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

Endorsed by the National Heart, Lung, and Blood Institute

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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 trials (33–37) 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

*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.

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The American Heart Association and American College of Cardiology make every effort to avoid any actual or potential conflicts of interest that might arise as a result of an outside relationship or personal interest of a member of the writing panel. Specifically, all members of the writing panel are asked to provide disclosure statements of all such relationships that might be perceived as real or potential conflicts of interest. These statements are reviewed by the parent task force, reported orally to all members of the writing panel at the first meeting, and updated as changes occur. The relationships with industry for writing committee members, as well as peer reviewers of the document, are located before the references.

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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: Goal Complete cessation. No exposure to environmental tobacco smoke.	• 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: Goal <140/90 mm Hg or <130/80 mm Hg if patient has diabetes or chronic kidney disease	**For all patients:** • 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)** **For patients with blood pressure ≥140/90 mm Hg (or ≥130/80 mm Hg for individuals with chronic kidney disease or diabetes):** • 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)** [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]
LIPID MANAGEMENT: Goal LDL-C <100 mg/dL If triglycerides are ≥200 mg/dL, non-HDL-C should be <130 mg/dL†	**For all patients:** • Start dietary therapy. Reduce intake of saturated fats (to <7% of total calories), *trans*-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)** **For lipid management:** 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: • 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 ≥100 mg/dL, initiate LDL-lowering drug therapy.§ **I (A)** • If on-treatment LDL-C is ≥100 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: ⇒ 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 ≥500 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: Goal 30 minutes, 7 days per week (minimum 5 days per week)	• 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: Goal Body mass index: 18.5 to 24.9 kg/m^2 Waist circumference: men <40 inches, women <35 inches	• 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/m^2. **I (B)** • If waist circumference (measured horizontally at the iliac crest) is ≥35 inches in women and ≥40 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)**

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TABLE 1. Continued

	Intervention Recommendations With Class of Recommendation and Level of Evidence
DIABETES MANAGEMENT: Goal HbA_{1c} <7%	• 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:	• 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:	**ACE inhibitors:** • 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. **IIa (B)** **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 ≤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)** **Aldosterone blockade:** • 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:	• 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. **IIa (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.

such patients. When the <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

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.

risk factors and a 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 Guidelines (39) or the ACC's Guidelines Applied to Practice (40) 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.

TABLE 3. Applying Classification of Recommendations and Level of Evidence

"Size of Treatment Effect"

"Estimate of Certainty (Precision) of Treatment Effect"

	Class I *Benefit >>> Risk* Procedure/Treatment SHOULD be performed/administered	Class IIa *Benefit >> Risk* *Additional studies with focused objectives needed* IT IS REASONABLE to perform procedure/administer treatment	Class IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; Additional registry data would be helpful* Procedure/Treatment MAY BE CONSIDERED	Class III *Risk ≥ Benefit* *No additional studies needed* Procedure/Treatment should NOT be performed/administered SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL
Level A *Multiple (3-5) population risk strata evaluated** *General consistency of direction and magnitude of effect*	• Recommendation that procedure or treatment is useful/effective • Sufficient evidence from multiple randomized trials or meta-analyses	• Recommendation in favor of treatment or procedure being useful/effective • Some conflicting evidence from multiple randomized trials or meta-analyses	• Recommendation's usefulness/efficacy less well established • Greater conflicting evidence from multiple randomized trials or meta-analyses	• Recommendation that procedure or treatment not useful/effective and may be harmful • Sufficient evidence from multiple randomized trials or meta-analyses
Level B *Limited (2-3) population risk strata evaluated**	• Recommendation that procedure or treatment is useful/effective • Limited evidence from single randomized trial or non-randomized studies	• Recommendation in favor of treatment or procedure being useful/ effective • Some conflicting evidence from single randomized trial or non-randomized studies	• Recommendation's usefulness/efficacy less well established • Greater conflicting evidence from single randomized trial or non-randomized studies	• Recommendation that procedure or treatment not useful/effective and may be harmful • Limited evidence from single randomized trial or non-randomized studies
Level C *Very limited (1-2) population risk strata evaluated**	• Recommendation that procedure or treatment is useful/effective • Only expert opinion, case studies, or standard-of-care	• Recommendation in favor of treatment or procedure being useful/ effective • Only diverging expert opinion, case studies, or standard-of-care	• Recommendation's usefulness/efficacy less well established • Only diverging expert opinion, case studies, or standard-of-care	• Recommendation that procedure or treatment not useful/effective and may be harmful • Only expert opinion, case studies, or standard-of-care
Suggested phrases for writing recommendations †	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/ beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown /unclear/uncertain or not well established	is not recommended is not indicated should not is not useful/effective/beneficial may be harmful

*Data available from clinical trials or registries about the usefulness/efficacy in different sub-populations, such as gender, age, history of diabetes, history of prior MI, history of heart failure, and prior aspirin use. A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Even though randomized trials are not available, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

†In 2003, the ACC/AHA Task Force on Practice Guidelines developed a list of suggested phrases to use when writing recommendations. All recommendations in this guideline have been written in full sentences that express a complete thought, such that a recommendation, even if separated and presented apart from the rest of the document (including headings above sets of recommendations), would still convey the full intent of the recommendation. It is hoped that this will increase readers' comprehension of the guidelines and will allow queries at the individual recommendation level.

Appendix

Appendix: References and Supplemental Search Criteria Used to Support Each Recommendation and Level of Evidence

Recommendation	References and Supplemental Search Criteria
SMOKING:	Primary reference(s) used: 2, 3, 21, 22 Supplemental search done? No
BLOOD PRESSURE:	Primary reference(s) used: 2, 4 Supplemental search done? Yes Database(s) used: PubMed and EMBASE for all English-language human studies Key words: PubMed: *blood pressure* OR *hypertension* AND *practice guidelines* and/or *prevention* and/or *clinical trial* and/or *pharmacology* EMBASE: *secondary prevention* OR *guidelines* AND *blood pressure* AND *Cochrane review* OR *controlled clinical trial* OR *randomized controlled trial* AND *pharmacology* OR *hypertension* AND *Cochrane review* OR *controlled clinical trial* OR *randomized controlled trial* AND *pharmacology* Years searched: 2003–March 2005 Supplemental search did not alter recommendations.
LIPID MANAGEMENT:	Primary reference(s) used: 2, 5, 7 Supplemental search done? Yes Database used: PubMed for all English-language human studies Key words: *cholesterol/lipids/lipoproteins* AND *clinical trials* and/or *meta-analysis* and/or *practice guidelines* Years searched: 2002–November 2005 Supplemental search added references 6, 8–12, and 33–37 and altered the recommendations.
PHYSICAL ACTIVITY:	Primary reference(s) used: 2, 13–16, 21, 22 Supplemental search done? No
WEIGHT MANAGEMENT:	Primary reference(s) used: 2, 17–19, 21, 22 Supplemental search done? No
DIABETES MANAGEMENT:	Primary reference(s) used: 2, 20–22 Supplemental search done? No
ANTIPLATELET AGENTS/ ANTICOAGULANTS:	Primary reference(s) used: 2, 21–25, 27, 29 Supplemental search done? Yes, for use of ASA after CABG Database(s) used: PubMed for all English-language studies Key words: *antiplatelet agents*, *coronary artery bypass graft patency* Years searched: 2000–March 2005 Supplemental search did not alter the recommendations.
RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM BLOCKERS:	Primary reference(s) used: 2, 21, 22, 27, 28 Supplemental search done? Yes Database used: PubMed for all English-language studies Key words: *ACE inhibitor* or *angiotensin receptor antagonist* or *aldosterone antagonist* AND *clinical trials* and/or *meta-analysis* and/or *practice guidelines* Years searched: 2003–March 2005 Supplemental search added references 25 and 30–32 and altered the recommendations.
β-BLOCKERS:	Primary reference(s) used: 2, 21, 22, 27, 28 Supplemental search done? Yes Database used: PubMed for all English-language studies Key words: *beta blockers* AND *clinical trials* and/or *meta-analysis* and/or *practice guidelines* Years searched: 2002–March 2005 Supplemental search did not alter recommendations.
INFLUENZA VACCINATION:	Primary reference(s) used: 38 Supplemental search done? No

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Disclosures

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*Modest.

†Significant.

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "Significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "Modest" if it is less than "Significant" under the preceding definition.

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