ICSI

INSTITUTE FOR CLINICAL SYSTEMS IMPROVEMENT

Health Care Guideline:
Stable Coronary Artery Disease

Thirteenth Edition
April 2009

The information contained in this ICSI Health Care Guideline is intended primarily for health professionals and the following expert audiences:

- physicians, nurses, and other health care professional and provider organizations;
- health plans, health systems, health care organizations, hospitals and integrated health care delivery systems;
- health care teaching institutions;
- health care information technology departments;
- medical specialty and professional societies;
- researchers;
- federal, state and local government health care policy makers and specialists; and
- employee benefit managers.

This ICSI Health Care Guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. If you are not one of the expert audiences listed above you are urged to consult a health care professional regarding your own situation and any specific medical questions you may have. In addition, you should seek assistance from a health care professional in interpreting this ICSI Health Care Guideline and applying it in your individual case.

This ICSI Health Care Guideline is designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and is not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition. An ICSI Health Care Guideline rarely will establish the only approach to a problem.

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Stable Coronary Artery Disease

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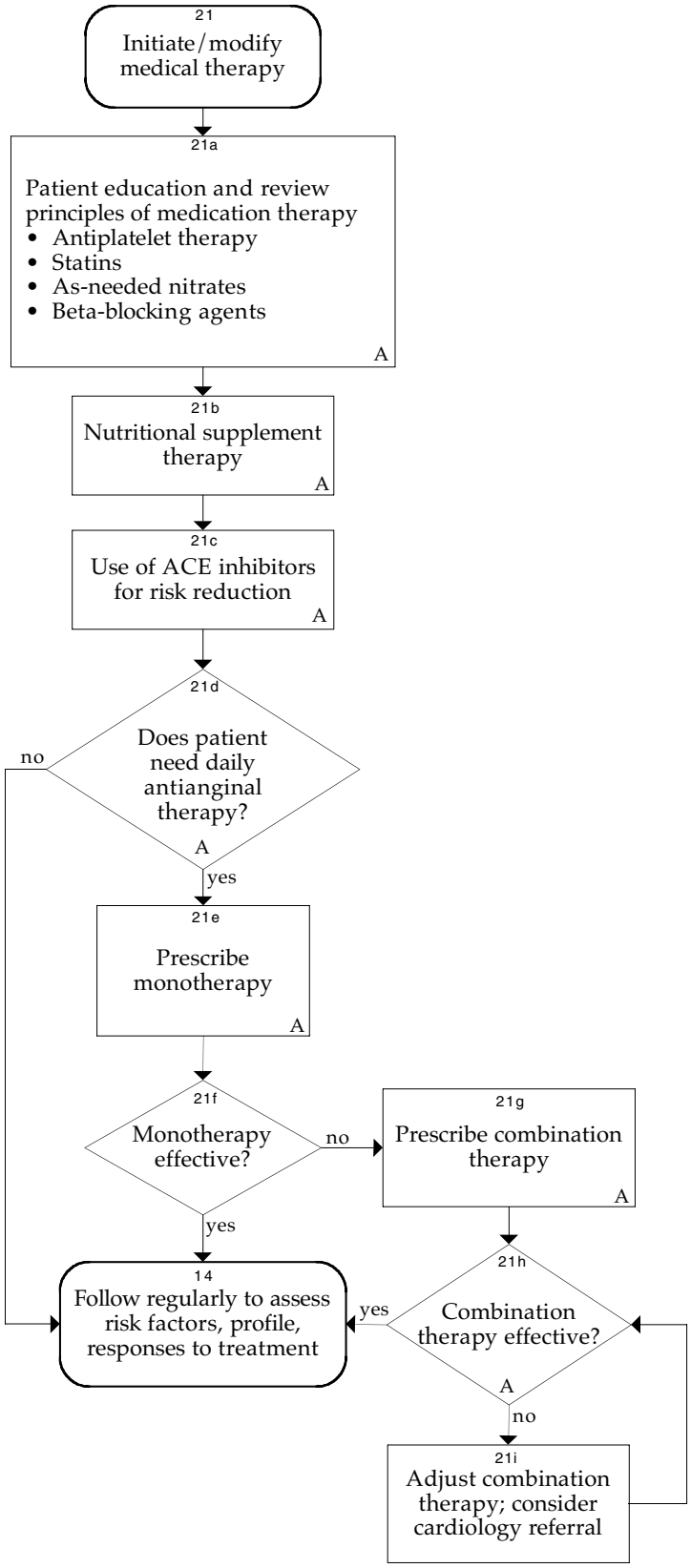
Main Algorithm

A = Annotation

Thirteenth Edition
April 2009

Pharmacologic Algorithm

A = Annotation



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Work Group Leader
Greg Lehman, MD
Internal Medicine, Park Nicollet Clinic

Work Group Members
Cardiology
Joe H. Nguyen, MD
CentraCare

Family Medicine
Spencer Bershow, MD
Fairview Health Services

General Internist
Phil Kofron, MD, MPH
Park Nicollet Clinic

Health Education
Susan M. Hanson, RD
Park Nicollet Institute

Nursing
Shauna Schad, RN, CNS
Mayo Clinic

Pharmacy
Peter Marshall, PharmD
HealthPartners Medical Group

Facilitators
Penny Fredrickson
ICSI

Myounghee Hanson
ICSI

Foreword

Scope and Target Population

Adults who have a diagnosis of stable coronary artery disease. The criteria, as noted on the Main algorithm, includes patient presenting with:

- previously diagnosed coronary artery disease without angina, or symptom complex that has remained stable for at least 60 days;
- no change in frequency, duration, precipitating causes or ease of relief of angina for at least 60 days; and
- no evidence of recent myocardial damage.

Clinical Highlights and Recommendations

- Prescribe aspirin in patients with stable coronary artery disease if there are no medical contraindications. *(Annotations #2, 21a; Aim #2)*
- Evaluate and treat the modifiable risk factors, which include smoking, sedentary activity level, stress, hyperlipidemia, obesity, hypertension and diabetes. *(Annotation #5; Aim #3)*
- Patients with chronic stable coronary artery disease should be on statin therapy regardless of their lipid levels unless contraindicated. (*Annotation #21a; Aim #3)*
- Perform prognostic testing in patients whose risk determination remains unclear. This may precede or follow an initial course of pharmacologic therapy. *(Annotation #7; Aim #7)*
- Refer the patient for cardiovascular consultation when clinical assessment indicates the patient is at high risk for adverse events, the non-invasive imaging study or electrocardiography indicates the patient is at high risk for an adverse event, or medical treatment is ineffective. *(Annotations #15, 16; Aim #4)*
- For relief of angina, prescribe beta-blockers as first-line medication. If beta-blockers are contraindicated, nitrates are the preferred alternative. Calcium channel blockers may be an alternative medication if the patient is unable to take beta-blockers or nitrates. *(Annotations #21a, 21e; Aim #1)*

Priority Aims

1. Increase the percentage of appropriate patients with an appropriate diagnosis of stable coronary artery disease (SCAD), who are prescribed aspirin and antianginal medications. *(Annotation #21a)*
2. Improve education/understanding around the management of stable coronary artery disease.
3. Increase the percentage of patients with stable coronary artery disease who receive an intervention for modifiable risk factors.
4. Improve the assessment of patients with a diagnosis of stable coronary artery disease who present with angina symptoms.
5. Increase the use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBS) in patients with coronary artery disease, including those patients with a diagnosis of diabetes, chronic kidney disease, and hypertension.

6. Increase the percentage of patients with a diagnosis of stable coronary artery disease who receive education around nutritional supplement therapy.
7. Increase prognostic testing for patients whose risk determination remains unclear.

Key Implementation Recommendations

The following system changes were identified by the guideline work group as key strategies for health care systems to incorporate in support of the implementation of this guideline.

1. Develop systems for providing patient education around:
   - Proper use of nitroglycerin
   - Consistent use of aspirin (unless contraindicated) or consistent use of clopidogrel as directed
   - When to call 911

   Education should also provide for patient to "teach back" in order to demonstrate their understanding of what they should do in an acute cardiac event.
2. Develop/provide patients education materials around use of aspirin (unless contraindicated), interventions around modifiable risk factors.
3. Provide patient education around the use and benefits of angiotensin-converting enzmes (ACE inhibitors) and/or angiotensin II receptor blockers (ARBs).

Related ICSI Scientific Documents

Guidelines

- Diagnosis and Treatment of Chest Pain and Acute Coronary Syndrome (ACS)
- Heart Failure in Adults
- Hypertension Diagnosis and Treatment
- Lipid Management in Adults
- Major Depression in Adults in Primary Care
- Diagnosis and Management of Type 2 Diabetes Mellitus
- Preventive Services for Adults
- Prevention and Management of Obesity in Adults and Mature Adolescents
- Primary Prevention of Chronic Disease Risk Factors

Technology Assessment Reports

- Biochemical Markers of Cardiovascular Disease Risk (#66, 2003)
- B-type Natriuretic Peptide (BNP) for the Diagnosis and Management of Congestive Heart Failure (#91, 2005)
- Cardiac Rehabilitation (#12, 2002)
- Drug-Eluting Stents for the Prevention of Restenosis in Native Coronary Arteries (#78, 2003)

- Electron-Beam and Helical Computed Tomography for Coronary Artery Disease (#34, 2004)
- Intracoronary Brachytherapy to Treat Restenosis after Stent Placement (In-stent Restenosis) (#34, 2002)
- Omega-3 Fatty Acids for Coronary Artery Disease (#94, 2006)

Disclosure of Potential Conflict of Interest

ICSI has adopted a policy of transparency, disclosing potential conflict and competing interests of all individuals who participate in the development, revision and approval of ICSI documents (guidelines, order sets and protocols). This applies to all work groups (guidelines, order sets and protocols) and committees (Committee on Evidence-Based Practice, Cardiovascular Steering Committee, Women's Health Steering Committee, Preventive & Health Maintenance Steering Committee and Respiratory Steering Committee).

Participants must disclose any potential conflict and competing interests they or their dependents (spouse, dependent children, or others claimed as dependents) may have with any organization with commercial, proprietary, or political interests relevant to the topics covered by ICSI documents. Such disclosures will be shared with all individuals who prepare, review and approve ICSI documents.

No work group members have potential conflicts of interest to disclose.

Introduction to ICSI Document Development

This document was developed and/or revised by a multidisciplinary work group utilizing a defined process for literature search and review, document development and revision, as well as obtaining input from and responding to ICSI members.

For a description of ICSI's development and revision process, please see the Development and Revision Process for Guidelines, Order Sets and Protocols at http://www.icsi.org.

Evidence Grading System

A. Primary Reports of New Data Collection:

Class A: Randomized, controlled trial

Class B: Cohort study

Class C: Non-randomized trial with concurrent or historical controls
Case-control study
Study of sensitivity and specificity of a diagnostic test
Population-based descriptive study

Class D: Cross-sectional study
Case series
Case report

B. Reports that Synthesize or Reflect Upon Collections of Primary Reports:

Class M: Meta-analysis
Systematic review
Decision analysis
Cost-effectiveness analysis

Class R: Consensus statement
Consensus report
Narrative review

Class X: Medical opinion

Citations are listed in the guideline utilizing the format of *(Author, YYYY [report class])*. A full explanation of ICSI's Evidence Grading System can be found at http://www.icsi.org.

Algorithm Annotations

Main Algorithm Annotations

1. Patient with Stable Coronary Artery Disease

This guideline applies to patients with coronary artery disease either with or without angina. Examples include patients with prior myocardial infarctions, prior revascularization (i.e., percutaneous transluminal coronary angioplasty [PTCA], coronary artery bypass graft [CABG]), angiographically proven coronary atherosclerosis, or reliable non-invasive evidence of myocardial ischemia.

A patient presenting with angina must meet all the following criteria *(Hurst, 1990 [R]; Rutherford, 1992 [R]; Shub, 1990 [R])*:

- Symptom complex has remained stable for at least 60 days
- No significant change in frequency, duration, precipitating causes or ease of relief of angina for at least 60 days
- No evidence of recent myocardial damage

The patient may already have undergone some diagnostic workup as a result of a prior presentation of chest pressure, heaviness and/or pain with or without radiation of the pain and/or shortness of breath. The clinician should have heightened awareness that many patients have atypical symptoms that reflect cardiac ischemia, especially women and the elderly. Initial care of such patients falls under the auspices of the ICSI Diagnosis and Treatment of Chest Pain and Acute Coronary Syndrome (ACS) guideline.

2. Perform Appropriate History, Physical Examination, Laboratory Studies and Patient Education

Thorough history taking and physical examination, including medication and compliance reviews, are important to confirm diagnosis, to assist in risk stratification, and to develop a treatment plan (*Rutherford, 1992 [R]; Shub, 1990 [R])*. Important points to elicit on history taking are:

- recognition that women may have atypical symptoms of cardiac ischemia. These may include fatigue, shortness of breath (SOB) without chest pain, nausea and vomiting, back pain, jaw pain, dizziness and weakness *(Bell, 2000 [R]; Harvard Medical School, 2005 [R]; Kordella, 2005 [R]);*
- history of previous heart disease;
- possible non-atheromatous causes of angina pectoris (e.g., aortic stenosis);
- comorbid conditions affecting progression of coronary artery disease;
- symptoms of systemic atherosclerosis (e.g., claudication, transischemic attack [TIAs] and bruits); and
- severity and pattern of symptoms of angina pectoris.

The physical examination should include a thorough cardiovascular examination, as well as evaluation for evidence of hyperlipidemia, hypertension, peripheral vascular disease, heart failure, anemia, thyroid disease, and renal disease.

Initial laboratory studies should include an electrocardiogram and a fasting lipid profile (total cholesterol, HDL-cholesterol, calculated LDL-cholesterol and triglycerides). Further tests, based on history and physical

examination findings, may include chest x-ray, measurement of hemoglobin, and tests for diabetes, thyroid function, and renal function.

An important aspect to treatment of stable coronary artery disease is education to help the patient understand the disease processes, prognosis, treatment options, and signs of worsening cardiac ischemia so that prompt medical assistance is sought when necessary and appropriate. Education may be accomplished in a number of ways among the various medical groups. It may be ongoing, occur in a formal class, and/or be done at the provider visit. Instruction on the proper use of aspirin and sublingual nitroglycerin, as needed, should also be reviewed at this time.

3. Non-Atherogenic Causes (e.g., Aortic Stenosis)?

Aortic stenosis is an important non-atherogenic cause of angina. This and any other non-atherogenic causes are considered to be outside the scope of this clinical guideline *(Shub, 1990 [R])*.

5. Address Modifiable Risk Factors and Comorbid Conditions

Comorbid conditions that could affect myocardial ischemia may include hypertension, anemia, thyroid disease, hypoxemia and others.

Modifiable risk factors for coronary heart disease need to be evaluated and may include smoking, inadequate physical activity, stress, hyperlipidemia, obesity, hypertension and diabetes mellitus. Intervention involving any risk factor pertinent to the patient is encouraged and may include education, goal setting, and follow-up as necessary *(Rutherford, 1992 [R]; Shub, 1990 [R])*.

Please see Appendix A, "Comorbid Conditions," for treatment recommendations in the presence of comorbid conditions.

Emerging Risk Factors

An association between homocysteine levels and cardiovascular disease has been demonstrated. The NORVIT trial and HOPE 2 trial found that folate and vitamins B6 and B12 did not reduce the risk of recurrent cardiovascular events in patients with vascular disease. These supplements cannot be recommended as routine treatment in patients with stable coronary artery disease *(Bønaa, 2006 [A]; HOPE 2 Investigators, 2006 [A])*.

In select patients, clinicians may want to consider obtaining a lipoprotein (a) and highly sensitive C-reactive protein (hsCRP) *(Ridker, 2005 [A])*. Highly sensitive C-reactive protein and related markers of inflammation may provide useful prognostic information and help guide further therapy for patients with coronary artery disease.

Influenza

Patients with cardiovascular disease should have an influenza vaccination as recommended by the American College of Cardiology/American Heart Association (ACC/AHA) Chronic Stable Coronary Artery Disease guideline *(Smith, 2006 [R])*.

Smoking

Cigarette smoking may cause an acute cardiac ischemic event and may interfere with the efficacy of medications to relieve angina.

Please refer to the ICSI Preventive Services for Adults guideline for recommendations regarding smoking cessation.

Sedentary Activity Level

An important aspect of the provider's role is to counsel patients regarding appropriate work, leisure activities, eating habits and vacation plans. Patients should be encouraged to exercise regularly to obtain cardiovascular benefit and to enhance their quality of life. The American College of Cardiology (ACC) endorses a minimum schedule of 30-60 minutes of aerobic activity (walking, jogging, etc.) three to four times per week, supplemented by an increase in daily lifestyle activities (walking breaks at work, gardening, etc.) Medically supervised programs are recommended for moderate- to high-risk patients. Exercise can be an important adjunct to modification of risk factors such as hypertension, hyperlipidemia and obesity. In addition, it can enhance patients' perception of their quality of life. Strenuous activities should be modified if they produce severe or prolonged angina; caution is needed to avoid consistent reproduction of ischemic symptoms or situations that may precipitate ischemic complications. Education is critical in achieving these goals. A study *(Hambrecht, 2005 [A])* showed less progression of coronary artery disease and significantly fewer ischemic events in patients who regularly exercised.

Stress

Psychophysiologic stress is a notable feature of the relationship between myocardial ischemia and the patient's daily environment. Depressive symptoms are common in stable coronary artery disease patients, with prevalence estimates ranging from 15% to 30% *(Kop, 2001 [R])*. The American Heart Association recommends that depression be routinely screened for and appropriately treated in patients with coronary heart disease *(Lichtman, 2008 [R])*.

Hyperlipidemia

A fasting lipid profile should be evaluated for appropriate patients with stable coronary artery disease. Secondary prevention is important in these patients, who should be treated aggressively for hyperlipidemia. Many patients will require both pharmacologic and non-pharmacologic interventions to reach target goals. Target goals for hyperlipidemic patients with coronary artery disease include:

LDL – less than 100 mg/dL

HDL – 40 mg/dL or greater

Triglycerides – less than 150 mg/dL

Please refer to the ICSI Lipid Management in Adults guideline for recommendations on lowering lipid levels.

Obesity

The American Heart Association considers obesity to be a major risk factor for coronary artery disease. Obesity is defined as a body mass index greater than 30. The loss of 5%-10% of an individual's weight can have health benefits such as decreasing blood pressure, cholesterol, decreasing the severity of obstructive sleep apnea, and improving glucose tolerance *(Eckel, 1998 [X])*.

Hypertension

General health measures include the treatment of hypertension, which is not only a risk factor for development and progression of atherosclerosis, but also causes cardiac hypertrophy, augments myocardial oxygen requirements, and thereby intensifies myocardial ischemia in patients with obstructive coronary disease.

Please refer to the ICSI Hypertension Diagnosis and Treatment guideline for recommendations regarding blood pressure management. The recommended target blood pressure is 130/80 mmHg or less.

Diabetes

Diabetes is associated with a marked increase in coronary artery disease. Patients with diabetes without known coronary artery disease have as high risk of a myocardial infarction as patients without diabetes with coronary artery disease. Therefore, patients with diabetes should have aggressive lipid and blood pressure management (similar to patients with coronary artery disease), and should be treated per the recommendations of the ICSI Diagnosis and Management of Type 2 Diabetes Mellitus in Adults guideline, ICSI Lipid Management in Adults guideline and ICSI Hypertension Diagnosis and Treatment guidelines.

Please refer to the ICSI Management of Type 2 Diabetes Mellitus guideline for recommendations regarding management of diabetes.

Every attempt should be made to achieve meticulous glucose control in patients with diabetes, because there is a clear relationship between lower hemoglobin Alc's and lower risk of myocardial infarction *(Haffner, 1998 [B])*. In the UKPDS *(United Kingdom Prospective Diabetes Study Group, 1998 [A])*, obese patients with type 2 diabetes who were treated with metformin showed a statistically significant reduction in rates of myocardial infarction, suggesting metformin as a possible therapy of choice for these patients. A meta-analysis (*Selvin, 2004 [M])* showed a 20% increase in cardiovascular events and mortality for every 1% increase in HbA_1c over 5%.

The Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial showed an increase rate of mortality in the intensive treatment arm compared to the standard arm (hazard ratio of 1.22), and there was a similar increase in cardiovascular deaths *(ACCORD, 2008 [A])*. Many of these patients were treated with insulin and multiple oral agents, with a target of A1c < 6. There were more hypoglycemic reactions in the intensively treated group, and more weight gain compared to the standard treatment group. Compared to other trials of intensive control, patients in the ACCORD trial may have had diabetes for a longer period of time and started with a higher A1c before entering the intensive treatment arm. Implications for SCAD patients can be summarized in a joint paper published by the American Diabetes Association, the American College of Cardiology, and the American Heart Association *(Skyler, 2009 [R])*. In general older, more frail SCAD patients with more comorbid disease (like chronic kidney disease) may be at greater risk for hypoglycemia and other complications of intensive diabetes therapy; perhaps patients such as these should be allowed higher A1c goals, such as maintaining A1c < 8.0. Other SCAD patients with a more recent diagnosis of diabetes, and those with less risk for hypoglycemia and other complications of intensive treatment will still warrant aggressive therapy to a target of < 7.0. For all patients, lifestyle modification, including exercise, smoking cessation, maintaining ideal body weight, and proven risk factor reduction *(Boden, 2007 [A])* will continue to be the focus of primary and secondary cardiovascular disease prevention. The A1c goal ought to be individualized based on each patient's particular cardiovascular risk factors.

Hormone Therapy (HT)

The HERS II trial showed no cardioprotective benefit from hormone therapy, and in fact showed an increase in risk of other complications (breast cancer, venous thromboembolism, etc.) *(Hulley, 1998 [A])*. Risk-benefit analyses unequivocally support NOT starting hormone therapy for primary prevention. Should a patient already on hormone therapy present with acute coronary syndrome or be at risk for venous thromboembolism (e.g., prolonged immobilization), hormone therapy should be discontinued immediately. Clinical judgement is required in making the decision whether to continue hormone therapy in other circumstances.

6. Assessment Yields High Risk of Adverse Event?

Some patients are considered to be at high risk for infarction or death on the basis of history, physical examination and initial laboratory findings. Patients presenting with accelerating symptoms of angina (NYHA (New York Heart Association) Class III or IV, see Appendix C, "Grading of Angina Pectoris"), symptoms of

peripheral vascular disease, or symptoms of left ventricular dysfunction should be referred to a cardiologist unless precluded by other medical conditions.

7. Need for Prognostic Testing?

Prognostic testing is appropriate for patients in whom risk determination remains unclear after initial evaluations have been completed, or in whom cardiac catheterization is deemed inappropriate by the cardiologist. Prognostic testing may precede or follow an initial course of pharmacological therapy *(Frye 1989 [R]; Shub, 1990 [R])*.

8. Patient/Electrocardiogram Allows Exercise Electrocardiography?

Sensitivity of exercise electrocardiography (Masters 2-Step Exercise Test, Graded Exercise Test, Bicycle Test, Ergometry) may be reduced for patients unable to reach the level of exercise required for near maximal effort, such as:

- patients taking beta-blockers;
- patients in whom fatigue, dyspnea or claudication symptoms develop; and
- patients with vascular, orthopedic or neurological conditions who cannot perform leg exercises.

Reduced specificity may be seen in patients with abnormalities on baseline electrocardiography, such as those taking digitalis medications, and in patients with left ventricular hypertrophy or left bundle branch block *(Rutherford, 1992 [R])*.

9. Perform Exercise Electrocardiography

Most patients with normal resting electrocardiographys who can exercise and are not taking digoxin can undergo standard treadmill exercise testing.

10. Perform Non-Invasive Imaging Study

A non-invasive imaging study such as myocardial perfusion scintigraphy or stress echocardiography should best meet the patient's needs while providing the most clinical usefulness and cost effectiveness within the provider's institution. An imaging study should be selected through discussion with the cardiologist or imaging expert *(Frye, 1989 [R])*.

11. Results Yield High Risk of Adverse Event?

Exercise electrocardiography and prognostic imaging studies may yield results that indicate high, intermediate or indeterminate or low risk of adverse clinical events. High-risk patients should have a cardiology consultation unless they are not considered to be potential candidates for revascularization. Patients who are at intermediate or indeterminate risk may benefit from cardiology consultation and/or further non-invasive imaging if an exercise electrocardiogram has been performed. Low-risk patients can generally be managed medically, with a good prognosis. Low-risk patients may benefit from angiography if the diagnosis remains unclear; however, angiography is unlikely to alter outcome in these patients *(Rutherford, 1992 [R])*.

13. Is Medical Treatment Effective?

Effectiveness of pharmacologic treatment is measured by whether the anginal pain is controlled within the definition of stable coronary artery disease as stated in Annotation #1, "Patient with Stable Coronary Artery Disease."

14. Follow Regularly to Assess Risk Factors, Profile, Responses to Treatment

There is no consensus in the literature regarding frequency of follow-up; ongoing management needs and follow-up should be individualized *(Nease, 1995 [D])*.

Patient perception of symptoms may impact the effect of the symptoms on quality of life and medical management.

Please refer to Appendix C, "Grading of Angina Pectoris," for information on grading angina pectoris.

15. Worsening in Angina Pattern?

A new occurrence of angina or a worsening in the chronic stable angina pattern is considered to be present when any of the following occur:

- The symptom complex becomes less stable
- There is change in frequency, duration, precipitating causes, or ease in relief of angina
- There is evidence of recent myocardial damage

16. Change Suggests Need for Cardiology Referral?

When such change is no longer managed by alterations in the pharmacologic therapy prescribed, cardiology consultation or referral for possible invasive intervention may be appropriate *(Gibbons, 2002 [R]; Shub, 1990 [R])*.

Please see Appendix C, "Grading of Angina Pectoris," for information on grading angina pectoris.

20. Percutaneous Transluminal Coronary Angioplasty (PCTA), Coronary Artery Bypass Graft (CABG) or Other Revascularization Procedures

The relative benefits of revascularization compared with medical therapy are enhanced by an increase in absolute number of severely narrowed coronary arteries, the degree of left ventricular systolic dysfunction and the magnitude of myocardial ischemia. Among patients with lesser disease, percutaneous transluminal coronary angioplasty and coronary artery bypass graft have not been shown to reduce mortality or the risk of myocardial infarction, but do reduce the symptoms of angina and the intensity of antianginal therapy, as well as increase exercise capacity.

The COURAGE trial was a randomized controlled trial involving 2,287 patients with at least 70% stenosis in *at least one* coronary artery. They were randomized to either percutaneous transluminal coronary angiography (PTCA)/stenting or aggressive medical therapy. These patients were followed for a median of 4.6 years. The primary outcome was death from any cause and non-fatal myocardial infarction. Other outcomes included no difference in outcomes at the three-year mark (end of study). Drug eluting stents weren't used, and some think that may make a difference.

(Boden, 2007 [A]; Bourassa, 1988 [R]; Frye, 1989 [R]; Kirklin, 1991 [R]; Ryan, 1993 [R]).

Although the actual intervention of an invasive modality such as angiography, percutaneous transluminal coronary angioplasty or coronary artery bypass graft is outside this guideline and may be found within another, those patients undergoing such procedures may, at best, be restored to a chronic stable anginal pattern, thus continuing to receive medical treatment under the purview of this guideline.

Aggressive modification of cardiac risk factors in the COURAGE trial should be pursued if similar clinical results are to be obtained.

These interventions include (when clinically appropriate):

- Metoprolol XL * (50-100 mg), amlodipine * (10 mg), and/or isosorbide mononitrate * (30-120 mg), with lisinopril * (2.5-40 mg) or losartan
- Aggressive statin * (20-80 mg) therapy alone or in combination to target LDL of 60-85 mg per deciliter (1.55-2.20 mmol/liter). Note: all statins were added in the COURAGE trial
- After LDL target achieved, attempt to raise HDL to > 40 mg/dL (1.03 mmol/l) AND lower triglyceride to < 150 mg/dL (1.69 mmol/l) with exercise, niacin SR, or fibrates *, alone or in combination
- Antiplatelet therapy

* generic medications

(Boden, 2007 [A])

Pharmacologic Algorithm Annotations

21a. Patient Education and Review Principles of Medication Therapy

Antiplatelet Therapy

The use of one aspirin tablet daily (81-162 mg) is strongly recommended unless there are medical contraindications *(Antiplatelet Trialists' Collaboration, 1994 [A]; CAPRI, 1996 [A]; Fuster, 1993 [R]; Juul-Möller, 1992 [A]; Kurth, 2003 [A]; Ridker, 1991 [A])*.

The *Antithrombotic Trialists' Collaboration* is a meta-analysis that analyzed 287 studies involving 135,000 patients for different aspects of antiplatelet therapy. When comparing the 500-1,500 mg versus 160-325 mg versus 75-150 mg daily regimens of aspirin in multiple trials, there was a trend of reduction in vascular events with decreased dose (odds reduction: 19% versus 26% versus 32%, respectively) *(Antithrombotic Trialists Collaboration; 2002 [M])*. Although the meta-analysis concludes that risk of gastrointestinal bleed was similar among doses 325 mg or less, other studies such as the CURE study showed increased bleeding risk with increasing the dose, without any increase in efficacy *(Peters, 2003 [A])*.

The authors conclude that aspirin dose in the range of 75-150 mg should be given for the long-term prevention of serious vascular events in high risk patients, and that there may be a reduced benefit when increasing the dose over 150 mg daily. Doses available to most clinicians are in increments of 81 mg; therefore, the recommended dose range is 81-162 mg daily.

A multicenter case-controlled study by Kelly et al. on 550 incident cases of first-time major upper gastrointestinal bleed showed that the relative risks of bleeding in patients taking plain, enteric-coated and buffered aspirin at average daily dose of 325 mg or less were 2.6, 2.7 and 3.1, respectively *(Kelly, 1996 [C])*. The study cites few other endoscopic studies showing the opposite (gastro-protection of enteric-coated aspirin), but explains such differences by differences in trial design and population characteristics.

It remains difficult to conclude whether enteric-coated aspirin is gastro-protective or not, but clinicians should not assume that it is any safer than regular or buffered aspirin, and should treat it with the same level of caution.

Patients for whom aspirin is contraindicated (or insufficient) should be treated with clopidogrel 75 mg daily indefinitely *(Harrington, 2004 [R])*. The recently published CHARISMA trial involved 15,603 patients

with vascular disease or multiple atherothrombotic risk factors who were randomized to clopidogrel (75 mg daily) plus low-dose aspirin (75-162 mg daily) or placebo plus low-dose aspirin.

After a median follow-up of 28 months, there was no difference between the two groups in the trial's primary composite end point of myocardial infarction, stroke or death from cardiovascular causes, with an increased risk of moderate bleeding in the clopidogrel group. Rate of hospitalization was lower in the clopidogrel group when compared with placebo. Subgroup analysis showed (marginally significant) reduction in primary end point in those with documented atherothrombotic disease on the clopidogrel protocol. In contrast, those without documented atherothrombotic disease and only risk factors on the clopidogrel protocol had higher incidence of death from all causes and from cardiovascular causes. Accordingly, addition of clopidogrel to aspirin in stable coronary artery disease patients comes with little benefit and some cost, and should not be recommended on routine basis. However, there may be proven benefits of clopidogrel such as in the setting of acute vascular injury (percutaneous transluminal coronary angioplasty or acute coronary syndromes) or in selected patients with ongoing ischemic events on aspirin therapy *(Bhatt, 2006 [A])*.

In appropriately selected patients, an aspirin dose of 81 mg is recommended for patients who are on chronic clopidogrel therapy. Different doses of aspirin may apply in the setting of acute coronary syndrome; refer to the ICSI Diagnosis and Treatment of Chest Pain and Acute Coronary Syndrome (ACS) guideline for aspirin dosing.

Examples of precautions/contraindications to aspirin are:

- Patients allergic to aspirin
  - Dose-related intolerance is not a contraindication for taking aspirin
- Patients with gastrointestinal disorders
  - Recent gastrointestinal bleeding and active treatment for peptic ulcer disease are contraindications
  - The use of H-2 antagonists or proton pump inhibitor (PPI) is not a contraindication to aspirin use
  - Consideration should be given for low-dose enteric-coated (81 mg) aspirin for patients with a questionable history of gastrointestinal disorders
- Patients with recent intracranial bleeding
  - Intracranial bleeding within the past six weeks is a contraindication
  - Any history of intracranial bleeding necessitates evaluation on a case-by-case basis
- Patients with bleeding disorders or those receiving other anticoagulants
  - Certain patients receiving anticoagulants may justifiably be on aspirin, as well
- Patients with uncontrolled hypertension
  - Systolic blood pressure is greater than 180 mmHg
  - Diastolic blood pressure is greater than 110 mmHg
- Patients regularly taking non-steroidal anti-inflammatory drugs (NSAIDs)
  - Combined use of aspirin and non-steroidal anti-inflammatory drugs may increase the risk of bleeding. Enteric-coated aspirin with careful monitoring for clinical signs of gastropathy may be an acceptable strategy for patients regularly taking non-steroidal anti-inflammatory drugs.

Use of non-steroidal anti-inflammatory drugs and COX-2 inhibitors may reduce the cardioprotective benefits of aspirin. Regular, not intermittent, use of non-steroidal anti-inflammatory drugs inhibit the clinical benefits of aspirin. Caution should be used in prescribing COX-2 inhibitors to patients with coronary artery disease, because there is evidence of a class effect on cardiovascular risks *(Bresalier, 2005 [A]; Mukherjee, 2001 [R]; Nussmeier, 2005 [A]; Solomon, 2005 [A]; U.S. Food and Drug Administration, 2006 [R])*.

In patients who have undergone drug-eluting stent (DES) placement for treatment of coronary artery disease, continuation of dual antiplatelet therapy with aspirin (325 mg each day) and clopidogrel (75 mg each day) is strongly recommended for a period of at least one year in the absence of contraindications (Grines, 2007). The importance of continued dual antiplatelet therapy during this period should be discussed with patients in an effort to improve compliance, and instructions should be given to contact a health care provider prior to discontinuation of antiplatelet therapy for elective surgical or dental procedures. Due to the risk of catastrophic stent thrombosis, cessation of antiplatelet therapy should be carefully considered during the first year after drug-eluting stent (DES) implantation and particularly during the first three (post-sirolimus-eluting stent) or six months (paclitaxel-eluting stent). In combination with clopidogrel, the dose of aspirin should remain 325 mg each day for at least three months after sirolimus-eluting stent implantation or at least six months after paclitaxel-eluting stent implantation, after which time the dose can be lowered to 75-162 mg each day in combination with clopidogrel *(Grines, 2007 [R])*. Aspirin should be prescribed to all patients with stable coronary disease. If patient is aspirin intolerant, use clopidogrel. See the ICSI Antithrombotic Therapy Supplement for more information.

Statins

Many patients will require both pharmacologic and non-pharmacologic interventions to reach target goals. Target goals for hyperlipidemic patients with coronary artery disease include:

LDL – less than 100 mg/dL

HDL – 40 mg/dL or greater

Triglycerides – less than 150 mg/dL

There is now an *ideal* LDL-C goal of less than 70 mg/dL for patients considered to be very high risk. Several trials have shown clinical benefit using high-dose statins to treat to lower LDL levels. The Treat to Numbers Trial (TNT) assigned 10,001 patients with stable coronary artery disease to either 80 mg atorvastatin with achieved LDL level of 77 mg/dL, or a 10 mg dose with LDL level of 101 mg/dL, and followed them for a median of 4.9 years. In the high-dose group there was a 22% relative reduction in the primary outcome of death from coronary heart disease, non-fatal myocardial infarction, cardiac arrest and stroke. There was no reduction in overall mortality due to a 25% increase in non-cardiovascular deaths in the high-dose atorvastatin group. Another concern was significantly higher rates of side effects in the high-dose group, including myalgias and elevated liver enzymes; this higher rate of side effects occurred even with a run-in period that excluded patients intolerant to the study drug *(LaRosa, 2005 [A])*. The Prove It TIMI-22 trial compared 4,162 patients with acute coronary syndrome treated with 80 mg of atorvastin to 40 mg of pravastatin, and followed for a mean of 24 months. The atorvastatin group achieved an LDL level of 62 mg/dL and the pravastatin group had an average LDL level of 95 mg/dL. There was a 16% reduction in the hazard ratio for the combined primary end point death, myocardial infarction, unstable angina, need for revascularization, and stroke. Most of the benefit occurred within 30 days of randomization and was unaccompanied by further incremental benefit through the end of the follow-up period *(Ridker, 2005 [B])*.

At present the clinician will need to individualize therapy with statins by the degree of risk in their patients, considering a target LDL of 70 or less, especially for patients at highest risks as described by Grundy (2004). Very high risk patients include patients with established cardiovascular disease plus any of the following: 1)

multiple major risk factors, such as diabetes; 2) severe or poorly controlled risk factors, especially smoking; 3) metabolic syndrome associated risk factor (triglycerides greater than 200 mg/dL, HDL less than 40 mg/dL); and 4) patients with acute coronary syndromes. The benefits in reducing cardiac events with high-dose statin therapy will need to be weighed against the higher potential for side effects, and the potential for increased non-cardiac mortality as seen in the TNT trial, which is either real or due to chance. Further trials comparing different treatment intensities of statins should bring more clarity regarding which patients benefit most with the least side effects *(LaRosa, 2005 [A])*.

Benefit has been demonstrated in all stable coronary artery disease patients treated with statins, regardless of pretreatment cholesterol levels. This was well demonstrated in the MRC/BHF Heart Protection Study *(Heart Protection Study Collaborative Group, 2002 [A])*. Simvastatin was shown to reduce major cardiovascular events, including death, non-fatal myocardial infarction, and stroke, by 15%-20% in the subgroup of patients with pretreatment levels of less than 100 mg/dL. A similar reduction in events was also observed in patients without documented coronary artery disease, but with peripheral vascular disease, diabetes or hypertension.

This recommendation reflects the analysis of the National Cholesterol (NCEP) report, the American College of Cardiology/American Heart Association (ACC/AHA) Chronic Stable Angina guideline, and compelling evidence of mortality reduction from multiple clinical trials *(Gibbons, 2002 [R]; Grundy, 2004 [R]; Heart Protection Study Group, 2002 [A]; Hunninghake, 1998 [A])*.

Please refer to the ICSI Lipid Management in Adults guideline for recommendations on cholesterol lowering.

Every effort should be made to ensure all patients with coronary artery disease receive optimal lipid therapy. Statin medications are strongly supported as first-line medications due to compelling evidence of mortality reduction from multiple clinical trials *(Hunninghake, 1998 [A]; Sacks, 1996 [A]; Scandinavian Simvastatin Survival Study Group, 1994 [A])*.

If patients are intolerant to a statin, clinicians are strongly encouraged to have the patient try other statins in reduced doses before ruling out all statins.

The PROSPER trial showed a significant risk reduction in myocardial infarction in the elderly; therefore, age alone should not preclude treatment. The Heart Protection Study also showed benefit in patients up to age 80 years *(Heart Protection Study Group, 2002 [A]; Shepherd, 2002 [A])*.

Patients with chronic stable coronary artery disease should be on statin therapy regardless of their lipid levels unless contraindicated.

As-Needed Nitrates

In patients with mild, stable coronary artery disease, drug therapy may be limited to short-acting sublingual nitrates on an as-needed basis. Use of lower dose (e.g., 0.3 mg or one-half of a 0.4 mg tablet) may reduce the incidence of side effects such as headache or hypotension in susceptible patients.

For more information regarding drug selection, please see Appendix B, "Medication Tables."

Beta-Blocking Agents

Beta-blockers should be used in all status post-myocardial infarction patients, based on studies showing mortality reduction. They are also the preferred first-line therapy for reducing symptoms of angina in patients with stable coronary artery disease. Drugs with intrinsic sympathomimetic activity should be avoided. Abrupt withdrawal of all beta-blockers should be avoided *(Cucherat, 1997 [A]; Frye, 1989 [R]; Shub, 1990 [R])*.

21b. Nutritional Supplement Therapy

The American Heart Association *(Gibbons, 2002 [R])* recommends inclusion of omega-3 fatty acids in patients with stable coronary artery disease because of evidence from randomized controlled trials. The GISSI study *(GISSI-Heyenzione Investigators, 1999 [A])*, using 850 mg of eicosopentaenoic acid (EPA) and docosahexaenoic acid (DHA) daily, showed a 20% overall mortality reduction, and a 45% reduction in sudden death. The JELIS trial used 1.8 grams EPA supplement daily and showed 19% relative reduction in major coronary events after mean follow-up of 4.6 years *(Yokoyama, 2007 [A])*. Other studies showing benefit include the DART trial and the Lyon trial, and data have been recently summarized by meta-analysis indicating significant reduction in risk of sudden death and overall mortality *(Bucher, 2002 [M]; Burr, 1989 [A]; deLorgeril, 1999 [A]; Kris-Etherton, 2002 [R])*.

The recommended daily amount of omega-3 fatty acids in patients with stable coronary artery disease is 1 gram of eicosopentaenoic acid (EPA) plus docosahexaenoic acid (DHA) by capsule supplement or by eating at least two 4-ounce servings per week of fatty fish. The amounts of omega-3 fatty acids in various foods are found in Appendix D, "Omega-3 Fatty Acids." To obtain the recommended daily amount of 1,000 mg EPA plus DHA per day, patients ought to be counseled in the proper way to interpret the supplement label. The goal is to consume 1,000 mg of EPA plus DHA, but not all omega-3 in a fish oil concentrate is EPA and DHA. The product label defines what constitutes a dose. Because there is variation in doses across products, it is necessary to calculate the EPA and DHA amount per dose, and consume the number of doses that together equate one gram *(Lee, 2008 [R])*. For example, if one serving size is two softgels, each serving containing 360 mg EPA plus 240 mg DHA, one would take two servings (four softgels) to attain the recommended dose of at least 1,000 mg of EPA plus DHA per day.

In addition to EPA and DHA supplements, patients with stable coronary artery disease should be encouraged to follow a diet rich in alpha-linolenic acid (ALA). According to published data, 1.5 gram-3 grams ALA per day appears to benefit the general population, and those at risk of heart disease also demonstrate benefit (based on level III evidence) *(Kris-Etherton, 2002 [R])*. Plant-based sources of omega-3 fatty acids would be ground flax seed, flax seed oil, walnuts, walnut oil, canola oil, soybeans and soybean oil. Fish meals can be difficult for patients to maintain, and there are issues of potential environmental contaminants including mercury, polychlorinated biphenyl (PCB), dioxin and others. Because of this, capsule supplements may be preferred, although there is no uniformity of EPA and DHA content or purity. Patients should consult their health providers or nutritionists regarding this issue. Please see the ICSI Omega-3 Fatty Acids for Coronary Artery Disease Technology Assessment #94 for more information.

Dietary and non-dietary intake of n-3 polyunsaturated fatty acids may reduce overall mortality, mortality due to myocardial infarction, and sudden death in patients with stable coronary artery disease.

High doses of vitamin E supplement (greater than 400 IU/day) may increase or cause mortality and should be avoided *(Lee, 2005 [A]; Miller, 2005 [M])*.

21c. Use of ACE Inhibitors for Risk Reduction

Among patients with stable angina, ACE inhibitors are most beneficial to patients with left ventricular dysfunction post-myocardial infarction, persistent hypertension and diabetes *(HOPE Study Investigators, 2000 [A])*. Patients with normal left ventricular function who also have hypertension, type II diabetes mellitus or chronic kidney disease should be on ACE inhibitors *(European Trial on Reduction of Cardiac Events with Perindopril in Stable Coronary Artery Disease Investigators 'EUROPA', 2003 [A]; HOPE Study Investigators, 2000 [A])*. If the patient cannot tolerate ACE inhibitors, a potential substitute would be angiotensin II receptor blockers *(Mann, 2008 [A])*. Results of the PEACE trial showed no statistically significant benefit for patients with stable coronary artery disease with preserved left ventricular function who are receiving "current standard" therapy, including statins *(PEACE Trial Investigators, 2004 [A])*.

A recent meta-analysis of five placebo randomized controlled trials involving different ACE inhibitors showed reduction in all cause and cardiovascular mortality, as well as myocardial infarction, that were statistically significant. The degree of benefit needs to be assessed individually and may depend on patient characteristics *(Danchin, 2006 [M])*.

21d. Does Patient Need Daily Antianginal Therapy?

The decision to initiate daily drug therapy for coronary artery disease is based upon the symptom complex of the patient in combination with findings from the history, physical examination, laboratory studies and prognostic testing *(Frye, 1989 [R]; Gorlin, 1992 [R]; ISIS-4, 1995 [A]; Rutherford, 1992 [R]; Shub, 1990 [R]; SOLVD Investigators, 1991 [A])*.

Ranolazine is a newly approved drug indicated for treatment of angina. Due to concerns of QT prolongation with its use, the work group can not recommend for or against its use at the current time. More evidence is needed to evaluate.

21e. Prescribe Monotherapy

Beta-Blocking Agents

Beta-blockers should be used in all status post-myocardial infarction patients, based on studies showing mortality reduction. They are also the preferred first-line therapy for reducing symptoms of angina in patients with stable coronary artery disease. Drugs with intrinsic sympathomimetic activity should be avoided. Abrupt withdrawal of all beta-blockers should be avoided *(Cucherat, 1997 [A]; Frye, 1989 [R]; Shub, 1990 [R])*.

Long-Acting Nitrates

If beta-blockers cannot be prescribed as first-line therapy, nitrates are the preferred alternative first-line therapy because of efficacy, low cost and relatively few side effects. Tolerance to long-acting nitrates is an important clinical issue in some patients and can be avoided by appropriate daily nitrate-free intervals *(Cheitlin, 1999 [R]; Frye, 1989 [R]; Parker, 1998 [R])*.

Adverse Interactions between Nitrates and Phosphodiesterase-5 Inhibitors

Patients with stable coronary artery disease should be advised that due to potentially life-threatening hypotension, phosphodiesterase-5 inhibitors (such as sildenafil, vardenafil and tadalafil) are absolutely contraindicated if they have used nitrates within the last 24 hours.

In any patient evaluated for acute coronary insufficiency, nitrates must also be avoided if there is a history of sildenafil or phosphodiesterase-5 inhibitor use in the previous 24-48 hours (avoid nitrates for 24 hours after sildenafil and verdenafil; avoid nitrates for 48 hours after tadalafil). All other interventions, including all non-nitrate antianginal medications may be used for these patients.

Calcium Channel Blocker

For patients who are unable to take beta-blockers or long-acting nitrates, the use of calcium channel blockers has been shown to be clinically effective in decreasing symptoms of angina. Calcium channel blockers have not been proven to reduce mortality. Because beta-blockers have reduced mortality in the post-myocardial infarction period, they are the preferred agent for patients with stable coronary artery disease *(Shub, 1990 [R])*. Dihydropyridines as monotherapy may exacerbate angina.

21g. Prescribe Combination Therapy

Combination therapy may be necessary in selected patients, but it increases side effects and cost. A combination of beta-blockers and long-acting nitrates is preferred because of cost, efficacy and reduced potential for adverse side effects *(Akhras, 1991 [A]; Rutherford, 1992 [R]; Tolins, 1984 [A])*. The following factors should be considered when beta-blockers and calcium channel blockers are combined *(Strauss, 1988 [R])*:

- This combination may not be better than either agent used alone in maximum tolerated doses.
- If angina persists at the maximum optimal dose of beta-blocker, addition of a calcium channel blocker is likely to reduce angina and improve exercise performance.
- Addition of verapamil or diltiazem to a beta-blocker does not usually enhance therapy and may precipitate symptomatic bradycardia, but addition of a beta-blocker to nifedipine can have enhanced effects.
- With left ventricular dysfunction, sinus bradycardia, or conduction disturbances, combination treatment with calcium channel blockers and beta-blockers should be avoided or initiated with caution. In patients with conduction system disease, the preferred combination is nifedipine and a beta-blocker.
- The combination of dihydropyridines and long-acting oral nitrates is usually not optimal because both are potent vasodilators.
- If side effects prohibit increased doses but symptoms persist, selected patients may need low doses of multiple drug therapy.

21h. Combination Therapy Effective?

If after several attempts at adjusting the medications, a therapeutic combination is not achieved for the patient, a cardiology consultation or referral may be appropriate.

Appendix A – Comorbid Conditions

Medical Conditions

Condition	Recommended Treatment (and alternative)	Avoid
Systemic hypertension	Beta-blockers (calcium antagonists)	
Migraine or vascular headaches	Beta-blockers (verapamil or diltiazem)	
Asthma or COPD w/ bronchospasm	Verapamil **or** diltiazem	Gradual titration with low initial doses may allow some patients to tolerate beta-blockers; careful monitoring is required.
Hyperthyroidism	Beta-blockers	
Raynaud's syndrome	Long-acting, slow-release calcium antagonists	Beta-blockers
Diabetes mellitus	ACE inhibitors, beta-blockers (particularly if prior myocardial infarction) **or** long-acting, slow-release calcium antagonists Optimize medical therapy per the ICSI Management of Type 2 Diabetes Mellitus guideline	
Mild peripheral vascular disease	Beta-blockers **or** calcium antagonists	
Severe peripheral vascular disease with rest ischemia	Calcium antagonists	Beta-blockers

Cardiac Arrhythmias and Conduction Abnormalities

Sinus bradycardia	Long-acting, slow-release calcium antagonists that do not decrease heart rate	Beta-blockers, diltiazem, verapamil
Sinus tachycardia (not due to heart failure)	Beta-blockers	
Supraventricular tachycardia	Verapamil, diltiazem **or** beta-blockers	
Atrioventricular block	Long-acting, slow-release calcium antagonists that do not slow A-V conduction	Beta-blockers, verapamil, diltiazem
Rapid atrial fibrillation (with digitalis)	Verapamil, diltiazem, **or** beta-blockers	
Ventricular arrythmias	Beta-blockers	

Special Conditions

Hypertrophic cardiomyopathy	Beta-blockers, non-dihydropyridine calcium antagonists	Nitrates, dihydropyridine calcium antagonists

Appendix B – Medication Tables

Antiplatelet Medication Therapies		
Generic name	**Usual dosage**	**Comments**
Aspirin	81-162 mg daily	Everyday administration is preferable, but 325 mg every other day is acceptable. Enteric-coated tablets or dosing with meals can minimize stomach upset. Patients on warfarin may take low-dose aspirin (81 mg). Patients using aspirin should avoid regular use of NSAIDs.
Clopidogrel	75 mg daily	Clopidogrel is recommended for all patients with coronary artery disease who are truly intolerant of aspirin.
As-Needed Nitrates		
Sublingual nitroglycerin	0.3-0.6 mg SL, may repeat x3.	If pain worsens or is not relieved after five minutes of first dose, call 911. Some patients take nitroglycerin regularly and should consult their physician about when to call 911.

Antianginal Therapies			
	Generic name	**Usual dosage**	**Comments**
Beta-blockers	Atenolol	50-200 mg daily	A target heart rate is 55-60 beats per minute. Abrupt withdrawal of beta-blockers should be avoided.
	Metoprolol	50-200 mg twice daily	
	Propanolol	20-80 mg twice daily	
	Other beta-blockers are available.		
Long-acting nitrates	Isosorbide mononitrate	30-60 mg once daily in morning. Maximum 240 mg daily 20 mg twice daily (7 hours apart) 20 mg twice daily (7 hours apart)	Tolerance can be avoided by appropriate daily nitrate-free intervals. Isordil can be given at 7A, 12N and 5P.
	Other forms of nitroglycerin are available.		
Calcium channel blockers	Verapamil long-acting	120-480 mg daily	Monotherapy with nifedipine should be avoided because of a reflex increase in heart rate.
	Diltiazem long-acting	120-320 mg daily	
	Nifedipine long-acting	30-180 mg daily	
	Amlodipine	5-10 mg daily	
	Other calcium channel blockers are available.		

See prescribing information for complete details. For the most up-to-date medication information consider the following sources: www.epocrates.com, www.micromedex.com, uptodate.com, www.pdr.net.

Appendix C – Grading of Angina Pectoris

Grading of Angina Pectoris by the New York Heart Association Classification System

Class I

Cardiac disease without resulting limitation of physical activity.

Class II

Slight limitation of physical activity – comfortable at rest, but ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

Class III

Marked limitations in physical activity – comfortable at rest, but less than ordinary physical activity causes fatigue, palpitation, dyspnea, or anginal pain.

Class IV

Inability to carry on any physical activity without discomfort – or symptoms at rest.

Source: ACC/AHA/ACP-ASIM Chronic Stable Angina Guidelines

Appendix D – Omega-3 Fatty Acids

Omega-3 fatty acids are found in fish oil and in some vegetable oils, nuts, seeds and soy. You can get omega-3 fatty acids from some foods or from over-the-counter and prescription supplements. Fish oil contains two important omega-3 fatty acids: **EPA** (eicosapentanoic acid) and **DHA** (docosahexanoic acid). Plant sources provide **ALA** (alpha-linolenic acid). Studies of EPA and DHA suggest that:

- doses of up to 1,000 mg per day reduce risk of heart attacks in high-risk patients; and
- doses of 2,000 mg-4,000 mg per day lower serum triglyceride levels, particularly for patients with triglyceride levels over 500 mg/L.

Tips for Getting More Omega-3 Fatty Acids

- Select fish from the chart below and eat at least 7 ounces per week. Prepare fish by grilling, baking, broiling or poaching.
- Omega-3 fatty acid supplements should be refrigerated and eaten with food. This will reduce the possibility of a mild fishy aftertaste.
- For those who cannot or will not consume fish-based products, an alternate source of omega-3 in the form of ALA from may be found in plant sources (level III evidence).
- Use vegetable oils that are high in omega-3 fatty acids. Examples are canola oil, soybean oil, flaxseed oil and walnut oil.
- Add walnuts or ground flaxseed to cereals, yogurt and salads. Whole flaxseeds will not work as well – they simply pass through the body undigested.
- Snack on edamame (steamed soybeans, sold fresh or frozen).

(Kris-Etherton, 2002 [R])

Amounts of EPA+DHA in Fish and Fish Oils and the Amount of Fish Consumption Required to Provide ~1 g of EPA+DHA Per Day

	EPA+DHA Content, g/3-oz Serving Fish (Edible Portion) or g/g Oil	Amount Required to Provide ~1 g of EPA+DHA per Day, oz (Fish) or g (Oil)
Fish		
Tuna		
Light, canned in water, drained	0.26	12
White canned, in water, drained	0.73	4
Fresh	0.24-1.28	2.5-12
Sardines	0.98-1.70	2-3
Salmon		
Chum	0.68	4.5
Sockeye	1.05	2.5
Pink	1.09	2.5
Chinook	1.48	2
Atlantic, farmed	1.09-1.83	1.5-2.5
Atlantic, wild	0.9-1.56	2-3.5
Mackerel	0.34-1.57	2-8.5
Herring		
Pacific	1.81	1.5
Atlantic	1.71	2
Trout, rainbow		
Farmed	0.98	3
Wild	0.84	3.5
Halibut	0.4-1.0	3-7.5
Cod		
Pacific	0.24	12.5
Atlantic	0.13	23
Haddock	0.2	15
Catfish		
Farmed	0.15	20
Wild	0.2	15
Flounder/Sole	0.42	7
Oyster		
Pacific	1.17	2.5
Eastern	0.95	3
Farmed	0.37	8
Lobster	0.07-0.41	7.5-42.5
Crab, Alaskan King	0.35	8.5
Shrimp, mixed species	0.27	11
Clam	0.24	12.5
Scallop	0.17	17.5
Capsules		
Cod liver oil*	0.19	5
Standard fish body oil	0.30	3
Omega-3 fatty acid concentrate	0.50	2
Omacor (Pronova Biocare) †	0.85	1

Data from the USDA Nutrient Data Laboratory. The intakes of fish given above are very rough estimates because oil content can vary markedly (> 300%) with species, season, diet, and packaging and cooking methods.

* This intake of cod liver oil would provide approximately the Recommended Dietary Allowance (RDA) of vitamin A and twice the RDA for vitamin D.

† Not currently available in the United States.

α-Linolenic Acid Content of Selected Vegetable Oils, Nuts and Seeds

	α-Linolenic Acid Content, g/tbsp
Olive oil	0.1
Walnuts, English	0.7
Soybean oil	0.9
Canola oil	1.3
Walnut oil	1.4
Flaxseeds	2.2
Flaxseed (linseed) oil	8.5

Permission granted by Wolters Kluwer, Kris-Etherton PM, Harris WS, Appel LJ. Consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Circulation* 2002;106:2747-57.

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Original Work Group Members

Dan Anderson
Measurement Advisors
HealthPartners

Fritz Arnason, MD
General Internist
Park Nicollet Clinic

Steve Benton, MD
Cardiology
HealthPartners

Bryon Dockter, RN, MSA
Facilitator
The Bryter Group

Dale J. Duthoy, MD
Family Practice
MinnHealth Family Physicians

Marilyn Eelkema, RPh
Pharmaceutics
HealthPartners

Susan M. Hanson, RD
Health Education
Park Nicollet Medical Foundation

Greg Lehman, MD
General Internist, Work Group Leader
HealthPartners

Trish Lester-Rux, RN
Adult Medicine
North Region Group Practice Org

Todd Mestad
Business Health Care Action Group
IDS Financial Services

Hugh Smith, MD
Cardiology
Mayo Clinic

Anthony Spagnolo, MD
Family Practice
Park Nicollet Clinic

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Contact ICSI at:
8009 34th Avenue South, Suite 1200; Bloomington, MN 55425; (952) 814-7060; (952) 858-9675 (fax)
Online at http://www.ICSI.org

Brief Description of Evidence Grading

Individual research reports are assigned a letter indicating the class of report based on design type: A, B, C, D, M, R, X.

A full explanation of these designators is found in the Foreword of the guideline.

References

Action to Control Cardiovascular Risk in Diabetes Study Group, The. Effects of intensive glucose lowering in type 2 diabetes. *N Engl J Med* 2008;358:2545-59. (Class A)

Akhras F, Jackson G. Efficacy of nifedipine and isosorbide mononitrate in combination with atenolol in stable angina. *Lancet* 1991;338:1036-39. (Class A)

Antiplatelet Trialists' Collaboration. Collaborative overview of randomised trials of antiplatelet therapy – I: Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. *BMJ* 1994;38:81-106. (Class M)

Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002;324:71-86. (Class M)

Bell DM, Nappi J. Myocardial infarction in women: a critical appraisal of gender differences in outcomes. *Pharmacotherapy* 2000;20:1034-44. (Class R)

Bhatt DL, Fox KAA, Hacke W, et al. Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. *N Engl J Med* 2006;354:1706-17. (Class A)

Boden WE, O'Rourke RA, Teo KK, et al. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med* 2007;356:1503-16. (Class A)

Bønaa KH, Njølstad I, Ueland PM, et al. Homocysteine lowering and cardiovascular events after acute myocardial infarction. *N Engl J Med* 2006;354:1578-88. (Class A)

Bourassa MG, Alderman EL, Bertrand M, et al. Report of the Joint ISFC/WHO Task Force on coronary angioplasty. *Circulation* 1988;78:780-89. (Class R)

Bresalier RS, Sandler RS, Quan H, et al. Cardiovascular events associated with rofecoxib in a colorectal adenoma chemoprevention trial. *N Engl J Med* 2005;352:1092-102. (Class A)

Bucher HC, Hengstler P, Schindler C, Meier G. N-3 polyunsaturated fatty acids in coronary heart disease: a meta-analysis of randomized controlled trials. *Am J Med* 2002;112:298-304. (Class M)

Burr ML, Gilbert JF, Holliday RM, et al. Effects of changes in fat, fish, and fibre intakes on death and myocardial reinfarction: diet and reinfarction trial (DART). *Lancet* 1989;8666:757-61. (Class A)

CAPRIE Steering Committee. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). *Lancet* 1996;348:1329-39. (Class A)

Cheitlin MD, Hutter AM, Brindis RG, et al. Use of sildenafil (viagra) in patients with cardiovascular disease. *JACC* 1999;33:273-82. (Class R)

Cucherat M, Boissel JP, Leizorovicz (for the APSI investigators). Persistent reduction of mortality for five years after one year of acebutolol treatment initiated during acute myocardial infarction. *Am J Cardiol* 1997;79:587-89. (Class A)

Danchin N, Cucherat M, Thuillez C, et al. Review: ACE inhibitors reduce mortality and cardiovascular endpoints in stable coronary artery disease. *Arch Intern Med* 2006;166:787-96. (Class M)

de Lorgeril M, Salen P, Martin J-L, et al. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon diet heart study. *Circulation* 1999;99:779-85. (Class A)

Eckel RH, Krauss RM (for the AHA Nutrition Committee). American Heart Association call to action: obesity as a major risk factor for coronary heart disease. *Circulation* 1998;97:2099-100. (Class X)

EURopean Trial on Reduction of Cardiac Events with Perindopril in Stable Coronary Artery Disease Investigators, The. Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomised, double-blind, placebo-controlled, multicentre trial (the EUROPA study). *Lancet* 2003;362:782-88. (Class A)

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). *JAMA* 2001;285:2486-97. (Class R)

Frye RL, Gibbons RJ, Schaff HV, et al. Treatment of coronary artery disease. *JACC* 1989;13:957-68. (Class R)

Fuster V, Dyken ML, Vokonas PS, et al. Aspirin as a therapeutic agent in cardiovascular disease. *Circulation* 1993;87:659-75. (Class R)

Gibbons RJ, Abrams J, Chatterjee K, et al. ACC/AHA 2002 guideline update for the management of patients with chronic stable angina: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (committee to update the 1999 guidelines for the management of patients with chronic stable angina). 2002. Available at: www.acc.org/clinical/guidelines/stable/stable.pdf. (Class R)

GISSI-Prevenzione Investigators. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the gastrointestinalSSI-Prevenzione trial. *Lancet* 1999;354:447-55. (Class A)

Gorlin R. Treatment of chronic stable angina pectoris. *Am J Cardiol* 1992;70:26G-31G. (Class R)

Grines CL, Bonow RO, Casey Jr DE, et al. Prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents: a science advisory from the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association, with representation from the American College of Physicians. *Circulation* 2007;115:813-18. (Class R)

Grundy SM, Cleeman JI, Bairey Merz CN, et al. Implications of recent clinical trials for the national cholesterol education program adult treatment panel III guidelines. *Circulation* 2004;110:227-39. (Class R)

Haffner SM, Lehto S, Rönnemaa T, et al. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. *N Engl J Med* 1998;339:229-34. (Class B)

Hambrecht R, Walther C, Möbius-Winkler S, et al. Exercise training reduced ischemic events more than percutaneous coronary intervention in stable coronary artery disease. *Circulation* 2004;109:1371-78. (Class A)

Harrington RA, Becker RC, Ezekowitz M, et al. Antithrombotic therapy for coronary artery disease: the seventh ACCP conference on antithrombotic and thrombolytic therapy. *Chest* 2004;126:513S-48S. (Class R)

Harvard Medical School. More research on women's unique heart risks: now that studies of heart disease include women, we're learning about "heart-felt" sex differences. *Harv Women's Health Watch* 2005;12:1-2 (Class R)

Heart Outcomes Prevention Evaluation (HOPE) 2 Investigators, The. Homocysteine lowering with folic acid and B vitamins in vascular disease. *N Engl J Med* 2006;354:1567-77. (Class A)

Heart Protection Study Collaborative Group. MRC/BHF heart protection study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002;360:7-22. (Class A)

HOPE Study Investigators, The. The effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *N Engl J Med* 2000;342:145-53. (Class A)

Hulley S, Grady D, Bush T, et al. Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women (HERS). *JAMA* 1998;280:605-13. (Class A)

Hunninghake DB. Therapeutic efficacy of the lipid-lowering armamentarium: the clinical benefits of aggressive lipid-lowering therapy. *Am J Med* 1998;104:9s-13s. (Class A)

Hurst JW, Schlant RC, Rackley CE, et al, eds. Methods of study and clinical features. *In* The Heart, Arteries and Veins. New York: McGraw-Hill, 1990:963-71. (Class R)

ISIS-4. A randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. *Lancet* 1995;345:669-85. (Class A)

Juul-Möller S, Edvardsson N, Jahnmatz B, et al. Double-blind trial of aspirin in primary prevention of myocardial infarction in patients with stable chronic angina pectoris. *Lancet* 1992;340:1421-25. (Class A)

Kelly JP, Kaufman DW, Jurgelon JM, et al. Risk of aspirin-associated major upper-gastrointestinal bleeding with enteric-coated or buffered product. *Lancet* 1996;348:1413-16. (Class C)

Kirklin JW, Akins CW, Blackstone EH, et al. Guidelines and indications for coronary artery bypass graft surgery: a report of the ACC/AHA task force on assessment of diagnostic and therapeutic cardiovascular procedures. *JACC* 1991;17:543-89. (Class R)

Kop WJ, Ader DN. Assessment and treatment of depression in coronary artery disease patients. *Ital Heart J* 2001;2:890-94. (Class R)

Kordella T. The heart of a woman. *Diabetes Forecast* 2005;58:42-47. (Class R)

Kris-Etherton PM, Harris WS, Appel LJ. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Circulation* 2002;106:2747-57. (Class R)

Kurth T, Glynn RJ, Walker AM, et al. Inhibition of clinical benefits of aspirin on first myocardial infarction by nonsteroidal anti-inflammatory drugs. *Circulation* 2003;108:1191-95. (Class A)

LaRosa JC, Grundy SM, Waters DD, et al. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. *N Engl J Med* 2005;352:1425-35. (Class A)

Lee IM, Cook NR, Gaziano JM, et al. Vitamin E in the primary prevention of cardiovascular disease and cancer: the women's health study: a randomized controlled trial. *JAMA* 2005;294:56-65. (Class A)

Lee JH, O'Keefe JH, Lavie CJ, et al. Omega-3 fatty acids for cardioprotection. *Mayo Clin Proc* 2008;83:324-32. (Class R)

Lichtman JH, Bigger Jr JT, Blumenthal JA, et al. Depression and coronary heart disease: recommendations for screening, referral, and treatment: a science advisory from the American heart association prevention committee of the council on cardiovascular nursing, council on clinical cardiology, council on epidemiology and prevention, and interdisciplinary council on quality of care and outcomes research: endorsed by the American psychiatric association. *Circulation* 2008;118:1768-75. (Class R)

Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group, The. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and broad range of initial cholesterol levels. *N Engl J Med* 1998;339:1349-57. (Class A)

Mann JFE, Schmieder RE, McQueen M, et al. Renal outcomes telmisartan, ramipril, or both, in people at high vascular risk (the ONTARGET study): a multicenter, randomised, double-blind, controlled trial. *Lancet* 2008;372:547-53. (Class A)

Miller III ER, Pastor-Barriuso R, Dalal D, et al. Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. *Ann Intern Med* 2005;142:37-46. (Class M)

Mukherjee D, Nissen SE, Topol EJ. Risk of cardiovascular events associated with selective COX-2 inhibitors. *JAMA* 2001;286:954-59. (Class R)

NCEP Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, The. Summary of the second report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. *JAMA* 1993;269:3015-23. (Class R)

Nease RF, Kneeland T, O'Connor GT, et al. Variation in patient utilities for outcomes of the management of chronic stable angina: implications for clinical practice guidelines. *JAMA* 1995;273:1185-90. (Class D)

Nussmeier NA, Whelton AA, Brown MT, et al. Complications of the COX-2 inhibitors parecoxib and valdecoxib after cardiac surgery. *N Engl J Med* 2005;352:1081-91. (Class A)

Parker JD, Parker JO. Nitrate therapy for stable angina pectoris. *N Engl J Med* 1998;338:520-31. (Class R)

PEACE Trial Investigators, The. Angiotensin-converting-enzyme inhibition in stable coronary artery disease. *N Engl J Med* 2004;351:2058-68. (Class A)

Peters RJG, Mehta SR, Fox KAA, et al. Effects of aspirin dose when used alone or in combination with clopidogrel in patients with acute coronary syndromes: observations from the clopidogrel in unstable angina to prevent recurrent events (CURE) study. *Circulation* 2003;108:1682-87. (Class A)

Ridker PM, Cannon CP, Morrow D, et al. C-reactive protein levels and outcomes after statin therapy. *N Engl J Med* 2005:352:20-28. (Class B)

Ridker PM, Manson JE, Gaziano M, et al. Low-dose aspirin therapy for chronic stable angina: a randomized, placebo-controlled clinical trial. *Ann Intern Med* 1991;114:835-39. (Class A)

Rutherford JD, Braunwald E. *In* Chronic Ischemic Heart Disease, 4th ed. W.B. Saunders, 1992:1292-1317. (Class R)

Ryan TJ, Bauman WB, Kennedy JW, et al. ACC/AHA guidelines for percutaneous transluminal coronary angioplasty: a report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Committee on Percutaneous Transluminal Coronary Angioplasty). *J Am Coll Cardiol* 1993;22:2033-54. (Class R)

Sacks FM, Pfeffer MA, Moye LA, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels (CARE). *N Engl J Med* 1996;335:1001-09. (Class A)

Scandinavian Simvastatin Survival Study Group, The. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet* 1994;344:1383-89. (Class A)

Selvin E, Marinopoulos S, Berkenblit G, et al. Meta-analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. *Ann Intern Med* 2004;141:421-31. (Class M)

Shepherd J, Blauw GJ, Murphy MB, et al. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. *Lancet* 2002;360:1623-30. (Class A)

References

Shub C. Stable angina pectoris: 1. clinical patterns. *Mayo Clin Proc* 1990;64:233-42. (Class R)

Skyler JS, Bergenstal R, Bonow RO, et al. Intensive glycemic control and the prevention of cardiovascular events: implications of the ACCORD, ADVANCE and VA diabetes trials: a position statement of the American diabetes association and a scientific statement of the American college of cardiology foundation and the American heart association. *Diabetes Care* 2009;32:187-92. (Class R)

Smith SC, Allen J, Blair SN, et al. AHA/ACC guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 update. *J Am Coll Cardiol* 2006;47:2130-39. (Class R)

SOLVD Investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. *N Engl J Med* 1991;325:293-302. (Class A)

Solomon SD, McMurray JJV, Pfeffer MA, et al. Cardiovascular risk associated with celecoxib in a clinical trial for colorectal adenoma prevention. *N Engl J Med* 2005:352:1071-80. (Class A)

Strauss WE, Parisi AF. Combined use of calcium-channel and beta-adrenergic blockers for the treatment of chronic stable angina: rationale, efficacy, and adverse effects. *Ann Intern Med* 1988;109:570-81. (Class R)

Tolins M, Weir EK, Chesler E, et al. Maximal drug therapy is not necessarily optimal in chronic angina pectoris. *JACC* 1984;3:1051-57. (Class A)

UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes. *Lancet* 1998;352:837-53. (Class A)

U.S. Food and Drug Administration. Concomitant use of ibuprofen and aspirin: potential for attenuation of the anti-platelet effect of aspirin. Available at: http://www.fda.gov/cder/drug/infopage/ibuprofen/science_paper.htm. September 8, 2006. (Class R)

Yokoyama M, Origasa H, Matsuzaki M, et al. Effects of eicosapentaenoic acid on major coronary events in hypercholesterolaemic patients (JELIS): a randomised open-label, blinded endpoint analysis. *Lancet* 2007;369:1090-98. (Class A)

This section provides resources, strategies and measurement specifications for use in closing the gap between current clinical practice and the recommendations set forth in the guideline.

The subdivisions of this section are:

- Priority Aims and Suggested Measures
  - Measurement Specifications
- Key Implementation Recommendations
- Knowledge Resources
- Resources Available

Priority Aims and Suggested Measures

1. Increase the percentage of appropriate patients with an appropriate diagnosis of stable coronary artery disease (SCAD), who are prescribed aspirin and antianginal medications. *(Annotation #21a)*

   Possible measure of accomplishing this aim:

   a. Percentage of patients with stable coronary artery disease who have aspirin (unless contraindicated) use documented in the medical record.

   b. Percentage of patients with SCAD who have antianginal medication use documented in the medical record.

2. Improve education/understanding around the management of stable coronary artery disease.

   Possible measure of accomplishing this aim:

   a. Percentage of patients with stable coronary artery disease with documentation in the medical record indicating they have demonstrated an understanding of how to respond in an acute cardiac event:

      - Proper use of nitroglycerin
      - Consistent use of aspirin (unless contraindicated), or consistent use of clopidogrel as directed
      - When to call 911

   b. Percentage of patients who are able to "teach back" and demonstrate their knowledge of an acute cardiac event, to include the following: proper use of nitroglycerin, consistent use of aspirin (unless contraindicated) or clopidogrel as directed, and when to call 9ll.

3. Increase the percentage of patients with stable coronary artery disease who receive an intervention for modifiable risk factors.

   Possible measures of accomplishing this aim:

   a. Percentage of patients who smoke, with documentation in the medical record that advice to quit was provided and/or help to quit was provided.

   b. Percentage of patients with cardiovascular disease who receive an annual flu shot.

   c. Percentage of patients with documentation in the medical record of education around the importance of exercise and physical activity.

   d. Percentage of patients with documentation in the medical record of an activity goal and when goal was met.

   e. Percentage of patients who were screened for depression using the PHQ-9 (see the ICSI Major Depression in Adults in Primary Care guideline).

   f. Percentage of patients with documentation in the medical record that an LDL was obtained within the last 12 months.

   g. Percentage of patients with documentation in the medical record that an LDL was obtained and the result was less than 100 mg/dL within the last 12 months.

   h. Percentage of patients with a body mass index (BMI) documented in the medical record within the last 12 months.

   i. Percentage of patients with a documented blood pressure in the medical record of 130/80 mmHg or less.

4. Improve the assessment of patients with a diagnosis of stable coronary artery disease who present with angina symptoms.

   Possible measure of accomplishing this aim:

   a. Percentage of patients with documentation in the medical record of angina symptoms within the last 12 months.

   b. Percentage of patients with accelerated symptoms of angina, symptoms or peripheral vascular disease, or symptoms indicating left ventricular function (LVF) dysfunction who were referred to a cardiologist (unless precluded by other medical condiditons).

5. Increase the use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) in patients with coronary artery disease, including those patients with a diagnosis of diabetes, chronic kidney disease and hypertension.

   Possible measure of accomplishing this aim:

   a. Percentage of patients who are prescribed an ACE inhibitor or ARB.

   b. Percentage of patients with a diagnosis of SCAD as well as diabetes who are prescribed an ACE inhibitor or ARB.

   c. Percentage of patients with a diagnosis of SCAD along with chronic kidney disease who are prescribed an ACE inhibitor or ARB.

   d. Percentage of patients with a diagnosis of SCAD along with hypertension who are prescribed an ACE inhibitor or ARB.

6. Increase the percentage of patients with a diagnosis of stable coronary artery disease who receive education around nutritional supplement therapy.

   Possible measure for accomplishing this aim:

   a. Percentage of patients with documentation in the medical record indicating that education was provided around the benefits of omega-3, and recommended daily amount of omega-3 fatty acids in patients with SCAD.

7. Increase prognostic testing for patients whose risk determination remains unclear.

   Possible measure for accomplishing this aim:

   a. Percentage of patients with documentation in the medical record of prognostic testing preceding or following a course of pharmologic therapy.

Measurement Specifications

Possible Success Measure #1a

Percentage of patients with stable coronary artery disease who have aspirin use documented in the medical record.

Population Definition

All patients age 18 and over with stable coronary artery disease.

Data of Interest

$$\frac{\text{\# patient records containing documentation of aspirin use}}{\text{Total \# records reviewed for stable coronary artery disease patients}}$$

Numerator/ Denominator Definitions

Numerator: Aspirin documentation should be treated as any medication and assessed at every visit. Any mention or documentation of regular aspirin intake found on the Medications List or in the progress notes should be counted as a "yes" for this measure.

For the purpose of this measure, the medical record should be reviewed for care provided during the previous two years. Documentation of regular aspirin use and/or contraindication to use should be found within this time span of current care.

Contraindications to aspirin use are not defined in the guideline (Algorithm box #12), but left to the provider's discretion. Some commonly found contraindications are allergy to the drug and history of bleeding ulcer or gastric hemorrhage. When contraindications are present, they need to be noted in the patient's record.

Denominator: Patients with documented contraindications to aspirin are included in this measure as it is written. Patients with documented contraindications to aspirin may be excluded from the denominator of this measure at the discretion of the individual medical group.

Method/Source of Data Collection

The population for this measure is a subset of the population used for the Lipid Management in Adults measure. When a patient with a diagnosis of stable coronary artery disease is identified while doing the Lipid Management in Adults data collection, that patient's record will also be assessed for evidence that the patient is using low-dose aspirin on a regular basis. Data needs to be collected for at least 10 patients. If the sample for Lipid Management in Adults does not produce enough patients, other patients may be identified using the procedure that follows.

If not collecting data for the Lipid Management in Adults guideline or when it is necessary to identify more patients with coronary artery disease, use a computer run to select patients with the suggested ICD-9 codes or the ICD-9 codes you determine your providers use to describe the type of patients included in the guideline. The medical records of these patients are reviewed for evidence that the patient is using low-dose aspirin on a regular basis. Data needs to be collected for at least 10 patients.

Count as patients in the denominator all patients whose records verify the stable coronary artery disease diagnosis. Count in the numerator all patients whose records contain documentation of regular use of low-dose aspirin.

Medical groups have the option to exclude patients with a documented contraindication to aspirin from this measure. It will be each medical group's determination whether the cost of doing this more specific measure is worth the benefit of the more precise result.

Time Frame Pertaining to Data Collection

Data may be collected monthly.

Notes

This measure may be done in conjunction with the data collection for the Lipid Management in Adults guideline. The evidence for low-dose aspirin regular use is Grade A. It is estimated that over 95% of the population would not have any contraindication to aspirin use.

Key Implementation Recommendations

The following system changes were identified by the guideline work group as key strategies for health care systems to incorporate in support of the implementation of this guideline:

1. Develop systems for providing patient education around:
   - Proper use of nitroglycerin
   - Consistent use of aspirin (unless contraindicated) or consistent use of clopidogrel as directed
   - When to call 911

   Education should also provide for patient to "teach back" in order to demonstrate their understanding of what they should do in an acute cardiac event.
2. Develop/provide patients education materials around use of aspirin (unless contraindicated), interventions around modifiable risk factors.
3. Provide patient education around the use and benefits of angiotensin-converting enzymes (ACE inhibitors) and/or angiotensin II receptor blockers (ARBs).

Knowledge Resources

Criteria for Selecting Resources

The following resources were selected by the Stable Coronary Artery Disease guideline work group as additional resources for providers and/or patients. The following criteria were considered in selecting these resources.

- The site contains information specific to the topic of the guideline.
- The content is supported by evidence-based research.
- The content includes the source/author and contact information.
- The content clearly states revision dates or the date the information was published.
- The content is clear about potential biases, noting conflict of interest and/or disclaimers as appropriate.

Resources Available to ICSI Members Only

ICSI has a wide variety of knowledge resources that are ***only*** available to ICSI members (these are indicated with an asterisk in far left-hand column of the Resources Available table). In addition to the resources listed in the table, ICSI members have access to a broad range of materials including tool kits on CQI processes and Rapid Cycling that can be helpful. To obtain copies of these or other Knowledge Resources, go to http://www.icsi.org/improvement_resources. To access these materials on the Web site, you must be logged in as an ICSI member.

The resources in the table on the next page that are not reserved for ICSI members are available to the public free-of-charge.

Resources Available

*	Author/Organization	Title/Description	Audience	Web sites/Order Information
	AMA Foundation	Health information translation: provides a number of medical conditions translated in a variety of languages.	Patients and Families; Health Care Professionals	http://www.healthinfotranslations.com
	American College of Cardiology	The American College of Cardiology is a trusted source of up-to-date clinical cardiovascular and health policy information.	Health Care Professionals	http://www.acc.org/media/media.htm
	American Diabetes Association	The American Diabetes Association is leading the fight against the deadly consequences of diabetes and fighting for those affected by diabetes. The association funds research to prevent, cure and manage diabetes; delivers services to hundreds of communities; provides objective and credible information; and gives voice to those denied their rights because of diabetes.	Patients and Families	http://www.diabetes.org
	American Heart Association	The American Heart Association is a national voluntary health agency whose mission is "building healthier lives, free of cardiovascular diseases and stroke."	Patients and Families	http://my.americanheart.org/portal/professional/ourmission
	National Heart, Lung and Blood Institute	The institute plans, conducts, fosters and supports an integrated and coordinated program of basic research, clinical investigations and trials, observational studies, and demonstration and education projects.	Patients and Families; Health Care Professionals	http://www.nhlbi.nih.gov/
	National Institutes of Health	Helping to lead the way toward important medical discoveries that improve people's health and save lives, NIH scientists investigate ways to prevent disease as well as the causes, treatments and even cures for common and rare diseases.	Patients and Families; Health Care Professionals	http://www.nih.gov/
	Park Nicollet Health Services	Understanding Lipids (Brochure)	Health Care Professionals	http://www.icsi.org/guidelines_and_more/patient_education_resources/cardiovascular_8490/
	Park Nicollet Health Services	Understanding Hypertension (Brochure)	Health Care Professionals	http://www.icsi.org/guidelines_and_more/patient_education_resources/cardiovascular_8490/

* Available to ICSI members only.

Resources Available

*	Author/Organization	Title/Description	Audience	Web sites/Order Information
	Park Nicollet Health Services	Coronary Artery Disease: Steps to Stay Healthy (brochure)	Health Care Professionals	http://www.icsi.org/guidelines_and_more/patient_education_resources/cardiovascular_8490/
	U.S. Food and Drug Administration	What You Need to Know About Mercury in Fish and Shellfish (trifold brochure)	Health Care Professionals	http://www.fda.gov

* Available to ICSI members only.