Policy Analysis Centre

Europe's Lost Patients

Untreated and Poorly Treated Gastroesophageal Reflux Disease (GERD)

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Foreword

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In the face of advancing medical opportunities and the increasing demands of an ageing and better informed population, health systems across Europe, and elsewhere, are struggling to work within their budgets. It is very important that the approaches taken by individual systems to manage this process of change do not neglect the evolving needs of patients.

Faced with the need to identify and apply cost containment measures, which can deliver tangible improvements on projected spend within typical funding cycles of five years or less, it is perhaps no surprise that the management of serious but non life-threatening conditions falls into the spotlight. Here, more effective screening, streamlined treatment methodologies and greater reliance on generic versions of brand name pharmaceuticals are all examples of favoured options where the overall negative impact on the patient population is deemed to be negligible.

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This report provides insight into the way in which the health policy environment is changing. It also describes a new interest in wider public health, including preventative strategies to improve diet and lifestyle and better chronic disease management to tackle the impact of disease on lifelong health and wellbeing. The relevance of those diseases, which have low level but long-term health impacts as well as more severe consequences when combined with associated conditions (co-morbidities), are now becoming widely accepted amongst policymakers.

One such example is gastroesophageal reflux disease (GERD) which is featured as the core case study on the basis of the particular challenge it presents for health systems. At present, most people with GERD will either suffer the untreated consequences of their condition or self-medicate to better cope with the symptoms – a widespread approach which can have adverse consequences both for the individual and the society within which they live.

Despite the sheer scale of the estimated prevalence of GERD at more than 10 percent of any European population,[1] the fact that the disease rarely leads directly to hospitalisation or premature mortality has led to its relative neglect by health systems. Nevertheless, as a result of the increasing volume of the proton pump inhibitor (PPI) class of medicines, which now form the mainstay of the way the disease is managed, the costs of drug treatment for those who are diagnosed are rising rapidly and forming a major area of focus for healthcare decision makers.

The challenge facing policymakers is that they must balance longer-term societal benefits from more effective and pervasive treatments with the direct and immediate costs being borne by their health budgets

The commentaries on Germany, Italy, and Spain in these pages all report on recent initiatives to develop public health strategies and disease management programmes, albeit at the local level in many cases. The evidence on the prevalence and impact of GERD sufficiently demonstrates the costs of neglecting chronic conditions, to be balanced against ongoing concerns at the costs of their treatment. The challenge facing policymakers is that they must balance longer-term societal benefits from more effective and pervasive treatments with the direct and immediate costs being borne by their health budgets. This is also at the root of the policy challenge that lies within the new emphasis on health promotion and tackling the deep-rooted epidemics of lifestyle-associated conditions.

Professor Josep Darba

Senior Health Economist, University of Barcelona

The severity of gastroesophageal reflux disease varies from person to person, but its potential to bring about long-term complications align it with a number of formidable disease entities in Europe which adversely affect patient quality of life and are costly to healthcare systems.

In my own country, Spain, a recent study found that many previously diagnosed patients suffered from poor control of their condition, and only a minority were referred to a specialist, with their physicians often underestimating the patient's symptom load. This is a situation which also applies in many other parts of Europe, although, as this report demonstrates, there are marked differences between the way different countries approach the management of such conditions.

In GERD, a conjugation of lack of diagnosis and poor treatment standards for those who are diagnosed together impact significantly upon the daily lives of a sizeable proportion of the patient population.

Sleep disturbance due to episodes of gastroesophageal reflux are assumed to reduce quality of life and work productivity, with an even more significant impact on work absenteeism, healthcare resource consumption and leisure activities.

By way of solution some country regions have created regional health technology assessment agencies and regulating bodies that establish their own chronic disease targets that aim to control current pharmaceutical expenditure. This situation makes prescription patterns quite different among different areas in the same country.

When compared, the net result is a high probability that a patient with GERD or other chronic conditions of its kind does not receive the appropriate drug treatment, leading to complications that have a considerable socio-economic cost. Decision makers must do more to take into account the impact that this can have.

Professor Marcello Tonini

Professor of Pharmacology, University of Pavia

The health economic environment in Italy dictates that the risk of patient under-treatment for those with long-term, chronic condition is high. This is reflected in other European national healthcare systems which also show relevant discrepancies which may contribute to inappropriate therapeutic management. A harmonisation on this matter is highly desirable.

It is possible to draw many learnings from the Italian healthcare system where, following a devolution process that started in the early 1990s, the prevailing system is mainly based on transferred funding from the central government to the regions to warrant 'essential levels of care' for the vast majority of diseases requiring prescription-based medicines. Regions are entirely responsible for healthcare deficit recovery due to hospital drug over-expenditure, and partially responsible for retail drug over-expenditure and the downstream effects of measures to control the situation.

This report capably compares these findings with the approaches adopted in Spain and Germany to draw valuable conclusions and recommendations about current shortcomings and what can be done to improve the health of patients moving forward.

Of particular note, this report references a measure introduced by some regions in Italy and other parts of Europe to control healthcare expenditure, namely reference pricing for several drugs within the same therapeutic class. These measures, exclusively aimed at cost containment, cannot address the medical need of each individual patient, who requires a personalised therapy to adequately control any underlying disease. These are the 'lost patients' which are described in the following pages – they must be found!

Professor Joachim Labenz

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In the countries of the western world, including Germany, GERD is an extremely common disease currently affecting 20 percent or more of the population, but with a continuously increasing tendency. Although many of the patients affected have a good prognosis in terms of survival, the condition is associated with a considerable impairment of their quality of life and performance, both in the private and occupational sectors. In some cases, however, GERD may prove fatal due either to a haemorrhage, the development of a cancer, or failed surgery.

Over the last 20 years, following the introduction of the proton pump inhibitors, therapeutic options for the treatment of reflux disease have improved dramatically. With the aid of these substances, the quality of life and performance of virtually all those affected can be restored, benignly and with little risk, and in many cases serious complications can be prevented. In the meantime it has been shown that in particular patients with severe forms of reflux disease (e.g. Los Angeles grade C and D reflux esophagitis, Barrett´s esophagus) require – and gain lasting profit from – intensive and consistent PPI treatment.

Owing to the ubiquitous nature of GERD, treatment with PPI has developed into an appreciable cost factor for many health service systems, including that in Germany. Accordingly, political measures aimed at containing the cost of PPI therapy have not been lacking. Stepwise in Germany, maximum reimbursement has repeatedly been reduced, and the pressure on physicians to prescribe inexpensive generics increased. However, these measures have failed to bring about any substantial savings. Owing to the urgency of the need to cut costs, there has been a clearly recognisable and progressive decrease in the quality of treatment of GERD due to a recourse to non-PPI drugs, inadequate PPI dosage, or the practical unavailability of effective PPI therapy because of current pricing policy and/or the need for considerable additional payments on the part of the patient. The particular victims of this development are those patients with the most severe manifestations of GERD – these are Germany´s lost patients. In the eyes of a scientist who has for decades been actively concerned with the optimisation of GERD and PPI therapy, and whose passion as a physician is to heal his patients, this negative development is totally unexpected and intolerable.

Executive Summary

The Lost Patient

Health systems in Europe are struggling to contain costs amidst the pressures of ageing populations and the service expectations of informed patients, alongside the constantly evolving landscape of medicines management. Long-term conditions are at the heart of the struggle. The chronic diseases that are responsible for the highest burden of premature mortality are often manageable through medical intervention, if not also preventable.

Socialised health systems that are typical throughout Europe, with high levels of state intervention in the provision of universal healthcare coverage, are most readily judged by measures of acute care inputs and outcomes. Where chronic conditions lead to hospitalisation and premature mortality, as may be the case with cardiovascular disease, asthma and diabetes, then they can achieve some degree of priority in such a system. However, those chronic diseases whose adverse effects are largely confined to the individual's quality of life can more readily be neglected by socialised health systems.

Diseases that are commonly regarded as primarily lifestyle-related and self-inflicted are often subjected to health policies that are focused on minimisation of costs to the health system, whether through the promotion of over-the-counter (OTC) remedies, restrictive drug reimbursement lists, patient out-of-pocket payments, or drug price regulation. In particular, this report takes an in-depth look at the implications of the management of these conditions which are perceived to fall into the 'lifestyle' category[2] and the implications of always taking a short-term view on the prioritisation of their treatment in the context of the need to safeguard existing healthcare budgets at national and regional level.

Some patients' needs may be lost within such a broad-brush approach

Specific emphasis is placed on how some patients' needs may be lost within such a broad-brush approach, when a disease encompasses a range of patient's and treatment options. Whilst most patients can be very effectively treated using the cheapest possible therapeutic options, others' disease severity may warrant a different approach tailored to their needs. In these circumstances a 'one size fits all' approach to treatment can have damaging consequences for both patients and European health systems. These victims of all-encompassing health policies are Europe's 'lost patients'.

GERD – A Case in Practice

GERD provides an excellent example of a disease area in which this scenario is easily identifiable. Despite being one of the most widespread medical conditions in Europe, patients are often poorly served in comparison with the best possible standards of care. Approximately, 10 to 15 percent of the European population experience weekly or more frequent incidents of reflux.[3] However, only a quarter of these people actually receive treatment, and most are left to suffer in silence.[3] Even amongst those few who are treated, physicians can be ill-equipped to face the task of matching treatment to each patient's needs.[3]

As the consequences of GERD on a *health system* are difficult to quantify in comparison to the well documented effect this condition can have in terms of reduced quality of life, impact in the workplace and effect on family and wider relationships,[4, 5] it is easy for policymakers to only consider the costs of treatment without balancing them against savings which might apply in the longer term for certain patients by preventing the development of serious co-morbidities.

Taking examples from other disease areas, it is clear that advances in survival rates for the most important causes of premature mortality, particularly cardiovascular diseases and cancers, have encouraged European health policy leaders to also consider their health systems' contributions to the wider public health. Elsewhere, the rapid growth of obesity and diabetes has led to a new focus on diet, lifestyle and chronic disease management.

When considered from a societal perspective, it is clear that GERD requires similar levels of commitment from policymakers that are being given to the other important long-term conditions. Unlike other chronic conditions, poor management of GERD only rarely leads to a tangible increase in health system costs in the short-term and ultimately to premature mortality. As a result, even amongst the major chronic diseases of Western societies which have long been neglected, tackling GERD is still relatively absent from the list of policy priorities. In the three countries looked at in this paper, Germany is the first to begin work on a significant scale to develop clinical guidelines for GERD.

This report includes summaries of the current situation in three European countries: Germany, Italy, and Spain. In Germany, where the annual GDP impact of GERD has been estimated at €668 million,[6] clinical guidelines for GERD are being developed between insurers in one region. In addition, a number of pilot projects for disease management are now underway. In Italy and Spain, health system decentralisation has exacerbated the fragmentation of care planning and funding. Furthermore, structural issues, combined with the co-payments systems undermine the efficiency of the treatment of chronic diseases.

European countries can learn from one another in managing the costs of treating GERD effectively

There is evidently much that European countries can learn from one another in managing the costs of treating GERD effectively within an overall disease management strategy to minimise long-term health system costs and the impact on individual patients' lives. GERD affects more than one-in-ten of the European population,[1] with a significant impact upon their quality of life and productivity. Effective treatment is nominally available but with little policy priority at the national level to ensure that those affected are, in fact, treated. As the European Union endeavours to meet its Lisbon Agenda on global competitiveness and play an increasing role in pursuit of high standards of public health across the EU, a European strategy on GERD could do much to address its inevitable neglect amongst competing local health priorities.

GERD Management: Current Approaches

GERD, which is one of the most widespread ailments in Western society, occurs when acid rises from the stomach to the esophagus. This is generally associated with symptoms such as 'heartburn' or 'regurgitation' leading to burning and painful sensations in the upper stomach and esophagus. It has been estimated that as much as 40 percent of the population will suffer from some occasional if not regular form of this condition,[7] which is a major cause of sleep disturbance.[4] In some people acid reflux only occurs during physical exercise.[4]

Defining GERD

Despite significant international efforts to agree a definition for GERD, a multitude of differing definitions are still used in health systems across Europe. Despite international consensus to the contrary, many health systems still use a definition of GERD that relates only to damage to the lining of the esophagus caused by acid reflux from the stomach due to problems with the muscle at the sphincter between them. This captures just one aspect of the disease. The authoritative *Montreal Definition* clearly states that GERD develops:

'when the reflux of stomach contents causes troublesome symptoms and/or complications'.[8]

This modern definition of GERD was supported by most of the panel of 44 experts from 14 countries (who 'agreed strongly' with the wording). Support increased to 95 percent with the inclusion of those who also agreed but with 'minor reservations'. According to this authoritative definition, the boundary beyond which occasional heartburn becomes a 'disease' is when reflux symptoms are troublesome, so that *'they adversely affect the individual's wellbeing'*. This would be the case, for example, if mild symptoms were occurring two or more days a week, or more severe symptoms one day a week. The Montreal Definition does, however, warn that underlying complications can also occur in asymptomatic individuals, so that the boundary can also be crossed even in the absence of troublesome symptoms.[8]

GERD is usually separated into either erosive (ERD), with reflux esophagitis (mucosal breaks of the esophagus), or non-erosive GERD (i.e.NERD), without esophagitis. Erosive GERD is then further broken down into four categories of severity using the 'Los Angeles' classification system: from A to D, according to the severity of damage to the lining of the esophagus.[8] Additionally, Barrett's esophagus (BE) is a condition that can develop when reflux into the esophagus leads to replacement of squamous epithelium by columnar lined epithelium (a change to the cells of the esophagus), which is associated with an increased risk of adenocarcinoma, a type of esophageal cancer.

Prevalence of GERD

Whilst as much as 40 percent of the Western population may experience heartburn, a typical symptom of GERD, at least occasionally, it is estimated that perhaps 10 to 20 percent of most Western populations suffer from regular symptoms of GERD.[1] Rates of GERD are rising, partly due to the decreasing prevalence of *Helicobacter pylori* infection which is supposed to have a protective effect against GERD, changes in lifestyle and diet, increasing rates of obesity, and the use of reflux-provoking drugs such as calcium channel blockers. Estimates of the actual incidence of GERD are complicated by the fact that many people with the condition do not seek medical attention.

Diagnosing GERD

GERD is usually identified from patients' own reporting of their symptoms. Physicians can then also use endoscopy and other tests to assist their diagnosis. However, there is no gold standard test for GERD. Diagnosis is further complicated by the fact that GERD can develop with or without symptoms, and with or without any of the range of established and possibly associated conditions. The doctor, therefore, usually has to work with the patient to gauge the severity of their symptoms and the impact on their wellbeing.

Various tools to assist with the diagnosis and management of GERD have been developed. The GERD Impact Scale,[9] for example, is one such tool, comprising just nine questions which measure the burden of GERD on the patient's quality of life.

It is important to note that approximately two-thirds of GERD patients will have typical symptoms – this can lead to misclassification of at least one-third of the GERD population as having dyspepsia or other diseases.[10] Additionally, more than 5 percent of the adult population in Western countries will have clinically silent reflux esophagitis or even Barrett´s esophagus.[11] It is also important to note that in about 95 percent of the patients with the most serious sequela of GERD – adenocarcinoma of the distal esophagus (Barrett´s cancer) – the diagnosis of the underlying disorder GERD with Barrett´s metaplasia has not been made previously.[10] The incidence of Barrett´s cancer is increasing rapidly, and it is very likely that many cases could be prevented by earlier and adequate treatment of GERD or be detected at an earlier curable stage.[10]

Health Consequences of GERD

Several of the syndromes and associations of GERD have specific health consequences of their own in addition to the direct impact of GERD on patients' daily lives. The most common complication due to GERD is esophagitis, when the lining of the esophagus is damaged. This can be diagnosed using an endoscopy, which is also subsequently necessary to monitor the effects of treatment. There are, however, several other forms of damage to the esophagus that can occur as a result of GERD, including ulceration, stricture, bleeding, Barrett's esophagus and adenocarcinoma.[8] One recent study of co-morbidities in US employees found that GERD patients were much more likely than non-GERD patients to suffer gastritis, duodenitis, gastrointestinal haemorrhage and a range of other stomach-related disorders as well as respiratory and thyroid disorders.[12] The duration and frequency of GERD symptoms have been shown to be closely associated with esophageal adenocarcinoma,[13] the prevalence of which is also rising.

Esophageal Manifestations & Complications	Extra-Esophageal Complications
GERD without esophagitis GERD with esophageal: – erosions – stricture – ulcers and bleeding Barrett's esophagus Esophageal adenocarcinoma	Pulmonary: – chronic obstructive pulmonary disease & asthma – cough Ear, nose & throat: – hoarseness – laryngitis – sinusitis Other: – unexplained chest pain – angina – sleep disturbance – dental erosion

Source: Malfertheiner P, Hallerback B. *Int J Clin Prac* 2005

Treating GERD

A range of treatment options are now available to GERD patients.[14] Antacids are routinely available without prescription, and certain low-dose forms of an H_2-receptor antagonist or PPIs may also be available directly from pharmacies.

- **Antacids** neutralise stomach acids. They are intended only to relieve the symptoms of occasional heartburn and not the treatment of GERD. Some antacids also contain sodium alginate, which floats on the top of stomach contents to form a physical barrier to reflux. Antacids should not be taken with other medicines. Common brands include Gaviscon, Rennies, and Tums.
- **H_2-Receptor Antagonists (H_2RAs)** work by blocking the action of histamine, which otherwise plays a part in boosting levels of acidity in the stomach through the release of hydrogen ions. Prior to the introduction of PPIs in the late-1980s, these had been the most effective form of GERD treatment available. Common H_2RAs are cimetidine, famotidine, nizatidine, and ranitidine.

- **Proton Pump Inhibitors (PPIs)**, which may now be available in a low-dose form without prescription in some countries, are usually the first line treatment for GERD. They quickly block the hydrogen ion-pumping action of the proton pump to reduce stomach acid levels. Available PPIs are omeprazole, lansoprazole, pantoprazole, rabeprazole, and esomeprazole. PPIs are also effective in the treatment of gastrointestinal bleeding, with GERD.[15]

Over the past 15 years, PPIs have been repeatedly demonstrated to be superior to the earlier therapies in treating GERD, although H_2RAs also perform well in symptom relief.[16] PPIs are particularly valuable for the prevention of serious GERD complications related to some of the forms of the disease,[17] as well as common problems with sleep disturbance.[18] In recent years the range of available therapies has increased as the oldest PPIs are subject to patent expiry, and the advent of generic versions, and the arrival of newer, more potent PPIs, notably esomeprazole. The increasing range of options allows treatment to be adapted to each patient's clinical need.[19] The arrival of generic PPIs has seen recent increases in the volume of PPI prescriptions offset in many countries by decreases in the volume of H_2Antagonists and the average price (and total cost) of PPIs. IMS data show, for example that increased volumes of PPIs in Germany between the second quarter of 2006 and the same quarter of 2007 were accompanied by a 30 percent fall in total spending on PPIs.[20]

Motility stimulants to speed up the emptying of the stomach may also be used, as may **surgery** to tighten the sphincter between the stomach and the esophagus.

European Clinical Practice in GERD

Drug Use per 100,000 Population

	Prescriptions		Over-the-Counter	
Country	PPI	H_2 RA	PPI + H_2 RA	Antacids
Belgium	157	81	238	112
Czech	93	60	153	72
Germany	138	23	161	60
Spain	267	31	298	152
France	236	14	250	156
Italy	169	25	194	35
Netherlands	182	31	213	19
Poland	81	77	158	38
Portugal	192	15	207	207
UK	198	49	247	166

Source: IMS Health & Eurostat

Note:
Drug use measured as standard units in thousands, one standard unit is equivalent to one pill.
Drug data is not separated by indication, so that uses other than GERD will be included. Greece has been excluded from the list of countries due to apparent data error.

GERD Impact

Untreated or poorly treated GERD will have significant impacts on individual patients, with associated consequences for European countries' health systems and economies. GERD affects an individual's quality of life at a level similar to other major chronic diseases, and it has a greater negative impact on emotional wellbeing than diabetes or hypertension.[21]

Health System Impact

The diagnosis and treatment of GERD carries significant costs for European health systems. For example, in Sweden the direct costs of drug treatment for GERD and other gastroesophageal disorders has been estimated to be over a hundred million Euros every year[22] and around 40 percent of the total costs of GERD, dyspepsia and peptic ulcer bleed treatment.[22] A German follow-up study on patients diagnosed with GERD and Barrett's mucosa found that three-quarters of these received medication during the year, 61 percent had been back to the doctor, and 2 percent were admitted to hospital. The mean cost was €342 per patient per year, but with huge variations around this sum.[23] As a major cause of unexplained chest pain, GERD places a serious burden on hospital emergency departments, and is estimated to account for between 2 and 5 percent of emergency patients.[24]

Personal Impact

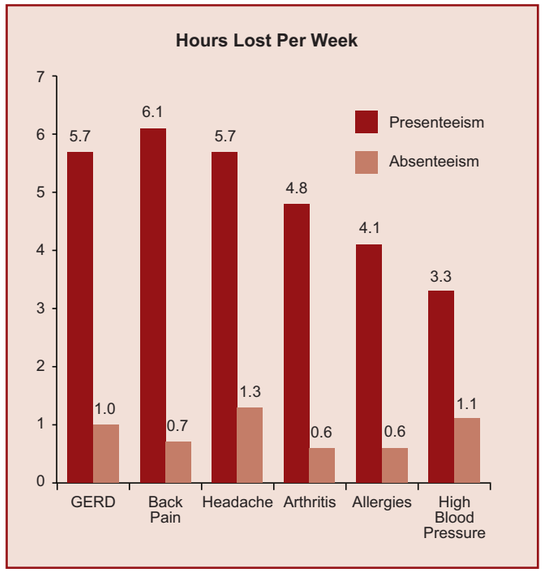
The most commonly reported impacts relate to sleep disturbance. A Gallup survey of 1000 heartburn sufferers showed that about 80 percent of these individuals reported heartburn at night and among those, 75 percent experienced sleep disturbances in relation to their heartburn and the majority of them believed that heartburn negatively affected their ability to sleep well, and a significant proportion indicated that this sleep disturbance ultimately affected their ability to perform work.[25]

European people with GERD who are being treated for the condition also face direct treatment costs, when they must pay directly for prescription and OTC therapies.

Across Europe, patients in the different EU Member States face very different financial burdens according to the local regime of prescription charges, co-payment and reliance upon OTC therapies outside of health system or insurance reimbursement.

Productivity Impact

A systematic review of research on work productivity effects found productivity losses amongst individuals with GERD between 6 and 42 percent, mainly through reduced productivity whilst at work, known as 'presenteeism' rather than through absenteeism, and primarily due to sleep disturbance. The review, which was published during 2006, estimated a mean productivity loss per employee with GERD between $62 and $430 per week.[5]



The chart shows a calculation of hours lost per week due to GERD in comparison with a selection of other common chronic conditions.[26]

A German study found almost 15 percent of GERD patients reported an average of almost 2 days off work due to their condition in the first year of follow-up on their diagnosis, falling to less than 1 day in the second year.[27] This relates to the minority of people with GERD who are diagnosed and receiving treatment.

Productivity does not relate solely to working hours. In fact, an even greater impact is reported with regard to leisure activities, where sufferers have reported 14 percent impairment in their non-work activities.[25]

The Cost of GERD

Professor Josep Darba

University of Barcelona

Using published health economic data, it is possible to estimate the economic implications of poorly treated GERD and its complications; for patients, health providers, and employers.

This analysis of the implications for patients suffering from poorly controlled GERD was estimated for six countries in Europe (France, Germany, Italy, Spain, Sweden and UK) and was compiled using population figures and the rates of prevalence for GERD and its complications in each country. From this estimation, the economic implications for healthcare providers and employers were estimated.

Table 1. Implications for patients of poorly controlled GERD (per year)

Implications for patients of poorly controlled GERD	**France**	**Germany**	**Italy**	**Spain**	**Sweden**	**UK**
Total actual Population (A)[a]	61.350.000	82.370.000	58.880.000	44.100.000	9.090.000	60.210.000
Mean GERD prevalence (+/-) (%) (P_G)	7,80%[b]	15%[c]	18,0%[d]	15,6%[e]	12,6%[f]	12,6%[f]
Incidence Barrett's oesophagus in patients with GERD (%) (I_B)[g]	10%	10%	10%	10%	10%	10%
Incidence Adenocarcinoma in patients with Barrett's esophagus (%) (I_A)[g]	8%	8%	8%	8%	8%	8%
Incidence Esophagitis in patients with GERD (%) (I_{EN})[g]	20%	20%	20%	20%	20%	20%
Incidence Esophagitis in GERD patients poorly treated (%) (I_{EP})[h]	50	50%	50%	50%	50%	50%
Estimated ratio exceed incidence esophagitis (I_{EP} / I_{EN})	2,5	2,5	2,5	2,5	2,5	2,5
Estimation of GERD prevalence and complications GERD incidence in all population						
GERD population (A x P_G)	4.785.300	12.355.500	10.598.400	6.879.600	1.140.795	7.556.355
Patients with Barrett's oesophagus (BO) (A x P_G x I_B)	478.530	1.235.550	1.059.840	687.960	114.080	755.636
Patients with Adenocarcinoma (A x P_G x I_B x I_A)	38.282	98.844	84.787	55.037	9.126	60.451
Patients with esophagitis (A x P_G x I_{EN})	957.060	2.471.100	2.119.680	1.375.920	228.159	1.511.271
Consequences of poorly controlled GERD						
Patients un-treated with severe esophagitis (%) (P_P)[i]	5%	5%	5%	5%	5%	5%
Patients poorly treated with severe esophagitis (A x P_G x P_P)	239.265	617.775	529.920	343.980	57.040	377.818
Patients poorly treated with Barrett's oesophagus (A x P_G x P_P x I_A x I_{EP} / I_{EN})	59.816	154.444	132.480	85.995	14.260	94.454
Patients poorly treated with Adenocarcinoma (A x P_G x P_P x I_B x I_{EP} / I_{EN} x I_A)	4.785	12.356	10.598	6.880	1.141	7.556

a Monthly bulletin of statistics of the United Nations, estimations for 2006.

b Bretagne JF *et al.* Gastroesophageal reflux in the French general population: national survey of 8000 adults. *Presse Med* 2006; **35**: 23–31

c Leodolter A *et al.* Gastro esophageal reflux disease is associated with absence from work: Results from a prospective cohort study. *World J Gastroenterol* 2005; **11**: 7148–7151

d Epi database, Update 9/29/2006

e Ortiz V *et al.* Value of Heartburn for Diagnosing Gastroesophageal Reflux Disease in Severely Obese Patients. *Obesity* 2006; **14**: 696–700

f Dent J *et al.* Epidemiology of gastro-oesophageal reflux disease: a systematic review, *Gut* 2005; **54**: 710–717

g Klaus A *et al.* Relación entre el reflujo gastroesofágico, esófago de Barrett y cancer de esófago. *Revis Gastroenterol* 2000; **4**: 189–194

h Fennerty MB *et al.* The diagnosis and treatment of gastroesophageal reflux disease in a managed care environment: suggested disease management guidelines. *Arch Intern Med* 1996; **156**: 477–484

i Dent J *et al.* An evidence-based appraisal of reflux disease managements – The Genval workshop report. *Gut* 1999; **44**(Supl.2): S1–S16

Table 2. Estimated economic implications for heath service of poorly controlled GERD (per year)

Cost estimations for health service of poorly controlled GERD	**France**	**Germany**	**Italy**	**Spain**	**Sweden**	**UK**
Total actual Population (A)[a]	61.350.000	82.370.000	58.880.000	44.100.000	9.090.000	60.210.000
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Incidence Adenocarcinoma in patients with Barrett's esophagus (%) (I_A)[g]	8%	8%	8%	8%	8%	8%
Incidence Esophagitis in patients with GERD (%) (I_{EN})[g]	20%	20%	20%	20%	20%	20%
Incidence Esophagitis in GERD patients poorly treated (%) (I_{EP})[h]	50%	50%	50%	50%	50%	50%
Estimated ratio exceed incidence esophagitis (I_{EP} / I_{EN})	2,5	2,5	2,5	2,5	2,5	2,5
Mean annual cost per patient						
Mean annual GERD treatment cost (€)[i]	242 €	242 €	242 €	242 €	242 €	242 €
Mean annual Barrett's oesophagus treatment cost (€)[i]	449 €	449 €	449 €	449 €	449 €	449 €
Mean annual Hospital cost by GERD (€)[i]	74 €	74 €	74 €	74 €	74 €	74 €
Mean annual Hospital cost by Barrett's esophagus (€)[i]	145 €	145 €	145 €	145 €	145 €	145 €
Mean annual Doctor's visits cost by GERD (€)[i]	26 €	26 €	26 €	26 €	26 €	26 €
Mean annual Doctor's visits cost by Barrett's esophagus (€)[i]	37 €	37 €	37 €	37 €	37 €	37 €
Cost estimation of GERD and BO in patients well treated						
Total direct cost of GERD (millions)	1.555 €	4.014 €	3.443 €	2.235 €	371 €	2.455 €
Total direct cost of BO (millions)	302 €	780 €	669 €	434 €	72 €	477 €
Total direct cost of GERD + BO (millions)	1.857 €	4.794 €	4.112 €	2.669 €	443 €	2.932 €
Cost consequences of poorly controlled GERD						
Cost by patients poorly treated with Barrett's oesophagus (millions)	38 €	97 €	84 €	54 €	9 €	60 €

a Monthly bulletin of statistics of the United Nations, estimations for 2006.

b Bretagne JF *et al.* Gastroesophageal reflux in the French general population: national survey of 8000 adults. *Presse Med* 2006; **35**: 23–31

c Leodolter A *et al.* Gastro esophageal reflux disease is associated with absence from work: Results from a prospective cohort study. *World J Gastroenterol* 2005; **11**: 7148–7151

d Epi database, Update 9/29/2006

e Ortiz V *et al.* Value of Heartburn for Diagnosing Gastroesophageal Reflux Disease in Severely Obese Patients. *Obesity* 2006; **14**: 696–700

f Dent J *et al.* Epidemiology of gastro-oesophageal reflux disease: a systematic review, *Gut* 2005; **54**: 710–717

g Klaus A *et al.* Relación entre el reflujo gastroesofágico, esófago de Barrett y cancer de esófago. *Revis Gastroenterol* 2000; **4**: 189–194

h Fennerty MB *et al.* The diagnosis and treatment of gastroesophageal reflux disease in a managed care environment: suggested disease management guidelines. *Arch Intern Med* 1996; **156**: 477–484

i Willich SN *et al.* Cost-of-disease analysis in patients with gastro-oesophageal reflux disease and Barrett's mucosa *Aliment Pharmacol & Ther* 2006; **23**: 371–376

Footnote

The mean annual direct costs of GERD and Barrett's esophagus (BE) were obtained from a study by Willich *et al.*[i] This estimate was taken from data from a German cohort. It has been assumed that this estimated cost is equal for all European countries and detailed in Euros (France, Germany, Italy and Spain). For Sweden and UK, the estimates are based on the exchange rate for each currency (SEK and Libra) with respect to Euro to the 31 December 2006.

Total cost was estimated by adding the direct medical costs of GERD to the cost of Barrett's esophagus disease likely to be caused by inadequate GERD treatment. Also, the *cost consequences of poorly controlled GERD* took into account the additional cost to the healthcare system incurred in dealing with Barrett's esophagus disease.

Table 3. Estimated economic implications for employers of poorly controlled GERD

Cost estimations for employer of poorly controlled GERD	**France**	**Germany**	**Italy**	**Spain**	**Sweden**	**UK**
Total actual Population (A)[a]	61.350.000	82.370.000	58.880.000	44.100.000	9.090.000	60.210.000
Mean GERD prevalence (+/-) (%) (P_G)	7,80%[b]	15%[c]	18,0%[d]	15,6%[e]	12,6%[f]	12,6%[f]
Incidence Barrett's oesophagus in patients with GERD (%) (I_B)[g]	10%	10%	10%	10%	10%	10%
Incidence Adenocarcinoma in patients with Barrett's esophagus (%) (I_A)[g]	8%	8%	8%	8%	8%	8%
Incidence Esophagitis in patients with GERD (%) (I_{EN})[g]	20%	20%	20%	20%	20%	20%
Incidence Esophagitis in GERD patients poorly treated (%) (I_{EP})[h]	50%	50%	50%	50%	50%	50%
Estimated ratio exceed incidence esophagitis (I_{EP} / I_{EN})	2,5	2,5	2,5	2,5	2,5	2,5
Percentage of population older 60 years old[i]	21%	21%	20%	20%	19%	16%
Percentage of younger 15 years old[i]	18%	14%	14%	15%	16%	18%
% active full time[k]	84%	84%	84%	84%	84%	84%
Average daily wage	140 €[k]	150 €[c]	140 €[i]	131 €[k]	1.269 SEK[k]	£95[k]
Incremental average absenteeism rate[j]	1,2	1,2	1,2	1,2	1,2	1,2
Presenteeism rate[j]	15	15	15	15	15	15
Prevalence of presenteeism (%)[j]	33%	33%	33%	33%	33%	33%
Cost estimation for employers of GERD and BO in patients well treated						
Absenteeism cost impact to employer by GERD	413 €	1.214 €	990 €	590 €	105 €	706 €
Absenteeism cost impact to employer by BO related-GERD	41 €	121 €	99 €	59 €	10 €	71 €
Presenteeism cost impact to employer by GERD	1.705 €	5.009 €	4.085 €	2.434 €	433 €	2.912 €
Preenteeism cost impact to employer by BO related-GERD	136 €	401 €	327 €	195 €	35 €	233 €
Absenteeism cost impact to employer by patients poorly treated with BO complications	4 €	12 €	10 €	6 €	1 €	7 €
Total Cost						
Per Absenteeism	459 €	1.348 €	1.099 €	655 €	117 €	784 €
Per Presenteeism	1.858 €	5.460 €	4.452 €	2.653 €	472 €	3.174 €

a Monthly bulletin of statistics of the United Nations, estimations for 2006.

b Bretagne JF *et al.* Gastroesophageal reflux in the French general population: national survey of 8000 adults. *Presse Med* 2006; **35**: 23–31

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h Fennerty MB *et al.* The diagnosis and treatment of gastroesophageal reflux disease in a managed care environment: suggested disease management guidelines. *Arch Intern Med* 1996; **156**: 477–484

i National Statistical Spanish Institute

j Willich SN *et al.* Cost-of-disease analysis in patients with gastro-oesophageal reflux disease and Barrett's mucosa *Aliment Pharmacol & Ther* 2006; **23**: 371–376

k Supposed (mean of average daily wage of Germany and Spain) and actualised by change rate for Sweden and UK

GERD in Spain

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Consideration of the management of GERD in Spain reveals a situation in which chronically ill patients receive different treatments and face different user charges, according to how they access care. A system of fragmented financing provides little incentive to develop patient-centred networks of care, with clear pathways for chronic disease management.

The current situation reflects the fact that between 1981 and 2002 the Spanish National Health System underwent a programme of devolution of responsibility to the regions. The end result was a system which provides universal and free access to most aspects of care, with the exception of user co-payments for pharmaceuticals, when those patients who are not in an exempt group must usually pay 40 percent of the price of an NHS prescribed medicine. For chronic conditions the co-payment is reduced to 10 percent with an upper limit per prescription. Additionally, Spain has a reference price system for pharmaceuticals and some regions (ACs) have created regional health technology assessment agencies (HTA) as well as establishing their own chronic disease targets.

In Spain some regions (ACs) have created regional health technology assessment agencies (HTA) as well as establishing their own chronic disease targets

In particular, GERD is a common cause for primary care consultation, and the main epidemiological study for Spain suggests a prevalence of 15.6 percent for the general population.[28] A more recent study has also estimated GERD prevalence at 15 percent. A causal analysis of Spanish data has shown a strong association between obesity and GERD,[29] which is consistent with evidence suggesting that obesity is linked to several chronic conditions.[30] The department of surgery of the Hospital Clínico San Carlos reported that 9.8 percent of the population suffers GERD symptoms on a weekly basis. The same study shows that 5.4 percent of patients who suffer from GERD will use inpatient care, (compared to just 5 percent in the US).[31] This may be related to the low barriers accessing inpatient care in Spain and the fact the pharmaceutical co-payments do not apply to hospital-dispensing.

In addition to high rates of hospitalisation for GERD, in 2002 there were around 2 million GERD-related primary care consultations.[31] A recent study estimated that for each 1,000 inhabitants the condition accounts each year for almost 300 consultations, 32.4 endoscopies, and for the loss of 201 working days (per 1,000 employed inhabitants with GERD).[31] On medication it estimates were 4,092 treatment days with H_2 antagonists, 9,030 treatment days with PPIs, and 1,082 treatment days with prokinetics per 1,000 inhabitants per year.[31]

Evidence from clinicians suggests that patients are generally allowed to choose their own drug treatment option from the available therapies. The most common strategy is to use a highly potent treatment and to decrease its potency over time.[31]

Spanish evidence on GERD treatment demonstrates the importance of distinguishing between patients, and tailoring the drug selection according to each patient's condition.[31]

Major GERD Treatments 1998–2002

Treatment Units (000)	*1998*	*2002*
PPI	10024	22688
H_2RA	13803	8679
Gastroprokinetics	9337	9343
Treatment value (€000)		
PPI	188206	309496
H_2RA	124423	64957
Gastroprokinetics	9337	9343

Source: Alvarez, Revista Española de Economia de la salud 2007

GERD in Germany

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GERD management in Germany is governed by a health system where there is a predominance of mandatory social health insurance, with a substantial number of competing sickness funds and a private/public mix of providers. In 2003, nearly 88 percent of the population was covered by comprehensive social health insurance.[32] Ambulatory healthcare is mainly delivered by private for-profit providers working in a single practice. Regional physicians' associations negotiate annual collective contracts for ambulatory services for all physicians affiliated with health insurance companies in their region.[32]

Patient co-payments have, with some exceptions, been standardised at €10 per inpatient day and €5–10 for prescribed pharmaceuticals. Co-payments of €10 also need to be made per quarter for the first contact with a physician or when other physicians are seen without referral during the same quarter. Without prescription, patients have to cover the full costs of pharmaceuticals.

According to the countrywide representative National Health Interview and Examination Survey, involving 7,124 subjects in 1997/98, the overall prevalence of reflux symptoms in the adult population was 43 percent. In total, 25 percent of participants reported mild, 14 percent moderate, and 4 percent severe symptoms.[33]

According to an analysis of the ProGERD cohort study, involving 6,215 patients in Germany, Austria and Switzerland, the loss of gross domestic product due to GERD in Germany amounts to at least €668 million per year.[6] According to another analysis of the same study, GERD caused mean direct costs of €342 and indirect mean costs of €40 per patient each year. Expenses for medication (particularly PPIs) were the largest single cost factor, amounting to 64 percent of overall disease-related costs.[34]

In 2001, health insurance companies spent €230 million on the PPIs esomeprazole, omeprazole and pantoprazole.[35] In 2006 some 1158.2 million Defined Daily Doses of PPIs were prescribed for reimbursement by general health insurance, having increased by 11.6 percent on the previous year.[36] Data on prescriptions under private health insurance reimbursement are not available.

In 2005, the German Society for Gastroenterology and Endocrinology *(Deutsche Gesellschaft für Verdauungs- und Stoffwechselerkrankungen)* issued clinical guidelines for GERD. In the case of erosive reflux disease, the use of PPIs is recommended, with subsequent attempts to step down. Similarly, patients with non-erosive reflux disease (NERD) should be treated with a PPI for 4 weeks followed by on-demand intake of such a drug.[35]

As in many other countries in Europe, primary care physicians manage the majority of GERD patients. These are the same physicians who are under some pressure to prescribe generics as a result of healthcare insurers making discounted contracts with pharmaceutical companies, with an associated effect on the upper limit of reimbursement. This has an impact on the quality of care patients receive.

The chronic disease management programmes which are currently offered by statutory health insurance are also important. These apply to the following diseases: type 1 and 2 diabetes, asthma, chronic obstructive pulmonary disease (COPD), breast cancer, and coronary heart disease. While no chronic disease management programme yet exists for GERD, a pilot project in southern Lower Saxony *(Niedersachsen)* starting in October 2007 has seen the development of an integrated model for the treatment of GERD, based on clinical guidelines and pathways. The model aims to improve the quality of care and to improve the efficiency of healthcare provision by avoiding unnecessary medications.

GERD in Italy

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In Italy, the needs of GERD patients are governed by the approaches adopted by the country's regions. This follows a devolution process which has been rolling out since the early 1990s, that has transferred legislative, administrative and, partly, fiscal powers to the 21 regions. As far as the healthcare system is concerned, the central government assures fundings to each region in order to reach the so-called 'essential levels of care', which include the vast majority of prescription-based medicinal products. In this context, regions are responsible for providing adequate healthcare services through expenditure of resources determined at national level and, notably, for healthcare deficit recovery.[37]

Price cuts, which can be generalised or selective to certain categories of drugs, have been extensively used as a measure to reduce national healthcare expenditure with an average decrease of 3 percent per year in the last 5 years.[38] Co-payments have played a relevant role in cost-containment policies up to the early 1990s, although they were subsequently abolished by central government. Since 2002, co-payment has been reintroduced at regional level with marked differences across regions.

Another measure introduced by some regions to control healthcare expenditure is the reference pricing for several drugs within the same therapeutic class. This is the case with proton pumps inhibitors (PPIs) which are important in the management of GERD patients for which 8 regions out of 21 adopted a reference price corresponding to the price of generic lansoprazole (the least expensive of the category), whereas in 4 regions a pre-definite level of generic PPI prescription was established (ranging from 40 percent to 70 percent of the entire PPI market).[39]

Under these conditions, if a physician prescribes a more expensive PPI, the patient is asked to pay for the difference exceeding the reference price. Nonetheless, the specialist or the general practitioner can prescribe a more expensive PPI, by justifying their choice due to a peculiar clinical condition of the patient. In this case co-payment by the patient is avoided. Currently, two generic PPIs are present in the Italian market, lansoprazole (branded and unbranded) and omeprazole (branded and unbranded). The still in-patent pantoprazole has recently reduced its price to the level of generic PPIs.

Omeprazole, lansoprazole and pantoprazole are referred to as 'first generation PPIs'.[40] Their antisecretory potency is lower compared to the 'second generation PPIs', rabeprazole and esomeprazole, whose prices are higher compared to generic PPIs or pantoprazole.[41]

Since 1994, the list of drugs covered by the national or regional healthcare system has been associated with prescribing guidelines (or notes), which define the clinical conditions for the use of certain classes of drugs, treatment approaches and reimbursement limits. Notes are mandatory and doctors are responsible for their application. Any violation can be sanctioned by the local health authorities.

Guidelines and reference prices for PPIs are perceived by healthcare professionals as restrictive measures aimed at controlling their prescription behaviour purely for reasons of cost containment and can adversely affect patients. Most relevantly, these measures cannot pay attention to the medical need of each individual patient, who requires a personalised therapy to control a disorder with a number of distinct clinical presentations, such as GERD.[8] In addition, the adoption of reference prices by some regions and not by others has led to profound differences among the Italian citizens regarding the therapeutic opportunities for acid-related disorders, in particular for GERD.[41]

Despite these considerations, the needs of lost patients did receive an important boost recently at a consensus conference sponsored by the Italian Federation of Digestive Diseases (FIMAD), held in Rome on 14–15 June, 2007, where it was agreed that *"the various clinical presentations of GERD may require different therapeutic approaches"*.[42] The therapy is based on the use of PPIs, which differ in their biochemical, pharmacokinetic and pharmacodynamic profile, which, in turn, influence their antisecretory potency.

GERD Europe – The Challenge

These country case studies provide an example of how catering for a majority of patients under the favoured national system, can effectively isolate a smaller group of patients whose needs are highly specific and require more specialised treatment. This has the potential to cost the system more in the long-term through the impact of co-morbidities than the cost of specific intervention.

By the most widely accepted definition of GERD currently available, as set out in the 'Montreal Definition', GERD is one of the most prevalent medical conditions in European society, albeit largely undiagnosed.[8] Despite the abundance of evidence to support good practice in its diagnosis and treatment, standards of both vary widely across Europe, between and within countries. The capacity of state-controlled health systems to neglect widespread but 'low-grade' chronic conditions is a major weakness of such systems. GERD, which affects more than 10 percent of adult Europeans, amply demonstrates this weakness.[1]

Areas of Neglect

Where easily measurable outputs have paramount importance in health policymaking, short-term costs and avoidable mortality can easily take precedence over long-term improvements in the population's quality of life. This can lead not only to perverse incentives to avoid diagnosis and treatment, but also decisions based on cost rather than maximum health-related effect. Worryingly, it is not just policymakers who may neglect the impact of GERD, but also primary care physicians: A recent study in Spain found that many previously diagnosed patients suffered from poor control of their condition, and only a minority were referred to a specialist, with their physicians often underestimating the patient's symptom load.[43] Clinical Guidelines developed by GI specialists and family doctors together should help to improve this situation. However, two to three years after the publication of these guidelines most primary care physicians in Spain experienced difficulties adhering to the recommendations.[44]

It is not just policymakers who may neglect the impact of GERD, but also primary care physicians

Lack of diagnosis and poor treatment standards for those who are diagnosed with GERD impact significantly upon the daily lives of a sizeable proportion of the European population. Sleep disturbance due to episodes of gastroesophageal reflux are estimated to reduce work productivity by around 10 percent, with an even more significant impact on leisure activities.[5] It also impacts health systems. For example, the disconcerting similarity between chest pain associated with GERD and chest pain due to coronary illness, which are not readily distinguished, places an often avoidable burden on emergency health services, while well-managed and treated GERD can reduce reliance upon physician consultations and hospital stays. With a very wide range of effective and safe treatment options available, with off-patent medicines available in each of the main therapeutic classes improving access to GERD, care is easier than ever.

The figures produced by Professor Darba highlight the costs when treatment standards fall below the levels that are nowadays easily attainable.

Data on the use of the various therapies available demonstrates the effects of local cultures and systems upon patient care in this area. Whilst the ratio between the use of PPI and H_2RAs in Belgium is 2-1, neighbouring countries have ratios as high as 8–1. At the other extreme, Greece, according to the IMS data, offers very little pharmaceutical treatment for GERD and uses 3 times as many units of H_2RAs as PPIs.[45]

National Disparities

As the country commentaries have demonstrated, European citizens with GERD face a lottery of care and costs. Most of them are lost to their health systems and consequently suffer the impact of GERD in their daily lives with no recourse to their health system. For those who are diagnosed and treated they still face a dramatic lottery of care according to where they live. The devolution of responsibility that has taken place in many European health systems means that not only are there different levels of access to care and different treatment options, but also very different treatment costs to the individual. Geographical inequities in access to PPIs is particularly evident in Italy, where regional budget deficits can remove the capacity for physicians to select the best treatment for each patient.

European citizens with GERD face a lottery of care and costs

The three health systems covered in the summaries show widely differing policy responses to improved awareness and improved treatment options for GERD. Germany has begun to see initiatives to manage care and its costs through clinical guidelines and defined care pathways. However, with the concomitant effect where the treatment pathways for individual patients are determined at the level of government, insurer, regional/speciality physician associations and PCP, there is more scope than in Spain and Italy for German patients to be 'lost' to the system.

In Spain, the decentralised Spanish health system faces high prescribing rates, but as the Spanish system is an arguably less regulated system than the German example, patients may be lost to the care provided by the system for geographic reasons and disparities in the provision of care. Italian policymakers have so far concentrated on supply-side measures, including direct price controls and a reimbursement system that encourages a reversal of current best practice; so that patients start on the least-potent therapies and are subsequently stepped-up to PPIs if and when necessary. In many ways and by its very nature, this system takes a slightly longer term view and patients may not be locked away from the most appropriate therapeutic interventions indefinitely.

Each country context is different

It is clear that each country context is different. Whilst Spain and Italy have seen shifts towards tax-based funding, albeit with high levels of private spending by European standards, and a degree of decentralisation to regional authorities, Germany has long maintained a complex 'plural' system for health policymaking and funding, with decisions taken at the national and regional levels of government and by provider associations. Nevertheless, improved understanding of GERD, its impact, and its treatment is much needed if the quality of life and productivity of this sizeable proportion of the European population is to be brought up to acceptable and manageable levels.

Conclusions

GERD offers important lessons for policymakers needing to meet the challenge presented by the major chronic diseases that affect Europe's working populations. The use of broad-brush policies in pursuit of short-term ambitions, and the subsequent neglect of long-term costs and consequences, should not be allowed to swell the ranks of 'lost patients', whose needs are no longer met by their national health systems.

Whilst there are several local initiatives to develop clinical guidelines for GERD, which is greatly assisted by the agreement of the Montreal Definition, these are so far very sporadic.

In the context of European health systems with high levels of public funding it is inevitable that health policy will more readily focus on direct health system costs, than on the economic and personal costs of a disease. It is also largely inevitable that prevention and treatment strategies within such systems will focus on the major causes of premature mortality rather than diseases that have widespread but usually moderate impact on individual wellbeing. The risk when decisions on healthcare are taken at the macro level is that whilst the resulting policies will suit the 'average' patient they can badly neglect the requirements of others. Analysis of the benefits of GERD patient segmentation and treatment tailored to individual needs, and the potential consequences of poor treatment of those in greatest need, demonstrates the appropriateness of GERD as a case study for health policymakers.

It is increasingly important that Europe's lost patients no longer suffer in silence:

- Considerable advances in tackling the major causes of premature mortality, particularly through reductions in smoking and the extensive use of statins in cardiovascular disease, are shifting the focus of health policy onto chronic diseases'
- Europe's 'Lisbon Agenda' for global competitiveness requires that individuals are supported by national and European policies to maximise their productive contribution.
- There is clear evidence that well-managed and tailored treatment can reduce the subsequent long-term burden of chronic diseases on health systems.

GERD can be readily and effectively treated with a range of therapies available to address the clinical needs of the individual patient. But the lack of consistent clinical guidelines, and systems of funding that neglect long-term costs and skew resources against best practice in disease management have produced barriers between those with GERD and the health systems that they fund.

Those patients with the greatest need may be 'lost' to their healthcare system, despite an accurate diagnosis

As European health systems begin to develop strategies to support economic development and combat the effects of an increasingly aged and overweight population, they will need to establish ambitious targets to manage the chronic conditions that adversely affect their working population. As demonstrated by the case study of GERD, those patients with the greatest need may be 'lost' to their healthcare system, despite an accurate diagnosis, due to policies that mitigate against personalised care. Much greater efforts will be required to identify and support these patients and their wellbeing to mutual benefit.

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