



Secondary Prevention of Coronary Artery Disease

Secondary Prevention of Coronary Artery Disease

Guideline Team

Team Leader

Denise Campbell-Scherer, MD, PhD
Family Medicine

Team Members

- R. Van Harrison, PhD Medical Education
Robert V. Hogikyan, MD, MPH Geriatric Medicine
Mark J. Lowell, MD Emergency Medicine
Thomas P. O'Connor, MD General Medicine
Brahmajee K. Nallamothu, MD Cardiovascular Medicine

Developed March 2009

UMMC Guidelines Oversight Team

William E. Chavey, MD
R. Van Harrison, PhD
Connie J. Standiford, MD

Literature search service
Taubman Medical Library

For more information call GUIDES: 936-9771

©Regents of the University of Michigan

These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

Patient population: Adults with coronary artery disease (CAD), CAD equivalent such as diabetes, other atherosclerotic vascular disease, or a risk factor calculation of greater than 20% for a future CAD event.

Objectives: Improve secondary prevention of CAD by assembling in one location core recommendations for the actions that should be taken or considered.

Key points:

High risk patients. This high-risk population should receive intensive secondary prevention interventions, as these interventions offer large absolute risk reductions for subsequent cardiovascular events and mortality [IA]\*.

Secondary prevention. Table 1 summarizes secondary prevention recommendations for patients with coronary and other vascular disease in general order of descending relative risk reduction:

- Smoking cessation
Antiplatelet agents & anticoagulants
Blood pressure control
Lipid management
beta blockers
Renin-angiotensin-aldosterone system blockers
Diabetes management
Pain control (caution with NSAIDs)
Depression screening
Physical activity
Weight management
Nutrition
Immunization
Supplements

\* Strength of recommendation: I= generally should be performed; II = may be reasonable to perform; III = generally should not be performed.

Levels of evidence for the most significant recommendations

A = randomized controlled trials; B=controlled trials, no randomization; C=observational trials; D=opinion of expert panel

Clinical Background

Clinical Problem

Heart disease is the leading cause of death in the United States with 217 deaths/100,000 population annually. (National Center for Health Statistics). An estimated 15,800,000 Americans have coronary artery disease, with 7,900,000 having a history of myocardial infarction and 8,900,000 with angina pectoris and 5,200,000 with heart failure.

Patients with CAD and other vascular disease are at appreciably higher risk for subsequent cardiac events and mortality. Several treatments and lifestyle changes for patients with CAD and other vascular disease have demonstrated large absolute risk reductions.

Although effective secondary prevention is available, a number of studies have shown that it does not occur for many patients and that only some aspects of secondary prevention are performed for many other patients. A more comprehensive approach is needed for secondary prevention of CAD and other vascular disease.

Prevalence of coronary artery disease in Americans:

- Native Hawaiians or other Pacific Islanders 13.8%
American Indians or Alaska Natives 7.6%
white ancestry 6.6%
Hispanics or Latinos 6.0%
African Americans 5.2%
Asians 4.2%

(continued on page 5)

**Table 1. Recommendations for Secondary Prevention of CAD**

<p><b><u>Smoking Cessation</u></b> Goal: Complete Cessation</p>	<p>Ask about smoking status, and document in medical record regularly [IC].</p> <p>Advise quit attempt [IA] and assess willingness.</p> <p>Assist with a quit plan [IC], consider pharmacological interventions, educate, and follow-up as quitting often requires multiple attempts.</p> <p>Counseling can assist a patient in quitting with or without pharmacological therapy [IA].</p> <p>Pharmacological therapy [IA] is used to reduce nicotine withdrawal symptoms and includes:</p> <p>1) nicotine replacement, 2) bupropion hydrochloride, and 3) varenicline (On 2/1/08 the FDA issued an alert regarding serious neuropsychiatric symptoms occurring in patients taking varenicline, but it still continues to be considered first line therapy).</p> <p>Nicotine transdermal formulations are contraindicated in patients with arrhythmias, worsening angina, severe angina, and within 2 weeks of myocardial infarction. It is recommended to use them with caution in patients with CAD.</p>
<p><b>Antiplatelet agents &amp; anticoagulants</b></p>	<p>In patients with established CAD, aspirin should be prescribed at a dose of 81-162 mg daily [IA]. (See text regarding those with coronary event while already on aspirin.)</p> <p>In patients with recent acute coronary syndromes who are treated with medical therapy, the addition of clopidogrel should be considered at a dose of 75 mg daily for at least 1 month [IA] and ideally up to 1 year post-event. NSTEMI (non-ST-elevation myocardial infarction) [IA], STEMI (ST-elevation myocardial infarction) [IIC]. Benefit of prolonged dual therapy is not proven.</p> <p>Clopidogrel at a dose of 75 mg daily (or ticlodipine) should be considered indefinitely in those patients with established coronary artery disease who are intolerant of aspirin [IA].</p> <p><u>Following stent placement:</u></p> <p>Aspirin should be used at a dose of 162 to 325 mg daily for at least 1 month after a bare-metal stent, 3 months after a sirolimus-eluting stent, and 6 months after a paclitaxel-eluting stent. After that period of time, the dose of aspirin can be reduced to 75 to 162 mg daily but continued indefinitely [IA].</p> <p>Clopidogrel at a dose of 75 mg daily should be prescribed for at least 4 weeks after a bare-metal stent, but ideally up to 1 year. For drug-eluting stents, clopidogrel should be used at a dose of 75 mg daily for 1 year [IB]. Continuation of clopidogrel beyond 1 year may be considered in patients at low-risk for bleeding and high-risk for late stent thrombosis [IID].</p>
<p><b><u>Blood Pressure Control</u></b> Goal: &lt; 135/80 more aggressive control may be warranted, particularly for renal disease</p>	<p>A general blood pressure (BP) goal of &lt; 135/80 is reasonable based on available data. Few studies have targeted or achieved systolic BP below 140 mmHg, so recommendations for systolic BP goals are largely based on extrapolations and expert opinion.</p> <p>The Joint National Commission (JNC 7 2003) recommended a goal of blood pressure (BP) &lt;140/90 mm Hg in patients with coronary artery disease (CAD) and a lower BP goal (&lt;130/80 mm Hg) in patients with diabetes mellitus or proteinuric kidney disease. Published trials, some after JNC 7, provide some support for a BP goal less than 130/80 mm Hg in patients with atherosclerotic cardiovascular disease. A similar BP goal was recommended in the 2007 American Heart Association statement on the treatment of blood pressure in ischemic heart disease and the 2007 European Society of Hypertension/European Society of Cardiology guidelines on the management of hypertension.</p> <p>For patients not at target, recommend initiation of lifestyle modification and blood pressure medications [IA]. Useful lifestyle interventions include sodium reduction, weight control, increased physical activity, and alcohol moderation. First line agents <math>\beta</math> blockers, ACE-I or ARB, and thiazides to achieve goal.</p>

<p><b><u>Lipid Management</u></b></p> <p>Goal: LDL-C <math>\leq</math> 100 If at very high risk, <math>&lt;70</math> mg/dl is a reasonable therapeutic option</p>	<p>Obtain a full fasting lipid panel (total cholesterol, LDL-C, HDL-C, and triglycerides) [IA].</p> <p>Assess and recommend lifestyle modification when indicated [IA].</p> <p>Assess the patient for secondary causes of lipid disorders and optimize if identified.</p> <p>LDL-C should be less than 100 mg/dL [IA], further reduction to LDL-C <math>&lt;70</math> mg/dL is reasonable [IIA]. If baseline LDL-C is 70-100 mg/dL, it is reasonable to treat to LDL-C <math>&lt;70</math> mg/dL [IIA].</p> <p>Consider statin therapy for all patients –moderate potency statin even if low LDL-C [IA]. (Note: in DM patients age <math>&lt;40</math> with no other CHD risk, statin is only marginally cost-effective.)</p> <p>Non-statin lipid agents (fibrates, Niacin, resins, ezetimibe) have less or no evidence for improved outcomes compared to statins [IA].</p> <p>Combination therapy (statin + any other lipid agent) improves lipids, but may increase myopathy risk, and has not yet been shown to improve outcomes compared to statins [IIC].</p> <p>Note: use of resins relatively contraindicated if triglycerides <math>\geq</math> 200 mg/dL.</p>
<p><b><math>\beta</math> blockers</b></p>	<p>It is beneficial to start and continue oral <math>\beta</math> blocker therapy indefinitely in all patients who have had a myocardial infarction, acute coronary syndrome, or left ventricle dysfunction with or without heart failure symptoms, unless contraindicated [IA] <i>unstable angina (UA)/NSTEMI (IB)</i>.</p> <p>Patients with moderate or severe LV failure should receive oral <math>\beta</math> blocker therapy with a gradual titration scheme (carvedilol, metoprolol succinate, bisoprolol) [IB].</p> <p>Prescribing <math>\beta</math> blockers is reasonable for low-risk patients (i.e., normal LV function, revascularized, no high-risk features) recovering from UA/NSTEMI in the absence of absolute contraindications [IIA].</p> <p>(see text for recommendations regarding <math>\beta</math> blocker use in the acute setting)</p>
<p><b>Renin-angiotensin-aldosterone system blockers</b></p>	<p>ACE inhibitors are first line therapy in all patients who have: heart failure or asymptomatic left ventricular dysfunction (LVEF <math>\leq</math> 40%); ST elevation MI; in non-ST elevation MI with anterior infarct, diabetes, or systolic dysfunction; proteinuric chronic kidney disease; or severe left ventricular hypertrophy [IA]. The data support a similar effect for ARB's in all these settings (STEMI [IA], UA/NSTEMI [IIA]).</p> <p>ACE inhibitors are reasonable for patients recovering from unstable angina or NSTEMI in the absence of LV dysfunction, hypertension or diabetes mellitus, unless otherwise contraindicated. The data for benefit are mixed [IIA].</p> <p>In patients with either symptomatic heart failure or diabetes mellitus, prescribe long-term aldosterone receptor blockade for unstable angina or acute coronary syndrome patients without significant kidney dysfunction (estimated creatinine clearance should be greater than 30 mL per min) or hyperkalemia (potassium should be less than or equal to 5 mEq per liter) who are already receiving therapeutic doses of an ACE inhibitor, and have an LVEF less than or equal to 40% [IA]. (See caution in text.)</p>
<p><b><u>Diabetes Management</u></b></p> <p><b>Goals:</b></p> <ul style="list-style-type: none"> <li>• Check LDL annually</li> <li>• Consider statin</li> <li>• BP <math>\leq</math> 130-135/80</li> <li>• Smoking status and cessation</li> <li>• Glycemic control: <ul style="list-style-type: none"> <li>- tight for Type 1 (HbA1c <math>&lt;7\%</math>),</li> <li>- reasonable for Type 2 (level debatable), consider <math>&lt; 8\%</math></li> </ul> </li> </ul>	<p>Check lipid profile- fasting or with direct LDL- annually</p> <p>Prescribe moderate dose statin (e.g. generic simvastatin 40 mg po daily) [IA]. In patients <math>&lt;40</math> years of age and without CAD, statins are optional.</p> <p>Goal LDL <math>&lt;100</math> mg/dL recommended [IA]; lower target levels not yet clearly defined in trials. (See lipid section above.)</p> <p>Target blood pressure <math>\leq</math> 130-135 <math>f\ddagger</math>/80 [IA].</p> <p>Check smoking status annually and recommend nonsmoking, educate and encourage cessation [IC].</p> <p>Tight glycemic control in Type I diabetes [IA],</p> <p>Glycemic control has not been of proven benefit in prevention of macrovascular complications of Type 2 diabetes. The target level is under debate and less stringent goals might be appropriate.</p> <p>For individuals with CAD, HEDIS is recommending a level <math>&lt; 8\%</math>, although no new data to guide this specific recommendation.</p> <p>In patients with Type 2 diabetes and microvascular complications or other compelling comorbidities, tight control (HbA1C <math>&lt; 7\%</math>) is recommended.</p>

<b>Pain Control</b>	<p>At the time of admission for acute coronary syndrome discontinue all COX-2 inhibitors and NSAIDs, EXCEPT aspirin as above [IC].</p> <p>In patients with established CAD requiring analgesia, COX-2 inhibitors and NSAIDs with COX-2 activity should be avoided whenever possible [IC]. To minimize risk, a stepwise approach to pain management is recommended (see text).</p>
<b><u>Depression Screening</u></b>	<p>Screen patients with CAD for depression [IB]. Care providers should treat or refer when indicated. Patients often present with somatic complaints. Initial screening can be performed by asking:</p> <p>During the past month, have you been bothered by:</p> <ul style="list-style-type: none"> <li>• Little interest or pleasure in doing things?</li> <li>• Feeling down, depressed or hopeless?</li> </ul> <p>If the patient responds “yes” to either question, consider more detailed assessment.</p>
<b>Physical Activity</b>	<p>Assess risk with a physical activity history and/or exercise test to guide prescription [IB].</p> <p>Encourage 30-60 minutes of moderate intensity aerobic activity on 5-7 days per week, supplemented by an increase in daily lifestyle activities [IIB].</p> <p>Encourage resistance training 2 days per week [IID].</p> <p>Advise medically supervised programs for high risk patients (e.g. recent acute coronary syndromes or revascularization, stable angina, heart failure) [IB].</p>
<b>Weight Management</b>	<p>Assess body mass index and/ or waist circumference on each visit, and consistently encourage weight maintenance/ reduction through an appropriate balance of physical activity, caloric intake and formal behavioral programs when indicated to achieve and maintain a body mass index between 18.5 and 24.9 kg/m<sup>2</sup> [IB].</p> <p>If waist circumference (measured horizontally at iliac crest) is ≥ 35 inches in women and ≥ 40 inches in men, initiate lifestyle change and consider treatment strategies for metabolic syndrome as indicated [IB].</p> <p>Initial goal of weight loss strategy should be to reduce body weight 10% from baseline. With success further weight loss can be attempted if indicated through further assessment [IB].</p>
<b>Nutrition</b>	<p>Achieve and maintain ideal body weight by limiting foods high in calories and low in nutrient density, including those high in sugar, such as soft drinks and candy.</p> <p>Eat a variety of fruits, vegetables, legumes, nuts, soy products, low-fat dairy products, and whole grain breads, cereals and pastas.</p> <p>Eat baked or broiled fish at least twice per week [IIB].</p> <p>Choose oils and margarines low in saturated fats and trans fat and high in omega-3 fat [IB], such as canola, soybean, walnut and flaxseed oils, including those fortified with stanols and sterols. Monounsaturated fats like olive oil are also preferred over saturated fats.</p> <p>Avoid foods high in saturated and trans fats, such as red meat, whole milk products, and pastries. Limit intake of saturated fats to less than 7% of daily calories, trans fatty acids and cholesterol to less than 200 mg per day [IB].</p> <p>Limit alcohol to no more than 2 drinks per day (men) or 1 drink per day (women).</p> <p>Eat less than 6 g of salt or less than 2400 g of sodium per day.</p>
<b><u>Immunizations</u></b>	<p>Influenza vaccination annually (inactivated, injectable) [IB].</p> <p>Pneumococcal polysaccharide vaccine [IB].</p>

Note: Abbreviations:

- CAD – coronary heart disease (or coronary artery disease)
- NSTEMI- non-ST segment elevation myocardial infarction
- STEMI – ST segment elevation myocardial infarction
- UA – unstable angina

**Table 2. Supplements: Summary of Recommendations by ACC Foundation Complementary Medicine Expert Consensus Panel**

Can be recommended:

- Omega-3 supplements 1-2 g per day if insufficient intake from fish
- Stanol / sterol ester margarines (2 g per day)
- Soluble fiber (5 to 20 g per day)
- Soy foods and soy protein (equivalent to 25 g of soy protein daily)

Possibly useful for indications noted

- Moderate alcohol intake for cardiovascular risk reduction, with caution to avoid in patients with history of dependency
- Tea (1-2 c) for cardiovascular risk reduction
- Recommended dietary intake of magnesium (men 420 mg, women 320 mg daily)

Cannot recommend at this time (for some individuals in some situations, probably not harmful)

- Folic acid if homocysteine not elevated for vascular disease
- Garlic for lipid lowering
- Soy isoflavones for lipid lowering
- L-arginine supplementation for nutritional support
- CoQ10 for nutritional support
- Hawthorn for mild heart failure
- Ginko biloba for peripheral vascular disease
- HCSE for peripheral vascular disease

Not recommended (possibly harmful)

- Levels exceeding the upper tolerable limits for vitamins C (2,000 mg/day) and E (1,000 mg/day); and beta-carotene supplementation not recommended; limit to food sources.
- Ephedra, oleander and other herbal/ botanicals with well-defined contraindications to cardiovascular drug and or CVD conditions

Note: [Detailed tables of interactions of supplements](#) are available in the American College of Cardiology Foundation clinical consensus document on Integrating Complementary Medicine into Cardiovascular Medicine.

## Rationale for Recommendations

### Approach

An initial step to increasing the secondary prevention of CAD and other vascular disease is to assemble in one place the most important recommendations for this care. The practical value of the overview is enhanced by listing the recommendations ordered from those generally providing more benefit to those providing less benefit for absolute risk reduction. Physicians and other clinicians can use this information to plan and assess care for individual patients.

The overview of secondary prevention recommendations was assembled from existing guidelines. The University of Michigan Health System (UMHS) has already developed guidelines addressing many of the components of secondary prevention (i.e. smoking cessation, hypertension, lipid management, diabetes mellitus, immunizations). The American Heart Association (AHA) and the American College of Cardiology (ACC) have also developed guidelines addressing overall secondary prevention of CAD and specific components of preventive care. The search for evidence and recommendations focused on guidelines of these organizations published since 2000.

The search was supplemented with very recent clinical trials known to expert members of the panel. Negative trials were specifically sought. Conclusions were based on prospective randomized clinical trials if available, to the exclusion of other data; if randomized controlled trials were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

### Recommendations for Secondary Prevention

The major recommendations are summarized in Table 1. The text of the recommendations closely mirrors the relevant national and UMHS guidelines. Discrepancies are highlighted in the text and reflect new data and controversies. Additionally, recommendations concerning supplements are summarized in Table 2. Further information regarding each of the recommendation categories is presented in the following sections. The sources for each recommendation category are listed at the end of this guideline. The focused guidelines present more detail, and can be accessed by hyperlink from this guideline.

**Smoking cessation.** In patients with CAD cessation of smoking is estimated to reduce the risk of mortality 36% 3-

---

5 years after quitting. Recommendations in this guideline follow those of the Public Health Service (updated in 2008) and the [University of Michigan Health System \(UMHS\) Smoking Cessation Guideline](#).

- The provider should ask about smoking status and document status in the medical record [IC]. A clinical screening system prompting clinicians increases the rate of physicians remembering to ask.
- Advising the patient to quit increases the rate of smoking cessation [IA]. Even three-minute physician interventions meaningfully increase rates of abstinence.
- Assessing a patient's willingness to quit [IC] is an appropriate predecessor to assisting them with developing a quit plan.

The combination of counseling and medication is more effective than either alone.

**Counseling.** Counseling sessions by a variety of clinician types are successful. More intensive interventions are more successful – a target of four or more interventions is reasonable.

**Pharmacologic therapy.** Pharmacologic interventions should be considered [IA].

- Bupropion and nicotine supplementation (gum, patch, inhaler, or nasal spray) are proven to be effective in assisting patients in tobacco cessation.
- Varenicline is also proven to be effective in assisting patients to quit smoking. The FDA issued an alert regarding serious neuropsychiatric symptoms occurring in patients taking varenicline, however it still continues to be considered first line therapy. Clinicians should elicit information on their patients' psychiatric history and monitor them for changes in mood or behavior on therapy.

Nicotine transdermal formulations are contraindicated in patients with arrhythmias, worsening angina, severe angina, and within 2 weeks of myocardial infarction. Use nicotine supplementation with caution in patients with CAD.

**Antiplatelet and anticoagulant therapy.** In general, recommendations for antiplatelet and anticoagulant therapy are consistent with ACC/AHA guidelines for these agents. Table 1 summarizes the key recommendations. (The strong recommendation for dual therapy with aspirin and clopidogrel immediately following NSTEMI and STEMI with medical management is based on the COMMIT trial.)

In patients with established CAD, aspirin should be prescribed at a dose of 81-162 mg daily [IA]. Expert opinion suggests an exception for those having a coronary event on 162mg or less daily. This could be assumed to be aspirin resistance and warrant a dose of 325mg daily or the addition of clopidogrel. This is an area of controversy.

This guideline expands on two areas of controversy below: (1) Use of “triple” therapy and (2) Post-stent antiplatelet therapy.

**“Triple” antiplatelet and anticoagulant therapy.** In general, long-term therapy with warfarin should be prescribed only for those patients with established indications for anticoagulation, such as atrial fibrillation, left ventricular thrombus or mechanical heart valves even when they are on dual antiplatelet therapy. There are limited data on the safety of “triple therapy” with aspirin, clopidogrel and warfarin, leading to significant concerns about the risk of bleeding. In this setting, therapies should be individualized and strong consideration should be made for low-dose aspirin (81 mg daily) and close monitoring of anticoagulation with an INR goal of between 2.0 and 2.5 (ID).

**Post-stent antiplatelet therapy.** Appropriate use of dual anti-platelet therapy is critical in the early period after stent placement and varies depending upon whether a bare-metal or drug-eluting stent was used.

In general, aspirin should be used at a dose of 162 to 325 mg daily for at least 1 month after a bare-metal stent, 3 months after a sirolimus-eluting stent, and 6 months after a paclitaxel-eluting stent. After that period of time, the dose of aspirin can be reduced to 75 to 162 mg daily but continued indefinitely [IB].

Clopidogrel should be given at a dose of 75 mg daily for at least 4 weeks after a bare-metal stent, but ideally up to 1 year [IB]. For drug-eluting stents, clopidogrel should be used at a dose of 75 mg daily for 1 year [IB]. If clopidogrel requires discontinuation within 1 year of drug-eluting stent placement, consultation with interventional cardiology may be helpful to assess whether technical or angiographic factors place the patients at very-high risk for late stent thrombosis, necessitating additional measures [IID]. Continuation of clopidogrel beyond 1 year may be considered in patients at low-risk for bleeding and high-risk for late stent thrombosis [IID].

Considerations about patient adherence with dual anti-platelet therapy are critical before the placement of a stent, particularly drug-eluting stents. Pay special attention to a patient's ability to pay for costly clopidogrel.

Of note, even after PCI without stent placement (i.e., balloon angioplasty), aspirin should be used indefinitely at the doses recommended for a bare-metal stent and clopidogrel should be used at a dose of 75 mg daily for at least 2 weeks and ideally up to 1 year [IB].

**Blood pressure control.** Studies have shown that aggressive treatment of elevated BP in patients with end organ damage (e.g., retinopathy, CHF, CAD, PVOD, cerebrovascular disease) provides significant improvements in clinical outcomes. A general goal is BP < 135/80, with more aggressive control considered based on the conditions present, particularly renal disease. This goal recognizes the importance of targeting lower BP levels in patients with CAD and the lack of evidence for setting the specific target for even lower systolic BP levels in CAD patients who also have diabetes or renal disease.

For diastolic BP, a target of 80 mmHg has shown marked benefit in patients with diabetes. However, in patients with diabetes, mortality increased for diastolic BP < 70 mmHg. Diastolic BP levels < 60 mmHg are a general concern for all patients.

Few studies have targeted or achieved systolic BP below 140 mmHg. Recommendations regarding systolic BP goals are expert opinion based on extrapolations, not randomized controlled trials. The Joint National Commission on Prevention, Detection, and Treatment of High Blood Pressure (JNC 7) recommended target BP of  $\leq 140/90$  ( $\leq 130/80$  for diabetes mellitus and CKD). The American Diabetes Association recommends 130/80 for patients with diabetes.

In all patients with CAD, initiate or maintain lifestyle modification - weight control; increased physical activity; alcohol moderation; sodium intake reduction; emphasize increased consumption of fresh fruits, vegetables, and low-fat dairy products [IB].

For patients with blood pressure greater not at target, add blood pressure medication as tolerated, treating initially with  $\beta$  blockers and/or ACE inhibitors, with addition of other drugs such as thiazides as needed to achieve goal blood pressure [IA].

(For indications for individual drug classes in specific vascular diseases, see [UMHS Essential Hypertension Guideline](#).)

**Lipid management.** For secondary prevention patients can be classified as high risk or very high risk. All patients with CAD are at least high risk. Very high risk is CAD or other atherosclerotic vascular disease plus one or more of: major risk factors (e.g. diabetes mellitus, metabolic syndrome, active cigarette smoking), or acute coronary syndrome.

Lifestyle changes that can improve lipid levels would include optimizing diet, quitting smoking, losing excessive body weight and regular physical exercise [IA].

Secondary prevention trials demonstrate a reduction in cardiac events and total mortality. This reduction is related to the reduction in LDL-C. Patients who experience a larger reduction in LDL-C will benefit from a larger relative risk reduction [IA].

The National Cholesterol Education Program Adult Treatment Panel III 2004 update recommended that high risk persons be treated to an LDL  $\leq 100$  mg/dL [IA]. For very high risk individuals it is reasonable to consider < 70 mg/dL. [IIB]. . This is an area of controversy particularly given that the benefits of reaching these targets with non-statin drugs is unknown and the safety of this approach has not been clearly established.

Even if LDL-C is low, a moderate potency statin (e.g. simvastatin 40 mg/daily) provides benefit. In the Heart Protection Study secondary prevention patients with a

normal cholesterol benefited from statin therapy [IA]. For patients with diabetes and no other CAD risk, statin therapy may reasonably be delayed until age 40 since statin use in this younger population is only marginally cost-effective.

If a patient is unable to tolerate a statin, other medications to consider include bile acid resins (e.g. cholestyramine), ezetimibe, niacin, and fibrates. Resins are relatively contraindicated in patients with triglycerides over 200 mg/dL.

Although recommended in the AHA/ACC guidelines, combination therapy is controversial [IIC].

**$\beta$  blockers.** The ACC/AHA STEMI guideline revision 2007 advises that it is beneficial to start and continue oral  $\beta$  blocker therapy indefinitely in all patients who have had an MI, acute coronary syndrome, or LV dysfunction with or without heart failure symptoms, unless contraindicated [IA]. Patients with moderate or severe LV failure should receive  $\beta$  blocker therapy with a gradual titration scheme [IB]. Although less evidence exists, prescribing  $\beta$  blockers is reasonable for low-risk patients (i.e. normal LV function, revascularized, no high-risk features) recovering from UA/NSTEMI in the absence of absolute contraindications [IIA].

It should be noted that in the *acute* setting, the routine use of IV  $\beta$  blockers for all patients is no longer recommended, as it may be harmful to administer them to those with contraindications to beta blockade, signs of heart failure or low output state, or other risk factors for cardiogenic shock. These include age greater than 70, SBP less than 120 mmHg, heart rate greater than 110 or less than 60, or increased time since onset of symptoms. (IIIA) IV  $\beta$  blockers may be used to treat concomitant hypertension in patients without any contraindications. (IIB) Oral  $\beta$  blocker therapy should be initiated within the first 24 hours in patients without contraindications. (IB)

**Renin-angiotensin-aldosterone system blockers.** Choice of blockade mechanism depends on the medical conditions present.

**ACE inhibitors.** Start ACE inhibitors and continue indefinitely in all patients with left ventricular ejection fraction less than or equal to 40%, in those with hypertension (with microalbuminuria), diabetes mellitus (with microalbuminuria), or chronic kidney disease, unless contraindicated [IA]. Consider ACE inhibitors for all other patients. Note that the data of usefulness are mixed in the lower risk groups [IB]. Among lower risk patients with normal left ventricular ejection fraction in whom cardiovascular risk factors are well controlled and revascularization has been performed, use of ACE inhibitors is optional [IIB].

**Angiotensin receptor blockers.** Use in patients who are intolerant of ACE inhibitors and have heart failure or have had a myocardial infarction with left ventricular ejection fraction less than or equal to 40% [IA]. Consider in other

patients who are ACE inhibitor intolerant [IB]. Consider use in combination with ACE inhibitors in systolic-dysfunction heart failure [IIB]. This is controversial and should be used with caution given risk for adverse events.

**Aldosterone blockade.** Use in post-myocardial infarction patients, without significant kidney dysfunction or hyperkalemia, who are already receiving therapeutic doses of an ACE inhibitor and  $\beta$  blocker, have left ventricular ejection fraction less than or equal to 40%, and have either diabetes mellitus or heart failure. Creatinine should be  $<2.5$  mg/dl in men and  $<2.0$  mg/dl in women. Potassium should be  $<5.0$  mg/dl [IA].

There is no evidence on the safety of combining ACE inhibitors, ARBs, and aldosterone blockers (EPHESUS).

**Diabetes mellitus management.** Diabetes mellitus is a coronary artery disease equivalent, and these patients should receive intensive secondary prevention interventions. These interventions offer large absolute risk reductions for subsequent events and mortality [IA].

Of paramount importance is hypertension control and cholesterol control. JNC-7 sites a target of SBP $<130$  and DBP $<80$  in this population. There is some debate about the systolic target and the [UMHS Essential Hypertension Guideline](#) recommends a target of SBP $<135$ .

Moderate dose statins are recommended in patients over 40 years of age; under 40 the data is less robust. LDL goal is  $<100$  mg/dL, lower target levels are not yet clearly substantiated in trials. Currently there is debate around treating to a target LDL versus moderate dose statins.

Smoking cessation is highly recommended (see [UMHS Smoking Cessation Guideline](#)). Encouraging physical activity and a healthy diet are also very important.

Tight glycemic control for the prevention of coronary artery disease is critically important in Type 1 diabetes.

Glycemic control has not been shown to be of importance in the prevention of macrovascular complications of Type 2 diabetes. The ACCORD and ADVANCE studies have raised concerns about the potential for increasing adverse outcomes with tight control. The target for HbA1c is not clear. For individuals with CAD, HEDIS is currently recommending a level of  $<8\%$ , though no new evidence on which to base this specific recommendation. (HEDIS recommends a level of  $<7\%$  for most other patients.) Tight glycemic control  $<7\%$  is important in DM Type 2 patients with microvascular complications and other compelling comorbidities.

Recent systematic reviews and meta-analyses have raised concerns about rosiglitazone increasing risks of myocardial infarction and heart failure, with no increased risk in cardiovascular mortality or all cause mortality demonstrated (see annotated reference). All of the initial trials used surrogate end points (HbA1c reduction) and there is no RCT data with this medication looking at patient

important outcomes such as myocardial infarction and death as primary end points. Given that there is no proven benefit and there may be harm with rosiglitazone, caution is recommended. The other CAD prevention recommendations are the same as for all patients requiring secondary prevention.

**Pain control – NSAIDs.** The selective cyclooxygenase-2 inhibitors (COX-2 inhibitors) and other nonselective NSAIDs have been associated with increased cardiovascular risk. The risk of cardiovascular events is proportional to COX-2 selectivity. With the exception of aspirin, all NSAIDs and COX-2 inhibitors should be discontinued immediately at the time of an acute coronary syndrome presentation [IC].

The American Heart Association recommends the following treatment for chronic pain in patients with known cardiovascular disease or risk factors for ischemic heart disease. Non-pharmacologic approaches such as physical therapy, heat or cold application, or the use of orthotic devices should be attempted first. If symptoms are not controlled use a stepwise pharmacologic approach, emphasizing using the lowest effective dose for the shortest possible time. Initial choices include acetaminophen or aspirin, tramadol, or small doses of narcotics, or non-acetylated salicylates (e.g. salasalate).

If these measures are insufficient, NSAIDs may be tried next. The practitioner and patient should understand that pain relief may come at the cost of increased risk of cardiovascular or cerebrovascular complications. Additionally, the long-term use of NSAIDs or aspirin also increases the risk of gastrointestinal bleeding, and high dose acetaminophen can cause hepatic toxicity.

If an NSAID must be used, available evidence suggests that the selective COX-2 inhibitors pose a greater risk than the nonselective ones, so therapy with a nonselective NSAID such as **naproxen** should be used initially. Only in the event of failure of this therapy should NSAIDs with some COX-2 selectivity be considered, with the COX-2 selective agents being the last resort. The lowest effective dose of any medicine should be used for the shortest possible time.

**Depression screening.** Coronary artery disease is associated with depression. Estimates of 15%-20% of patients hospitalized with acute myocardial infarction, unstable angina, angioplasty, bypass surgery, and valve surgery suffer with major depressive disorder. Significantly larger percentages suffer with symptoms of depression. Major depression and elevated depressive symptoms are associated with worse prognosis in patients with CAD. While biological mechanisms have been proposed for this relationship, behavioral mechanisms are clear. Untreated depression will likely make it harder for patients to engage in preventive activities (e.g., smoking cessation, medication adherence, physical activity, weight management, and nutrition modification).

An October 2008 American Heart Association science advisory recommends that patients with CAD be screened

for depression and referred or treated appropriately. Screening and treatment methods for this population are the similar to those for the general patient population. While no single screening tool has been demonstrated to be better than others, a common approach is to perform an initial screening with the two questions listed in Table 1. For those who respond “yes” to either item, more detailed screening items and treatment recommendations are described in the [UMHS Depression Guideline](#).

Some studies have been performed in this population to determine the safety and efficacy of psychotherapeutic and psychopharmacologic interventions. As yet the limited trials done have failed to show that these interventions significantly reduce mortality in patients after myocardial infarction.

**Physical activity and weight management.** The ACC/AHA recommends encouraging 30-60 minutes of moderate intensity aerobic activity on 5-7 days per week, supplemented by an increase in daily lifestyle activities [IB] and encouraging resistance training 2 days per week [IID]. Moderate intensity includes walking more than 3 mph, vacuuming, lawn mowing, bicycling on flat ground, light effort and leisurely swimming and playing golf, with walking and pulling clubs.

To guide prescription of increased intensity exercise, assess risk with a physical activity history and/or exercise test [IB]. Medically supervised programs are advised for high risk patients (e.g. recent acute coronary syndromes or revascularization, heart failure) [IB]. Check insurance coverage prior to referral, as some insurers will not cover these programs.

Recommendations are to assess body mass index and/ or waist circumference on each visit, and consistently encourage weight maintenance/ reduction through an appropriate balance of physical activity, caloric intake and formal behavioral programs when indicated to achieve and maintain a body mass index between 18.5 and 24.9 kg/m<sup>2(B1)</sup> [IB]. If waist circumference (measured horizontally at iliac crest) is ≥ 35 inches in women and ≥ 40 inches in men, initiate lifestyle change and consider treatment strategies for metabolic syndrome as indicated [IB]. Initial goal of weight loss strategy should be to reduce body weight 10% from baseline. With success further weight loss can be attempted if indicated through further assessment [IB].

**Nutrition.** Key recommendations are highlighted in Table 1.

**Immunizations.** Patients with coronary artery disease fall into the high priority category for the influenza vaccination as this places them at high-risk for influenza-related hospitalization and death [IB]. Influenza vaccine as an inactivated vaccine, administered intramuscularly is recommended. It is contraindicated in patients with severe egg allergy or previous allergy/ anaphylaxis to influenza vaccine, and caution with previous Guillian-Barre

syndrome. Due to antigenic shift and drift in circulating influenza A and B strains, the vaccine is manufactured and administered annually. Pneumococcal polysaccharide vaccination is recommended in all patients with heart disease. (See the [UMHS Adult Immunization Guideline](#) for more information on immunization)

**Supplements.** There is increasing patient interest in the area of herbal supplements and other complementary medical therapies for secondary prevention of heart disease. This is a large, complex area beyond the scope of this guideline. Please see the American College of Cardiology Foundation Complementary Medicine Expert Consensus Document (2005) for a review. Their highlighted recommendations are in Table 2. Of note, some herbal remedies can have cardiotoxic properties, some may lower serum potassium, and some may interact with cardiovascular drugs.

## Disclosures

University of Michigan Health System endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Disclosure of a relationship is not intended to suggest bias in the information presented, but is made to provide readers with information that might be of potential importance to their evaluation of the information.

Team Member	Company	Relationship
Denise Campbell-Scherer, MD, PhD	(none)	
R. Van Harrison, PhD	(none)	
Robert V. Hogikyan, MD, MPH	Pfizer	Shareholder
Mark J. Lowell, MD	(none)	
Thomas P. O'Connor, MD	(none)	
Brahmajee K. Nallamouth, MD	(none)	

## References

### Smoking Cessation

Frohna JG, Harrison RV, Serlin DC, Thomas LA. Smoking Cessation [update 2006]. Ann Arbor, Michigan: University of Michigan Health System, 2006. (Available at [www.guideline.gov](http://www.guideline.gov) and [www.med.umich.edu/1info/fhp/practiceguides/ccg.html](http://www.med.umich.edu/1info/fhp/practiceguides/ccg.html))

Critchley J.A., Capewell S. Mortality risk reduction associated with coronary heart disease: a systematic review. JAMA 2003; 290:86-97.

---

## Antiplatelet agents & anticoagulants

King SB et al. 2007 Focused Update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention. *J Am Coll Cardiol*, 2008; 51:172-209, doi:10.1016/j.jacc.2007.10.002 (Published online 13 December 2007).

Anderson JL et al. ACC/AHA 2007 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction. *J Am Coll Cardiol*, 2007; 50:1-157, doi:10.1016/j.jacc.2007.02.013 (Published online 6 August 2007).

Antman EM et al. 2007 Focused Update of the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction. *J Am Coll Cardiol*, 2008; 51:210-247, doi:10.1016/j.jacc.2007.10.001 (Published online 10 December 2007).

Eisenstein EL et al. Clopidogrel Use and Long-term Clinical Outcomes After Drug-Eluting Stent Implantation. *JAMA*, January 10, 2007; 297: 159 - 168.

COMMIT Collaborative Group. Addition of clopidogrel to aspirin in 45852 patients with acute myocardial infarction: randomised placebo-controlled trial. *Lancet*. 2005; 366: 1607-21.

## Blood Pressure Control

Jimbo M, Barrie W, Dorsch MP, Harrison RV, Jamerson K. Essential Hypertension [update 2008]. Ann Arbor, Michigan: University of Michigan Health System, 2008. (To be available at [www.guideline.gov](http://www.guideline.gov) and [www.med.umich.edu/1info/fhp/practiceguides/ccg.html](http://www.med.umich.edu/1info/fhp/practiceguides/ccg.html))

## Lipid Management

Barrie WE, Harrison RV, Khanderia UB, Kinningham RB, Rosenson RS. Screening and Management of Lipids [update 2008]. Ann Arbor, Michigan: University of Michigan Health System, 2008. (To be available at [www.guideline.gov](http://www.guideline.gov) and [www.med.umich.edu/1info/fhp/practiceguides/ccg.html](http://www.med.umich.edu/1info/fhp/practiceguides/ccg.html))

Antman EM et al. 2007 Focused Update of the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction. *J Am Coll Cardiol*, 2008; 51:210-247, doi:10.1016/j.jacc.2007.10.001 (Published online 10 December 2007). (Secondary Prevention Section)

Ridker PM, Danielson E, Fonseca FA, et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. *N Engl J Med*. 2008;359:2195-207.

## β blockers & Renin-angiotensin-aldosterone system blockers

Antman EM et al. 2007 Focused Update of the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction. *J Am Coll Cardiol*, 2008;

51:210-247, doi:10.1016/j.jacc.2007.10.001 (Published online 10 December 2007). (Secondary Prevention Section)

ACC/AHA 2007 guidelines for the management of patients with unstable angina/non ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2007 Aug 14;116(7):e148-304.

COMMIT Collaborative Group. Early intravenous then oral metoprolol in 45852 patients with acute myocardial infarction; randomized placebo-controlled trial. *Lancet*. 2005; 366: 1622-32.

Pitt B, et al. Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction. *N Engl J Med* 2003;348:1309-21. (EPHESUS)

## Diabetes Management

Vijan S, Choe HM, Funnell MM, Bernstein SJ, Harrison RV, Herman WH, Campbell-Scherer D, Lash RW. Management of Type 2 Diabetes Mellitus [update 2008]. Ann Arbor, Michigan: University of Michigan Health System, 2008. (Available at: [www.guideline.gov](http://www.guideline.gov) and [www.med.umich.edu/1info/fhp/practiceguides/ccg.html](http://www.med.umich.edu/1info/fhp/practiceguides/ccg.html))

Singh S., Loke Y.K., Furberg C.D. Long-term risk of cardiovascular events with rosiglitazone. *JAMA* 2007; 298(10): 1189—1195.

The Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of intensive glucose lowering in type 2 diabetes. *New England Journal of Medicine* 2008; 358: 2545-59.

The Advance Collaborative Group. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *New England Journal of Medicine* 2008;358:2560-72.

## Pain Control

Elliott M. Antman, et al, Use of Nonsteroidal Antiinflammatory Drugs: An Update for Clinicians: A Scientific Statement From the American Heart Association. *Circulation* 2007;115;1634-1642.

ACC/AHA 2007 guidelines for the management of patients with unstable angina/non ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2007 Aug 14;116(7):e148-304.

Gislason G.H., Jacobsen S., Rasmussen J.N., et al. Risk of death or reinfarction associated with the use of selective cyclo-oxygenase inhibitors and nonselective nonsteroidal anti-inflammatory drugs after acute myocardial infarction. *Circulation* 2006; 113:2906-2913.

---

## Depression Screening

Lichtman JH, Bigger JT Jr, 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; 118:1768-1775. Available at: [circ.ahajournals.org/cgi/reprint/CIRCULATIONAHA.108.190769](http://circ.ahajournals.org/cgi/reprint/CIRCULATIONAHA.108.190769)

Rudisch B., Nemeroff C.B. Epidemiology of comorbid coronary artery disease and depression. *Biol Psychiatry* 2003; 54(3): 227-240.

Schwenk TL, Terrell LB, Harrison RV, Shadigian EM, Valenstein MA. Depression [update Oct. 2005]. *Ann Arbor, Michigan: University of Michigan Health System, 2005.* (Available at [www.guideline.gov](http://www.guideline.gov) and [www.med.umich.edu/1info/fhp/practiceguides/ccg.html](http://www.med.umich.edu/1info/fhp/practiceguides/ccg.html))

## Physical Activity

AHA/ACC guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 update. *Circulation* 2006; 113:2363-2372. (Endorsed by NHLBI)

Haskell W.L. et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Med Sci Sports Exerc.*, Vol.39, No. 8, pp.1423-1434, 2007.

## Weight Management

AHA/ACC guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 update. *Circulation* 2006; 113:2363-2372. (Endorsed by NHLBI)

## Nutrition

American College of Cardiology Foundation expert consensus document: Integrating complementary medicine into cardiovascular medicine. *Journal of the American College of Cardiology* 2005; 46 (1): 184-221

Antman EM et al. 2007 Focused Update of the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction. *J Am Coll Cardiol*, 2008; 51:210-247, doi:10.1016/j.jacc.2007.10.001 (Published online 10 December 2007). (Secondary Prevention Section)

Hooper L, Summerbell CD, Higgins JPT, Thompson RL, Clements G, Capps N, Davey Smith G, Riemersma RA, Ebrahim S. Reduced or modified dietary fat for preventing cardiovascular disease (Review). *Cochrane Collaboration* 2008:4.

## Immunizations

Andreae M, Luughkin C, Barry-Bodine M, Blitz S, DeLoach SL, Engert SF, Garrett SD, Malouin J, McGrath L. [Adult Preventive Care: Immunizations](http://www.med.umich.edu/1info/fhp/practiceguides/ccg.html) [update 2009]. *Ann Arbor, Michigan: University of Michigan Health System, 2009.* (Available at [www.med.umich.edu/1info/fhp/practiceguides/ccg.html](http://www.med.umich.edu/1info/fhp/practiceguides/ccg.html))

Recommended Adult Immunization Schedule United States, October 2007 – September 2008: Summary of Recommendations Published by the Advisory Committee on Immunization Practices. *Atlanta, GA: Centers for Disease Control and Prevention, MMWR* 2007;56:Q1–Q4. [www.cdc.gov/mmwr/preview/mmwrhtml/mm5641-Immunizational.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5641-Immunizational.htm)

## Supplements

ACCF complementary medicine expert consensus document: Integrating complementary medicine into cardiovascular medicine. *Journal of the American College of Cardiology* 2005; 46 (1): 184-221

## Burden of Disease

AHA Statistical Update, Heart Disease and Stroke Statistics- 2007 Update. Report from the American Heart Association Statistics Committee and Stroke Statistics Committee. *Circulation*, 2007; 115: e69-e171The online-only Data Supplement, which consists of 3 supplemental charts, is available with this article at <http://circ.ahajournals.org/cgi/content/full/115/5/e69/DC1>.

National Center for Health Statistics  
<http://www.cdc.gov/nch>