



Guidelines for Secondary Prevention for Patients with Coronary and Other Atherosclerotic Vascular Disease: 2006 Update

American Heart Association/American College of Cardiology
Endorsed by the National Heart, Lung, and Blood Institute

Adopted by Capital Health Plan
Quality Improvement Committee 9/8/09

AHA/ACC Guidelines for Secondary Prevention for Patients With Coronary and Other Atherosclerotic Vascular Disease: 2006 Update

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Since the 2001 update of the American Heart Association (AHA)/American College of Cardiology (ACC) consensus statement on secondary prevention,¹ important evidence from clinical trials has emerged that further supports and broadens the merits of aggressive risk-reduction therapies for patients with established coronary and other atherosclerotic vascular disease, including peripheral arterial disease, atherosclerotic aortic disease, and carotid artery disease. This growing body of evidence confirms that aggressive comprehensive risk factor management improves survival, reduces recurrent events and the need for interventional procedures, and improves quality of life for these patients.

Compelling evidence from recent clinical trials and revised practice guidelines provided the impetus for this update of the 2001 recommendations with evidence-based results (Table 1). Classification of Recommendations and Level of Evidence are expressed in ACC/AHA format, as detailed in Tables 2 and 3. Recommendations made herein are based largely on major practice guidelines from the National Institutes of Health and ACC/AHA. In many cases, these practice guidelines were supplemented by research findings published

after the publication of the primary reference(s). Thus, the development of the present statement involved a process of partial adaptation of other guideline statements and reports and supplemental literature searches.²⁻³² (For specific search criteria, see the Appendix.) The findings from additional lipid reduction trials³³⁻³⁷ involving more than 50 000 patients resulted in new optional therapeutic targets, which were outlined in the 2004 update of the National Heart, Lung, and Blood Institute's Adult Treatment Panel (ATP) III report.⁶ These changes defined optional lower target cholesterol levels for very high-risk coronary heart disease (CHD) patients, especially those with acute coronary syndromes, and expanded indications for drug treatment. Subsequent to the 2004 update of ATP III, 2 additional trials^{8,9} demonstrated cardiovascular benefit for lipid lowering significantly below current cholesterol goal levels for those with chronic CHD. These new trials allow for alterations in guidelines, such that low-density lipoprotein cholesterol (LDL-C) should be <100 mg/dL for all patients with CHD and other clinical forms of atherosclerotic disease, but in addition, it is reasonable to treat to LDL-C <70 mg/dL in such patients. When the

*Dr Pasternak withdrew from the Writing Group on June 22, 2004, when he accepted an offer of employment as Vice President, Clinical Research, Cardiovascular and Atherosclerosis, at Merck Research Laboratories. The remaining members of the Writing Group were advised of his change in status before this Scientific Statement was finalized, and they affirmed their support of the Statement with subsequent revisions after his departure.

†Deceased.

This document was approved by the American Heart Association Science Advisory and Coordinating Committee on November 11, 2005, and by the American College of Cardiology Foundation Board of Trustees on November 10, 2005.

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When this document is cited, the American Heart Association requests that the following citation format be used: Smith SC, Allen J, Blair SN, Bonow RO, Brass LM, Fonarow GC, Grundy SM, Hiratzka L, Jones D, Krumholz HM, Mosca L, Pasternak RC, Pearson T, Pfeffer MA, Taubert KA. AHA/ACC guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 update. *Circulation*. 2006;113:2363-2372. DOI: 10.1161/CIRCULATIONAHA.106.174516.

This article has been copublished in the May 16, 2006, issue of the *Journal of the American College of Cardiology (J Am Coll Cardiol)*. 2006;47:2130-2139.

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(*Circulation*. 2006;113:2363-2372.)

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DOI: 10.1161/CIRCULATIONAHA.106.174516

TABLE 1. AHA/ACC Secondary Prevention for Patients With Coronary and Other Vascular Disease*: 2006 Update

	Intervention Recommendations With Class of Recommendation and Level of Evidence
SMOKING: <u>Goal</u> Complete cessation. No exposure to environmental tobacco smoke.	<ul style="list-style-type: none"> • Ask about tobacco use status at every visit. I (B) • Advise every tobacco user to quit. I (B) • Assess the tobacco user's willingness to quit. I (B) • Assist by counseling and developing a plan for quitting. I (B) • Arrange follow-up, referral to special programs, or pharmacotherapy (including nicotine replacement and bupropion). I (B) • Urge avoidance of exposure to environmental tobacco smoke at work and home. I (B)
BLOOD PRESSURE CONTROL: <u>Goal</u> <140/90 mm Hg or <130/80 mm Hg if patient has diabetes or chronic kidney disease	<p>For all patients:</p> <ul style="list-style-type: none"> • Initiate or maintain lifestyle modification—weight control; increased physical activity; alcohol moderation; sodium reduction; and emphasis on increased consumption of fresh fruits, vegetables, and low-fat dairy products. I (B) <p>For patients with blood pressure \geq140/90 mm Hg (or \geq130/80 mm Hg for individuals with chronic kidney disease or diabetes):</p> <ul style="list-style-type: none"> • As tolerated, add blood pressure medication, treating initially with β-blockers and/or ACE inhibitors, with addition of other drugs such as thiazides as needed to achieve goal blood pressure. I (A) <p>[For compelling indications for individual drug classes in specific vascular diseases, see Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7).]⁴</p>
LIPID MANAGEMENT: <u>Goal</u> LDL-C <100 mg/dL If triglycerides are \geq 200 mg/dL, non-HDL-C should be <130 mg/dL [†]	<p>For all patients:</p> <ul style="list-style-type: none"> • Start dietary therapy. Reduce intake of saturated fats (to <7% of total calories), <i>trans</i>-fatty acids, and cholesterol (to <200 mg/d). I (B) • Adding plant stanol/sterols (2 g/d) and viscous fiber (>10 g/d) will further lower LDL-C. • Promote daily physical activity and weight management. I (B) • Encourage increased consumption of omega-3 fatty acids in the form of fish[‡] or in capsule form (1 g/d) for risk reduction. For treatment of elevated triglycerides, higher doses are usually necessary for risk reduction. Iib (B) <p>For lipid management:</p> <p>Assess fasting lipid profile in all patients, and within 24 hours of hospitalization for those with an acute cardiovascular or coronary event. For hospitalized patients, initiate lipid-lowering medication as recommended below before discharge according to the following schedule:</p> <ul style="list-style-type: none"> • LDL-C should be <100 mg/dL I (A), and • Further reduction of LDL-C to <70 mg/dL is reasonable. Iia (A) • If baseline LDL-C is \geq100 mg/dL, initiate LDL-lowering drug therapy.§ I (A) • If on-treatment LDL-C is \geq100 mg/dL, intensify LDL-lowering drug therapy (may require LDL-lowering drug combination). I (A) • If baseline LDL-C is 70 to 100 mg/dL, it is reasonable to treat to LDL-C <70 mg/dL. Iia (B) • If triglycerides are 200 to 499 mg/dL, non-HDL-C should be <130 mg/dL. I (B), and • Further reduction of non-HDL-C to <100 mg/dL is reasonable. Iia (B) • Therapeutic options to reduce non-HDL-C are: <ul style="list-style-type: none"> ⇒ More intense LDL-C-lowering therapy I (B), or ⇒ Niacin¶ (after LDL-C-lowering therapy) Iia (B), or ⇒ Fibrate therapy# (after LDL-C-lowering therapy) Iia (B) • If triglycerides are \geq500 mg/dL#, therapeutic options to prevent pancreatitis are fibrate¶ or niacin¶ before LDL-lowering therapy; and treat LDL-C to goal after triglyceride-lowering therapy. Achieve non-HDL-C <130 mg/dL if possible. I (C)
PHYSICAL ACTIVITY: <u>Goal</u> 30 minutes, 7 days per week (minimum 5 days per week)	<ul style="list-style-type: none"> • For all patients, assess risk with a physical activity history and/or an exercise test, to guide prescription. I (B) • For all patients, encourage 30 to 60 minutes of moderate-intensity aerobic activity, such as brisk walking, on most, preferably all, days of the week, supplemented by an increase in daily lifestyle activities (eg, walking breaks at work, gardening, household work). I (B) • Encourage resistance training 2 days per week. Iib (C) • Advise medically supervised programs for high-risk patients (eg, recent acute coronary syndrome or revascularization, heart failure). I (B)
WEIGHT MANAGEMENT: <u>Goal</u> Body mass index: 18.5 to 24.9 kg/m ² Waist circumference: men <40 inches, women <35 inches	<ul style="list-style-type: none"> • 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 maintain/achieve a body mass index between 18.5 and 24.9 kg/m². I (B) • If waist circumference (measured horizontally at the iliac crest) is \geq35 inches in women and \geq40 inches in men, initiate lifestyle changes and consider treatment strategies for metabolic syndrome as indicated. I (B) • The initial goal of weight loss therapy should be to reduce body weight by approximately 10% from baseline. With success, further weight loss can be attempted if indicated through further assessment. I (B)

TABLE 1. Continued

	Intervention Recommendations With Class of Recommendation and Level of Evidence
DIABETES MANAGEMENT: Goal HbA _{1c} <7%	<ul style="list-style-type: none"> • Initiate lifestyle and pharmacotherapy to achieve near-normal HbA_{1c}. I (B) • Begin vigorous modification of other risk factors (eg, physical activity, weight management, blood pressure control, and cholesterol management as recommended above). I (B) • Coordinate diabetic care with patient's primary care physician or endocrinologist. I (C)
ANTIPLATELET AGENTS/ ANTICOAGULANTS:	<ul style="list-style-type: none"> • Start aspirin 75 to 162 mg/d and continue indefinitely in all patients unless contraindicated. I (A) ⇒ For patients undergoing coronary artery bypass grafting, aspirin should be started within 48 hours after surgery to reduce saphenous vein graft closure. Dosing regimens ranging from 100 to 325 mg/d appear to be efficacious. Doses higher than 162 mg/d can be continued for up to 1 year. I (B) • Start and continue clopidogrel 75 mg/d in combination with aspirin for up to 12 months in patients after acute coronary syndrome or percutaneous coronary intervention with stent placement (≥1 month for bare metal stent, ≥3 months for sirolimus-eluting stent, and ≥6 months for paclitaxel-eluting stent). I (B) ⇒ Patients who have undergone percutaneous coronary intervention with stent placement should initially receive higher-dose aspirin at 325 mg/d for 1 month for bare metal stent, 3 months for sirolimus-eluting stent, and 6 months for paclitaxel-eluting stent. I (B) • Manage warfarin to international normalized ratio=2.0 to 3.0 for paroxysmal or chronic atrial fibrillation or flutter, and in post-myocardial infarction patients when clinically indicated (eg, atrial fibrillation, left ventricular thrombus). I (A) • Use of warfarin in conjunction with aspirin and/or clopidogrel is associated with increased risk of bleeding and should be monitored closely. I (B)
RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM BLOCKERS:	<p>ACE inhibitors:</p> <ul style="list-style-type: none"> • Start and continue indefinitely in all patients with left ventricular ejection fraction ≤40% and in those with hypertension, diabetes, or chronic kidney disease, unless contraindicated. I (A) • Consider for all other patients. I (B) • 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 may be considered optional. Ila (B) <p>Angiotensin receptor blockers:</p> <ul style="list-style-type: none"> • Use in patients who are intolerant of ACE inhibitors and have heart failure or have had a myocardial infarction with left ventricular ejection fraction ≤40%. I (A) • Consider in other patients who are ACE inhibitor intolerant. I (B) • Consider use in combination with ACE inhibitors in systolic-dysfunction heart failure. Iib (B) <p>Aldosterone blockade:</p> <ul style="list-style-type: none"> • Use in post-myocardial infarction patients, without significant renal dysfunction** or hyperkalemia††, who are already receiving therapeutic doses of an ACE inhibitor and β-blocker, have a left ventricular ejection fraction ≤40%, and have either diabetes or heart failure. I (A)
β-BLOCKERS:	<ul style="list-style-type: none"> • Start and continue indefinitely in all patients who have had myocardial infarction, acute coronary syndrome, or left ventricular dysfunction with or without heart failure symptoms, unless contraindicated. I (A) Consider chronic therapy for all other patients with coronary or other vascular disease or diabetes unless contraindicated. Ila (C)
INFLUENZA VACCINATION:	Patients with cardiovascular disease should have an influenza vaccination. I (B)

*Patients covered by these guidelines include those with established coronary and other atherosclerotic vascular disease, including peripheral arterial disease, atherosclerotic aortic disease, and carotid artery disease. Treatment of patients whose only manifestation of cardiovascular risk is diabetes will be the topic of a separate AHA scientific statement. ACE indicates angiotensin-converting enzyme.

†Non-HDL-C=total cholesterol minus HDL-C.

‡Pregnant and lactating women should limit their intake of fish to minimize exposure to methylmercury.

§When LDL-lowering medications are used, obtain at least a 30% to 40% reduction in LDL-C levels. If LDL-C <70 mg/dL is the chosen target, consider drug titration to achieve this level to minimize side effects and cost. When LDL-C <70 mg/dL is not achievable because of high baseline LDL-C levels, it generally is possible to achieve reductions of >50% in LDL-C levels by either statins or LDL-C-lowering drug combinations.

||Standard dose of statin with ezetimibe, bile acid sequestrant, or niacin.

¶The combination of high-dose statin+fibrate can increase risk for severe myopathy. Statin doses should be kept relatively low with this combination. Dietary supplement niacin must not be used as a substitute for prescription niacin.

#Patients with very high triglycerides should not consume alcohol. The use of bile acid sequestrant is relatively contraindicated when triglycerides are >200 mg/dL.

**Creatinine should be <2.5 mg/dL in men and <2.0 mg/dL in women.

††Potassium should be <5.0 mEq/L.

<70-mg/dL target is chosen, it may be prudent to increase statin therapy in a graded fashion to determine a patient's response and tolerance. Furthermore, if it is not possible to attain LDL-C <70 mg/dL because of a high baseline LDL-C, it generally is possible to achieve LDL-C reductions of

>50% with either statins or LDL-C-lowering drug combinations. Moreover, this guideline for patients with atherosclerotic disease does not modify the recommendations of the 2004 ATP III update for patients without atherosclerotic disease who have diabetes or multiple risk factors and a

TABLE 2. Classification of Recommendations and Level of Evidence***Classification of Recommendations**

- Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective.
- Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.
- Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.
- Class IIb: Usefulness/efficacy is less well established by evidence/opinion.
- Class III: Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful.

Level of Evidence

- Level of Evidence A: Data derived from multiple randomized clinical trials or meta-analyses.
- Level of Evidence B: Data derived from a single randomized trial or nonrandomized studies.
- Level of Evidence C: Only consensus opinion of experts, case studies, or standard-of-care.

*Classification of Recommendations and Level of Evidence are expressed in the ACC/AHA format and described in more detail in Table 3.

10-year risk level for CHD >20%. In the latter 2 types of high-risk patients, the recommended LDL-C goal of <100 mg/dL has not changed. Finally, to avoid any misunderstanding about cholesterol management in general, it must be emphasized that a reasonable cholesterol level of <70 mg/dL does not apply to other types of lower-risk individuals who do not have CHD or other forms of atherosclerotic disease; in such cases, recommendations contained in the 2004 ATP III update still pertain.

Trials involving other secondary prevention therapies also have influenced major practice guidelines used to formulate the recommendations in this update. Thus, specific recommendations for clopidogrel use in post-acute coronary syndrome or post-percutaneous coronary intervention-stented patients are now included in this 2006 update. The present update also recommends lower-dose aspirin for chronic

therapy. The results of additional studies have further confirmed the benefit of aldosterone antagonist therapy among patients with impaired left ventricular function. Finally, recently published findings of a trial involving angiotensin-converting enzyme inhibitor therapy among patients at relatively low risk with stable coronary disease and normal left ventricular function influenced the recommendations.²⁶

The writing group has for the first time added a recommendation with regard to influenza vaccination. According to the US Centers for Disease Control and Prevention, vaccination with inactivated influenza vaccine is recommended for individuals who have chronic disorders of the cardiovascular system because they are at increased risk for complications from influenza.³⁸

The writing group emphasizes the importance of giving consideration to the use of cardiovascular medications that have been proved in randomized clinical trials to be of benefit. This strengthens the evidence-based foundation for therapeutic application of these guidelines. The committee acknowledges that ethnic minorities, women, and the elderly are underrepresented in many trials and urges physician and patient participation in trials that will provide additional evidence with regard to therapeutic strategies for these groups of patients.

In the 11 years since the guidelines were first published, 2 other developments have made them even more important in clinical care. First, the aging of the population continues to expand the number of patients living with a diagnosis of cardiovascular disease (now estimated at 13 million for coronary heart disease alone) who might benefit from these therapies. Second, multiple studies of the use of these recommended therapies in appropriate patients, although showing slow improvement, continue to support the discouraging conclusion that many patients in whom therapies are indicated are not receiving them in actual clinical practice. The AHA and ACC recommend the use of programs such as the AHA's Get With The Guidelines³⁹ or the ACC's Guidelines Applied to Practice⁴⁰ to identify appropriate patients for therapy, provide practitioners with useful reminders based on the guidelines, and continuously assess the success achieved in providing these therapies to the patients who can benefit from them.

Quality Indicators to Measure Effectiveness of Guideline

- HEDIS[®]:
 - Cholesterol Management for Patients with Cardiovascular Conditions
 - Persistence of Beta Blocker Treatment Following A Heart Attack
 - Controlling High Blood Pressure
 - Advising Smokers to Quit
 - Use of Aspirin / Discussion of Aspirin Risks and Benefits (HEDIS 2010)