ACP Clinical Practice® American College of Physicians GUIDELINES

CLINICAL GUIDELINE

Management of Stable Ischemic Heart Disease: Summary of a Clinical Practice Guideline From the American College of Physicians/American College of Cardiology Foundation/ American Heart Association/American Association for Thoracic Surgery/Preventive Cardiovascular Nurses Association/Society of Thoracic Surgeons

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Description: The American College of Physicians (ACP) developed this guideline with the American College of Cardiology Foundation (ACCF), American Heart Association (AHA), American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, and Society of Thoracic Surgeons to present the available evidence on the management of stable known or suspected ischemic heart disease.

Methods: Literature on this topic published before November 2011 was identified by using MEDLINE, Embase, Cochrane CENTRAL, PsychINFO, AMED, and SCOPUS. Searches were limited to human studies published in English. This guideline grades the evidence and recommendations according to a translation of the ACCF/AHA grading system into ACP's clinical practice guidelines grading system.

Recommendations: The guideline includes 48 specific recommendations that address the following issues: patient education, management of proven risk factors (dyslipidemia, hypertension, diabetes, physical activity body weight, and smoking), risk factor reduction strategies of unproven benefit, medical therapy to prevent myocardial infarction and death and to relieve symptoms, alternative therapy, revascularization to improve survival and symptoms, and patient follow-up.

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EXECUTIVE SUMMARY

This guideline presents the available evidence on the management of stable known or suspected ischemic heart disease (IHD). This is the second of 2 guidelines addressing stable IHD; the first guideline addresses the diagnosis of patients with stable IHD (1). Internists and other primary care physicians are the target audiences for this guideline. The target population is all adult patients with stable known or suspected IHD. These recommendations are based on the joint American College of Cardiology Foundation (ACCF), American Heart Association (AHA), American College of Physicians (ACP), American Association for Thoracic Surgery (AATS), Preventive Cardiovascular Nurses Association (PCNA), Society for Cardiovascular Angiography and Interventions (SCAI), and Society of Thoracic Surgeons (STS) guideline for the diagnosis and management of patients with stable IHD published in 2012, which ACP recognized as a scientifically valid, high-quality review of the evidence (2). Full details about methods and evidence are available in the **Appendix** at www.annals.org.

Methods

The databases used for the literature search included MEDLINE, Embase, Cochrane CENTRAL, PsychINFO, AMED, and SCOPUS for studies published up until November 2011. The criteria for search included human participants and English-language articles. For more details on the methods, please refer to the **Appendix** and the ACCF, AHA, ACP, AATS, PCNA, SCAI, and STS guideline for the diagnosis and management of patients with stable IHD (2).

See also:

Print

Related article 729
Editorial comment 749
Summary for Patients I-48

Web-Only

Appendix: Full Guideline Summary

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Table 1. **The American College of Physicians Guideline Grading System***

Quality of Evidence	Strength of Recommendation	
	Benefits Clearly Outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced With Risks and Burden
High	Strong	Weak
Moderate	Strong	Weak
Low	Strong	Weak
Insufficient evidence to determine net benefits or risks		

* Adopted from the classification developed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) workgroup.

Because this document is based on the joint guideline, ACP translated the ACCF/AHA evidence and recommendation grades into ACP's guideline grading system (**Tables 1** and **2**) (3). We included only class I and class III statements from the joint guideline because the evidence very clearly demonstrates the tradeoff between benefits and harms (**Table 2**). For details on other recommendations, please refer to the ACCF, AHA, ACP, AATS, PCNA, SCAI, and STS guideline for the diagnosis and management of patients with stable IHD (2).

The objective of this guideline is to synthesize the evidence for the following key questions:

1: What should be the approach to modifying cardiovascular risk factors to reduce the mortality and morbidity associated with stable IHD?

2: What is the role of coronary revascularization in reducing mortality and morbidity associated with stable IHD?

3: How should chronic anginal symptoms be managed with medications?

General Approach to Treatment

The goals of treating patients with stable IHD are to 1) prevent premature cardiovascular death and complications of stable IHD, including nonfatal acute myocardial infarction (MI) and heart failure, and 2) maintain or restore a quality of life that is satisfactory to the patient while eliminating avoidable adverse effects of tests and treatments, preventing hospital admissions, and eliminating unnecessary tests and treatments. This approach acknowledges that certain interventions are primarily aimed at improving survival, whereas others are undertaken largely to reduce symptoms, although under some circumstances, a treatment may be provided to achieve both aims simultaneously. The evolving approach to management of patients with stable IHD entails a "package" of therapies that are appropriate for most patients who do not have specific contraindications. These include lifestyle changes and specific medications, which together are called *guideline-directed medical therapy* and are prescribed regardless of decisions regarding revascularization (**Figure 1**).

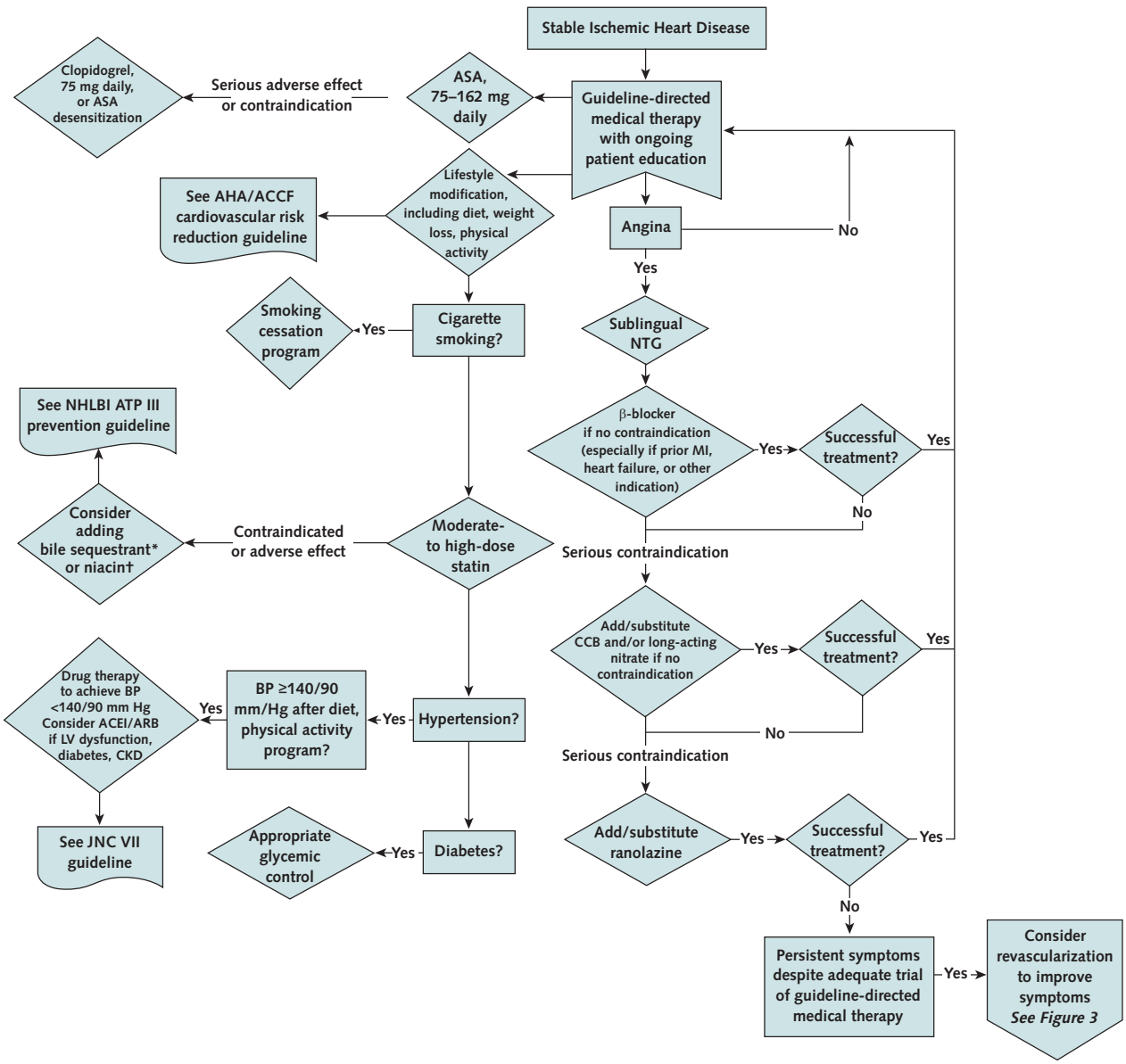
The initial approach to all patients should be focused on eliminating unhealthy behaviors, such as smoking, and effectively promoting lifestyle changes that reduce cardiovascular risk, such as increasing weight loss, physical activity, and adopting a healthy diet. In addition, for most patients, an evidence-based set of pharmacologic interventions is indicated to reduce the risk for future events. The presumed mechanism by which these interventions are effective is by stabilizing the coronary plaque to prevent rupture and thrombosis (4). These include antiplatelet agents (5); lipid-lowering agents, in particular hydroxymethylglutaryl coenzyme A reductase inhibitors (statins) (6–13); and β-blockers (14, 15). Angiotensin-converting enzyme (ACE) inhibitors are indicated in many patients with stable IHD, especially those with diabetes or left ventricular (LV) dysfunction (16–18). Similarly, although tight glycemic control has not been shown to reduce the risk for macrovascular complications in patients with type 2 diabetes, weight loss, aerobic exercise, an AHA Step II diet, and ACE inhibitors in those with proteinuria can all improve patients' risks for microvascular complications and, potentially, cardiac events. Revascularization improves survival in specific subgroups of patients, whereas it should be undertaken to relieve symptoms in others.

Table 2. **Comparison of Grading Systems From the ACP and ACCF/AHA**

ACP's Grading System			ACCF/AHA's Grading System (Size vs. Certainty)		
Description	Grade (For or Against Intervention)		Grade	Class	
	Recommendation	Evidence		For	Against
Benefits clearly outweigh risks and burden or vice versa	Strong	High-quality	A	I	III
Benefits clearly outweigh risks and burden or vice versa	Strong	Moderate-quality	B	I	III
Benefits clearly outweigh risks and burden or vice versa	Strong	Low-quality	C	I	III
Benefits closely balanced with risks and burden	Weak	High-quality	A	IIa, IIb	NER
Benefits closely balanced with risks and burden	Weak	Moderate-quality	B	IIa, IIb	NER
Uncertainty, benefits may be closely balanced with risks and burden	Weak	Low-quality	C	IIa, IIb	NER

ACCF = American College of Cardiology Foundation; ACP = American College of Physicians; AHA = American Heart Association; NER = no equivalent rating.

Figure 1. **Guideline-directed medical therapy for patients with stable ischemic heart disease.**



ACCF = American College of Cardiology Foundation; ACEI = angiotensin-converting enzyme inhibitor; AHA = American Heart Association; ARB = angiotensin-receptor blocker; ASA = aspirin; ATP III = Adult Treatment Panel III; BP = blood pressure; CCB = calcium-channel blocker; CKD = chronic kidney disease; JNC VII = Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; LV = left ventricular; MI = myocardial infarction; NHLBI = National Heart, Lung, and Blood Institute; NTG = nitroglycerin.
* The use of bile acid sequestrant is relatively contraindicated when triglyceride levels are 200 mg/dL or greater and is contraindicated when triglyceride levels are 500 mg/dL or greater.
† Dietary supplement niacin must not be used as a substitute for prescription niacin.

Recommendations

Patient Education

Recommendation 1: The organizations recommend that patients with stable IHD should have an individualized education plan to optimize care and promote wellness, including:

A. Education on the importance of medication adherence for managing symptoms and reducing disease progression (Grade: strong recommendation; low-quality evidence).

B. An explanation of medication management and cardiovascular risk reduction strategies in a manner that respects the patient's level of understanding, reading comprehension, and ethnicity (Grade: strong recommendation; moderate-quality evidence).

C. A comprehensive review of all therapeutic options (Grade: strong recommendation; moderate-quality evidence).

D. A description of appropriate levels of exercise with encouragement to maintain recommended levels of daily physical activity (Grade: strong recommendation; low-quality evidence).

E. Introduction to self-monitoring skills (Grade: strong recommendation; low-quality evidence).

F. Information on how to recognize worsening cardiovascular symptoms and take appropriate action (Grade: strong recommendation, low-quality evidence).

Recommendation 2: The organizations recommend that patients with stable IHD should be educated regarding the following lifestyle elements that may influence prognosis (Grade: strong recommendation; low-quality evidence):

A. Weight control and maintenance of a body mass index of 18.5 to 24.9 kg/m^2 and waist circumference less than 40 inches for men and less than 35 inches for women (less for certain racial groups).

B. Lipid management.

C. Blood pressure control.

D. Smoking cessation and avoidance of exposure to second-hand smoke.

E. Individualized medical, nutrition, and lifestyle education for patients with diabetes mellitus to supplement diabetes treatment goals and education.

Risk Factor Modification

Lipid Management. *Recommendation 3: The organizations recommend lifestyle modifications for lipid management in all patients with stable IHD, including daily physical activity and weight management (Grade: strong recommendation; moderate-quality evidence).*

Recommendation 4: The organizations recommend dietary therapy for all patients, which should include reduced intake of saturated fats (to <7% of total calories), trans-fatty acids (to <1% of total calories), and cholesterol (to <200 mg per day) (Grade: strong recommendation; moderate-quality evidence).

Recommendation 5: The organizations recommend that in addition to therapeutic lifestyle changes, a moderate or high dose of a statin therapy should be prescribed in the absence of contraindications or documented adverse effects. (Grade: strong recommendation; high-quality evidence).

Hypertension. *Recommendation 6: The organizations recommend that patients with stable IHD who have high blood pressure should be counseled regarding the need for lifestyle modifications, including maintenance of recommended weight; increased physical activity; moderation of alcohol consumption; limitation of dietary sodium; and emphasis on increased consumption of fresh fruits, vegetables, and low-fat dairy products (Grade: strong recommendation; moderate-quality evidence).*

Recommendation 7: The organizations recommend that patients with stable IHD with blood pressure of 140/90 mm Hg or higher should be treated with antihypertensive drug therapy in addition to following a trial of lifestyle modifications (Grade: strong recommendation; high-quality evidence). The specific medications used for treatment of high blood pressure should be based on specific patient characteristics, and may include ACE inhibitors and/or β-blockers, with addition of other drugs, such as thiazide diuretics or calcium-channel blockers, if needed to achieve a goal blood pressure of less than 140/90 mm Hg (Grade: strong recommendation; moderate-quality evidence).

Diabetes. *Recommendation 8: The organizations recommend that therapy with rosiglitazone should not be initiated in diabetic patients with stable IHD (Grade: strong recommendation; low-quality evidence).*

Physical Activity. *Recommendation 9: The organizations recommend risk assessment with a physical activity history to guide prognosis and prescription for all patients. An exercise test should be obtained when clinically indicated (Grade: strong recommendation; moderate-quality evidence). As indicated, based on this assessment, patients with stable IHD should be encouraged to engage in 30 to 60 minutes of moderate-intensity aerobic activity, such as brisk walking, at least 5 days and preferably 7 days of the week, supplemented by an increase in daily activities (such as walking breaks at work, gardening, or household work) to improve cardiorespiratory fitness and motivate patients of the least fit, least active high-risk cohort (bottom 20%) (Grade: strong recommendation; moderate-quality evidence). Medically supervised programs (cardiac rehabilitation) and physician-directed, home-based programs are recommended for at-risk patients at first diagnosis (Grade: strong recommendation; high-quality evidence).*

Weight Management. *Recommendation 10: The organizations recommend assessing body mass index and/or waist circumference at every visit and consistently encouraging 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^2, and waist circumference less than 40 inches in men and less than 35 inches in women (less for certain racial groups) (Grade: strong recommendation; moderate-quality evidence). 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 (Grade: strong recommendation; low-quality evidence).*

Smoking Cessation. *Recommendation 11: The organizations recommend that smoking cessation and avoidance of exposure to environmental tobacco smoke at work and at home should be encouraged for all patients with stable IHD. A stepwise strategy for smoking cessation (Ask, Advise, Assess, Assist, Arrange), follow-up, referral to special programs, and/or pharmacotherapy are recommended (Grade: strong recommendation; moderate-quality evidence).*

Risk Factor Reduction Strategies of Unproven Benefits. *Recommendation 12: The organizations recommend that estrogen therapy should not be initiated in postmenopausal*

women with stable IHD with the intent of reducing cardiovascular risk or improving clinical outcomes (Grade: strong recommendation; high-quality evidence).

Recommendation 13: The organizations recommend that vitamin C, vitamin E, and β-carotene supplementation should not be used with the intent of reducing cardiovascular risk or improving clinical outcomes in patients with stable IHD (Grade: strong recommendation; high-quality evidence).

Recommendation 14: The organizations recommend that treatment of elevated homocysteine with folate and/or vitamins B_6 and B_{12} should not be used with the intent of reducing cardiovascular risk or improving clinical outcomes in patients with stable IHD (Grade: strong recommendation; high-quality evidence).

Recommendation 15: The organizations recommend that chelation therapy should not be used with the intent of improving symptoms or reducing cardiovascular risk in patients with stable IHD (Grade: strong recommendation; low-quality evidence).

Recommendation 16: The organizations recommend that treatment with garlic, coenzyme Q_{10}, selenium, or chromium should not be used with the intent of reducing cardiovascular risk or improving clinical outcomes in patients with stable IHD (Grade: strong recommendation; low-quality evidence).

Medical Therapy to Prevent MI and Death in Patients With Stable IHD

Recommendation 17: The organizations recommend that aspirin, 75 to 162 mg daily, should be continued indefinitely in the absence of contraindications in patients with stable IHD (Grade: strong recommendation; high-quality evidence).

Recommendation 18: The organizations recommend treatment with clopidogrel as a reasonable option when aspirin is contraindicated in patients with stable IHD (Grade: strong recommendation; moderate-quality evidence).

Recommendation 19: The organizations recommend that dipyridamole should not be used as antiplatelet therapy for patients with stable IHD (Grade: strong recommendation; low-quality evidence).

Recommendation 20: The organizations recommend that β-blocker therapy should be initiated and continued for 3 years in all patients with normal LV function following MI or acute coronary syndromes (Grade: strong recommendation; moderate-quality evidence).

Recommendation 21: The organizations recommend that metoprolol succinate, carvedilol, or bisoprolol should be used for all patients with systolic LV dysfunction (ejection fraction ≤40%) with heart failure or prior MI, unless contraindicated (Grade: strong recommendation; high-quality evidence).

Recommendation 22: The organizations recommend that ACE inhibitors should be prescribed in all patients with stable IHD who also have hypertension, diabetes, LV systolic dysfunction (ejection fraction ≤40%), and/or chronic kidney disease, unless contraindicated (Grade: strong recommendation; high-quality evidence).

Recommendation 23: The organizations recommend angiotensin-receptor blockers for patients with stable IHD who have hypertension, diabetes, LV systolic dysfunction, or chronic kidney disease and have indications for, but are intolerant of, ACE inhibitors (Grade: strong recommendation; high-quality evidence).

Recommendation 24: The organizations recommend an annual influenza vaccine for patients with stable IHD (Grade: strong recommendation; moderate-quality evidence).

Medical Therapy for Relief of Symptoms in Patients With Stable IHD

Recommendation 25: The organizations recommend that β-blockers should be prescribed as initial therapy for relief of symptoms in patients with stable IHD (Grade: strong recommendation; moderate-quality evidence).

Recommendation 26: The organizations recommend that calcium-channel blockers or long-acting nitrates should be prescribed for relief of symptoms when β-blockers are contraindicated or cause unacceptable side effects in patients with stable IHD (Grade: strong recommendation; moderate-quality evidence).

Recommendation 27: The organizations recommend that calcium-channel blockers or long-acting nitrates, in combination with β-blockers, should be prescribed for relief of symptoms when initial treatment with β-blockers is unsuccessful in patients with stable IHD (Grade: strong recommendation; moderate-quality evidence).

Recommendation 28: The organizations recommend that sublingual nitroglycerin or nitroglycerin spray should be used for immediate relief of angina in patients with stable IHD (Grade: strong recommendation; moderate-quality evidence).

Alternative Therapy for Relief of Symptoms in Patients With Stable IHD

Recommendation 29: The organizations recommend that acupuncture should not be used for the purpose of improving symptoms or reducing cardiovascular risk in stable IHD patients (Grade: strong recommendation; low-quality evidence).

Revascularization

Recommendation 30: The organizations recommend that a shared decision-making approach should be utilized when making decisions about revascularization in patients with unprotected left main or complex coronary artery disease and should include a cardiac surgeon, an interventional cardiologist, and the patient (Grade: strong recommendation; low-quality evidence).

Revascularization to Improve Survival. *Recommendation 31: The organizations recommend coronary artery bypass graft to improve survival for patients with significant (≥50% diameter stenosis) left main coronary artery stenosis (Grade: strong recommendation; moderate-quality evidence).*

Recommendation 32: The organizations recommend that percutaneous coronary intervention to improve survival should

not be performed in stable patients with significant (≥50% diameter stenosis) unprotected left main coronary artery disease who have unfavorable anatomy for percutaneous coronary intervention and who are good candidates for coronary artery bypass graft (Grade: strong recommendation; moderate-quality evidence).

Recommendation 33: The organizations recommend the use of coronary artery bypass graft to improve survival in patients with significant (≥70% diameter) stenoses in 3 major coronary arteries (with or without involvement of the proximal left anterior descending artery) or in the proximal left anterior descending artery plus 1 other major coronary artery (Grade: strong recommendation; moderate-quality evidence).

Recommendation 34: The organizations recommend the use of coronary artery bypass graft or percutaneous coronary intervention to improve survival in survivors of sudden cardiac death with presumed ischemia-mediated ventricular tachycardia caused by significant (≥70% diameter) stenosis in a major coronary artery (Grade: strong recommendation; moderate-quality evidence for coronary artery bypass graft, low-quality evidence for percutaneous coronary intervention).

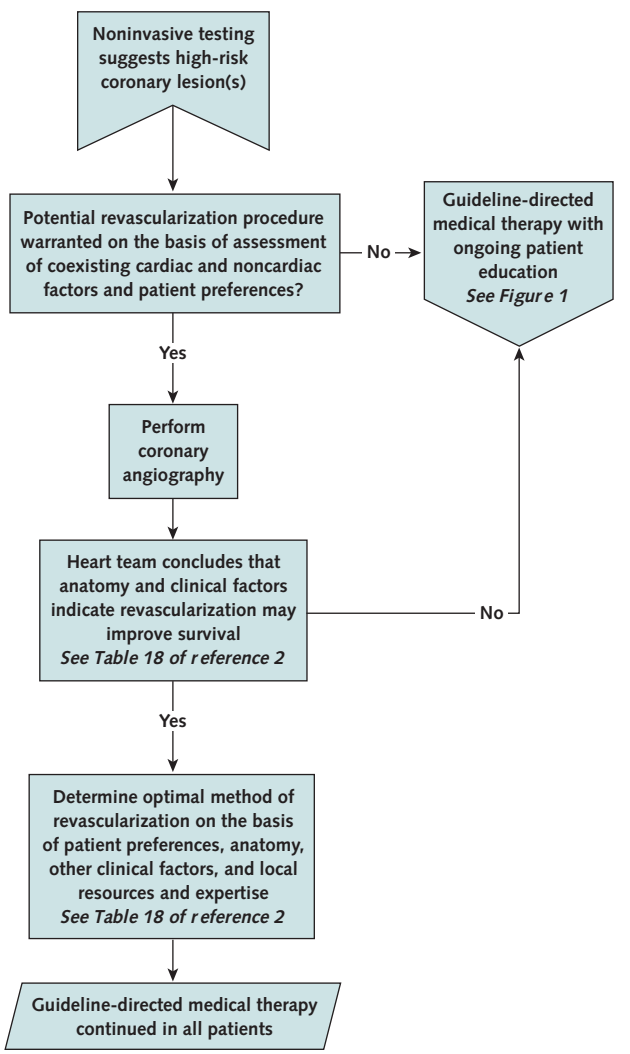
Recommendation 35: The organizations recommend that coronary artery bypass graft or percutaneous coronary intervention should not be performed with the primary or sole intent to improve survival in patients with stable IHD with 1 or more coronary stenoses that are not anatomically or functionally significant (for example, <70% diameter non–left main coronary artery stenosis, fractional flow reserve >0.80, no or only mild ischemia on noninvasive testing), involve only the left circumflex or right coronary artery, or subtend only a small area of viable myocardium (Grade: strong recommendation; moderate-quality evidence).

Revascularization to Improve Symptoms. *Recommendation 36: The organizations recommend the use coronary artery bypass graft or percutaneous coronary intervention to improve symptoms in patients with 1 or more significant (≥70% diameter) coronary artery stenoses amenable to revascularization and unacceptable angina despite guideline-directed medical therapy (Grade: strong recommendation; high-quality evidence).*

Recommendation 37: The organizations recommend that the use coronary artery bypass graft or percutaneous coronary intervention to improve symptoms should not be performed in patients who do not meet anatomical (≥50% diameter left main or ≥70% non–left main stenosis diameter) or physiologic (for example, abnormal fractional flow reserve) criteria for revascularization (Grade: strong recommendation; low-quality evidence).

Recommendation 38: The organizations recommend that percutaneous coronary intervention with coronary stenting (bare-metal stent or drug-eluting stent) should not be performed if the patient is not likely to be able to tolerate and comply with dual antiplatelet therapy for the appropriate duration rof treatment based on the type of stent implanted (Grade: strong recommendation; moderate-quality evidence).

Figure 2. **Revascularization to improve survival of patients with stable ischemic heart disease.**



Patient Follow-up

Recommendation 39: The organizations recommend that patients with stable IHD should receive periodic follow-up at least annually that includes all of the following (Grade: strong recommendation; low-quality evidence):

A. Assessment of symptoms and clinical function.

B. Surveillance for complications of stable IHD, including heart failure and arrhythmias.

C. Monitoring of cardiac risk factors.

D. Assessment of the adequacy of and adherence to recommended lifestyle changes and medical therapy.

Recommendation 40: The organizations recommend assessment of LV ejection fraction and segmental wall motion by

echocardiography or radionuclide imaging in patients with new or worsening heart failure or evidence of intervening MI by history or electrocardiogram (Grade: strong recommendation; low-quality evidence).

Recommendation 41: The organizations recommend that measurement of LV function with a technology such as echocardiography or radionuclide imaging should not be used for routine periodic reassessment of patients who have not had a change in clinical status or who are at low risk of adverse cardiovascular events (Grade: strong recommendation; low-quality evidence).

Recommendation 42: The organizations recommend standard exercise electrocardiogram in patients with known stable IHD who have new or worsening symptoms not consistent with unstable angina and who have a) at least moderate physical functioning and no disabling comorbidity and b) an interpretable electrocardiogram (Grade: strong recommendation; moderate-quality evidence).

Recommendation 43: The organizations recommend exercise with radionuclide myocardial perfusion imaging or echocardiography in patients with known stable IHD who have new or worsening symptoms not consistent with unstable angina, and who have a) at least moderate physical functioning or no disabling comorbidity but b) an uninterpretable electrocardiogram (Grade: strong recommendation; moderate-quality evidence).

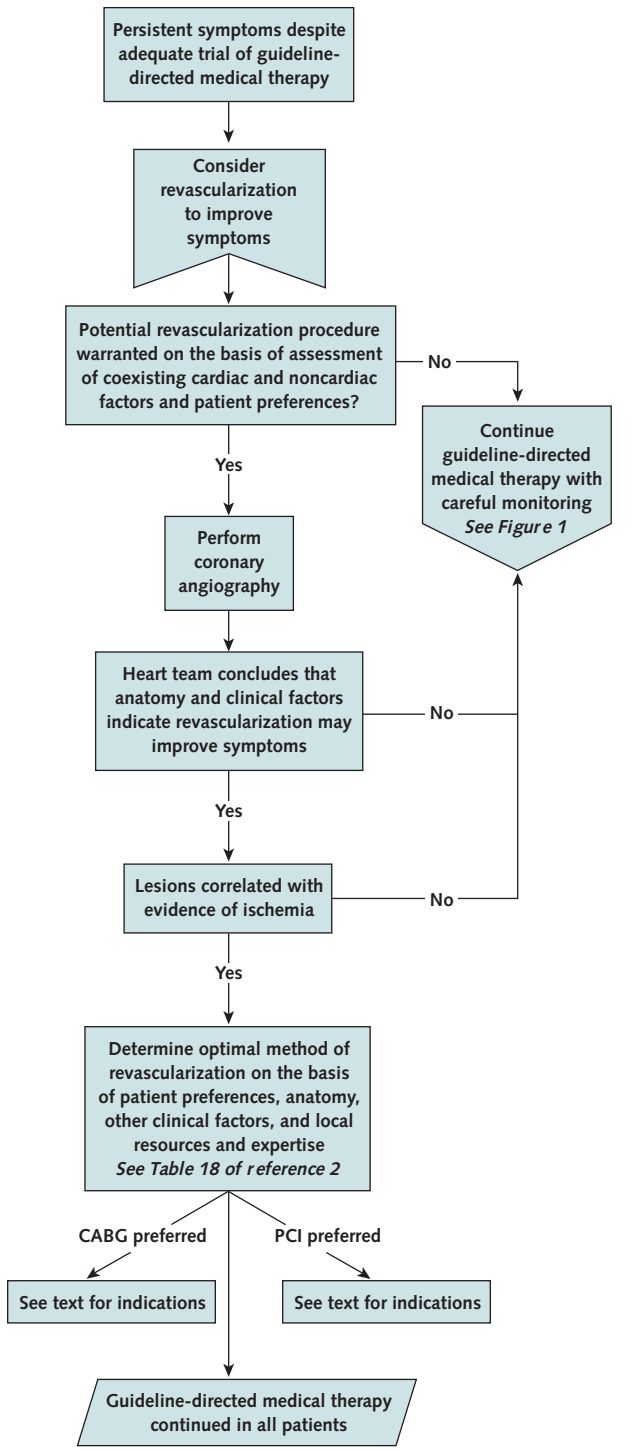
Recommendation 44: The organizations recommend that pharmacologic stress imaging with radionuclide myocardial perfusion imaging, echocardiography, or cardiac magnetic resonance should not be used in patients with known stable IHD who have new or worsening symptoms not consistent with unstable angina and who are capable of at least moderate physical functioning or have no disabling comorbidity (Grade: strong recommendation; low-quality evidence).

Recommendation 45: The organizations recommend pharmacologic stress imaging using radionuclide myocardial perfusion or echocardiography in patients with known stable IHD who have new or worsening symptoms not consistent with unstable angina and who are incapable of at least moderate physical functioning or have disabling comorbidity (Grade: strong recommendation; moderate-quality evidence).

Recommendation 46: The organizations recommend that standard exercise electrocardiogram testing should not be performed in patients with known stable IHD who have new or worsening symptoms not consistent with unstable angina and who a) are incapable of at least moderate physical functioning or have disabling comorbidity or b) have an uninterpretable electrocardiogram (Grade: strong recommendation; low-quality evidence).

Recommendation 47: The organizations recommend that coronary/cardiac computed tomography angiography should not be performed for assessment of native coronary arteries with known moderate or severe calcification or of coronary stents less than 3 mm in diameter in patients with known

Figure 3. **Revascularization to improve symptoms of patients with stable ischemic heart disease.**



CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention.

stable IHD who have new or worsening symptoms not consistent with unstable angina, irrespective of ability to exercise (Grade: strong recommendation; moderate-quality evidence).

Recommendation 48: The organizations recommend that radionuclide myocardial perfusion imaging, echocardiography, or cardiac magnetic resonance, with either exercise or pharmacologic stress or coronary/cardiac computed tomography angiography, should not be used for follow-up assessment in patients with stable IHD, if performed more frequently than at a) 5-year intervals after coronary artery bypass graft or b) 2-year intervals after percutaneous coronary intervention (Grade: strong recommendation; low-quality evidence).

Summary

The goals of managing patients with stable IHD include reducing premature cardiovascular death and nonfatal MI while maintaining a level of activity, functional capacity, and quality of life that is satisfactory to the patient. See **Figures 1** to **3** for algorithms on medical care, revascularization to improve survival, and revascularization to improve symptoms.

Because of the variation in symptoms and clinical characteristics among patients, as well as their unique perceptions, expectations, and preferences, there is clearly no single correct approach to any given set of clinical circumstances. Patient education regarding various therapeutic options, appropriate levels of exercise, diet and weight control, and the importance of various clinical manifestations play a key role in achieving the treatment goal. Lifestyle modifications are also critical for all patients with stable IHD to control weight and high blood pressure and manage diabetes. Various pharmacologic approaches can be used to prevent MI or death in patients with stable IHD, including daily aspirin, β-blockers, ACE inhibitors or angiotensin-receptor blockers, and influenza vaccination. For patients with symptoms, various pharmacologic options are available to relieve symptoms. Although there is limited evidence of the efficacy of specific strategies for the follow-up of patients with stable IHD, there is emerging consensus that patients with a variety of chronic illnesses have improved outcomes when they receive coordinated care. Patients with stable IHD require regular monitoring to assess changes in their status, their response, and adherence to guideline-directed medical therapy.

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Appendix: Management of Stable Ischemic Heart Disease: A Clinical Practice Guideline Summary From the American College of Physicians/ American College of Cardiology Foundation/ American Heart Association/American Association for Thoracic Surgery/Preventive Cardiovascular Nurses Association/ Society of Thoracic Surgeons

Ischemic heart disease (IHD) is a major public health issue that affects an estimated 1 in 3 adults in the United States (19). It is the single leading cause of death and is responsible for 1 of every 4 deaths. Approximately 71 million Americans have some form of cardiovascular disease, including more than 13 million with coronary artery disease (CAD) and more than 9 million with angina pectoris (19). The prevalence of IHD increases with age; approximately 23% of men and 15% of women in the United States have IHD. The costs of caring for patients with IHD are enormous: an estimated $156 billion in the United States for both direct and indirect costs in 2008 (20). These costs include hospitalizations, invasive procedures, emergency department visits, and long-term care.

The purpose of this guideline is to present the available evidence on the management of stable known or suspected IHD in adult patients. This is the second of 2 guidelines addressing stable IHD; the first guideline addressed the diagnosis of patients with stable IHD (21). The target audience for this guideline is all internists and other primary care physicians. The target population is all adult patients with stable known or suspected IHD. These recommendations are based on the joint guideline on the diagnosis and management of patients with stable IHD from the American College of Cardiology Foundation (ACCF), American Heart Association (AHA), American College of Physicians (ACP), American Association for Thoracic Surgery (AATS), Preventive Cardiovascular Nurses Association (PCNA), Society for Cardiovascular Angiography and Interventions (SCAI), and Society of Thoracic Surgeons (STS) published in 2012, which ACP recognized as a scientifically valid, high-quality review of the evidence (22).

Methods

The databases used for the literature search included MEDLINE, Embase, Cochrane CENTRAL, PsychINFO, AMED, and SCOPUS for studies published up until November 2011. The criteria for search included human participants and English-language articles. For more details on the methods, please refer to the ACCF, AHA, ACP, AATS, PCNA, SCAI, and STS guideline for the diagnosis and management of patients with stable IHD (22).

ACP guideline recommendations are based on evidence from systematic reviews of high-quality evidence (several well-designed randomized, controlled trials) and meta-analyses where appropriate. Because this document is based on the joint ACCF, AHA, ACP, AATS, PCNA, SCAI, and STS guideline, ACP translated the ACCF/AHA evidence and recommendation grading system into ACP's guideline grading system (**Tables 1** and **2**, in Executive Summary). We included only class I and class III statements from the ACCF, AHA, ACP, AATS, PCNA, SCAI, and STS guideline because the evidence very clearly demonstrated that benefits outweigh harms or vice versa (**Table 2**, in Executive Summary). For details on other recommendations, please refer to the ACCF, AHA, ACP, AATS, PCNA, SCAI, and STS guideline for the diagnosis and management of patients with stable IHD (22).

The objective of this guideline is to synthesize the evidence for the following key questions:

1: What should be the approach to modifying cardiovascular risk factors to reduce the mortality and morbidity associated with stable IHD?

2: What is the role of coronary revascularization in reducing mortality and morbidity associated with stable IHD?

3: How should chronic anginal symptoms be managed with medications?

General Approach to Treatment

The goals of treating patients with stable IHD are to 1) prevent premature cardiovascular death and complications of stable IHD, including nonfatal acute myocardial infarction (MI) and heart failure, and 2) maintain or restore a quality of life that is satisfactory to the patient while eliminating avoidable adverse effects of tests and treatments, preventing hospital admissions, and eliminating unnecessary tests and treatments. This approach acknowledges that certain interventions are primarily aimed at improving survival, whereas others are undertaken largely to reduce symptoms; under some circumstances, however, a treatment may be provided to achieve both aims simultaneously. The evolving approach to management of patients with stable IHD entails a "package" of therapies that are appropriate for most patients who do not have specific contraindications. These include lifestyle changes and specific medications that together are called *guideline-directed medical therapy* (GDMT) and are prescribed irrespective of decisions regarding revascularization (**Figure 1**, in Executive Summary).

The initial approach to all patients should be focused on eliminating unhealthy behaviors, such as smoking, and effectively promoting lifestyle changes that reduce cardiovascular risk, such as increasing weight loss, physical activity, and adopting a healthy diet. In addition, for most patients, an evidence-based set of pharmacologic interventions is indicated to reduce the risk for future events. The presumed mechanism by which these interventions are effective is by stabilizing the coronary plaque to prevent rupture and thrombosis (23). These include antiplatelet agents (24); lipid-lowering agents, in particular hydroxymethylglutaryl coenzyme A reductase inhibitors (statins) (25–32); and β-blockers (33, 34). Angiotensin-converting enzyme (ACE) inhibitors are indicated in many patients with stable IHD, especially those with diabetes or left ventricular (LV) dysfunction (35–37). Similarly, although tight glycemic control has not been shown to reduce the risk for macrovascular complications in patients with type 2 diabetes, weight loss, aerobic exercise, an AHA Step II diet, and ACE inhibitors in those with proteinuria can all

improve patients' risks for microvascular complications and, potentially, cardiac events. Revascularization improves survival in specific subgroups of patients, whereas it should be undertaken to relieve symptoms in others.

Patient Education for Persons With Stable IHD

Patients with stable IHD usually have multiple risk factors for heart disease, vascular disease, and stroke (38, 39). These risk factors include hypertension, cigarette smoking, dyslipidemia, diabetes, obesity, physical inactivity, and psychological states (such as depression) that contribute to higher rates of morbidity and mortality (38, 39). The approach to the management for all risk factors requires partnerships among the health care team, the patient and family, and the community. The goal of this partnership is to assure an effective exchange of information, sharing of concerns, and improved understanding of treatments with the aim of improving quality-of-life and health outcomes. Effective patient education and counseling as well as active patient involvement are crucial (40). Successful clinical management depends on patients' understanding of their condition, their ability to safely adhere to complex medical therapies, and their willingness to communicate on a regular basis with their health care team. Effectively communicating with patients about their condition; management of and adherence to recommended lifestyle changes and medications, diagnostic tests, and procedures; and the necessity of reporting adverse effects is essential (23, 41). It is also important to integrate patients' individual cognitive, behavioral, and sociodemographic characteristics into the communication and to incorporate them into the communication process.

Evidence supports the use of an individualized plan of education that addresses various therapeutic options (23, 40–45), diet (23, 46–49), physical activity (23, 50–52), importance of weight control (23, 41, 53–57), blood pressure control (49, 58), smoking cessation (23, 59, 60), and medication adherence (61–63).

Risk Factor Modification

Lipid Management

Serum cholesterol is a well-established independent risk factor for coronary heart disease (64–67), and this also holds true in patients with stable IHD (68–70). Effective dietary approaches to lowering low-density lipoprotein (LDL) cholesterol include replacing saturated and trans-fatty acids with dietary carbohydrates or unsaturated fatty acids, as well as reducing dietary cholesterol (71–74). Evidence suggests decreasing intake of saturated fats to less than 7% of total calories, with trans-fatty acids, and total cholesterol to less than 200 mg/d (71–74). In addition, regular physical activity is also a key component of therapeutic lifestyle modification because it facilitates weight loss and has other beneficial effects on the lipid profile (75–77).

In addition to dietary modification, evidence has established the efficacy of statins in the primary and secondary prevention of coronary events (15–17, 31, 78–83). Each 40-mg/dL reduction in LDL cholesterol was associated with a 12% reduction in all-cause mortality and 19% reduction in coronary mortality, with corresponding reductions in MI, need for coronary revascularization, and fatal or nonfatal strokes (48). Data support intensive LDL cholesterol–lowering with statins in patients with stable IHD (31, 78, 79), including those who have LDL cholesterol levels less than 130 mg/dL (84). However, clinical trials to date have neither established an absolute or optimal threshold of benefit with regard to reduction in LDL cholesterol levels nor provided evidence that a particular statin drug in a particular dosage is preferred. An update of the Adult Treatment Panel III (ATP III) report recommends treatment to an LDL cholesterol level less than 100 mg/dL in patients with established coronary disease or other high-risk features and an LDL cholesterol goal of less than 70 mg/dL as a therapeutic option in patients at very high risk (85). Factors that identify patients at very high risk include the presence of established coronary vascular disease plus 1) multiple major risk factors, especially diabetes; 2) severe and poorly controlled risk factors, especially continued tobacco use; and 3) multiple risk factors for the metabolic syndrome.

When statins are insufficiently effective, not tolerated, or contraindicated or cause adverse effects, other lipid-lowering agents can be substituted or added. Evidence from randomized, controlled trials shows that treatment with cholesterol-binding resins (such as cholestyramine) and niacin improves survival compared with placebo. Less evidence favors fibric acid derivatives (such as gemfibrozil) for patients with hypercholesterolemia. Evidence from observational studies and treatment trials shows benefits of consumption of omega-3 fatty acids in reducing cardiovascular risk (86–88). Ezetimibe decreases cholesterol but has not been shown to improve clinical outcomes.

A secondary target of therapy introduced by the ATP III is non–high-density lipoprotein (HDL) cholesterol in patients with elevated triglyceride levels (46). Non-HDL cholesterol is defined as the difference between total cholesterol and HDL cholesterol. It includes all cholesterol and lipoprotein particles that are considered atherogenic, including LDL, lipoprotein(a), intermediate-density lipoprotein, and very-low-density lipoprotein, and is a predictor of cardiovascular death (89). Because statins reduce LDL cholesterol and non-HDL cholesterol to a similar extent, the relative benefits of decreasing these 2 lipid measures cannot be distinguished on the basis of recent clinical trials.

Hypertension

In a meta-analysis of prospective studies involving nearly 1 million adults without pre-existing vascular disease, the risk for vascular death increased linearly over the blood pressure range of 115/75 to 185/115 mm Hg, without a threshold effect (90). In general, the evidence supports a target blood pressure of 140/90 mm Hg or less in patients with stable IHD (91–97).

The first step in managing hypertension includes lifestyle modification. This includes maintenance of an appropriate body weight with a body mass index (BMI) less than 25 kg/m^2. However, a weight loss of 10 kg is also associated with a decrease in blood pressure of 5 to 20 mm Hg (98–102). In addition, dietary habits, such as consumption of fruits, vegetables, and low-fat dairy products (103, 104); reduction of sodium intake (98, 99, 104–106); regular physical activity (107); and moderation of

alcohol consumption (108), are also related to lower blood pressure.

In patients for whom lifestyle modification measures do not sufficiently reduce blood pressure, therapy with medications is warranted. Several treatment trials have definitively demonstrated a beneficial effect of antihypertensive drug therapy in reducing cardiovascular risk (92, 96, 109, 110). However, the appropriate blood pressure threshold for initiating medical therapy in patients with stable IHD remains controversial. Evidence from randomized, controlled trials has demonstrated a benefit from antihypertensive therapy in patients with a diastolic blood pressure greater than 90 mm Hg (74) and also in patients with isolated systolic hypertension and a systolic blood pressure greater than 160 mm Hg (92, 109, 110). The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VII) recommends a target blood pressure of less than 140/90 mm Hg in patients with uncomplicated hypertension (49). However, caution with regard to overly aggressive lowering of blood pressure in patients with stable IHD is warranted because excessive reduction in diastolic pressure has not conclusively been shown to improve outcomes and has been associated with an increase in mortality, potentially related to reduced coronary perfusion (111–113).

Clinical trials have shown no differences among available antihypertensive medications in preventing coronary events (114, 115). The choice of therapy is guided by an individualized assessment of patients who have stable IHD and the indications for specific classes of drugs. Angiotensin-converting enzyme inhibitors improve outcomes in most patients with coronary disease, especially those with a history of MI, LV dysfunction and heart failure, or chronic kidney disease or diabetes (36, 37, 116–121). Angiotensin-receptor blockers (ARBs) are beneficial in the same spectrum of patients and are recommended for patients who are unable to tolerate ACE inhibitors (122–125). β-Blockers are recommended for patients with angina pectoris, a history of MI, or LV dysfunction (126–130). Calcium antagonists are useful in the treatment of angina. Many patients with stable IHD will require a combination of drugs, including a diuretic, to achieve optimal blood pressure control.

Diabetes

Diabetes is an important independent risk factor for cardiovascular disease. Type 1 diabetes is associated with at least a 10-fold increase in cardiovascular events (131, 132), and type 2 diabetes is associated with a 2 to 6 times increased risk for death from cardiovascular events compared with persons without diabetes (133–135). Diabetes is also associated with poor outcomes in patients with stable IHD (136).

Good evidence supports the benefits of glycemic control in reducing microvascular complications of diabetes (137, 138). However, the efficacy of intensive diabetes therapy in reducing cardiovascular disease is not established (137, 139–141). The Diabetes Control and Complications Trial (DCCT), which studied patients with type 1 diabetes, showed that fewer cardiovascular events occurred in the patient group exposed to intensive therapy (average hemoglobin A_{1c} achieved, 7.4%) compared with conventional therapy (average hemoglobin A_{1c} achieved, 9.1%) but the difference between groups was not statistically significant (137). The UKPDS (United Kingdom Prospective Diabetes Study), which studied patients with type 2 diabetes (142), and the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation) trial (140) provided similar results, with no statistically significant effect on cardiovascular events with intensive glycemic control.

The most appropriate target level for hemoglobin A_{1c} in patients with diabetes has not been definitively established by clinical trials. According to the ACP recommendations, the goal for the hemoglobin A_{1c} level should be based on individualized assessment of risk for complications from diabetes, comorbidity, life expectancy, and patient preferences (143). A target hemoglobin A_{1c} level less than 7% based on individualized assessment is a reasonable goal for some but not all patients (143, 144). Younger patients with type 1 diabetes are more likely to benefit from tight glycemic control, whereas elderly patients with several coexisting chronic conditions are least likely to benefit.

Physical Activity

Counseling about physical activity is a critical component of a comprehensive strategy for coronary risk factor modification in patients with stable IHD. Evidence shows that regular exercise reduces coronary heart disease mortality (145). Benefits of exercise have also been shown in patients with stable IHD (45, 146–151). Exercise-based cardiac rehabilitation may ameliorate and reduce reporting of symptoms (146, 150, 152, 153).

Most patients with coronary disease should be encouraged to engage in 30 to 60 minutes of moderate-intensity aerobic activity, such as brisk walking, on most and preferably all days of the week (154). Resistance training can also be beneficial.

Evidence also shows the safety of exercise-based cardiac rehabilitation in patients with documented stable IHD (155–158). Patients at high risk for cardiac complications (that is, those with a history of multiple MIs or cardiac arrest, New York Heart Association functional class 3 or 4 or exercise capacity less than 6 METs [metabolic equivalents], or significant exercise-induced ischemia on treadmill testing) should participate in a medically supervised program for at least 8 to 12 weeks to establish the safety of the prescribed exercise regimen.

Weight Management

Increased body weight has been shown to be associated with coronary events (159). Cardiovascular risk is increased in patients with central obesity, which can be identified by a waist circumference greater than 40 inches in men or greater than 35 inches in women (160, 161). No clinical trials have specifically examined the effects of weight loss on cardiovascular event rates in patients with stable IHD. However, the association of adiposity with other cardiovascular risk factors suggests that weight reduction is beneficial in all overweight and obese patients.

Weight loss can be achieved through reducing caloric intake, nutritional counseling, and behavioral modification therapy. The

ACP recommends (162) that clinicians should 1) counsel all obese patients (defined as those with a BMI $\geq$30 kg/m^2) on lifestyle and behavioral modifications, such as appropriate diet and exercise; 2) individually determine the patient's goals for weight loss (these goals may encompass not only weight loss but also changes in other parameters, such as decreasing blood pressure or fasting blood glucose levels); and 3) offer pharmacologic therapy to obese patients who have not achieved their weight loss goals through diet and exercise alone. Regarding pharmacologic agents, however, there needs to be a physician–patient discussion of the drugs' side effects, the lack of long-term safety data, and the temporary nature of the weight loss achieved with medications before initiating therapy. Weight loss is a difficult target, and other adjunct therapies may be appropriate for certain patients.

Smoking Cessation

There is incontrovertible evidence that cigarette smoking is associated with increased risk for cardiovascular disease events (163, 164). In addition, the number of cigarettes smoked is also linked with increased relative risk for cardiovascular disease events (164). Although randomized clinical trials of smoking cessation have not been performed in patients with stable IHD, results of observational studies strongly suggest that smoking cessation is an effective strategy for secondary prevention of coronary events.

The most effective smoking cessation strategies include both nonpharmacologic and medical interventions. Various strategies include physician advice (165); self-help programs, telephone counseling, behavioral therapy, and exercise (166–170); and nicotine replacement therapy (gum, patch, tablet, lozenge, and nasal spray) (171). Physicians should approach smoking cessation using the 5 A's framework (Ask, Advise, Assess, Assist, Arrange), which seeks to understand treatment of tobacco dependence and organize clinicians to provide appropriate treatment (172).

Sustained-release bupropion has demonstrated effectiveness similar to that of nicotine replacement therapy (173). Varenicline, a partial agonist of the $\alpha 4\beta 2$ nicotinic receptor, compares favorably with placebo and with bupropion in clinical trials (174, 175). There have, however, been concerns about possible worsening of pre-existing depression and the risk for suicide due to varenicline. The Food and Drug Administration has issued an alert warning that serious neuropsychiatric symptoms may occur in patients taking this drug (176, 177).

Medical Therapy to Prevent MI and Death in Patients With Stable IHD

Antiplatelet Therapy

Platelet inhibition is indicated in patients with stable IHD to reduce platelet aggregation as a thrombotic response to plaque disruption. A comprehensive meta-analysis showed that aspirin use was associated with a 33% reduction in the risk for serious vascular events, including a 46% decrease in the risk for unstable angina and a 53% decrease in the risk for undergoing coronary angioplasty (178). Aspirin at a dosage of 75 to 162 mg/d is equally as effective as a 325-mg dose in secondary prevention and is associated with a lower risk for bleeding. Doses less than 75 mg have less proven benefit (178, 179). Aspirin is relatively contraindicated in patients with known allergies to nonsteroidal anti-inflammatory drugs and in patients with the syndrome of asthma, rhinitis, and nasal polyps.

Clopidogrel is a reasonable option if aspirin is contraindicated in patients with stable IHD (180). In certain high-risk patients, a combination of aspirin and clopidogrel has also been shown to be beneficial (181, 182).

Antithrombotic Therapy

The evidence does not support the use of antithrombotic therapy, such as warfarin, in patients with stable IHD in the absence of a specific indication, such as prevention of recurrent venous thromboembolism or chronic atrial fibrillation (183–186). The evidence also does not support dipyridamole (187, 188) or ticlopidine (189, 190) as antiplatelet therapy for patients with stable IHD.

β-Blockers

β-Blockers reduce death and recurrent MI in patients who have sustained an MI and are especially effective when an ST-segment elevation MI is complicated by persistent or recurrent ischemia or tachyarrhythmias early or after the onset of infarction (191, 192). However, no large trials have assessed the effects of β-blockers on survival or coronary event rates in patients with stable IHD.

The results of the APSIS (Angina Prognosis Study in Stockholm), TIBBS (Total Ischemic Burden Bisoprolol Study), and IMAGE (International Multicenter Angina Exercise) studies have shown that β-blockers are more effective than calcium-channel blockers in the control of angina, reduction of cardiovascular events, or need for revascularization (193–195). Although combining β-blocker with calcium-channel blockers increases exercise time and improves cardiovascular outcomes (196, 197), it is important to be aware that a β-blocker given with verapamil or diltiazem may cause bradycardia, atrioventricular block, or excessive fatigue. Also, in patients with stable IHD, combination of a β-blocker with a nitrite is more effective than either monotherapy alone (198, 199). Bisoprolol, carvedilol, and metoprolol have been shown to reduce the risk for death and improve symptoms, clinical status, and quality of life in patients with chronic heart failure with or without CAD (130, 200, 201). The dosing for a β-blocker should be adjusted to limit the heart rate to 55 to 60 beats/min at rest and not to exceed 75% of the exercise heart rate response at the onset of ischemia.

All β-blockers have similar efficacy in patients with stable IHD (202–206). However, there are clinically important differences among β-blockers relating to cardioselectivity, presence of intrinsic sympathomimetic activity, vasodilating properties, and relative lipid solubility in the presence of renal or hepatic impairment. In addition, β-blockers are associated with certain contraindications that should be kept in mind when treating a patient with stable IHD. Absolute contraindications to β-blockers include severe bradycardia, pre-existing high degree of atrioventricular block, sick sinus syndrome, and refractory heart failure. Rel-

ative contraindications include bronchospastic disease or active peripheral arterial disease (β-blockers without vasodilating properties or selective agents at low doses may be used). β-Blockers should be used with caution in patients with type 1 diabetes. Abrupt β-blocker withdrawal should be avoided, and the dose should be tapered during a 1- to 3-week period because of heightened β-receptor density and sensitivity causing a rebound phenomenon associated with an increased risk for acute MI and sudden death.

Renin–Angiotensin–Aldosterone Therapy

ACE Inhibitors. Evidence supports the cardiovascular protective effects of ACE inhibitors and their role in reducing the risks for future ischemic events, such as acute MI and unstable angina (117, 120, 207). Angiotensin-converting enzymes inhibitors are beneficial for all patients with stable IHD and diabetes, LV dysfunction, chronic kidney disease, or cardiovascular history or risk profile similar to those of participants in the HOPE (Heart Outcomes Prevention Evaluation) or EUROPA (EURopean trial On reduction of cardiac events with Perindopril in stable coronary Artery disease) trials (37, 119, 208–211). Although the available ACE inhibitors differ with respect to structure, bioavailability, potency, receptor-binding characteristics, tissue distribution, metabolism, and excretion properties, there is little evidence that these differences are associated with therapeutic advantages. Because the benefits of ACE inhibitors appear to reflect a class effect, the selection of a particular agent should be based on such factors as availability in local formularies, cost, and tolerability.

ARBs. Angiotensin-receptor blockers also play an important role in vascular protection by decreasing blood pressure (212) and reducing LV mass, stroke incidence, and improving outcomes in heart failure (122, 124, 213–216). These drugs should be substituted for ACE inhibitors in patients with stable IHD and hypertension or LV dysfunction who are intolerant of ACE inhibitors (122, 124, 212, 214, 216).

Influenza Vaccination

Influenza is associated with increased mortality and hospitalizations in patients with cardiovascular disease. The World Health Organization, Centers for Disease Control and Prevention, ACP, and AHA/ACC recommend annual vaccination with inactivated vaccine administered intramuscularly against seasonal influenza in all patients with underlying cardiovascular condition (217, 218).

Medical Therapy for Relief of Symptoms in Patients With Stable IHD

β-Blockers

β-Blockers should be used as the initial agents to relieve anginal symptoms in most forms of stable IHD (20, 192, 202, 203). Long-term treatment with β-blockers reduces the ischemic burden and threshold, improves survival, and is generally well-tolerated (191, 192, 202, 203). However, the adverse event profile of β-blockers may limit their use.

Calcium-Channel Blockers

Calcium-channel blockers can be used if β-blockers are contraindicated in a patient or if adverse effects limit their use (219). All 3 classes of calcium-channel blockers improve myocardial oxygen supply and are effective in several angina presentations (220–222). The choice between various calcium-channel blockers depends on individual characteristics of patients, potential drug interactions, and adverse events. Overall, calcium-channel blockers are well-tolerated and adverse effects are generally related to systemic hypotension. Diltiazem is usually the best tolerated of the 3 classes (dihydropyridines, phenylalkylamines, and benzothiazepines). However, use of a β-blocker with verapamil or diltiazem should generally be avoided because of the potential for development of bradycardia, atrioventricular block, or reduced cardiac contractility. Calcium-channel blockers should be used with caution in patients who are taking cyclosporine, carbamazepine, lithium carbonate, amiodarone, or digoxin because of potential drug interactions.

Nitrates

Nitrates are effective in the treatment of all forms of angina and exert their effects through vasodilatation (223), contributing to coronary blood flow redistribution (224), and antithrombotic and antiplatelet effects (225, 226). Long-term nitrate therapy in patients with stable IHD results in improvement in anginal tolerance. All patients should be prescribed sublingual nitroglycerin tablets or nitroglycerin spray for immediate relief of angina. Most patients respond within 5 minutes of taking 1 to 2 sublingual dose or doses of 0.3 to 0.6 mg. If additional doses are necessary, they should be taken at 5-minute intervals, but no more than 1.2 mg within 15 minutes; during this time frame, the patient should seek immediate medical assistance if no relief occurs (227). These products are also effective for prevention of effort-induced angina when administered 5 to 10 minutes before the angina-inducing action, with relief lasting approximately 30 to 40 minutes (228). Long-acting nitrate preparations (such as nitroglycerin, isosorbide dinitrate, and isosorbide-5-mononitrate) are beneficial for treatment of angina when initial therapy with a β-blocker or nondihydropyridine calcium-channel blocker is contraindicated, unacceptable side effects necessitate discontinuation of these therapies, or additional therapy is needed to control angina.

The most common side effects are headache, flushing, and hypotension. All short-acting nitrate preparations may result in hypotension, sometimes severe, and headaches that limit continued patient adherence with these agents. Nitrates are relatively well-tolerated if a titration schedule is used at initiation and with discontinuation.

Ranolazine

Ranolazine inhibits the late inward sodium current, indirectly reducing the sodium-dependent calcium current during ischemic conditions, and leading to improvement in ventricular diastolic tension and oxygen consumption. It is approved for the treatment of chronic angina but represents a fourth-line agent reserved for patients who have contraindications to, do not

respond to, or cannot tolerate β-blockers, calcium-channel blockers, or long-acting nitrates. Ranolazine may be used in combination with β-blockers, nitrates, dihydropyridine, and calcium-channel blockers. The extended-release preparation reduces the frequency of angina, improves exercise performance, and delays the development of exercise-induced angina and ST-segment depression (229–231). Among patients with acute coronary syndromes, ranolazine did not reduce the incidence of MI or death (232). Ranolazine is contraindicated in combination with potent inhibitors of the *CYP3A4* pathway, including ketoconazole (3.2-fold increase in ranolazine plasma levels) and other azole antifungal agents, macrolide antibiotics, HIV protease inhibitors, grapefruit products or juice, and diltiazem. The major adverse effects are constipation, nausea, dizziness, and headache. The incidence of syncope is less than 1%.

Revascularization

Revascularization by coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) is performed to improve survival, symptoms, or both. The decision to perform revascularization should be undertaken in consultation with a multidisciplinary heart team, including an interventional cardiologist and a cardiac surgeon. This team reviews relevant clinical data, determines whether revascularization using PCI or CABG is technically feasible and reasonable, and helps the patient select among available options (233–236).

Studies performed over the past 3 decades have established that in a select subgroup of patients, patients who have undergone CABG have lower mortality than patients treated medically. Because surgical techniques and the effectiveness of medical therapy have both improved over time, however, it is not entirely clear that the earliest studies remain fully applicable. Nonetheless, the strongest evidence that revascularization improves survival has been established for CABG performed in the following subgroups: 1) patients with operable left main coronary artery stenosis greater than 50% (237, 238), 2) patients with significant stenosis in 3 major vessels (with or without involvement of the proximal left anterior descending artery [LAD]) (239–241), 3) patients with significant stenosis in 2 major vessels with involvement of the proximal LAD (239–241), and 4) patients with significant stenosis in a major coronary artery who have survived sudden cardiac death or sustained ventricular tachycardia (242–244).

In general, the anatomical or clinical features that are associated with substantial ischemia and the extent of ischemia on noninvasive testing are predictors for subsequent adverse outcomes. In the most contemporary studies, however, no significant overall improvement in survival has been observed between patients randomly assigned to revascularization and those assigned to GDMT, even among patients who might be regarded as high risk. In the BARI 2D (Bypass Angioplasty Revascularization Investigation 2 Diabetes) study, survival did not improve among patients with diabetes randomly assigned to GDMT plus CABG, although the study was not powered for this end point, excluded patients with significant left main CAD, and included only a small percentage of patients with proximal LAD artery disease or LV ejection fraction less than 50% (245). In the STICH (Surgical Treatment for Ischemic Heart Failure) trial, in which 1212 patients with an LV ejection fraction of 35% or less and CAD amenable to revascularization were randomly assigned to CABG or medical therapy, there was no significant difference in overall mortality; however, during a median follow-up of 56 months, 28% of patients assigned to CABG died of a cardiovascular cause compared with 33% of those receiving medical therapy (246).

There is less strong evidence that revascularization using CABG (247–250) may enhance survival in patients with involvement of 1 or 2 major arteries, including proximal LAD with severe or extensive (>20% by myocardial perfusion stress imaging) myocardial ischemia (247, 251). In patients with stable IHD who do not meet these criteria, there is only limited evidence, derived from observational studies, that revascularization influences survival. As opposed to patients with acute coronary syndromes, there is no compelling evidence that PCI improves survival for any group of patients with stable IHD. Moreover, PCI may increase the short-term risk for MI (28, 252–254) but does not decrease the long-term risk (28, 245, 252, 253, 255, 256).

Even in patients who are unlikely to experience improvement in survival, revascularization is often performed to relieve anginal symptoms. In general, however, an adequate trial of GDMT should be undertaken before revascularization is contemplated. The COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial (251) demonstrated that this strategy is effective in the majority of patients with anginal symptoms, including those with considerable ischemia on noninvasive testing. Such patients can be evaluated for revascularization of significant lesions if GDMT is ineffective, poorly tolerated, or contraindicated, and deferring revascularization in this fashion was not associated with any detectable increase in mortality. Coronary stenoses in arteries other than the left main coronary artery that are greater than 70% should be considered significant, and lesions in the 50% to 70% range can be considered potentially significant. These latter lesions require additional evidence of physiologic significance, from either stress testing or intracoronary flow testing (such as fractional flow reserve), to establish their clinical significance (257–259). Clinical correlation between the patient's symptoms, stress test results, and coronary anatomy is essential. In general, the greater the extent and severity of ischemia on noninvasive stress testing, the greater the benefit to be derived from revascularization compared with medical therapy (237, 260–265).

Naturally, patient preferences play an important role in determining the preferred course of therapy, particular in deciding whether to consider revascularization. To effectively participate in decision making, patients must be furnished with accurate information about the relative risks, benefits, and costs of all therapeutic options. When revascularization is the preferred strategy, the choice between CABG and PCI should be based on a variety of factors, including coronary anatomy, coexisting medical conditions, local expertise, likelihood of achieving complete revascularization, and patient preferences. A meta-analysis (266) of studies comparing CABG and PCI found that survival was similar at 1 year after the procedure (96.4% for CABG vs. 96.5%

for PCI) and at 5 years (90.7% vs. 89.7%). The incidence of acute MI was similar at 5 years after CABG (10.9%) and PCI (11.9%). Procedural strokes were more common after CABG (1.2% vs. 0.6%; $P = 0.002$). Relief of angina was more common at 1 year after CABG (84% vs. 75%) and at 5 years (84% vs. 79%; $P < 0.001$ for both). Repeat coronary revascularization was less frequent at 1 year after CABG (3.8% vs. 26.5%; $P < 0.001$) and at 5 years (9.8% vs. 46.1%; $P < 0.001$), although this difference was reduced after introduction of stents.

For details on other recommendations for revascularization, please refer to the ACCF, AHA, ACP, AATS, PCNA, SCAI, and STS guideline for the diagnosis and management of patients with stable IHD (22). See **Figure 2** in the Executive Summary for an algorithm on revascularization to improve survival of patients with stable IHD and **Figure 3** in the Executive Summary for an algorithm on revascularization to improve symptoms of patients with stable IHD.

Special Considerations

Although differences exist in incidence of disease and approaches to diagnosis, the general approach in this guideline would be to apply the recommendations consistently among groups.

Women

Women generally have a lower incidence of IHD than men until older age. In younger women, microvascular disease is more common, and obstructive epicardial CAD is less prevalent. Stable angina is the most frequent initial manifestation of IHD in women, as opposed to acute MI and sudden death in men (267, 268). Atypical chest pain and anginal equivalent symptoms, such as dyspnea, are more common in women, although women still present with similar patterns, duration, and frequency of symptoms. Contrary to earlier perceptions, the prognosis of women with chest pain and nonobstructive disease is not necessarily better (269, 270), and their outcomes after an MI are worse (271–274). The lower prevalence of obstructive disease in conjunction with technical challenges makes the interpretation of ischemia on imaging studies somewhat more difficult. Younger women have higher false-positive rates on stress testing and nuclear imaging studies, which may be due, in part, to attenuation from breast tissue. Data from the COURAGE registry suggest that the benefits of medical therapy alone in comparison with medical therapy plus early PCI were similar for men and women (252, 275). In other studies, the outcomes of revascularization appear to be less favorable among women than men, as the odds of in-hospital mortality after PCI have ranged from 25% to 80% higher for women compared with men (276–280). This trend may have improved in recent years and after accounting for the higher incidence of diabetes and hypertension in women (281). The risk for procedural complications also appears to be significantly higher in women (282). On the basis of these observations, the initial approach to therapy for women with stable IHD should be to prescribe a full regimen of GDMT and to consider revascularization only for patients who do not obtain a satisfactory response or who experience unacceptable adverse effects. On the basis of the higher risk associated with PCI in women, it may be reasonable to adopt an even more conservative approach to this procedure than in men.

Older Adults

Coronary artery disease is more likely to be diffuse and more severe in older adults (>75 years). Common coexisting conditions of pulmonary, gastrointestinal, and musculoskeletal systems can cause chest pain, making diagnosis more difficult, even in patients with documented IHD. Physiologic changes in older adults, including alterations in cardiac output through various mechanisms, muscle loss and deconditioning, neuropathies, lung disease, and degenerative joint disease, make stress testing more difficult.

The higher prevalence of stable IHD disease in older adults leads to more false-negative test results. Although the prognostic value of the Duke treadmill score in older adults may be limited (283), exercise stress testing still provides good information for management (284). For patients who are unable to exercise, pharmacologic stress imaging is indicated and yields a similar degree of accuracy compared with testing in younger individuals who present with suspicion for IHD (285–288).

Despite the complexities and concerns related to evaluating and treating elderly patients with stable IHD, findings from the COURAGE and TIME (Trial of Invasive versus Medical therapy in Elderly patients) trials indicated that initial therapy with medical therapy was not significantly less effective than medical therapy plus PCI in relieving angina during a 12-month period. Moreover, considerable evidence indicates that elderly patients have 2- to 7-fold higher odds of mortality after PCI and CABG than do younger patients and that the risk appears to increase monotonically after age 65 years (276, 278–280, 289–291).

It is recommended that management using GDMT be the initial approach in most elderly patients. Given concerns about higher mortality, particularly in patients older than 75 or 80 years, decisions to recommend revascularization should be undertaken only after careful consideration of patient preferences, functional capacity, quality of life, and end-of-life issues (292).

Diabetes Mellitus

Diabetes (types 1 and 2) is an important risk factor for stable IHD. Cardiovascular mortality is 3-fold higher in diabetic men and between 2- and 5-fold higher in diabetic women compared with patients without diabetes (293, 294). Achievement and maintenance of optimal glycemic control and lipid management, along with careful attention to other risk factors (such as hypertension, smoking, and obesity) are paramount. For patients whose symptoms are inadequately managed or who experience intolerable adverse effects, revascularization should be considered. For diabetic patients with extensive coronary disease and active ischemia, early revascularization may be preferable and should be considered. Coronary artery bypass grafting may be associated with lower mortality in diabetic patients with multivessel disease than PCI, but this remains uncertain (295).

Chronic Kidney Disease

Chronic kidney disease is associated with greater risk for developing stable IHD, for its progression, and for worse outcomes (296–299). Physicians should consider creatinine clearance in pharmacotherapy and risk scores for prediction of contrast-induced nephropathy in addition to the use of renal protective strategies to avoid complications related to chronic kidney disease (300).

Obesity

Obese individuals may have limited physical capacity, exaggerated dyspnea on exertion, and excessive breast tissue that impairs imaging, and their weight may exceed the limits of diagnostic equipment (301–303). Enhancements to single-photon emission computed tomography, including prone imaging, and use of intravenous contrast with stress echocardiography may improve accuracy (304–308).

HIV

HIV infection and treatment appear to be associated with an increased risk for premature coronary and cerebrovascular atherosclerosis (309, 310). Acute MI is often the initial manifestation (311). The cause is probably multifactorial and related to both the underlying infection and antiretroviral therapy. The protease inhibitors amprenavir–fosamprenavir with or without ritonavir and lopinavir with ritonavir have the strongest association with risk for acute MI, whereas saquinavir may not be associated (312). Indinavir, lopinavir–ritonavir, didanosine, and abacavir were associated with increased risk for MI (313). Other agents, such as nonnucleoside reverse transcriptase inhibitors, entry inhibitors, and integrase inhibitors, do not appear to be associated with an increase in risk for IHD. Despite the increase in prevalence of IHD among patients with HIV, the absolute increase in incidence of acute MI is relatively low, and overall mortality does not appear to be increased (314, 315). It is likely that this reflects the otherwise enormous benefit conferred by treatment with antiretroviral therapy in the course of HIV infection. Nonetheless, patients receiving antiretroviral therapy should be assessed for cardiovascular risk factors and monitored for signs and symptoms of IHD. It is prudent to recommend a healthy diet, regular physical activity, and avoidance of smoking. Patients with hypercholesterolemia should be managed in a fashion similar to that used for other patients at risk for IHD (316).

Other Considerations

Rheumatoid arthritis has been shown to increase inflammation of coronary artery walls and increase frequency of vulnerable plaques (317). The adjusted rate of stable IHD in systemic lupus erythematosus is at least 50-fold higher than in patients without it.

Socioeconomic Factors

Low socioeconomic status is highly associated with the risk for developing and dying of cardiovascular disease (318, 319). Moreover, members of an ethnic minority (in particular African Americans and Hispanics) are less likely to receive a wide variety of diagnostic and therapeutic interventions, including preventive medications, cardiac procedures, and access to cardiologists (320, 321). Health care providers and systems should strive to eliminate barriers to care for patients who have stable IHD and are of low socioeconomic status or are ethnic minorities.

Patient Follow-up

The evidence is very limited, especially from high-quality studies, on the efficacy of specific strategies on patient outcomes that can be used to follow up with patients with stable IHD. However, this is an important clinical issue for primary care physicians. Although ACP does not usually issue recommendations unless they are based on high-quality evidence, this guideline summarizes the discussion on this issue that was developed on the basis of expert consensus in the joint ACCF, AHA, ACP, AATS, PCNA, SCAI, and STS guideline (22).

The clinical follow-up of patients with stable IHD seeks to maximize function and to minimize long-term mortality and morbidity. Ongoing reassessment of adherence to and effectiveness of the therapeutic regimen, including clinical response, occurrence of adverse effects, and treatment goals, should be based on evolving scientific evidence and preferences of the patient. Coexisting chronic medical conditions that may directly or indirectly affect the clinical course of stable IHD should be managed effectively.

Unnecessary testing should be avoided. When appropriate, follow-up exercise testing provides reassessment of the anatomical, functional, and prognostic severity of disease. Patients with stable IHD who have accelerating symptoms or decreasing functional capacity require prompt reassessment, and those who develop acute coronary syndromes should be managed according to established guidelines. Patients with stable IHD should be evaluated before elective or emergent surgery according to established perioperative guidelines.

Standard risk assessment tools for coronary disease that were developed from clinical and laboratory evaluation of ambulatory populations suspected of having IHD (as discussed in the guideline on diagnosis of stable IHD) included patients with noncardiac causes of presenting symptoms (67, 322, 323) and probably perform less well in populations of patients with known stable IHD. Moreover, although mortality and morbidity might intuitively be expected to be higher in patients with documented as opposed to suspected IHD, the former group is more likely to be receiving effective therapy to reduce risk, including revascularization; this could account for the generally low and declining risk for death observed in patients with established but stable IHD (119, 252, 324–330). Unfortunately, there is no accepted index for assessing ongoing risk by using clinical variables in patients with stable IHD.

Frequency and Methods

Patients with stable IHD should have a follow-up evaluation every 4 to 12 months. This interval should be 4 to 6 months during the first year of therapy. Annual evaluations are reasonable after the first year of therapy if the patient is stable and reliable

enough to call or make an appointment when angina symptoms become worse or other symptoms occur. In addition, effective communication between the primary care physician and cardiologist is essential when patients are jointly managed.

Key Components of Follow-up

In the follow-up of patients with stable IHD, key components of history include any changes in physical activity or symptoms; response to therapy, adverse effects, and adherence; and development of relevant or new conditions or changes in existing conditions.

Physical Examination

Physical examinations should include weight, blood pressure, and heart rate. Physicians should look for signs of heart failure, such as elevated jugular venous pressure, hepatojugular reflux, pulmonary crackles, new murmurs or gallops, or edema. The vascular examination should identify any change in peripheral pulses or new bruits.

Laboratory Examination

It is reasonable to screen patients not known to have diabetes with a fasting blood glucose measurement every 3 years and to annually measure hemoglobin A_{1c} levels in patients with established diabetes. Lipid profile assessment 6 to 8 weeks after initiation of lipid-lowering drug therapy and then periodically during the first year of therapy is reasonable (46). Routine measurement of hemoglobin, thyroid function, serum electrolytes, renal function, or oxygen saturation is not beneficial and should be done only when required by the patient's history, physical examination, or clinical course.

Electrocardiography

Repeated electrocardiography (ECG) is indicated when 1) medications affecting cardiac conduction are initiated or changed, 2) the anginal pattern changes, 3) symptoms or findings suggestive of a dysrhythmia or conduction abnormality are present, and 4) near or frank syncope occurs. Although periodic recording of standard 12-lead ECG provides a baseline waveform against which tracings taken during symptoms can reasonably be compared, there is no clear evidence showing that routine, periodic ECG is useful in the absence of a change in history or physical examination.

Follow-up Stress Testing

Strategies for the selection and use of noninvasive testing in the evaluation of new or worsening symptoms in patients with documented stable IHD are similar to those in patients with suspected stable IHD. Despite widespread use of follow-up stress testing in patients with stable angina, few published data have established the benefits of this approach. In the absence of a change in clinical status, low-risk patients with an estimated annual mortality rate of less than 1% over each year of the interval do not require repeated stress testing until 3 years after the initial evaluation. However, stress testing might be useful in high-risk patients with an estimated annual mortality rate greater than 3% because a marked decrease in exercise capacity or a marked increase in ischemic burden can warrant reevaluation of the medical regimen or interventional plan. Examples of such patients are those with a high-risk Duke treadmill score, an ejection fraction less than 50%, and significant CAD in 1 or more major vessels; diabetic patients; and those with multivessel disease who have not undergone CABG. Patients with an intermediate-risk ($>$1% and $<$3%) annual mortality rate may merit testing at an interval of 1 to 3 years, but only if decisions regarding a change in pharmacologic management, level of exercise, or revascularization will be directly influenced by the test result or if the patient has persistent symptoms despite adequate GDMT.

Whenever possible, initial and follow-up testing should be performed using the same stress and imaging techniques so that any interval change can more reliably be attributed to alterations in clinical status rather than merely differences in technique. In patients with interpretable results on resting ECG who are capable of exercise, treadmill exercise ECG testing remains the first choice. Loss of the ability to exercise on follow-up testing in and of itself suggests deterioration in functional and clinical status. In general, the diagnostic accuracy of stress testing is similar in patients with and without known stable IHD. A few meta-analyses examining the effect of prior MI on diagnostic accuracy have found that the specificity of exercise ECG was higher in mixed populations (331), whereas the diagnostic performance of exercise echocardiography was reduced. In contrast, the specificity of exercise single-photon emission computed tomography was increased because of the predictive value of total stress perfusion abnormalities, which includes both the risk for ischemia plus infarcted myocardium (332).

As discussed in the ACP guideline on diagnosis of stable IHD, the durability of information gained from a stress test over time varies widely according to the characteristics of the patients and the type of test performed. A normal stress test result is generally associated with a low risk for adverse cardiac events; however, among patients with negative results on perfusion imaging studies, the risk for cardiac death or MI can increase fairly rapidly over a 2-year follow-up period if a number of clinical risk factors are present. Among other groups, the risk remains low over 2 years and can be predicted to remain low for an extended period of time. Factors associated with an earlier increase in risk included diabetes, male sex, older age ($\geq$70 years), a history of previous MI or revascularization, and having undergone a pharmacologic stress test rather than an exercise test (333). Among patients who are younger, female, and not diabetic or do not have a history of MI or revascularization, the annual risk for adverse cardiovascular events is predicted to remain less than 1% for as long as 9 years.

Summary

The goals of managing patients with stable IHD include reducing premature cardiovascular death and nonfatal MI while maintaining a level of activity, functional capacity, and quality of life that is satisfactory to the patient. Because of the variation in

symptoms and clinical characteristics among patients, as well as their unique perceptions, expectations, and preferences, there is clearly no single correct approach to any given set of clinical circumstances. Patient education regarding various therapeutic options, appropriate levels of exercise, diet and weight control, and the importance of various clinical manifestations play a key role in achieving the treatment goal. Lifestyle modifications are also critical for all patients with stable IHD to control weight and high blood pressure and manage diabetes.

Various pharmacologic approaches can be used to prevent MI or death in patients with stable IHD, including daily aspirin, β-blockers, ACE inhibitors or ARBs, and influenza vaccination. For patients with symptoms, various pharmacologic options are available to relieve symptoms.

Despite limited evidence for the efficacy of specific strategies for the follow-up of patients with stable IHD, there is an emerging consensus that patients with a variety of chronic illnesses have improved outcomes when they receive coordinated care. Patients with stable IHD require regular monitoring to assess changes in their status, response, and adherence to GDMT.

Recommendations

The recommendations were jointly developed by ACP, ACCF, AHA, AATS, PCNA, and STS; however, ACP translated the ACCF/AHA evidence and recommendation grading system into ACP's guideline grading system (**Tables 1** and **2**, in the Executive Summary).

Patient Education

Recommendation 1: The organizations recommend that patients with stable IHD should have an individualized education plan to optimize care and promote wellness, including:

A. Education on the importance of medication adherence for managing symptoms and reducing disease progression (Grade: strong recommendation; low-quality evidence).

B. An explanation of medication management and cardiovascular risk reduction strategies in a manner that respects the patient's level of understanding, reading comprehension, and ethnicity (Grade: strong recommendation; moderate-quality evidence).

C. A comprehensive review of all therapeutic options (Grade: strong recommendation; moderate-quality evidence).

D. A description of appropriate levels of exercise with encouragement to maintain recommended levels of daily physical activity (Grade: strong recommendation; low-quality evidence).

E. Introduction to self-monitoring skills (Grade: strong recommendation; low-quality evidence).

F. Information on how to recognize worsening cardiovascular symptoms and take appropriate action (Grade: strong recommendation, low-quality evidence).

Recommendation 2: The organizations recommend that patients with stable IHD should be educated regarding the following lifestyle elements that may influence prognosis (Grade: strong recommendation; low-quality evidence):

A. Weight control and maintenance of a body mass index (BMI) of 18.5 to 24.9 kg/m^2 and waist circumference less than 40 inches for men and less than 35 inches for women (less for certain racial groups).

B. Lipid management.

C. Blood pressure control.

D. Smoking cessation and avoidance of exposure to second-hand smoke.

E. Individualized medical, nutrition, and lifestyle education for patients with diabetes mellitus to supplement diabetes treatment goals and education.

Risk Factor Modification

Lipid Management. *Recommendation 3: The organizations recommend lifestyle modifications for lipid management in all patients with stable IHD, including daily physical activity and weight management (Grade: strong recommendation; moderate-quality evidence).*

Recommendation 4: The organizations recommend dietary therapy for all patients, which should include reduced intake of saturated fats (to <7% of total calories), trans-fatty acids (to <1% of total calories), and cholesterol (to <200 mg per day) (Grade: strong recommendation; moderate-quality evidence).

Recommendation 5: The organizations recommend that in addition to therapeutic lifestyle changes, a moderate or high dose of a statin therapy should be prescribed in the absence of contraindications or documented adverse effects. (Grade: strong recommendation; high-quality evidence).

Hypertension. *Recommendation 6: The organizations recommend that patients with stable IHD who have high blood pressure should be counseled regarding the need for lifestyle modifications, including maintenance of recommended weight; increased physical activity; moderation of alcohol consumption; limitation of dietary sodium; and emphasis on increased consumption of fresh fruits, vegetables, and low-fat dairy products (Grade: strong recommendation; moderate-quality evidence).*

Recommendation 7: The organizations recommend that patients with stable IHD with blood pressure of 140/90 mm Hg or higher should be treated with antihypertensive drug therapy in addition to following a trial of lifestyle modifications (Grade: strong recommendation; high-quality evidence). The specific medications used for treatment of high blood pressure should be based on specific patient characteristics, and may include ACE inhibitors and/or β-blockers, with addition of other drugs, such as thiazide diuretics or calcium-channel blockers, if needed to achieve a goal blood pressure of less than 140/90 mm Hg (Grade: strong recommendation; moderate-quality evidence).

Diabetes. *Recommendation 8: The organizations recommend that therapy with rosiglitazone should not be initiated in diabetic patients with stable IHD (Grade: strong recommendation; low-quality evidence).*

Physical Activity. *Recommendation 9: The organizations recommend risk assessment with a physical activity history to guide prognosis and prescription for all patients. An exercise test should be obtained when clinically indicated (Grade: strong recommendation; moderate-quality evidence). As indicated, based on this assessment, patients with stable IHD should be encouraged to engage in 30 to 60 minutes of moderate-intensity aerobic activity, such as brisk walking, at least 5 days and preferably 7 days of the week, supplemented by an increase in daily activities (such as walking breaks at work, garden-*

ing, or household work) to improve cardiorespiratory fitness and motivate patients of the least fit, least active high-risk cohort (bottom 20%) (Grade: strong recommendation; moderate-quality evidence). Medically supervised programs (cardiac rehabilitation) and physician-directed, home-based programs are recommended for at-risk patients at first diagnosis (Grade: strong recommendation; high-quality evidence).

Weight Management. *Recommendation 10: The organizations recommend assessing BMI and/or waist circumference at every visit and consistently encouraging 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 BMI between 18.5 and 24.9 kg/m^2, and waist circumference less than 40 inches in men and less than 35 inches in women (less for certain racial groups) (Grade: strong recommendation; moderate-quality evidence). 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 (Grade: strong recommendation; low-quality evidence).*

Smoking Cessation. *Recommendation 11: The organizations recommend that smoking cessation and avoidance of exposure to environmental tobacco smoke at work and at home should be encouraged for all patients with stable IHD. A stepwise strategy for smoking cessation (Ask, Advise, Assess, Assist, Arrange), follow-up, referral to special programs, and pharmacotherapy are recommended (Grade: strong recommendation; moderate-quality evidence).*

Risk Factor Reduction Strategies of Unproven Benefits. *Recommendation 12: The organizations recommend that estrogen therapy should not be initiated in postmenopausal women with stable IHD with the intent of reducing cardiovascular risk or improving clinical outcomes (Grade: strong recommendation; high-quality evidence).*

Recommendation 13: The organizations recommend that vitamin C, vitamin E, and β-carotene supplementation should not be used with the intent of reducing cardiovascular risk or improving clinical outcomes in patients with stable IHD (Grade: strong recommendation; high-quality evidence).

Recommendation 14: The organizations recommend that treatment of elevated homocysteine with folate and/or vitamins B_6 and B_{12} should not be used with the intent of reducing cardiovascular risk or improving clinical outcomes in patients with stable IHD (Grade: strong recommendation; high-quality evidence).

Recommendation 15: The organizations recommend that chelation therapy should not be used with the intent of improving symptoms or reducing cardiovascular risk in patients with stable IHD (Grade: strong recommendation; low-quality evidence).

Recommendation 16: The organizations recommend that treatment with garlic, coenzyme Q_{10}, selenium, or chromium should not be used with the intent of reducing cardiovascular risk or improving clinical outcomes in patients with stable IHD (Grade: strong recommendation; low-quality evidence).

Medical Therapy to Prevent MI and Death in Patients With Stable IHD

Recommendation 17: The organizations recommend that aspirin, 75 to 162 mg daily, should be continued indefinitely in the absence of contraindications in patients with stable IHD (Grade: strong recommendation; high-quality evidence).

Recommendation 18: The organizations recommend treatment with clopidogrel as a reasonable option when aspirin is contraindicated in patients with stable IHD (Grade: strong recommendation; moderate-quality evidence).

Recommendation 19: The organizations recommend that dipyridamole should not be used as antiplatelet therapy for patients with stable IHD (Grade: strong recommendation; low-quality evidence).

Recommendation 20: The organizations recommend that β-blocker therapy should be initiated and continued for 3 years in all patients with normal LV function following MI or acute coronary syndromes (Grade: strong recommendation; moderate-quality evidence).

Recommendation 21: The organizations recommend that metoprolol succinate, carvedilol, or bisoprolol should be used for all patients with systolic LV dysfunction (ejection fraction ≤40%) with heart failure or prior MI, unless contraindicated (Grade: strong recommendation; high-quality evidence).

Recommendation 22: The organizations recommend that ACE inhibitors should be prescribed in all patients with stable IHD who also have hypertension, diabetes, LV systolic dysfunction (ejection fraction ≤40%), or chronic kidney disease, unless contraindicated (Grade: strong recommendation; high-quality evidence).

Recommendation 23: The organizations recommend ARBs for patients with stable IHD who have hypertension, diabetes, LV systolic dysfunction, or chronic kidney disease and have indications for, but are intolerant of, ACE inhibitors (Grade: strong recommendation; high-quality evidence).

Recommendation 24: The organizations recommend an annual influenza vaccine for patients with stable IHD (Grade: strong recommendation; moderate-quality evidence).

Medical Therapy for Relief of Symptoms in Patients With Stable IHD

Recommendation 25: The organizations recommend that β-blockers should be prescribed as initial therapy for relief of symptoms in patients with stable IHD (Grade: strong recommendation; moderate-quality evidence).

Recommendation 26: The organizations recommend that calcium-channel blockers or long-acting nitrates should be prescribed for relief of symptoms when β-blockers are contraindicated or cause unacceptable side effects in patients with stable IHD (Grade: strong recommendation; moderate-quality evidence).

Recommendation 27: The organizations recommend that calcium-channel blockers or long-acting nitrates, in combination with β-blockers, should be prescribed for relief of symptoms when initial treatment with β-blockers is unsuccessful in patients with stable IHD (Grade: strong recommendation; moderate-quality evidence).

Recommendation 28: The organizations recommend that sublingual nitroglycerin or nitroglycerin spray should be used for immediate relief of angina in patients with stable IHD (Grade: strong recommendation; moderate-quality evidence).

Alternative Therapy for Relief of Symptoms in Patients With Stable IHD

Recommendation 29: The organizations recommend that acupuncture should not be used for the purpose of improving symptoms or reducing cardiovascular risk in stable IHD patients (Grade: strong recommendation; low-quality evidence).

Revascularization

Recommendation 30: The organizations recommend that a shared decision-making approach should be utilized when making decisions about revascularization in patients with unprotected left main or complex coronary artery disease and should include a cardiac surgeon, an interventional cardiologist, and the patient (Grade: strong recommendation; low-quality evidence).

Revascularization to Improve Survival. *Recommendation 31: The organizations recommend CABG to improve survival for patients with significant (≥50% diameter stenosis) left main coronary artery stenosis (Grade: strong recommendation; moderate-quality evidence).*

Recommendation 32: The organizations recommend that PCI to improve survival should not be performed in stable patients with significant (≥50% diameter stenosis) unprotected left main CAD who have unfavorable anatomy for PCI and who are good candidates for CABG (Grade: strong recommendation; moderate-quality evidence).

Recommendation 33: The organizations recommend the use of CABG to improve survival in patients with significant (≥70% diameter) stenoses in 3 major coronary arteries (with or without involvement of the proximal left anterior descending artery) or in the proximal left anterior descending artery plus 1 other major coronary artery (Grade: strong recommendation; moderate-quality evidence).

Recommendation 34: The organizations recommend the use of CABG or PCI to improve survival in survivors of sudden cardiac death with presumed ischemia-mediated ventricular tachycardia caused by significant (≥70% diameter) stenosis in a major coronary artery (Grade: strong recommendation; moderate-quality evidence for CABG, low-quality evidence for PCI).

Recommendation 35: The organizations recommend that CABG or PCI should not be performed with the primary or sole intent to improve survival in patients with stable IHD with 1 or more coronary stenoses that are not anatomically or functionally significant (for example, <70% diameter non–left main coronary artery stenosis, fractional flow reserve >0.80, no or only mild ischemia on noninvasive testing), involve only the left circumflex or right coronary artery, or subtend only a small area of viable myocardium (Grade: strong recommendation; moderate-quality evidence).

Revascularization to Improve Symptoms. *Recommendation 36: The organizations recommend the use of CABG or PCI to improve symptoms in patients with 1 or more significant (≥70% diameter) coronary artery stenoses amenable to revascularization and unacceptable angina despite GDMT (Grade: strong recommendation; high-quality evidence).*

Recommendation 37: The organizations recommend that CABG or PCI to improve symptoms should not be performed in patients who do not meet anatomical (≥50% diameter left main or ≥70% non–left main stenosis diameter) or physiologic (for example, abnormal fractional flow reserve) criteria for revascularization (Grade: strong recommendation; low-quality evidence).

Recommendation 38: The organizations recommend that PCI with coronary stenting (bare-metal stent or drug-eluting stent) should not be performed if the patient is not likely to be able to tolerate and comply with dual antiplatelet therapy for the appropriate duration of treatment based on the type of stent implanted (Grade: strong recommendation; moderate-quality evidence).

Patient Follow-up

Recommendation 39: The organizations recommend that patients with stable IHD should receive periodic follow-up at least annually that includes all of the following (Grade: strong recommendation; low-quality evidence):

A. Assessment of symptoms and clinical function.

B. Surveillance for complications of stable IHD, including heart failure and arrhythmias.

C. Monitoring of cardiac risk factors.

D. Assessment of the adequacy of and adherence to recommended lifestyle changes and medical therapy.

Recommendation 40: The organizations recommend assessment of LV ejection fraction and segmental wall motion by echocardiography or radionuclide imaging in patients with new or worsening heart failure or evidence of intervening MI by history or ECG (Grade: strong recommendation; low-quality evidence).

Recommendation 41: The organizations recommend that measurement of LV function with a technology such as echocardiography or radionuclide imaging should not be used for routine periodic reassessment of patients who have not had a change in clinical status or who are at low risk of adverse cardiovascular events (Grade: strong recommendation; low-quality evidence).

Recommendation 42: The organizations recommend standard exercise ECG in patients with known stable IHD who have new or worsening symptoms not consistent with unstable angina and who have 1) at least moderate physical functioning and no disabling comorbidity and 2) an interpretable ECG (Grade: strong recommendation; moderate-quality evidence).

Recommendation 43: The organizations recommend exercise with radionuclide myocardial perfusion imaging or echocardiography in patients with known stable IHD who have new or worsening symptoms not consistent with unstable angina, and who have a) at least moderate physical functioning or no disabling comorbidity but b) an uninterpretable ECG (Grade: strong recommendation; moderate-quality evidence).

Recommendation 44: The organizations recommend that pharmacologic stress imaging with radionuclide myocardial perfusion imaging, echocardiography, or cardiac magnetic resonance imaging should not be used in patients with known stable IHD who have new or worsening symptoms not consistent with unstable angina and who are capable of at least moderate physical functioning or have no disabling comorbidity (Grade: strong recommendation; low-quality evidence).

Recommendation 45: The organizations recommend pharmacologic stress imaging using radionuclide myocardial perfusion or echocardiography in patients with known stable IHD who have new

or worsening symptoms not consistent with unstable angina and who are incapable of at least moderate physical functioning or have disabling comorbidity (Grade: strong recommendation; moderate-quality evidence).

Recommendation 46: The organizations recommend that standard exercise ECG testing should not be performed in patients with known stable IHD who have new or worsening symptoms not consistent with unstable angina and who a) are incapable of at least moderate physical functioning or have disabling comorbidity or b) have an uninterpretable ECG (Grade: strong recommendation; low-quality evidence).

Recommendation 47: The organizations recommend that coronary/cardiac computed tomography angiography should not be performed for assessment of native coronary arteries with known moderate or severe calcification or of coronary stents less than 3 mm in diameter in patients with known stable IHD who have new or worsening symptoms not consistent with unstable angina, irrespective of ability to exercise (Grade: strong recommendation; moderate-quality evidence).

Recommendation 48: The organizations recommend that radionuclide myocardial perfusion imaging, echocardiography, or cardiac magnetic resonance imaging, with either exercise or pharmacologic stress or coronary/cardiac computed tomography angiography, should not be used for follow-up assessment in patients with stable IHD, if performed more frequently than at a) 5-year intervals after CABG or b) 2-year intervals after PCI (Grade: strong recommendation; low-quality evidence).

Appendix References

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