university-ased research programme from a range of pharmaceutical companies: GlaxoSmithKline, Pfizer, Boeringher Ingelhiem, AstraZeneca, Abbott, Gilead, Novartis, Shire, Roche, MSD,

4. Personal non-pecuniary interest:

09/05/08
Approached by Buzienker to give a speech on MC in May, but did not attend.

Approached by Chandler Chicco to request advice on support service for patients with HIV.

30/01/07
I have developed several questionnaire-based tools for assessing patients perspectives of illness and treatment and adherence to medication

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Shaun Johnson

Patient Representative

1. Personal specific pecuniary or personal family interest:

Member of Board of Directors LAMP (the leicestershire action for mental health project)

Member of Policies Committee (Mind)

Member of publications committee
Member of Mind link national advisory panel

2. Personal family interest:

3. Non-personal pecuniary interest

4. Personal non-pecuniary interest:

Sean

Kelly

Consultant Physician and Gastrolenterologist

1. Personal specific pecuniary or personal family interest:

2. Personal family interest:

3. Non-personal pecuniary interest

4. Personal non-pecuniary interest:

Member of British Society of Gastroenterology
Fellow of the Royal College of Physicians
Lecturer Hull York Medical School.

Bunis

Packham

Nurse Consultant- Thrombosis and Anticoagulation

1. Personal specific pecuniary or personal family interest:

Nurse consultant- interested in standards and quality.
Keen to be involved in development of national guidelines.

2. Personal family interest:

3. Non-personal pecuniary interest

09/05/07
Invited by a scientific group to discuss MC. Non-paid role.

21/05/08
Asked to do a presentation on medication review for anticoagulation patients for NPC which is a follow on from the Medication review Level 2 in 2002

4. Personal non-pecuniary interest:

Member of Royal College of Nursing
Chair of Anticoagulation Specialist Association
Core Member of The Patient Safety Campaign 2008- VTE Lead

Mahendra

Patel

Lecturer/Research Fellow

Medicines Concordance

1. Personal specific pecuniary or personal family interest:	19/09/07 Guest speaker for the Cardio-diabetes event in collaboration with multiple organisations, held at the Barbican Theatre (London) to address Health inequalities: 'Mending the Gap: reducing cardiovascular risk in London (October 2007)" I was paid an honararium as a guest speaker for this event (plus travel expenses). The Honorarium offered was £200.00. I am attaching a copy of the event details for your information. As mentioned I have also just recently been appointed an Honorary Research Fellow at the University of Huddersfield. 28/02/07 Occasional professional services provided as a locum community pharmacist for Sainsbury's Pharmacy, Gordans Chemist Ltd, National CO-OP Ltd and other community pharmacy outlets 21/05/2008 Presentation at the conference Cardiopneumo in Italy 15-17 May 2008. Third International Conference on Cardiovascular and Respiratory Disease in Family Medicine. Implementing cares closer to home: the PhwSI's role
2. Personal family interest:	
3. Non-personal pecuniary interest	28/02/07 1. Part of a Phd Research programme by Merck Sharpe & Dohme (2005): analysing medicines management for patients discharged from hospital following a current CHD event and comparing differences and effects of pharmacist intervention within white and South Asian groups. Joint supervising of PhD student in within this area. For School of Pharmacy - University of Bradford 2. Developing and dvelivering a training programme to health advocates, health carer and interpreters working as volunteers primary within communities of BME groups - British Heart Foundation. For Institute of Pharmacutical Innovation (IPI) - University of Bradford.
4. Personal non-pecuniary interest:	Member of the royal Pharmaceutical Society (GB) member of the Cardiovascular Group - South Asian Health Foundation Member of the Ethnic Health Strategy Group - British Heart Foundation Trustee Member - Mouth Cancer Foundation Research fellow - University of Bradford

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Henry Smithson

General Practitioner

1. Personal specific pecuniary or personal family interest:	21/11/08 Attended ECE in Berlin- no conflict of interests 21/05/08

	Funding to attend ECE congress in Berlin by EISAI 09/04/08 Advisory Board for Carisbamate Health Ec Meeting (Janssen-Cilag) 28/07/07 Various honoraria from USB, Pfizer and Eisai for educational initiatives relating to care of epilepsy 14/11/2007 Speaker honorarium and chairs honorarium for a Vagal Nerve Stimulation meeting in Manchester funded by the manufacturers last month. Total came within allowed amounts
2. Personal family interest:	
3. Non-personal pecuniary interest	
4. Personal non-pecuniary interest:	

Jonathan Steel

GP, Chairman GP Comiitte RCP

1. Personal specific pecuniary or personal family interest:	1. General Practitioner -Glouchester PCT 2. Fellow -Royal College of Physicians 3. Clinical Associate - Price Waterhouse Coopers Has been invited by ABPI to their president's Gala Dinner in April- has offered to decline in case of incompatibility with NICE.
2. Personal family interest:	
3. Non-personal pecuniary interest	11-07-07 Met with Sanofi-Aventis who paid for dinner, more in relation to the work I am doing at RCP, I have not accepted any work.
4. Personal non-pecuniary interest:	

Sarah Willett

1. Personal specific pecuniary or personal family interest:	None
2. Personal family interest:	None
3. Non-personal pecuniary interest	None

4. Personal non-pecuniary interest: None

Marian Cotterell

Information Scientist

1. Personal specific pecuniary or personal family interest: None

2. Personal family interest: None

3. Non-personal pecuniary interest None

4. Personal non-pecuniary interest: None

Julie Neilson

Health Services Research Fellow

1. Personal specific pecuniary or personal family interest: None

2. Personal family interest: None

3. Non-personal pecuniary interest None

4. Personal non-pecuniary interest: None

Vanessa Nunes

Health Services Research Fellow/Project Manager

1. Personal specific pecuniary or personal family interest: None

2. Personal family interest: None

3. Non-personal pecuniary interest
None

4. Personal non-pecuniary interest:
None

Norma O'Flynn

Clinical Director

1. Personal specific pecuniary or personal family interest:
DOI - 06/03/07
Work half time as NHS general practitioner

2. Personal family interest:
None

3. Non-personal pecuniary interest
None

4. Personal non-pecuniary interest:
None
