

## AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients With Coronary and Other Atherosclerotic Vascular Disease: 2011 Update

### A Guideline From the American Heart Association and American College of Cardiology Foundation

*Endorsed by the World Heart Federation and the Preventive Cardiovascular Nurses Association*

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Since the 2006 update of the American Heart Association (AHA)/American College of Cardiology Foundation (ACCF) guidelines on secondary prevention,<sup>1</sup> important evidence from clinical trials has emerged that further supports and broadens the merits of intensive risk-reduction therapies for patients with established coronary and other atherosclerotic vascular disease, including peripheral artery disease, atherosclerotic aortic disease, and carotid artery disease. In reviewing this evidence and its clinical impact, the writing group believed it would be more appropriate to expand the title of this guideline to “Secondary Prevention and Risk Reduction Therapy for Patients With Coronary and Other Atherosclerotic Vascular Disease.” Indeed, the growing body of evidence confirms that in patients with atherosclerotic vascular disease, comprehensive risk factor management reduces risk as assessed by a variety of outcomes, including improved survival, reduced recurrent events, the need

for revascularization procedures, and improved quality of life. It is important not only that the healthcare provider implement these recommendations in appropriate patients but also that healthcare systems support this implementation to maximize the benefit to the patient.

Compelling evidence-based results from recent clinical trials and revised practice guidelines provide the impetus for this update of the 2006 recommendations with evidence-based results<sup>2–165</sup> (Table 1). Classification of recommendations and level of evidence are expressed in ACCF/AHA format, as detailed in Table 2. Recommendations made herein are largely based on major practice guidelines from the National Institutes of Health and updated ACCF/AHA practice guidelines, as well as on results from recent clinical trials. Thus, the development of the present guideline involved a process of partial adaptation of other guideline statements and reports and supplemental litera-

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**Table 1. AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients With Coronary and Other Atherosclerotic Vascular Disease: 2011 Update: Intervention Recommendations With Class of Recommendation and Level of Evidence**

Area for Intervention	Recommendations
<b>Smoking</b> Goal: Complete cessation. No exposure to environmental tobacco smoke	<b>Class I</b> 1. Patients should be asked about tobacco use status at every office visit. <sup>2,3,4,5,7</sup> ( <b>Level of Evidence: B</b> ) 2. Every tobacco user should be advised at every visit to quit. <sup>4,5,7,9</sup> ( <b>Level of Evidence: A</b> ) 3. The tobacco user's willingness to quit should be assessed at every visit. ( <b>Level of Evidence: C</b> ) 4. Patients should be assisted by counseling and by development of a plan for quitting that may include pharmacotherapy and/or referral to a smoking cessation program. <sup>4-9</sup> ( <b>Level of Evidence: A</b> ) 5. Arrangement for follow up is recommended. ( <b>Level of Evidence: C</b> ) 6. All patients should be advised at every office visit to avoid exposure to environmental tobacco smoke at work, home, and public places. <sup>10,11</sup> ( <b>Level of Evidence: B</b> )
<b>Blood pressure control</b> Goal: <140/90 mm Hg	<b>Note: The writing committee did not think that the 2006 recommendations for blood pressure control (below) should be modified at this time. The writing committee anticipates that the recommendations will be reviewed when the updated JNC guidelines are released.</b> <b>Class I</b> 1. All patients should be counseled regarding the need for 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. <sup>12-16</sup> ( <b>Level of Evidence: B</b> ) 2. Patients with blood pressure $\geq$ 140/90 mm Hg should be treated, as tolerated, with blood pressure medication, treating initially with $\beta$ -blockers and/or ACE inhibitors, with addition of other drugs as needed to achieve goal blood pressure. <sup>12,17,18</sup> ( <b>Level of Evidence: A</b> )
<b>Lipid management</b> Goal: Treatment with statin therapy; use statin therapy to achieve an LDL-C of <100 mg/dL; for very high risk* patients an LDL-C <70 mg/dL is reasonable; if triglycerides are $\geq$ 200 mg/dL, non-HDL-C† should be <130 mg/dL, whereas non-HDL-C <100 mg/dL for very high risk patients is reasonable	<b>Note: The writing committee anticipates that the recommendations will be reviewed when the updated ATP guidelines are released.</b> <b>Class I</b> 1. A lipid profile in all patients should be established, and for hospitalized patients, lipid-lowering therapy as recommended below should be initiated before discharge. <sup>20</sup> ( <b>Level of Evidence: B</b> ) 2. Lifestyle modifications including daily physical activity and weight management are strongly recommended for all patients. <sup>19,29</sup> ( <b>Level of Evidence: B</b> ) 3. Dietary therapy for all patients should include reduced intake of saturated fats (to <7% of total calories), <i>trans</i> fatty acids (to <1% of total calories), and cholesterol (to <200 mg/d). <sup>21-24,29</sup> ( <b>Level of Evidence: B</b> ) 4. In addition to therapeutic lifestyle changes, statin therapy should be prescribed in the absence of contraindications or documented adverse effects. <sup>25-29</sup> ( <b>Level of Evidence: A</b> ) 5. An adequate dose of statin should be used that reduces LDL-C to <100 mg/dL AND achieves at least a 30% lowering of LDL-C. <sup>25-29</sup> ( <b>Level of Evidence: C</b> ) 6. Patients who have triglycerides $\geq$ 200 mg/dL should be treated with statins to lower non-HDL-C to <130 mg/dL. <sup>25-27,30</sup> ( <b>Level of Evidence: B</b> ) 7. Patients who have triglycerides >500 mg/dL should be started on fibrate therapy in addition to statin therapy to prevent acute pancreatitis. ( <b>Level of Evidence: C</b> ) <b>Class IIa</b> 1. If treatment with a statin (including trials of higher-dose statins and higher-potency statins) does not achieve the goal selected for a patient, intensification of LDL-C-lowering drug therapy with a bile acid sequestrant‡ or niacin§ is reasonable. <sup>31-33</sup> ( <b>Level of Evidence: B</b> ) 2. For patients who do not tolerate statins, LDL-C-lowering therapy with bile acid sequestrants‡ and/or niacin§ is reasonable. <sup>35,36</sup> ( <b>Level of Evidence: B</b> ) 3. It is reasonable to treat very high-risk patients* with statin therapy to lower LDL-C to <70 mg/dL. <sup>26-28,37,38,166</sup> ( <b>Level of Evidence: C</b> ) 4. In patients who are at very high risk* and who have triglycerides $\geq$ 200 mg/dL, a non-HDL-C goal of <100 mg/dL is reasonable. <sup>25-27,30</sup> ( <b>Level of Evidence: B</b> )

(Continued)

Table 1. Continued

Area for Intervention	Recommendations
<b>Lipid management cont'd</b>	<p><b>Class IIb</b></p> <ol style="list-style-type: none"> <li>1. The use of ezetimibe may be considered for patients who do not tolerate or achieve target LDL-C with statins, bile acid sequestrants,<sup>‡</sup> and/or niacin.<sup>§</sup> (<b>Level of Evidence: C</b>)</li> <li>2. For patients who continue to have an elevated non-HDL-C while on adequate statin therapy, niacin<sup>§</sup> or fibrates<sup>  </sup> therapy<sup>32,35,41</sup> (<b>Level of Evidence: B</b>) or fish oil (<b>Level of Evidence: C</b>) may be reasonable.</li> <li>3. For all patients, it may be reasonable to recommend omega-3 fatty acids from fish<sup>¶</sup> or fish oil capsules (1 g/d) for cardiovascular disease risk reduction.<sup>44–46</sup> (<b>Level of Evidence: B</b>)</li> </ol>
<b>Physical activity</b> Goal: At least 30 minutes, 7 days per week (minimum 5 days per week)	<p><b>Class I</b></p> <ol style="list-style-type: none"> <li>1. For all patients, the clinician should encourage 30 to 60 minutes of moderate-intensity aerobic activity, such as brisk walking, at least 5 days and preferably 7 days per week, supplemented by an increase in daily lifestyle activities (eg, walking breaks at work, gardening, household work) to improve cardiorespiratory fitness and move patients out of the least fit, least active high-risk cohort (bottom 20%).<sup>54,55,58</sup> (<b>Level of Evidence: B</b>)</li> <li>2. For all patients, risk assessment with a physical activity history and/or an exercise test is recommended to guide prognosis and prescription.<sup>47–52,58</sup> (<b>Level of Evidence: B</b>)</li> <li>3. The clinician should counsel patients to report and be evaluated for symptoms related to exercise. (<b>Level of Evidence: C</b>)</li> </ol> <p><b>Class IIa</b></p> <ol style="list-style-type: none"> <li>1. It is reasonable for the clinician to recommend complementary resistance training at least 2 days per week.<sup>59</sup> (<b>Level of Evidence: C</b>)</li> </ol>
<b>Weight management</b> Goals: Body mass index: 18.5 to 24.9 kg/m <sup>2</sup> Waist circumference: women <35 inches (<89 cm), men <40 inches (<102 cm)	<p><b>Class I</b></p> <ol style="list-style-type: none"> <li>1. Body mass index and/or waist circumference should be assessed at every visit, and the clinician should consistently encourage weight maintenance/reduction through an appropriate balance of lifestyle physical activity, structured exercise, caloric intake, and formal behavioral programs when indicated to maintain/achieve a body mass index between 18.5 and 24.9 kg/m<sup>2</sup>.<sup>60–62,65–70</sup> (<b>Level of Evidence: B</b>)</li> <li>2. If waist circumference (measured horizontally at the iliac crest) is <math>\geq 35</math> inches (<math>\geq 89</math> cm) in women and <math>\geq 40</math> inches (<math>\geq 102</math> cm) in men, therapeutic lifestyle interventions should be intensified and focused on weight management.<sup>66–70</sup> (<b>Level of Evidence: B</b>)</li> <li>3. The initial goal of weight loss therapy should be to reduce body weight by approximately 5% to 10% from baseline. With success, further weight loss can be attempted if indicated. (<b>Level of Evidence: C</b>)</li> </ol>
<b>Type 2 diabetes mellitus management</b>	<p><b>Note: Recommendations below are for prevention of cardiovascular complications.</b></p> <p><b>Class I</b></p> <ol style="list-style-type: none"> <li>1. Care for diabetes should be coordinated with the patient's primary care physician and/or endocrinologist. (<b>Level of Evidence: C</b>)</li> <li>2. Lifestyle modifications including daily physical activity, weight management, blood pressure control, and lipid management are recommended for all patients with diabetes.<sup>19,22–24,29,56,58,59,62,66,74,162</sup> (<b>Level of Evidence: B</b>)</li> </ol> <p><b>Class IIa</b></p> <ol style="list-style-type: none"> <li>1. Metformin is an effective first-line pharmacotherapy and can be useful if not contraindicated.<sup>74–76</sup> (<b>Level of Evidence: A</b>)</li> <li>2. It is reasonable to individualize the intensity of blood sugar-lowering interventions based on the individual patient's risk of hypoglycemia during treatment. (<b>Level of Evidence: C</b>)</li> </ol> <p><b>Class IIb</b></p> <ol style="list-style-type: none"> <li>1. Initiation of pharmacotherapy interventions to achieve target HbA1c may be reasonable.<sup>71,72,74–80</sup> (<b>Level of Evidence: A</b>)</li> <li>2. A target HbA1c of <math>\leq 7\%</math> may be considered. (<b>Level of Evidence: C</b>)</li> <li>3. Less stringent HbA1c goals may be considered for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, or extensive comorbidities, or those in whom the goal is difficult to attain despite intensive therapeutic interventions. (<b>Level of Evidence: C</b>)</li> </ol>
<b>Antiplatelet agents/anticoagulants</b>	<p><b>Class I</b></p> <ol style="list-style-type: none"> <li>1. Aspirin 75–162 mg daily is recommended in all patients with coronary artery disease unless contraindicated.<sup>64,81,82,116</sup> (<b>Level of Evidence: A</b>) <ul style="list-style-type: none"> <li>• Clopidogrel 75 mg daily is recommended as an alternative for patients who are intolerant of or allergic to aspirin.<sup>117</sup> (<b>Level of Evidence: B</b>)</li> </ul> </li> <li>2. A P2Y<sub>12</sub> receptor antagonist in combination with aspirin is indicated in patients after ACS or PCI with stent placement.<sup>83–85</sup> (<b>Level of Evidence: A</b>) <ul style="list-style-type: none"> <li>• For patients receiving a bare-metal stent or drug-eluting stent during PCI for ACS, clopidogrel 75 mg daily, prasugrel 10 mg daily, or ticagrelor 90 mg twice daily should be given for at least 12 months.<sup>84,86,113,114</sup> (<b>Level of Evidence: A</b>)</li> </ul> </li> </ol>

(Continued)

Table 1. Continued

Area for Intervention	Recommendations
<b>Antiplatelet agents/anticoagulants cont'd</b>	<ol style="list-style-type: none"> <li>3. For patients undergoing coronary artery bypass grafting, aspirin should be started within 6 hours after surgery to reduce saphenous vein graft closure. Dosing regimens ranging from 100 to 325 mg daily for 1 year appear to be efficacious.<sup>87–90</sup> <b>(Level of Evidence: A)</b></li> <li>4. In patients with extracranial carotid or vertebral atherosclerosis who have had ischemic stroke or TIA, treatment with aspirin alone (75–325 mg daily), clopidogrel alone (75 mg daily), or the combination of aspirin plus extended-release dipyridamole (25 mg and 200 mg twice daily, respectively) should be started and continued.<sup>91,104,116</sup> <b>(Level of Evidence: A)</b></li> <li>5. For patients with symptomatic atherosclerotic peripheral artery disease of the lower extremity, antiplatelet therapy with aspirin (75–325 mg daily) or clopidogrel (75 mg daily) should be started and continued.<sup>92,107,116,117</sup> <b>(Level of Evidence: A)</b></li> <li>6. Antiplatelet therapy is recommended in preference to anticoagulant therapy with warfarin or other vitamin K antagonists to treat patients with atherosclerosis.<sup>93,94,105,110</sup> <b>(Level of Evidence: A)</b> <ul style="list-style-type: none"> <li>● If there is a compelling indication for anticoagulant therapy, such as atrial fibrillation, prosthetic heart valve, left ventricular thrombus, or concomitant venous thromboembolic disease, warfarin should be administered.<sup>95,99–102</sup> <b>(Level of Evidence: A)</b> (NOTE: Patients receiving low dose aspirin for atherosclerosis should continue to receive it.)</li> <li>● For patients requiring warfarin, therapy should be administered to achieve the recommended INR for the specific condition.<sup>81,96</sup> <b>(Level of Evidence: B)</b></li> <li>● Use of warfarin in conjunction with aspirin and/or clopidogrel is associated with increased risk of bleeding and should be monitored closely.<sup>97,98,110</sup> <b>(Level of Evidence: A)</b></li> </ul> </li> </ol>
	<b>Class IIa</b>
	<ol style="list-style-type: none"> <li>1. If the risk of morbidity from bleeding outweighs the anticipated benefit afforded by thienopyridine therapy after stent implantation, earlier discontinuation (eg, &lt;12 months) is reasonable. <b>(Level of Evidence: C)</b> (Note: the risk for serious cardiovascular events because of early discontinuation of thienopyridines is greater for patients with drug-eluting stents than those with bare-metal stents.)</li> <li>2. After PCI, it is reasonable to use 81 mg of aspirin per day in preference to higher maintenance doses.<sup>84,85,118–122</sup> <b>(Level of Evidence: B)</b></li> <li>3. For patients undergoing coronary artery bypass grafting, clopidogrel (75 mg daily) is a reasonable alternative in patients who are intolerant of or allergic to aspirin. <b>(Level of Evidence: C)</b></li> </ol>
	<b>Class IIb</b>
	<ol style="list-style-type: none"> <li>1. The benefits of aspirin in patients with asymptomatic peripheral artery disease of the lower extremities are not well established.<sup>108,109</sup> <b>(Level of Evidence: B)</b></li> <li>2. Combination therapy with both aspirin 75 to 162 mg daily and clopidogrel 75 mg daily may be considered in patients with stable coronary artery disease.<sup>112</sup> <b>(Level of Evidence: B)</b></li> </ol>
<b>Renin-angiotensin-aldosterone system blockers</b>	
ACE inhibitors	<b>Class I</b> <ol style="list-style-type: none"> <li>1. ACE inhibitors should be started and continued indefinitely in all patients with left ventricular ejection fraction <math>\leq 40\%</math> and in those with hypertension, diabetes, or chronic kidney disease, unless contraindicated.<sup>124,125</sup> <b>(Level of Evidence: A)</b></li> </ol>
	<b>Class IIa</b>
	<ol style="list-style-type: none"> <li>1. It is reasonable to use ACE inhibitors in all other patients.<sup>126</sup> <b>(Level of Evidence: B)</b></li> </ol>
ARBs	<b>Class I</b> <ol style="list-style-type: none"> <li>1. The use of ARBs is recommended in patients who have heart failure or who have had a myocardial infarction with left ventricular ejection fraction <math>\leq 40\%</math> and who are ACE-inhibitor intolerant.<sup>130–132</sup> <b>(Level of Evidence: A)</b></li> </ol>
	<b>Class IIa</b>
	<ol style="list-style-type: none"> <li>1. It is reasonable to use ARBs in other patients who are ACE-inhibitor intolerant.<sup>133</sup> <b>(Level of Evidence: B)</b></li> </ol>
	<b>Class IIb</b>
	<ol style="list-style-type: none"> <li>1. The use of ARBs in combination with an ACE inhibitor is not well established in those with systolic heart failure.<sup>132,134</sup> <b>(Level of Evidence: A)</b></li> </ol>
Aldosterone blockade	<b>Class I</b> <ol style="list-style-type: none"> <li>1. Use of aldosterone blockade in post-myocardial infarction patients without significant renal dysfunction# or hyperkalemia** is recommended in patients who are already receiving therapeutic doses of an ACE inhibitor and <math>\beta</math>-blocker, who have a left ventricular ejection fraction <math>\leq 40\%</math>, and who have either diabetes or heart failure.<sup>136,137</sup> <b>(Level of Evidence: A)</b></li> </ol>

(Continued)

Table 1. Continued

Area for Intervention	Recommendations
<b><math>\beta</math>-Blockers</b>	<b>Class I</b> 1. $\beta$ -Blocker therapy should be used in all patients with left ventricular systolic dysfunction (ejection fraction $\leq$ 40%) with heart failure or prior myocardial infarction, unless contraindicated. (Use should be limited to carvedilol, metoprolol succinate, or bisoprolol, which have been shown to reduce mortality.) <sup>138,140,141</sup> <b>(Level of Evidence: A)</b> 2. $\beta$ -Blocker therapy should be started and continued for 3 years in all patients with normal left ventricular function who have had myocardial infarction or ACS. <sup>139,142,143</sup> <b>(Level of Evidence: B)</b>
	<b>Class IIa</b> 1. It is reasonable to continue $\beta$ -blockers beyond 3 years as chronic therapy in all patients with normal left ventricular function who have had myocardial infarction or ACS. <sup>139,142,143</sup> <b>(Level of Evidence: B)</b> 2. It is reasonable to give $\beta$ -blocker therapy in patients with left ventricular systolic dysfunction (ejection fraction $\leq$ 40%) without heart failure or prior myocardial infarction. <b>(Level of Evidence: C)</b>
	<b>Class IIb</b> 1. $\beta$ -Blockers may be considered as chronic therapy for all other patients with coronary or other vascular disease. <b>(Level of Evidence: C)</b>
<b>Influenza vaccination</b>	<b>Class I</b> 1. Patients with cardiovascular disease should have an annual influenza vaccination. <sup>144–147</sup> <b>(Level of Evidence: B)</b>
<b>Depression</b>	<b>Class IIa</b> 1. For patients with recent coronary artery bypass graft surgery or myocardial infarction, it is reasonable to screen for depression if patients have access to case management, in collaboration with their primary care physician and a mental health specialist. <sup>148–152</sup> <b>(Level of Evidence: B)</b> <b>Class IIb</b> 1. Treatment of depression has not been shown to improve cardiovascular disease outcomes but may be reasonable for its other clinical benefits. <b>(Level of Evidence: C)</b>
<b>Cardiac rehabilitation</b>	<b>Class I</b> 1. All eligible patients with ACS or whose status is immediately post coronary artery bypass surgery or post-PCI should be referred to a comprehensive outpatient cardiovascular rehabilitation program either prior to hospital discharge or during the first follow-up office visit. <sup>55,154,161,163</sup> <b>(Level of Evidence: A)</b> 2. All eligible outpatients with the diagnosis of ACS, coronary artery bypass surgery or PCI <b>(Level of Evidence: A)</b> , <sup>55,154,155,161</sup> chronic angina <b>(Level of Evidence: B)</b> , <sup>161,163</sup> and/or peripheral artery disease <b>(Level of Evidence: A)</b> <sup>58,164</sup> within the past year should be referred to a comprehensive outpatient cardiovascular rehabilitation program. 3. A home-based cardiac rehabilitation program can be substituted for a supervised, center-based program for low-risk patients. <sup>153,159,160</sup> <b>(Level of Evidence: A)</b> <b>Class IIa</b> 1. A comprehensive exercise-based outpatient cardiac rehabilitation program can be safe and beneficial for clinically stable outpatients with a history of heart failure. <sup>159,159a–159c</sup> <b>(Level of Evidence: B)</b>

JNC indicates the report of the National Heart, Lung, and Blood Institute's Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure guidelines; ACE, angiotensin-converting enzyme; ATP, Adult Treatment Panel; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HbA1c, hemoglobin A1c; ACS, acute coronary syndrome; PCI, percutaneous coronary intervention; TIA, transient ischemic attack; INR, international normalized ratio; and ARB, angiotensin receptor blocker.

\*Presence of established CVD plus (1) multiple major risk factors (especially diabetes), (2) severe and poorly controlled risk factors (especially continued cigarette smoking), (3) multiple risk factors of the metabolic syndrome (especially high triglycerides  $\geq$ 200 mg/dL plus non-HDL-C  $\geq$ 130 mg/dL with low HDL-C  $<$ 40 mg/dL), and (4) patients with ACSs.

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

‡The use of bile acid sequestrants is relatively contraindicated when triglycerides are  $\geq$ 200 mg/dL and is contraindicated when triglycerides are  $\geq$ 500 mg/dL.

§Dietary supplement niacin must not be used as a substitute for prescription niacin.

||The combination of high-dose statin plus fibrate (especially gemfibrozil) can increase risk for severe myopathy. Statin doses should be kept relatively low with this combination.

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

#Estimated creatinine clearance should be  $>$ 30 mL/min.

\*\*Potassium should be  $<$ 5.0 mEq/L.

ture searches. The recommendations listed in this document are, whenever possible, evidence based. Writing group members performed these relevant supplemental literature searches with key search phrases including but not limited to tobacco/smoking/smoking cessation; blood pressure control/hypertension; chole-

sterol/hypercholesterolemia/lipids/lipoproteins/dyslipidemia; physical activity/exercise/exercise training; weight management/overweight/obesity; type 2 diabetes mellitus management; antiplatelet agents/anticoagulants; renin/angiotensin/aldosterone system blockers;  $\beta$ -blockers; influenza vaccination;

Table 2. Applying Classification of Recommendation and Level of Evidence

		SIZE OF TREATMENT EFFECT				
		CLASS I <i>Benefit &gt;&gt;&gt; Risk</i> Procedure/Treatment <b>SHOULD</b> be performed/administered	CLASS IIa <i>Benefit &gt;&gt; Risk</i> <i>Additional studies with focused objectives needed</i> <b>IT IS REASONABLE</b> to perform procedure/administer treatment	CLASS IIb <i>Benefit ≥ Risk</i> <i>Additional studies with broad objectives needed; additional registry data would be helpful</i> Procedure/Treatment <b>MAY BE CONSIDERED</b>	CLASS III <i>No Benefit or CLASS III Harm</i>	
				Procedure/ Test	Treatment	
				COR III: No benefit	No Proven Benefit	
				COR III: Harm	Excess Cost w/o Benefit or Harmful to Patients	
ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	<ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is useful/effective</li> <li>Sufficient evidence from multiple randomized trials or meta-analyses</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation in favor of treatment or procedure being useful/effective</li> <li>Some conflicting evidence from multiple randomized trials or meta-analyses</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation's usefulness/efficacy less well established</li> <li>Greater conflicting evidence from multiple randomized trials or meta-analyses</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is not useful/effective and may be harmful</li> <li>Sufficient evidence from multiple randomized trials or meta-analyses</li> </ul>	
	LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	<ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is useful/effective</li> <li>Evidence from single randomized trial or nonrandomized studies</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation in favor of treatment or procedure being useful/effective</li> <li>Some conflicting evidence from single randomized trial or nonrandomized studies</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation's usefulness/efficacy less well established</li> <li>Greater conflicting evidence from single randomized trial or nonrandomized studies</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is not useful/effective and may be harmful</li> <li>Evidence from single randomized trial or nonrandomized studies</li> </ul>	
	LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	<ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is useful/effective</li> <li>Only expert opinion, case studies, or standard of care</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation in favor of treatment or procedure being useful/effective</li> <li>Only diverging expert opinion, case studies, or standard of care</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation's usefulness/efficacy less well established</li> <li>Only diverging expert opinion, case studies, or standard of care</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is not useful/effective and may be harmful</li> <li>Only expert opinion, case studies, or standard of care</li> </ul>	
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	COR III: No Benefit is not recommended is not indicated should not be performed/administered/other is not useful/beneficial/effective	COR III: Harm potentially harmful causes harm associated with excess morbidity/mortality should not be performed/administered/other
Comparative effectiveness phrases†		treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B			

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. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

\*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

†For comparative effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

clinical depression/depression screening; and cardiac/cardiovascular rehabilitation. Additional searches cross-referenced these topics with the subtopics of clinical trials, secondary prevention, atherosclerosis, and coronary/cerebral/peripheral artery disease. These searches were limited to studies, reviews, and other evidence conducted in human subjects and published in English. In addition, the writing group reviewed documents related to the subject matter previously published by the AHA, the ACCF, and the National Institutes of Health.

With regard to lipids and dyslipidemias, the lipid reduction trials published between 2002 and 2006<sup>18,25,166–168</sup> included >50 000 patients and 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.<sup>169</sup> 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<sup>26,27</sup> demonstrated cardiovascular benefit for lipid lowering significantly below current cholesterol goal levels for those with chronic coronary heart disease. These trials allowed for alterations in the 2006 guideline, 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 patients at highest risk. The benefits of lipid-lowering therapy are in proportion to the reduction in LDL-C, and when LDL-C is above 100 mg/dL, an adequate dose of statin therapy should be used to achieve at least a 30% lowering of LDL-C. 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. For patients with triglyceride levels  $\geq$ 200 mg/dL, non-high-density lipoprotein cholesterol values should be used as a guide to therapy. Although no studies have directly tested treatment to target strategies, the target LDL-C and non-HDL-C levels are derived from several randomized controlled trials where the LDL-C levels achieved for patients showing benefit are used to suggest targets. Thus, references for the studies from which targets are derived are listed and targets are considered as level of evidence C. Importantly, this guideline statement for patients with atherosclerotic disease does not modify the recommendations of the 2004 ATP III update for patients without atherosclerotic disease who have diabetes mellitus or multiple 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. The writing group agreed that no further changes be made in the recommendations for treatment of dyslipidemia pending the expected publication of the National Heart, Lung, and Blood Institute's updated ATP guidelines in 2012. Similar recommendations were made for the treatment of hypertension by the writing group pending the publication of the updated report of the National Heart, Lung, and Blood Institute's Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure guidelines, expected in the spring of 2012.

Trials involving other secondary prevention therapies also have influenced major practice guidelines used to formulate the recommendations in the present update. Thus, specific recommendations for clopidogrel use in post-acute coronary syndrome or post-percutaneous coronary intervention stented patients were included in the 2006 update, and recommendations regarding prasugrel and ticagrelor are added to this guideline on the basis of the results of the TRITON-TIMI 38 trial (Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel-Thrombolysis in Myocardial Infarction) and PLATO (Study of Platelet Inhibition and Patient Outcomes). The present update continues to recommend 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. The results of several trials involving angiotensin-converting enzyme inhibitor therapy among patients at relatively low risk with stable coronary disease and normal left ventricular function influenced the current recommendations.<sup>32</sup> Finally, the recom-

mendations for  $\beta$ -blocker therapy have been clarified to reflect the fact that evidence supporting their efficacy is greatest among patients with recent myocardial infarction (<3 years) and/or left ventricular systolic dysfunction (left ventricular ejection fraction  $\leq$ 40%). For those patients without these Class I indications,  $\beta$ -blocker therapy is optional (Class IIa or IIb).

The writing group confirms the recommendation introduced in 2006 for this guideline 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.<sup>147</sup> Additionally, the writing group added new sections on depression and on cardiovascular rehabilitation.

The writing group continues to emphasize the importance of giving consideration to the use of cardiovascular medications that have been proven 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 15 years since these 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 16.3 million for CHD alone)<sup>170</sup> 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 ACCF recommend the use of programs such as the AHA's Get With The Guidelines,<sup>171</sup> the American Cancer Society/American Diabetes Association/AHA's Guideline Advantage Program,<sup>172</sup> and the ACC's PINNACLE (Practice INNOvation And CLinical Excellence) program<sup>173</sup> to identify appropriate patients for therapy, provide practitioners with useful reminders based on the guidelines, and continually assess the success achieved in providing these therapies to the patients who can benefit from them. In this regard, it is important that the healthcare provider not only implement the therapies according to their class of recommendation but also assess for and assist with patient compliance with these therapies in each patient encounter. Discussion of the literature and supporting references for many of the recommendations summarized in the present guideline can be found in greater detail in the upcoming ACCF/AHA guideline for management of patients undergoing PCI,<sup>174</sup> ACCF/AHA guideline for management of patients with peripheral artery disease,<sup>175,176</sup> the AHA effectiveness-based guidelines for cardiovascular disease prevention in women,<sup>46</sup> and in the AHA/American Stroke Association guidelines for the prevention of stroke in patients with stroke or transient ischemic attack.<sup>123</sup>

Finally, the practitioner should exercise judgment in initiating the various recommendations if the patient has recently experienced an acute event.

Disclosures

Writing Group Disclosures

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
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(Continued)



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James H. Stein	University of Wisconsin School of Medicine and Public Health	Sanofi-Aventis† (ended July 2009); Siemens Medical Solutions† (ended July 2009); SonoSite† (ended September 2009)	None	Abbott* and Takeda* (no permanent remuneration; all money to charity. Both were terminated December 2008)	None	None	Abbott*, Lilly*, and Takeda* (research trial DSMBs)	Takeda* (training grant to institution ended June 2009); Wisconsin Alumni Research Foundation* (royalties related to carotid ultrasound and cardiovascular disease risk prediction)
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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 (1) the person receives \$10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (2) 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.

\*Modest.

†Significant.

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This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (1) the person receives \$10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (2) 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.

\*Modest.  
†Significant.

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KEY WORDS: AHA Scientific Statements ■ secondary prevention ■ coronary disease ■ vascular disease ■ risk factors



# Correction

In the article by Smith et al, “AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients With Coronary and Other Atherosclerotic Vascular Disease: 2011 Update: A Guideline From the American Heart Association and American College of Cardiology Foundation,” which published online November 3, 2011, and appeared with the November 29, 2011, issue of the journal (*Circulation*. 2011;124:2458–2473. DOI: 10.1161/CIR.0b013e318235eb4d.), several corrections were needed.

1. In Table 1, the Antiplatelet agents/anticoagulants section on page 2461, Class I, recommendation 4, the recommendation read,

4. In patients with extracranial carotid or vertebral atherosclerosis who have had ischemic stroke or TIA, treatment with aspirin alone (75–325 mg daily), clopidogrel alone (75 mg daily), or the combination of aspirin plus extended-release dipyridamole (25 mg and 200 mg twice daily, respectively) should be started and continued.<sup>91,104,116</sup> (*Level of Evidence: B*)

The recommendation Level of Evidence has changed to “A”; the recommendation now reads,

4. In patients with extracranial carotid or vertebral atherosclerosis who have had ischemic stroke or TIA, treatment with aspirin alone (75–325 mg daily), clopidogrel alone (75 mg daily), or the combination of aspirin plus extended-release dipyridamole (25 mg and 200 mg twice daily, respectively) should be started and continued.<sup>91,104,116</sup> (*Level of Evidence: A*)

2. In Table 1, the Antiplatelet agents/anticoagulants section on page 2461, Class I, recommendation 6, first bullet, the recommendation read,

6. Antiplatelet therapy is recommended in preference to anticoagulant therapy with warfarin or other vitamin K antagonists to treat patients with atherosclerosis.<sup>93,94,105,110</sup> (*Level of Evidence: A*)
  - If there is a compelling indication for anticoagulant therapy, such as atrial fibrillation, prosthetic heart valve, left ventricular thrombus, or concomitant venous thromboembolic disease, warfarin should be administered in addition to the low-dose aspirin (75–81 mg daily).<sup>95,99–102</sup> (*Level of Evidence: A*)

The bullet now reads,

- If there is a compelling indication for anticoagulant therapy, such as atrial fibrillation, prosthetic heart valve, left ventricular thrombus, or concomitant venous thromboembolic disease, warfarin should be administered.<sup>95,99–102</sup> (*Level of Evidence: A*) (NOTE: Patients receiving low-dose aspirin for atherosclerosis should continue to receive it.)

The authors regret the errors.

These corrections have been made to the current online version of the article, which is available at <http://circ.ahajournals.org/content/124/22/2458>.

## **AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients With Coronary and Other Atherosclerotic Vascular Disease: 2011 Update: A Guideline From the American Heart Association and American College of Cardiology Foundation**

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