# 2010 ACCF/AHA Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults: Executive Summary

American College of Cardiology Foundation, American Heart Association Task Force on Practice Guidelines, American Society of Echocardiography, American Society of Nuclear Cardiology, Society of Atherosclerosis Imaging and Prevention, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, Philip Greenland, Joseph S. Alpert, George A. Beller, Emelia J. Benjamin, Matthew J. Budoff, Zahi A. Fayad, Elyse Foster, Mark.A. Hlatky, John McB. Hodgson, Frederick G. Kushner, Michael S. Lauer, Leslee J. Shaw, Sidney C. Smith, Jr, Allen J. Taylor, William S. Weintraub, and Nanette K. Wenger J. Am. Coll. Cardiol. published online Nov 15, 2010; doi:10.1016/j.jacc.2010.09.002

## This information is current as of November 17, 2010

The online version of this article, along with updated information and services, is located on the World Wide Web at:

http://content.onlinejacc.org/cgi/content/full/j.jacc.2010.09.002v1

# JACC JOURNAL of the American College of Cardiology



### **PRACTICE GUIDELINES**

# 2010 ACCF/AHA Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults: Executive Summary

A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the American Society of Echocardiography, American Society of Nuclear Cardiology, Society of Atherosclerosis Imaging and Prevention, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance

### Writing Committee Members

Philip Greenland, MD, FACC, FAHA, Chair

Joseph S. Alpert, MD, FACC, FAHA
George A. Beller, MD, MACC, FAHA
Emelia J. Benjamin, MD, ScM, FACC, FAHA\*†
Matthew J. Budoff, MD, FACC, FAHA‡\$||
Zahi A. Fayad, PhD, FACC, FAHA¶
Elyse Foster, MD, FACC, FAHA#
Mark. A. Hlatky, MD, FACC, FAHA\$\*\*
John McB. Hodgson, MD, FACC, FAHA,
FSCAI‡\$\*\*††

Frederick G. Kushner, MD, FACC, FAHA†‡‡ Michael S. Lauer, MD, FACC, FAHA Leslee J. Shaw, PhD, FACC, FAHA§§
Sidney C. Smith, JR, MD, FACC, FAHA|||¶¶
Allen J. Taylor, MD, FACC, FAHA##
William S. Weintraub, MD, FACC, FAHA
Nanette K. Wenger, MD, MACC, FAHA

\*ACCF/AHA Task Force on Performance Measures Liaison; †Recused from voting on Section 10, Lipoprotein-Associated Phospholipase A2; ‡Recused from voting on Section 21, Coronary Computed Tomography Angiography; §Recused from voting on Section 23, Diabetes Mellitus; |SAIP Representative; |SCMR Representative; #ASE Representative; \*\*Recused from voting on Section 20, Calcium Scoring Methods; ††SCAI Representative; ‡‡Recused from voting on Section 5, Lipoprotein and Apolipoprotein Assessments; §§ASNC Representative; |||ACCF/AHA Task Force on Practice Guidelines Liaison; ¶¶Recused from voting on Section 7, Measurement of C-Reactive Protein; ##SCCT Representative.

### ACCF/AHA Task Force Members

Alice K. Jacobs, MD, FACC, FAHA, Chair, 2009–2011

Sidney C. Smith, JR, MD, FACC, FAHA, Immediate Past Chair, 2006–2008††† Jeffrey L. Anderson, MD, FACC, FAHA, Chair-Elect

Nancy Albert, PhD, CCNS, CCRN Christopher E. Buller, MD, FACC††† Mark A. Creager, MD, FACC, FAHA Steven M. Ettinger, MD, FACC Robert A. Guyton, MD, FACC Jonathan L. Halperin, MD, FACC, FAHA
Judith S. Hochman, MD, FACC, FAHA
Frederick G. Kushner, MD, FACC, FAHA
Rick Nishimura, MD, FACC, FAHA†††
E. Magnus Ohman, MD, FACC
Richard L. Page, MD, FACC, FAHA†††
William G. Stevenson, MD, FACC, FAHA
Lynn G. Tarkington, RN†††
Clyde W. Yancy, MD, FACC, FAHA

†††Former ACCF/AHA Task Force member during this writing effort.

This document was approved by the American College of Cardiology Foundation Board of Trustees, the American Heart Association Science Advisory and Coordinating Committee, and all cosponsoring organizations in September 2010.

The American College of Cardiology Foundation requests that this document be cited as follows: Greenland P, Alpert JS, Beller GA, Benjamin EJ, Budoff MJ, Fayad ZA, Foster E, Hlatky MA, Hodgson JMcB, Kushner FG, Lauer MS, Shaw LJ, Smith SC, Jr., Taylor AJ, Weintraub WS, Wenger NK. 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2010;56:xxx-xxx.

This article is copublished in Circulation and the Journal of Cardiovascular Computed Tomography.

Copies: This document is available on the World Wide Web sites of the American College of Cardiology Foundation (www.cardiosource.org) and the American Heart Association (my.americanheart.org). For copies of this document, please contact the Elsevier Inc. Reprint Department, fax (212) 633-3820, e-mail reprints@elsevier.com.

Permissions: Modification, alteration, enhancement, and/or distribution of this document are not permitted without the express permission of the American College of Cardiology Foundation. Please contact Elsevier's permission department at healthpermissions@elsevier.com.

Greenland et al.

CV Risk Guideline: Executive Summary

JACC Vol. 56, No. 25, 2010 December 14/21, 2010:000-000

# **TABLE OF CONTENTS**

2

Pre	amble	.XXXX
1.	Introduction	.XXXX
	1.1. Methodology and Evidence Review	XXXX
	1.2. Organization of the Writing Committee	XXXX
	1.3. Document Review and Approval	
	1.4. Magnitude of the Problem of Cardiovascular Risk in Asymptomatic Adults	
	1.5. Assessing the Prognostic Value of Risk Factors and Risk Markers.	
	1.6. Usefulness in Motivating Patients or Guiding Therapy.	
	1.7. Economic Evaluation of Novel Risk Markers	
2.	Recommendation for Global Risk Scoring	
3.	Recommendation for Family History	.XXXX
4.	Recommendation for Genomic Testing	.XXXX
5.	Recommendation for Lipoprotein and Apolipoprotein Assessments	.XXXX
6.	Recommendation for Measurement of Natriuretic Peptides	.XXXX
7.	Recommendations for Measurement of C-Reactive Protein	.XXXX
8.	Recommendation for Measurement of Hemoglobin A1C	.XXXX
9.	Recommendations for Testing for Microalbuminuria	.XXXX
10.	Recommendation for Lipoprotein-Associated Phospholipase A2	.XXXX
11.	Recommendations for Resting Electrocardiogram	.XXXX
12.	Recommendations for Transthoracic Echocardiography	.XXXX
13.	Recommendation for Measurement of Carotid Intima-Media Thickness	.XXXX
14.	Recommendation for Brachial/Peripheral Flow-Mediated Dilation	XXXX

15.	Recommendation for Specific Measures of Arterial Stiffness	. XXXX
16.	Recommendation for Measurement of Ankle-Brachial Index	. XXXX
17.	Recommendation for Exercise Electrocardiography	. XXXX
18.	Recommendation for Stress Echocardiography	. XXXX
19.	Recommendations for Myocardial Perfusion Imaging	. XXXX
20.	Recommendations for Calcium Scoring Methods.	. XXXX
21.	Recommendation for Coronary Computed Tomography Angiography	XXXX
22.	Recommendation for Magnetic Resonance Imaging of Plaque	XXXX
23.	Recommendations for Patients With Diabetes Mellitus	XXXX
24.	Recommendations for Special Considerations in Women	. XXXX
25.	Clinical Implications of Risk Assessment: Concluding Comments	XXXX
	pendix 1. Author Relationships With Industry Other Entities	XXXX
	pendix 2. Reviewer Relationships With Indust Other Entities	

### **Preamble**

It is essential that the medical profession play a central role in critically evaluating the evidence related to drugs, devices, and procedures for the detection, management, or prevention of disease. Properly applied, rigorous, expert analysis of the available data documenting absolute and relative benefits and risks of these therapies and procedures can improve the effectiveness of care, optimize patient outcomes, and favorably affect the cost of care by focusing resources on the most effective strategies. One important use of such data is the production of clinical practice guidelines that, in turn, can provide a foundation for a variety of other applications,

Greenland *et al.*CV Risk Guideline: Executive Summary

such as performance measures, appropriate use criteria, clinical decision support tools, and quality improvement tools.

The American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) have jointly engaged in the production of guidelines in the area of cardiovascular disease since 1980. The ACCF/AHA Task Force on Practice Guidelines (Task Force) is charged with developing, updating, and revising practice guidelines for cardiovascular diseases and procedures, and the Task Force directs and oversees this effort. Writing committees are charged with assessing the evidence as an independent group of authors to develop, update, or revise recommendations for clinical practice.

Experts in the subject under consideration have been selected from both organizations to examine subject-specific data and write guidelines in partnership with representatives from other medical practitioner and specialty groups. Writing committees are specifically charged to perform a formal literature review; weigh the strength of evidence for or against particular tests, treatments, or procedures; and include estimates of expected health outcomes where data exist. Patient-specific modifiers, comorbidities, and issues of patient preference that may influence the choice of tests or therapies are considered. When available, information from studies on cost is considered, but data on efficacy and clinical outcomes constitute the primary basis for recommendations in these guidelines.

In analyzing the data and developing recommendations and supporting text, the writing committee used evidencebased methodologies developed by the Task Force that are described elsewhere (1). The committee reviewed and ranked evidence supporting current recommendations, with the weight of evidence ranked as Level A if the data were derived from multiple randomized clinical trials or metaanalyses. The committee ranked available evidence as Level B when data were derived from a single randomized trial or nonrandomized studies. Evidence was ranked as Level C when the primary source of the recommendation was consensus opinion, case studies, or standard of care. In the narrative portions of these guidelines, evidence is generally presented in chronological order of development. Studies are identified as observational, retrospective, prospective, or randomized when appropriate. For certain conditions for which inadequate data are available, recommendations are based on expert consensus and clinical experience and ranked as Level C. An example is the use of penicillin for pneumococcal pneumonia, where there are no randomized trials and treatment is based on clinical experience. When recommendations at Level C are supported by historical clinical data, appropriate references (including clinical reviews) are cited if available. For issues where sparse data are available, a survey of current practice among the clinicians on the writing committee was the basis for Level C recommendations and no references are cited. The schema for Classification of Recommendations (COR) and Level of Evidence (LOE) is summarized in Table 1, which also illustrates how the grading system provides an estimate of the size as well as the certainty of the treatment effect. A new addition to the ACCF/AHA methodology is a separation of the Class III recommendations to delineate whether the recommendation is determined to be of "no benefit" or associated with "harm" to the patient. In addition, in view of the increasing number of comparative effectiveness studies, comparator verbs and suggested phrases for writing recommendations for the comparative effectiveness of one treatment/strategy with respect to another for COR I and IIa, LOE A or B only, have been added.

The Task Force makes every effort to avoid actual, potential, or perceived conflicts of interest that may arise as a result of industry relationships or personal interests among the writing committee. Specifically, all members of the writing committee, as well as peer reviewers of the document, are asked to disclose all relevant relationships and those existing 24 months before initiation of the writing effort. All guideline recommendations require a confidential vote by the writing committee and must be approved by a consensus of the members voting. Members who were recused from voting are noted on the title page of this document and in Appendix 1. Members must recuse themselves from voting on any recommendation to which their relationships with industry and other entities (RWI) applies. Any writing committee member who develops new RWI during his or her tenure is required to notify guideline staff in writing. These statements are reviewed by the Task Force and all members during each conference call and meeting of the writing committee and are updated as changes occur. For detailed information about guideline policies and procedures, please refer to the ACCF/AHA methodology and policies manual (1). Authors' and peer reviewers' RWI pertinent to this guideline are disclosed in Appendixes 1 and 2, respectively. In addition, to ensure complete transparency, writing committee members' comprehensive disclosure information—including RWI not pertinent to this document—is available online as a supplement to this document. Disclosure information for the ACCF/ AHA Task Force on Practice Guidelines is also available online at www.cardiosource.org/ACC/About-ACC/ Leadership/Guidelines-and-Documents-Task-Forces.aspx. The work of the writing committee was supported exclusively by the ACCF and AHA without commercial support. Writing committee members volunteered their time for this effort.

The ACCF/AHA practice guidelines address patient populations (and health care providers) residing in North America. As such, drugs that are not currently available in North America are discussed in the text without a specific COR. For studies performed in large numbers of subjects outside of North America, each writing committee reviews the potential impact of different practice patterns and patient populations on the treatment effect and the relevance to the ACCF/AHA target population to de-

4 Greenland *et al.*CV Risk Guideline: Executive Summary

JACC Vol. 56, No. 25, 2010 December 14/21, 2010:000-000

Table 1. Applying Classification of Recommendations and Level of Evidence

.... .. ....... ....

		SIZE OF TREATM	ENT EFFECT -		<del></del>
		CLASS I  Benefit >>> Risk  Procedure/Treatment SHOULD be performed/ administered	CLASS IIa  Benefit >> Risk  Additional studies with focused objectives needed  IT IS REASONABLE to perform procedure/administer treatment	CLASS IIb  Benefit ≥ Risk  Additional studies with broad  objectives needed; additional  registry data would be helpful  Procedure/Treatment  MAY BE CONSIDERED	CLASS III No Benefit or CLASS III Harm  Procedure/ Test Treatment  COR III: Not No Proven No benefit Helpful Benefit  COR III: Excess Cost Harmful Harm W/o Benefit to Patients or Harmful
OF TREATMENT EFFECT	LEVEL A  Multiple populations evaluated*  Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
OF CERTAINTY (PRECISION) O	LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
ESTIMATE OF CERTA	LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
	Suggested phrases for writing recommendations <sup>†</sup>	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit  Is not potentially recommended is not indicated causes harm should not associated with
	Comparative effectiveness phrases <sup>†</sup>	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B		be done excess morbid- is not useful/ ity/mortality beneficial/ should not effective be done

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

termine whether the findings should inform a specific recommendation.

The ACCF/AHA practice guidelines are intended to assist health care providers in clinical decision making by describing a range of generally acceptable approaches to the diagnosis, management, and prevention of specific diseases or conditions. These practice guidelines represent a consensus of expert opinion after a thorough and systematic review of the available current scientific evidence and are intended to improve patient care. The guidelines attempt to define practices that meet the needs of most patients in most situations. The ultimate judgment regarding care of a particular patient must be made by the health care provider

and patient in light of all the circumstances presented by that patient. Thus, there are circumstances in which deviations from these guidelines may be appropriate. Clinical decision making should consider the quality and availability of expertise in the area where care is provided. When these guidelines are used as the basis for regulatory or payer decisions, the goal should be improvement in quality of care. The Task Force recognizes that situations arise in which additional data are needed to better inform patient care; these areas will be identified within each respective guideline when appropriate.

Prescribed courses of treatment in accordance with these recommendations are effective only if they are followed.

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

Greenland *et al.*CV Risk Guideline: Executive Summary

Because lack of patient understanding and adherence may adversely affect outcomes, physicians and other health care providers should make every effort to engage the patient's active participation in prescribed medical regimens and lifestyles.

The guidelines will be reviewed annually by the Task Force and considered current until they are updated, revised, or withdrawn from distribution. The full-text guideline is e-published in the *Journal of the American College of Cardiology, Circulation*, and the *Journal of Cardiovascular Computed Tomography*.

Alice K. Jacobs, MD, FACC, FAHA Chair, ACCF/AHA Task Force on Practice Guidelines

### 1. Introduction

### 1.1. Methodology and Evidence Review

The recommendations listed in this document are, whenever possible, evidence based. An extensive evidence review was conducted for the period beginning March 2008 through April 2010. Searches were limited to studies, reviews, and other evidence conducted in human subjects and published in English. Key search words included, but were not limited to, African Americans, Asian Americans, albuminuria, asymptomatic, asymptomatic screening and brachial artery reactivity, atherosclerosis imaging, atrial fibrillation, brachial artery testing for atherosclerosis, calibration, cardiac tomography, compliance, carotid intima-media thickness, coronary calcium, coronary computed tomography angiography, C-reactive protein (CRP), detection of subclinical atherosclerosis, discrimination, endothelial function, family history, flow-mediated dilation, genetics, genetic screening, guidelines, Hispanic Americans, hemoglobin A, glycosylated, meta-analysis, Mexican Americans, myocardial perfusion imaging (MPI), noninvasive testing, noninvasive testing and type 2 diabetes, outcomes, patient compliance, peripheral arterial tonometry, peripheral tonometry and atherosclerosis, lipoprotein-associated phospholipase A2, primary prevention of coronary artery disease, proteinuria, cardiovascular risk, risk scoring, receiver operating characteristics curve, screening for brachial artery reactivity, stress echocardiography, subclinical atherosclerosis, subclinical and Framingham, subclinical and Multi-Ethnic Study of Atherosclerosis (MESA), and type 2 diabetes. Additionally, the writing committee reviewed documents related to the subject matter previously published by the ACCF and AHA, American Diabetes Association, European Society of Cardiology, and the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC) 7. References selected and published in this document are representative and not all-inclusive.

To provide clinicians with a comprehensive set of data, whenever deemed appropriate or when published in the article, data from the clinical trial will be used to calculate the absolute risk difference and number needed to treat or

harm; data related to the relative treatment effects will also be provided, such as odds ratio, relative risk, hazard ratio, or incidence rate ratio, along with confidence interval when available.

The focus of this guideline is the initial assessment of the apparently healthy adult for risk of developing cardiovascular events associated with atherosclerotic vascular disease. The goal of this early assessment of cardiovascular risk in an asymptomatic individual is to provide the foundation for targeted preventive efforts based on that individual's predicted risk. It is based on the long-standing concept of targeting the intensity of drug treatment interventions to the severity of the patient's risk (2). This clinical approach serves as a complement to the population approach to prevention of cardiovascular disease (CVD), in which population-wide strategies are used regardless of an individual's risk.

This guideline pertains to initial assessment of cardiovascular risk in the asymptomatic adult. Although there is no clear age cut point for defining the onset of risk for CVD, elevated risk factor levels and subclinical abnormalities can be detected in adolescents as well as young adults. To maximize the benefits of prevention-oriented interventions, especially those involving lifestyle changes, the writing committee advises that these guidelines be applied in asymptomatic persons beginning at age 20 years. The writing committee recognizes that the decision about a starting point is an arbitrary one.

This document specifically excludes from consideration patients with a diagnosis of CVD or a coronary event, for example, angina or anginal equivalent, myocardial infarction, or revascularization with percutaneous coronary intervention or coronary artery bypass graft surgery. It also excludes testing for patients with known peripheral artery disease and cerebral vascular disease. This guideline is not intended to replace other sources of information on cardiovascular risk assessment in specific disease groups or in higher-risk groups such as those with known hypertension or diabetes who are receiving treatment.

### 1.2. Organization of the Writing Committee

The committee was composed of physicians and other experts in the field of cardiology. The committee included representatives from the American Society of Echocardiography, American Society of Nuclear Cardiology, Society of Atherosclerosis Imaging and Prevention, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance.

# 1.3. Document Review and Approval

This document was reviewed by 2 outside reviewers nominated by the ACCF and 2 outside reviewers nominated by

6

the AHA, as well as 2 reviewers each from the American Society of Echocardiography, American Society of Nuclear Cardiology, Society of Atherosclerosis Imaging and Prevention, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance, and 23 individual content reviewers (including members from the ACCF Appropriate Use Criteria Task Force, ACCF Cardiac Catheterization Committee, ACCF Imaging Council, and ACCF Prevention of Cardiovascular Disease Committee). All reviewer RWI information was collected and distributed to the writing committee and is published in this document (Appendix 2).

This document was approved for publication by the governing bodies of the ACCF and AHA and endorsed by the American Society of Echocardiography, American Society of Nuclear Cardiology, Society of Atherosclerosis Imaging and Prevention, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance.

# 1.4. Magnitude of the Problem of Cardiovascular Risk in Asymptomatic Adults

Atherosclerotic CVD is the leading cause of death for both men and women in the United States (3). It is estimated that if all forms of major CVD were eliminated, life expectancy would rise by almost 7 years (4). Coronary heart disease (CHD) has a long asymptomatic latent period, which provides an opportunity for early preventive interventions. One aim of this guideline is to provide an evidence-based approach to risk assessment in an effort to lower this high burden of coronary deaths in asymptomatic adults.

# **1.5.** Assessing the Prognostic Value of Risk Factors and Risk Markers

Many risk factors have been proposed as predictors of CHD (5,6). New risk factors or markers are frequently identified and evaluated as potential additions to standard risk assessment strategies. The AHA has published a scientific statement on appropriate methods for evaluating the predictive value of new risk factors or risk markers (7). The scientific statement endorsed previously published guidelines for proper reporting of observational studies in epidemiology (8) but also went beyond those guidelines to specifically address criteria for evaluation of established and "new" risk markers.

For any new risk marker to be considered a useful candidate for risk prediction, it must, at the very least, have an independent statistical association with risk after accounting for established readily available and inexpensive risk markers. This independent statistical association should be based on studies that include large numbers of outcome events. Traditionally, reports of novel risk markers have only

gone this far, reporting adjusted hazard ratios with confidence intervals and p values (9). Although this level of basic statistical association is often regarded by researchers as meaningful in prediction of a particular outcome of interest, the AHA scientific statement called for considerably more rigorous assessments that include analysis of the calibration, discrimination, and reclassification of the predictive model (7). Many of the tests reviewed in this guideline fail to provide these more comprehensive measures of test evaluation, and for this reason, many tests that are statistically associated with clinical outcomes cannot be judged to be useful beyond a standard risk assessment profile. In the absence of this evidence of "additive predictive information," the writing committee generally concluded that a new risk marker was not ready for routine use in risk assessment.

Calibration and discrimination are 2 separate concepts that do not necessarily track with each other. Calibration refers to the ability to correctly predict the proportion of subjects within any given group who will experience disease events. Among patients predicted to be at higher risk, there will be a higher number of events, whereas among patients identified as being at lower risk, there will be fewer events. For example, if a diagnostic test or a multivariable model splits patients into 3 groups with predicted risks of 5%, 10%, and 15% within each group, calibration would be considered good if in a separate group of cohorts with similar predicted risks, the actual rates of events were close to 5%, 10%, and 15%. Calibration is best presented by displaying observed versus expected event rates across quantiles of predicted risk for models that do and do not include the new risk marker.

Discrimination is a different concept that refers to the probability of a diagnostic test or a risk prediction instrument to distinguish between patients who are at higher compared with lower risk. For example, a clinician sees 2 random patients, 1 of whom is ultimately destined to experience a clinical event. A diagnostic test or risk model discriminates well if it usually correctly predicts which of the 2 subjects is at higher risk for an event. Mathematically this is described by calculating a C index or C statistic, parameters that are analogous to the area under the receiver operating characteristics curve. These statistics define the probability that a randomly selected person from the "affected group" will have a higher test score than a randomly selected person from the "nonaffected group." A test with no discrimination would have a C statistic of 0.50 and a perfect test would have a C statistic of 1.0. Throughout this document, C statistic information is cited where available.

Some investigators have called for evaluating the number of subjects reclassified into other risk categories based on models that include the new risk marker (10). One problem with this approach is that not all reclassification is necessarily clinically useful. If a patient is deemed to be at intermediate risk and is then reclassified as being at high or low risk, the clinician might find that information helpful. It may not be known, however, whether or not these reclassifications are correct for individual subjects. Two new

 JACC Vol. 56, No. 25, 2010
 Greenland et al.

 December 14/21, 2010:000-000
 CV Risk Guideline: Executive Summary

Table 2. Comparison of a Sample of Global Coronary and Cardiovascular Risk Scores

	Framingham	SCORE	PROCAM (Men)	Reynolds (Women)	Reynolds (Men)
Sample size	5,345	205,178	5,389	24,558	10,724
Age (y)	30 to 74; M: 49	19 to 80; M: 46	35 to 65; M: 47	>45; M: 52	>50; M: 63
Mean follow-up (y)	12	13	10	10.2	10.8
Risk factors considered	Age, sex, total cholesterol, HDL cholesterol, smoking, systolic blood pressure, antihypertensive medications	Age, sex, total-HDL cholesterol ratio, smoking, systolic blood pressure	Age, LDL cholesterol, HDL cholesterol, smoking, systolic blood pressure, family history, diabetes, triglycerides	Age, HbA1C (with diabetes), smoking, systolic blood pressure, total cholesterol, HDL cholesterol, hsCRP, parental history of MI at <60 y of age	Age, systolic blood pressure, total cholesterol, HDL cholesterol, smoking, hsCRP, parental history of MI at <60 y of age
Endpoints	CHD (MI and CHD death)	Fatal CHD	Fatal/nonfatal MI or sudden cardiac death (CHD and CVD combined)	MI, ischemic stroke, coronary revascularization, cardiovascular death (CHD and CVD combined)	MI, stroke, coronary revascularization, cardiovascular death (CHD and CVD combined)
URLs for risk calculators	http://hp2010. nhlbihin.net/ atpiii/calculator. asp?usertype=prof	http://www. heartscore.org/ pages/ welcome.aspx	http://www.chd- taskforce.com/ coronary_risk_ assessment.html	http://www. reynoldsriskscore.org/	http://www. reynoldsriskscore.org/

CHD indicates coronary heart disease; CVD, cardiovascular disease; HbA1C, hemoglobin A1C; HDL, high-density lipoprotein; hsCRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein; M, mean; MI, myocardial infarction; PROCAM, Münster Heart Study; and SCORE, Systematic Coronary Risk Evaluation.

approaches to risk reclassification have been introduced, namely "net reclassification improvement" and "integrated discrimination improvement," which provide quantitative estimates of correct reclassifications (11). Correct reclassifications are associated with higher predicted risks for cases and lower predicted risks for noncases.

# **1.6.** Usefulness in Motivating Patients or Guiding Therapy

Patients deemed to be at low risk for clinical events are unlikely to gain substantial benefits from pharmaceutical interventions and therefore might best be managed with lifestyle modifications. Conversely, patients deemed to be at high risk for events are more likely to benefit from pharmacologic interventions and therefore are appropriate candidates for intensive risk factor modification efforts. Among patients at intermediate risk, further testing may be indicated to refine risks and assess the need for treatment.

## 1.7. Economic Evaluation of Novel Risk Markers

The progressively rising costs of medical care have increased interest in documenting the economic effects of new tests and therapies. The most basic goal is to estimate the economic consequences of a decision to order a new test. The ultimate goal is to determine whether performing the test provides sufficient value to justify its use.

In general, testing strategies such as those assessed in this document have not included evaluations of the costs and cost-effectiveness of the tests. The writing committee was generally unable to find evidence to support the cost-effectiveness of any of the tests and testing approaches discussed here. Where exceptions were identified, cost-related information is included.

### 2. Recommendation for Global Risk Scoring

#### CLASS I

1. Global risk scores (such as the Framingham Risk Score) that use multiple traditional cardiovascular risk factors should be obtained for risk assessment in all asymptomatic adults without a clinical history of CHD. These scores are useful for combining individual risk factor measurements into a single quantitative estimate of risk that can be used to target preventive interventions (12). (Level of Evidence: B)

Table 2 summarizes a sample of published global risk score instruments that take into account modifiable risk markers that are also appropriate evidence-based targets for preventive interventions.

### 3. Recommendation for Family History

### CLASS I

 Family history of atherothrombotic CVD should be obtained for cardiovascular risk assessment in all asymptomatic adults (13,14). (Level of Evidence: B)

### 4. Recommendation for Genomic Testing

### **CLASS III: NO BENEFIT**

1. Genotype testing for CHD risk assessment in asymptomatic adults is not recommended (15,16). (Level of Evidence: B)

# **5. Recommendation for Lipoprotein and Apolipoprotein Assessments**

### **CLASS III: NO BENEFIT**

 Measurement of lipid parameters, including lipoproteins, apolipoproteins, particle size, and density, beyond a standard fasting Greenland et al.
CV Risk Guideline: Executive Summary

JACC Vol. 56, No. 25, 2010 December 14/21, 2010:000-000

lipid profile is not recommended for cardiovascular risk assessment in asymptomatic adults (17). (Level of Evidence: C)

# **6. Recommendation for Measurement of Natriuretic Peptides**

#### **CLASS III: NO BENEFIT**

 Measurement of natriuretic peptides is not recommended for CHD risk assessment in asymptomatic adults (18). (Level of Evidence: B)

# 7. Recommendations for Measurement of C-Reactive Protein

#### CLASS IIa

8

1. In men 50 years of age or older or women 60 years of age or older with low-density lipoprotein cholesterol less than 130 mg/dL; not on lipid-lowering, hormone replacement, or immunosuppressant therapy; without clinical CHD, diabetes, chronic kidney disease, severe inflammatory conditions, or contraindications to statins, measurement of CRP can be useful in the selection of patients for statin therapy (19). (Level of Evidence: B)

#### **CLASS IIb**

 In asymptomatic intermediate-risk men 50 years of age or younger or women 60 years of age or younger, measurement of CRP may be reasonable for cardiovascular risk assessment (14,20). (Level of Evidence: B)

### **CLASS III: NO BENEFIT**

- In asymptomatic high-risk adults, measurement of CRP is not recommended for cardiovascular risk assessment (21). (Level of Evidence: B)
- In low-risk men younger than 50 years of age or women 60 years of age or younger, measurement of CRP is not recommended for cardiovascular risk assessment (14,20). (Level of Evidence: B)

# 8. Recommendation for Measurement of Hemoglobin A1C

### **CLASS IIb**

 Measurement of hemoglobin A1C may be reasonable for cardiovascular risk assessment in asymptomatic adults without a diagnosis of diabetes (22–27). (Level of Evidence: B)

# 9. Recommendations for Testing for Microalbuminuria

### CLASS IIa

 In asymptomatic adults with hypertension or diabetes, urinalysis to detect microalbuminuria is reasonable for cardiovascular risk assessment (28–30). (Level of Evidence: B)

### **CLASS IIb**

 In asymptomatic adults at intermediate risk without hypertension or diabetes, urinalysis to detect microalbuminuria might be reasonable for cardiovascular risk assessment (31). (Level of Evidence: B)

# 10. Recommendation for Lipoprotein-Associated Phospholipase A2

#### **CLASS IIb**

 Lipoprotein-associated phospholipase A2 might be reasonable for cardiovascular risk assessment in intermediate-risk asymptomatic adults (32–35). (Level of Evidence: B)

# **11. Recommendations for Resting Electrocardiogram**

#### **CLASS IIa**

 A resting electrocardiogram (ECG) is reasonable for cardiovascular risk assessment in asymptomatic adults with hypertension or diabetes (36,37). (Level of Evidence: C)

### **CLASS IIb**

 A resting ECG may be considered for cardiovascular risk assessment in asymptomatic adults without hypertension or diabetes (38-40). (Level of Evidence: C)

# **12. Recommendations for Transthoracic Echocardiography**

#### CLASS IIb

 Echocardiography to detect left ventricular hypertrophy may be considered for cardiovascular risk assessment in asymptomatic adults with hypertension (41,42). (Level of Evidence: B)

### CLASS III: NO BENEFIT

 Echocardiography is not recommended for cardiovascular risk assessment of CHD in asymptomatic adults without hypertension. (Level of Evidence: C)

# **13. Recommendation for Measurement of Carotid Intima-Media Thickness**

### CLASS IIa

Measurement of carotid artery intima-media thickness is reasonable for cardiovascular risk assessment in asymptomatic adults at intermediate risk (43,44). Published recommendations on required equipment, technical approach, and operator training and experience for performance of the test must be carefully followed to achieve high-quality results (44). (Level of Evidence: B)

# 14. Recommendation for Brachial/Peripheral Flow-Mediated Dilation

### **CLASS III: NO BENEFIT**

1. Peripheral arterial flow-mediated dilation studies are not recommended for cardiovascular risk assessment in asymptomatic adults (45,46). (Level of Evidence: B)

Greenland *et al.*CV Risk Guideline: Executive Summary

# **15. Recommendation for Specific Measures of Arterial Stiffness**

#### **CLASS III: NO BENEFIT**

 Measures of arterial stiffness outside of research settings are not recommended for cardiovascular risk assessment in asymptomatic adults. (Level of Evidence: C)

# **16. Recommendation for Measurement of Ankle-Brachial Index**

#### **CLASS IIa**

1. Measurement of ankle-brachial index is reasonable for cardiovascular risk assessment in asymptomatic adults at intermediate risk (47). (Level of Evidence: B)

# 17. Recommendation for Exercise Electrocardiography

#### **CLASS IIb**

An exercise ECG may be considered for cardiovascular risk assessment in intermediate-risk asymptomatic adults (including sedentary adults considering starting a vigorous exercise program), particularly when attention is paid to non-ECG markers such as exercise capacity (48–50). (Level of Evidence: B)

# **18. Recommendation for Stress Echocardiography**

### **CLASS III: NO BENEFIT**

1. Stress echocardiography is not indicated for cardiovascular risk assessment in low- or intermediate-risk asymptomatic adults. (Exercise or pharmacologic stress echocardiography is primarily used for its role in advanced cardiac evaluation of symptoms suspected of representing CHD and/or estimation of prognosis in patients with known coronary artery disease or the assessment of patients with known or suspected valvular heart disease.) (Level of Evidence: C)

# **19. Recommendations for** Myocardial Perfusion Imaging

### **CLASS IIb**

 Stress MPI may be considered for advanced cardiovascular risk assessment in asymptomatic adults with diabetes or asymptomatic adults with a strong family history of CHD or when previous risk assessment testing suggests high risk of CHD, such as a coronary artery calcium (CAC) score of 400 or greater. (Level of Evidence: C)

### **CLASS III: NO BENEFIT**

 Stress MPI is not indicated for cardiovascular risk assessment in low- or intermediate-risk asymptomatic adults (Exercise or pharmacologic stress MPI is primarily used and studied for its role in advanced cardiac evaluation of symptoms suspected of representing CHD and/or estimation of prognosis in patients with known coronary artery disease.) (51). (Level of Evidence: C)

# 20. Recommendations for Calcium Scoring Methods

#### **CLASS II**a

Measurement of CAC is reasonable for cardiovascular risk assessment in asymptomatic adults at intermediate risk (10% to 20% 10-year risk) (52,53). (Level of Evidence: B)

#### CLASS III

 Measurement of CAC may be reasonable for cardiovascular risk assessment in persons at low to intermediate risk (6% to 10% 10-year risk) (53-55). (Level of Evidence: B)

### **CLASS III: NO BENEFIT**

 Persons at low risk (<6% 10-year risk) should not undergo CAC measurement for cardiovascular risk assessment (52,53,56). (Level of Evidence: B)

# **21. Recommendation for Coronary Computed Tomography Angiography**

#### CLASS III: NO RENEFIT

 Coronary computed tomography angiography is not recommended for cardiovascular risk assessment in asymptomatic adults (57). (Level of Evidence: C)

# 22. Recommendation for Magnetic Resonance Imaging of Plaque

### **CLASS III: NO BENEFIT**

 Magnetic resonance imaging for detection of vascular plaque is not recommended for cardiovascular risk assessment in asymptomatic adults. (Level of Evidence: C)

# 23. Recommendations for Patients With Diabetes Mellitus

### CLASS IIa

 In asymptomatic adults with diabetes, 40 years of age and older, measurement of CAC is reasonable for cardiovascular risk assessment (58-61). (Level of Evidence: B)

### **CLASS IIb**

- Measurement of hemoglobin A1C may be considered for cardiovascular risk assessment in asymptomatic adults with diabetes (62). (Level of Evidence: B)
- Stress MPI may be considered for advanced cardiovascular risk assessment in asymptomatic adults with diabetes or when previous risk assessment testing suggests a high risk of CHD, such as a CAC score of 400 or greater. (Level of Evidence: C)

# 24. Recommendations for Special Considerations In Women

### CLASS

 A global risk score should be obtained in all asymptomatic women (14,63). (Level of Evidence: B) 10 Greenland *et al.*CV Risk Guideline: Executive Summary

JACC Vol. 56, No. 25, 2010 December 14/21, 2010:000-000

Family history of CVD should be obtained for cardiovascular risk assessment in all asymptomatic women (13,14). (Level of Evidence: B)

# 25. Clinical Implications of Risk Assessment: Concluding Comments

The assessment of risk for development of clinical manifestations of atherosclerotic CVD is designed to aid the clinician in informed decision making about lifestyle and pharmacologic interventions to reduce such risk. Patients are broadly categorized into low-, intermediate-, and highrisk subsets, and level of intensity and type of treatments are based on these differing assessments of risk.

The initial step in risk assessment in individual patients involves the ascertainment of a global risk score (Framingham, Reynolds, etc.) and the elucidation of a family history of atherosclerotic CVD. These Class I recommendations, which are simple and inexpensive, determine subsequent strategies to be undertaken. Persons at low risk do not require further testing for risk assessment, as more intensive interventions are considered unwarranted, and those already documented to be at high risk (established CHD or coronary risk equivalents) are already candidates for intensive preventive interventions, so that added testing will not provide incremental benefit.

For the intermediate-risk patient, this guideline should help the clinician select appropriate test modalities that can further define risk status. Tests classified as Class IIa are those shown to provide benefit that exceeds costs and risk. Selection among these will vary with local availability and expertise, decisions regarding cost, and potential risks such as radiation exposure, etc. Tests classified as Class IIb have less robust evidence for benefit but may prove helpful in selected patients. Tests classified as Class III are not recommended for use in that there is no, or rather limited, evidence of their benefit in incrementally adding to the assessment of risk; therefore, these tests fail to contribute to changes in the clinical approach to therapy. In addition, a number of Class III tests discussed in this guideline require additional efforts to standardize the measurement or make the test more commonly available on a routine clinical basis. Furthermore, some of the Class III tests also pose potential harm (radiation exposure or psychological distress in the absence of a defined treatment strategy) and are therefore to be avoided for cardiovascular risk assessment purposes in the asymptomatic adult. Until additional research is accomplished to justify the addition of Class III tests, the writing committee recommends against their use for cardiovascular risk assessment.

# APPENDIX 1. AUTHOR RELATIONSHIPS WITH INDUSTRY AND OTHER ENTITIES: 2010 ACCF/AHA GUIDELINE FOR ASSESSMENT OF CARDIOVASCULAR RISK IN ASYMPTOMATIC ADULTS: EXECUTIVE SUMMARY

Committee Member	Employer	Consultant	Speaker	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Philip Greenland, Chair	Northwestern University Feinberg School of Medicine—Professor of Preventive Medicine and Professor of Medicine; Director, Northwestern University Clinical and Translational Sciences Institute	GE/Toshiba     Pfizer	None	None	None	NHLBI (MESA)	None
Joseph S. Alpert	University of Arizona— Professor of Medicine; Head, Department of Medicine	Bayer Bristol-Myers Squibb Exeter CME Johnson & Johnson King Pharmaceuticals Merck Novartis Roche Diagnostics Sanofi-aventis	None	None	None	None	None
George A. Beller	University of Virginia Health System—Ruth C. Heede Professor of Cardiology	BSP Advisory     Board	None	Adenosine Therapeutics	None	None	• Stress testing case, defense, 2009

JACC Vol. 56, No. 25, 2010 December 14/21, 2010:000-000

Medicine

Greenland *et al.*CV Risk Guideline: Executive Summary

Institutional, Ownership/ Organizational, or Committee Partnership/ Other Financial **Expert** Personal Member **Employer** Consultant Speaker **Principal** Research **Benefit** Witness Emelia J. **Boston University Schools** None None None GlaxoSmithKline None None Benjamin† of Medicine and Public • Itamar\* Health-Professor of NHLBI Medicine and • NIH/NHLBI\* Epidemiology; • NIH/NIA\* Framingham Heart Study-Director, Echocardiography/Vascular Laboratory Matthew J. Los Angeles Biomedical None • GE None None • CDC None Budoff‡§ Research Institute-Healthcare NIH/NHLBI • MESA Program Director. **Division of Cardiology** • BG Medicine Zahi A. Fayad Mount Sinai School of Merck None None None None Medicine-Professor of Merck Roche Radiology and Medicine Roche Siemens (Cardiology) VIA **Pharmaceuticals** Elyse Foster University of California San None None None Boston Scientific None None Francisco-Professor of Evalve **Clinical Medicine and**  EBR Systems Anesthesia: Director. Echocardiography Laboratory Stanford University School BCBS Technology Mark A. Hlatky§ None None Aviir None None of Medicine—Professor **Evaluation Center** of Health Research and Medical Advisory Policy; Professor of Panel\* Medicine California Pacific (Cardiovascular Medical Center\* Medicine) CV Therapeutics GE Medical\* • The Medicines Company John McB. Geisinger Health System— Volcano\* Boston Volcano\* Boston None None Scientific Scientific\* Hodgson‡§ Chairman of Cardiology • GE FAME Medical GE Medical\* Pfizer RADI Medical\* Volcano\* Volcano\* Frederick G. **Tulane University Medical** None Abbott None AstraZeneca FDA Science None Center—Clinical **Board Member** Kushner†¶ Bristol- Atherogenics Professor of Medicine; Myers Cogentus **Heart Clinic of** Squibb • Eli Lilly • CV Louisiana-Medical NIH Director **Therapeutics**  Novartis Pfizer NHLBI, NIH-Director, Michael S. Lauer None None None None None None Division of Cardiovascular Sciences Leslee J. Shaw **Emory University School of** None None • GE Healthcare\* None None None Medicine-Professor of

11

12 Greenland et al.

**CV Risk Guideline: Executive Summary** 

JACC Vol. 56, No. 25, 2010 December 14/21, 2010:000-000

Committee Member	Employer	Consultant	Speaker	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Sidney C. Smith, Jr.#	University of North Carolina at Chapel Hill— Professor of Medicine and Director, Center for Cardiovascular Science and Medicine	None	None	None	AstraZeneca (DSMB)	None	None
Allen J. Taylor	Washington Hospital Center, Cardiology Section—Director, Advanced Cardiovascular Imaging, Cardiovascular Research Institute	Abbott     Merck     Pfizer	None	None	- Abbott	• SAIP • SCCT	None
William S. Weintraub	Christiana Care Health System—Section Chief, Cardiology	Bristol-Myers     Squibb     Gilead     Eli Lilly     Sanofi-aventis	None	None	<ul> <li>Abbott*</li> <li>AstraZeneca*</li> <li>Bristol-Myers Squibb*</li> <li>Gilead*</li> <li>Otsuka*</li> <li>Sanofi-aventis*</li> </ul>	<ul><li>AstraZeneca*</li><li>Bayer*</li><li>Pfizer*</li></ul>	Quetiapine case, defense, 2008     Celebrex case, defense, 2008
Nanette K. Wenger	Emory University School of Medicine—Professor of Medicine (Cardiology)	Abbott AstraZeneca Boston Scientific Genzyme Gilead* LCIC Medtronic Merck Pfizer Sanofi-aventis Schering-Plough*	None	None	• Gilead* • Eli Lilly* • Merck* • NHLBI* • Pfizer* • Sanofi-aventis*	None	None

This table represents the relationships of committee members with industry and other entities that were reported by authors to be relevant to this document. These relationships were reviewed and updated in conjunction with all meetings and/or conference calls of the writing committee during the document development process. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of 5% or more of the voting stock or share of the business entity, or ownership of \$10,000 or more of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. A relationship is considered to be modest if it is less than significant under the preceding definition. Relationships in this table are modest unless otherwise noted. \*Significant relationship; †Recused from voting on Section 10, Lipoprotein-Associated Phospholipase A2; ‡Recused from voting on Section 21, Coronary Computed Tomography Angiography; §Recused from voting on Section 23, Diabetes Mellitus; |Recused from voting on Section 20, Calcium Scoring Methods; ¶Recused from voting on Section 5, Lipoprotein and Apolipoprotein Assessments; #Recused from voting on Section 7, Measurement of C-Reactive Protein.

ACCF indicates American College of Cardiology Foundation; AHA, American Heart Association; BCBS, Blue Cross Blue Shield; BSP, Biological Signal Processing; CDC, Centers for Disease Control; CME, continuing medical education; DSMB, Data Safety Monitoring Board; FAME, Fractional flow reserve (FFR) vs. Angiography in Multivessel Evaluation; FDA, Food and Drug Administration; LCIC, Leadership Council for Improving Cardiovascular Care; MESA, Multiethnic Study of Atherosclerosis; NHLBI, National Heart, Lung, and Blood Institute; NIA, National Institute on Aging; NIH, National Institutes of Health; SAIP, Society of Atherosclerosis Imaging and Prevention; and SCCT, Society of Cardiovascular Computed Tomography.

# APPENDIX 2. REVIEWER RELATIONSHIPS WITH INDUSTRY AND OTHER ENTITIES: 2010 ACCF/AHA GUIDELINE FOR ASSESSMENT OF CARDIOVASCULAR RISK IN ASYMPTOMATIC ADULTS: EXECUTIVE SUMMARY

				Ownership/ Partnership/	Personal	Institutional, Organizational, or Other Financial	r Expert
Peer Reviewer	Representation	Consultant	Speaker	Principal	Research	Benefit	Witness
Frederick G. Kushner	Official Reviewer— ACCF/AHA Task Force on Practice Guidelines	None	Abbott     Bristol-Myers     Squibb     CV Therapeutics	None	AstraZeneca     Atherogenics     Cogentus     Eli Lilly     NIH     Novartis     Pfizer	None	None
Marian C. Limacher	Official Reviewer—AHA	None	None	None	• NIH*	None	None

JACC Vol. 56, No. 25, 2010 December 14/21, 2010:000-000 Greenland *et al.*CV Risk Guideline: Executive Summary

Institutional, Ownership/ Organizational, or Other Financial Partnership/ **Expert** Personal **Peer Reviewer** Representation Consultant Speaker **Principal** Research **Benefit** Witness Thomas C. Piemonte Official Reviewer-None None None None Medtronic\* None **ACCF Board of** Governors **Paul Poirier** Official Reviewer—AHA None None None • CDA\* None None CIHR\* • FRSQ\* Official Reviewer-Jane E. Schauer None None None NIH None None **ACCF Board of Trustees** Daniel S. Berman Organizational Reviewer— • Astellas None None Astellas\* None None American Society of Bracco GF/Amersham **Nuclear Cardiology**  Cedars-Sinai Siemens Medical Center\* • Flora Pharma • Lantheus\* Magellan Spectrum Dynamics\* Roger S. Blumenthal Organizational Reviewer— None None None None None None Society of Atherosclerosis Imaging and Prevention Robin P. Choudhury Organizational Reviewer- None None None None None None Society for Cardiovascular Magnetic Resonance Abbott Vascular David A. Cox Organizational Reviewer— Abbott Vascular None None None None • Boston Scientific • Boston Scientific Society for Cardiovascular Angiography and Interventions **Daniel Edmundowicz** Organizational Reviewer— None None None None None None Society for Cardiovascular Angiography and Interventions Steven J. Lavine Organizational Reviewer— None None None None None None American Society of Echocardiography James K. Min Organizational Reviewer— • GE Healthcare GF Healthcare GF Healthcare<sup>3</sup> None None None American Society of **Nuclear Cardiology** Kofo O. Ogunyankin Organizational Reviewer— None None None None None None American Society of **Echocardiography** Donna M. Polk Organizational Reviewer— • Daiichi Sankyo\* GlaxoSmithKline Merck\* None None None American Society of Roche **Nuclear Cardiology** Timothy A. Sanborn Organizational Reviewer— None The Medicines None None None None Society for Company\* Cardiovascular Angiography and Interventions

13

14 Greenland et al.

**CV Risk Guideline: Executive Summary** 

JACC Vol. 56, No. 25, 2010 December 14/21, 2010:000-000

Peer Reviewer	Representation	Consultant	Speaker	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Gregory S. Thomas	Organizational Reviewer— American Society of Nuclear Cardiology	Astellas     GE Medical	Abbott     Astellas*	None	Astellas*     GE Medical     Isis     Pharmaceuticals*     Siemens	Past President,     American     Society of     Nuclear     Cardiology	None
Szilard Voros	Organizational Reviewer— Society for Cardiovascular Magnetic Resonance	None	• Merck Schering- Plough*	None	Abbott Vascular*     CardioDx*     Merck Schering-Plough*     Vital Images*     Volcano*	None	None
Karthikeyan Ananthasubramaniam	Content Reviewer— ACCF Imaging Council	None	Astellas Global Pharma	None	Astellas Global     Pharma*	None	None
Jeffrey L. Anderson	Content Reviewer— ACCF/AHA Task Force on Practice Guidelines	None	None	None	None	None	None
Vera Bittner	Content Reviewer— ACCF Prevention of Cardiovascular Disease Committee	None	None	None	• CV Therapeutics* • GlaxoSmithKline* • NHLBI* • NIH/Abbott* • Roche	None	None
James I. Cleeman	Content Reviewer	None	None	None	None	None	None
Mark A. Creager	Content Reviewer— ACCF/AHA Task Force on Practice Guidelines	<ul><li>Genzyme Biomarin</li><li>Sanofi-aventis</li><li>Sigma Tau</li><li>Vascutek</li></ul>	None	None	Merck     Sanofi-aventis	None	None
Gregg C. Fonarow	Content Reviewer	Abbott* AstraZeneca BMS/Sanofi GlaxoSmithKline* Medtronic* Merck* Novartis* Pfizer*	Abbott* AstraZeneca BMS/Sanofi* GlaxoSmithKline* Medtronic* Merck* Novartis* Pfizer*	None	None	None	None
David C. Goff, Jr.	Content Reviewer	• JAMA/Archives of Internal Medicine* • Scientific Evidence*	None	None	Merck	None	None
Thomas A. Haffey	Content Reviewer	Merck     Merck Schering- Plough	AstraZeneca     Merck     Merck Schering- Plough	Colorado Heart Institute	GlaxoSmithKline*	None	None

JACC Vol. 56, No. 25, 2010 December 14/21, 2010:000-000 Greenland *et al.*CV Risk Guideline: Executive Summary

Institutional, Ownership/ Organizational, or Partnership/ Other Financial Personal **Expert** Peer Reviewer Representation Consultant Speaker **Principal** Research **Benefit** Witness • NIH (NHLBI) Jonathan L. Halperin Content Reviewer- Astellas Pharma None None None None ACCF/AHA Task Force on Practice Guidelines **HealthCare** • Biotronik\* • Boehringer Ingelheim Daiichi Sankyo FDA Cardiorenal Advisory Committee Johnson & Johnson Portola **Pharmaceuticals**  Sanofi-aventis Jerome L. Hines Content Reviewer-None None None None None None **ACCF Imaging Council** Judith S. Hochman Content Reviewer— • Eli Lilly • GlaxoSmithKline None None None None ACCF/AHA Task Force on • Millennium Pharmaceuticals **Practice Guidelines** and Schering-Plough Research Institute (TIMI 50) Christopher M. Kramer Content Reviewer- Siemens None None Astellas\* None None **ACCF Imaging Council**  GlaxoSmithKline\* NHLBI\* • Merck Schering-Plough\* • Siemens Medical Solutions\* Donald M. Lloyd-Jones Content Reviewer None None None None None None Pamela B. Morris Content Reviewer-None Abbott None None None None ACCF Prevention of AstraZeneca Cardiovascular Disease Merck Committee · Merck Schering-Plough Takeda Srihari S. Naidu Content Reviewer— None None None None None None **ACCF Cardiac** Catheterization Committee Vasan S. Ramachandran Content Reviewer None None None • NIH\* None None Rita F. Redberg Content Reviewer None None None None None None Charanjit S. Rihal Content Reviewer— None None None None None None **ACCF Cardiac** Catheterization Committee Vincent L. Sorrell Content Reviewer-Lantheus\* GE Medical AtCor Medical None None None ACCF Prevention of • Lantheus\* Cardiovascular Disease Phillips Committee Laurence S. Sperling Content Reviewer— None None None None None None ACCF Prevention of Cardiovascular Disease Committee

15

16

# Greenland *et al.*CV Risk Guideline: Executive Summary

JACC Vol. 56, No. 25, 2010 December 14/21, 2010:000-000

Peer Reviewer	Representation	Consultant	Speaker	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Carl L. Tommaso	Content Reviewer— ACCF Interventional Council	None	None	None	None	None	None
Uma S. Valeti	Content Reviewer	None	None	None	• Medtronic*	None	None
Christopher J. White	Content Reviewer— ACCF Interventional Council	<ul><li>Baxter*</li><li>Boston</li><li>Scientific*</li></ul>	None	None	None	None	None
Kim A. Williams	Content Reviewer— ACCF Imaging Council	Astellas*     GE Healthcare*     King     Pharmaceuticals	Astellas*     GE Healthcare* *	None	GE Healthcare*     Molecular Insight     Pharmaceuticals*	Molecular     Insight     Pharmaceuticals	None *

This table represents the relevant relationships with industry and other entities that were disclosed at the time of peer review. It does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of 5% or more of the voting stock or share of the business entity, or ownership of \$10,000 or more of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. A relationship is considered to be modest if it is less than significant under the preceding definition. Relationships in this table are modest unless otherwise noted. Names are listed in alphabetical order within each category of review. \*Significant relationship.

ACCF indicates American College of Cardiology Foundation; AHA, American Heart Association; CDA, Canadian Diabetes Association; CIHR, Canadian Institutes of Health; FDA, Food and Drug Administration; FRSQ, Fonds de la recherche en santé du Québec; NHLBI, National Heart, Lung, and Blood Institute; NIH, National Institutes of Health; JAMA, Journal of the American Medical Association; and TIMI, Thrombolysis In Myocardial Infarction.

### **Staff**

American College of Cardiology Foundation
John C. Lewin, MD, Chief Executive Officer
Charlene May, Senior Director, Science and Clinical Policy
Lisa Bradfield, CAE, Director, Science and Clinical Policy
Sue Keller, BSN, MPH, Senior Specialist, Evidence-Based
Medicine

Erin A. Barrett, MPS, Senior Specialist, Science and Clinical Policy

Beth Denton, Specialist, Science and Clinical Policy

American Heart Association

Nancy Brown, Chief Executive Officer Gayle R. Whitman, PhD, RN, FAHA, FAAN, Senior Vice President, Office of Science Operations

### **REFERENCES**

- ACCF/AHA Task Force on Practice Guidelines. Methodologies and Policies from the ACCF/AHA Task Force on Practice Guidelines. Available at: http://assets.cardiosource.com/Methodology\_Manual\_for\_ACC\_AHA\_Writing\_Committees.pdf and http://circ.ahajournals.org/manual/. Accessed August 27, 2010.
- Califf RM, Armstrong PW, Carver JR, et al. 27th Bethesda Conference: matching the intensity of risk factor management with the hazard for coronary disease events. Task Force 5. Stratification of patients into high, medium and low risk subgroups for purposes of risk factor management. J Am Coll Cardiol. 1996;27:1007–19.
- D'Agostino RB, Russell MW, Huse DM, et al. Primary and subsequent coronary risk appraisal: new results from the Framingham Study. Am Heart J. 2000;139:272–81.
- Lloyd-Jones D, Adams R, Carnethon M, et al. Heart disease and stroke statistics—2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2009;119:e21–181.
- Haapanene-Niemi, N, Vuovi, I, Pasanen M, et al. Public health burden of coronary disease risk factors among middle-aged and elderly men. Prev Med. 2009;4:343–8.
- 6. Vinereau D. Risk factors for atherosclerotic disease: present and future. Herz 2006;31 Suppl 3:5–24.

- Hlatky MA, Greenland P, Arnett DK, et al. Criteria for evaluation of novel markers of cardiovascular risk: a scientific statement from the American Heart Association. Circulation. 2009;119:2408–16.
- 8. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Ann Intern Med. 2007;147:573–7.
- Greenland P, O'Malley PG. When is a new prediction marker useful? A consideration of lipoprotein-associated phospholipase A2 and C-reactive protein for stroke risk. Arch Intern Med. 2005;165:2454–6.
- Cook NR. Use and misuse of the receiver operating characteristic curve in risk prediction. Circulation. 2007;115:928-35.
- Pencina MJ, D'Agostino RB, Sr., D'Agostino RB, Jr., Vasan RS. Evaluating the added predictive ability of a new marker: from area under the ROC curve to reclassification and beyond. Stat Med. 2008;27:157–72.
- D'Agostino RB, Sr., Grundy S, Sullivan LM, Wilson P. Validation of the Framingham coronary heart disease prediction scores: results of a multiple ethnic groups investigation. JAMA. 2001;286:180–7.
- 13. Assmann G, Cullen P, Schulte H. Simple scoring scheme for calculating the risk of acute coronary events based on the 10-year follow-up of the prospective cardiovascular Munster (PROCAM) study. Circulation. 2002;105:310-5.
- Ridker PM, Buring JE, Rifai N, et al. Development and validation of improved algorithms for the assessment of global cardiovascular risk in women: the Reynolds Risk Score. JAMA. 2007;297:611–9.
- Paynter NP, Chasman DI, Buring JE, et al. Cardiovascular disease risk prediction with and without knowledge of genetic variation at chromosome 9p21.3. Ann Intern Med. 2009;150:65–72.
- Scheuner MT, Sieverding P, Shekelle PG. Delivery of genomic medicine for common chronic adult diseases: a systematic review. JAMA. 2008;299:1320–34.
- Ip S, Lichtenstein AH, Chung M, et al. Systematic review: association of low-density lipoprotein subfractions with cardiovascular outcomes. Ann Intern Med. 2009;150:474–84.
- DiAngelantonio E, Chowdhury R, Sarwar N, et al. B-type natriuretic peptides and cardiovascular risk: systematic review and meta-analysis of 40 prospective studies. Circulation. 2009;120:2177–87.
- Ridker PM, Danielson E, Fonseca FA, et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N Engl J Med. 2008;359:2195–207.
- Ridker PM, Paynter NP, Rifai N, et al. C-reactive protein and parental history improve global cardiovascular risk prediction: the Reynolds Risk Score for men. Circulation. 2008;118:2243–51.

Greenland *et al.*CV Risk Guideline: Executive Summary

- Baigent C, Keech A, Kearney PM, et al. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. Lancet. 2005; 366:1267–78.
- Khaw KT, Wareham N, Bingham S, et al. Association of hemoglobin A1c with cardiovascular disease and mortality in adults: the European prospective investigation into cancer in Norfolk. Ann Intern Med. 2004:141-413-20
- Khaw KT, Wareham N. Glycated hemoglobin as a marker of cardiovascular risk. Curr Opin Lipidol. 2006;17:637–43.
- Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346:393–403.
- 25. Lachin JM, Christophi CA, Edelstein SL, et al. Factors associated with diabetes onset during metformin versus placebo therapy in the diabetes prevention program. Diabetes. 2007;56:1153–9.
- Selvin E, Marinopoulos S, Berkenblit G, et al. Meta-analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. Ann Intern Med. 2004;141:421–31.
- Selvin E, Steffes MW, Zhu H, et al. Glycated hemoglobin, diabetes, and cardiovascular risk in nondiabetic adults. N Engl J Med. 2010; 362:800–11
- Ibsen H, Olsen MH, Wachtell K, et al. Reduction in albuminuria translates to reduction in cardiovascular events in hypertensive patients: losartan intervention for endpoint reduction in hypertension study. Hypertension. 2005;45:198–202.
- Ninomiya T, Perkovic V, Verdon C, et al. Proteinuria and stroke: a meta-analysis of cohort studies. Am J Kidney Dis. 2009;53:417–25.
- Wachtell K, Ibsen H, Olsen MH, et al. Albuminuria and cardiovascular risk in hypertensive patients with left ventricular hypertrophy: the LIFE study. Ann Intern Med. 2003;139:901–6.
- 31. Arnlov J, Evans JC, Meigs JB, et al. Low-grade albuminuria and incidence of cardiovascular disease events in nonhypertensive and nondiabetic individuals: the Framingham Heart Study. Circulation. 2005;112:969–75.
- 32. Ballantyne C, Cushman M, Psaty B, et al. Collaborative meta-analysis of individual participant data from observational studies of Lp-PLA2 and cardiovascular diseases. Eur J Cardiovasc Prev Rehabil. 2007;14:
- 33. Daniels LB, Laughlin GA, Sarno MJ, et al. Lipoprotein-associated phospholipase A2 is an independent predictor of incident coronary heart disease in an apparently healthy older population: the Rancho Bernardo Study. J Am Coll Cardiol. 2008;51:913–9.
- 34. Garza CA, Montori VM, McConnell JP, et al. Association between lipoprotein-associated phospholipase A2 and cardiovascular disease: a systematic review. Mayo Clin Proc. 2007;82:159–65.
- 35. Koenig W, Khuseyinova N, Lowel H, et al. Lipoprotein-associated phospholipase A2 adds to risk prediction of incident coronary events by C-reactive protein in apparently healthy middle-aged men from the general population: results from the 14-year follow-up of a large cohort from southern Germany. Circulation. 2004;110:1903–8.
- 36. De Bacquer D, DeBacker G. Electrocardiographic findings and global coronary risk assessment. Eur Heart J. 2002;23:268-70.
- 37. Okin PM, Roman MJ, Lee ET, et al. Combined echocardiographic left ventricular hypertrophy and electrocardiographic ST depression improve prediction of mortality in American Indians: the Strong Heart Study. Hypertension. 2004;43:769–74.
- Ashley EA, Raxwal V, Froelicher V. An evidence-based review of the resting electrocardiogram as a screening technique for heart disease. Prog Cardiovasc Dis. 2001;44:55–67.
- Schlant RC, Adolph RJ, DiMarco JP, et al. Guidelines for electrocardiography: a report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Committee on Electrocardiography). J Am Coll Cardiol. 1992;19:473–81.
- 40. U.S. Preventive Services Task Force. Screening for coronary heart disease: recommendation statement. Ann Intern Med. 2004;140:569–72.
- Verdecchia P, Carini G, Circo A, et al. Left ventricular mass and cardiovascular morbidity in essential hypertension: the MAVI study. J Am Coll Cardiol. 2001;38:1829–35.
- 42. Rodriguez CJ, Lin F, Sacco RL, et al. Prognostic implications of left ventricular mass among Hispanics: the Northern Manhattan Study. Hypertension. 2006;48:87–92.

- 43. Nambi V, Chambless L, Folsom A, and et al. Carotid intima-media thickness and the presence or absence of plaque improves prediction of coronary heart disease risk in the Atherosclerosis Risk in Communities (ARIC) study. J Am Coll Cardiol 2010;55:1600–7.
- 44. Stein JH, Korcarz CE, Hurst RT, et al. Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular disease risk: a consensus statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force. J Am Soc Echocardiogr. 2008;21:93–111.
- 45. Kuvin JT, Mammen A, Mooney P, et al. Assessment of peripheral vascular endothelial function in the ambulatory setting. Vasc Med. 2007;12:13-6.
- 46. Takase B, Uehata A, Akima T, et al. Endothelium-dependent flow-mediated vasodilation in coronary and brachial arteries in suspected coronary artery disease. Am J Cardiol. 1998;82:1535–8.
- Fowkes FG, Murray GD, Butcher I, et al. Ankle brachial index combined with Framingham Risk Score to predict cardiovascular events and mortality: a meta-analysis. JAMA. 2008;300:197–208.
- 48. Gulati M, Pandey DK, Arnsdorf MF, et al. Exercise capacity and the risk of death in women: the St James Women Take Heart Project. Circulation. 2003;108:1554–9.
- Adabag AS, Grandits GA, Prineas RJ, et al. Relation of heart rate parameters during exercise test to sudden death and all-cause mortality in asymptomatic men. Am J Cardiol. 2008;101:1437–43.
- Wei M, Kampert JB, Barlow CE, et al. Relationship between low cardiorespiratory fitness and mortality in normal-weight, overweight, and obese men. JAMA. 1999;282:1547–53.
- 51. Gibbons RJ, Abrams J, Chatterjee K, et al. ACC/AHA 2002 guideline update for the management of patients with chronic stable angina—summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Chronic Stable Angina). J Am Coll Cardiol. 2003;41:159–68.
- 52. Detrano R, Guerci AD, Carr JJ, et al. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. N Engl J Med. 2008;358:1336–45.
- 53. Greenland P, LaBree L, Azen SP, et al. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. JAMA. 2004;291:210–5.
- 54. Lakoski SG, Greenland P, Wong ND, et al. Coronary artery calcium scores and risk for cardiovascular events in women classified as "low risk" based on Framingham risk score: the Multi-Ethnic Study of Atherosclerosis (MESA). Arch Intern Med. 2007;167:2437–42.
- 55. Taylor AJ, Bindeman J, Feuerstein I, et al. Coronary calcium independently predicts incident premature coronary heart disease over measured cardiovascular risk factors: mean three-year outcomes in the Prospective Army Coronary Calcium (PACC) project. J Am Coll Cardiol. 2005;46:807–14.
- Budoff MJ, Nasir K, McClelland RL, et al. Coronary calcium predicts events better with absolute calcium scores than age-sex-race/ethnicity percentiles: MESA (Multi-Ethnic Study of Atherosclerosis). J Am Coll Cardiol. 2009;53:345–52.
- 57. Choi EK, Choi SI, Rivera JJ, et al. Coronary computed tomography angiography as a screening tool for the detection of occult coronary artery disease in asymptomatic individuals. J Am Coll Cardiol. 2008;52:357–65.
- 58. Anand DV, Lim E, Hopkins D, et al. Risk stratification in uncomplicated type 2 diabetes: prospective evaluation of the combined use of coronary artery calcium imaging and selective myocardial perfusion scintigraphy. Eur Heart J. 2006;27:713–21.
- Becker A, Leber AW, Becker C, et al. Predictive value of coronary calcifications for future cardiac events in asymptomatic patients with diabetes mellitus: a prospective study in 716 patients over 8 years. BMC Cardiovasc Disord. 2008;8:27.
- 60. Elkeles RS, Godsland IF, Feher MD, et al. Coronary calcium measurement improves prediction of cardiovascular events in asymptomatic patients with type 2 diabetes: the PREDICT study. Eur Heart J. 2008;29:2244–51.
- 61. Scholte AJ, Schuijf JD, Kharagjitsingh AV, et al. Prevalence of coronary artery disease and plaque morphology assessed by multi-slice computed tomography coronary angiography and calcium scoring in asymptomatic patients with type 2 diabetes. Heart. 2008;94:290–5.

18 Greenland *et al.*CV Risk Guideline: Executive Summary

JACC Vol. 56, No. 25, 2010 December 14/21, 2010:000-000

- 62. Becker A, Leber A, Becker C, Knez A. Predictive value of coronary calcifications for future cardiac events in asymptomatic individuals. Am Heart J. 2008;155:154–60.
- 63. Pasternak RC, Abrams J, Greenland P, et al. 34th Bethesda Conference: task force #1—identification of coronary heart disease risk: is there a detection gap? J Am Coll Cardiol. 2003;41:1863–74.

**Key Words:** ACCF/AHA practice guidelines ■ asymptomatic adults ■ cardiovascular risk assessment ■ cardiovascular screening of asymptomatic adults ■ detection of coronary artery disease ■ risk factor assessment ■ subclinical coronary artery disease.

# 2010 ACCF/AHA Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults: Executive Summary

American College of Cardiology Foundation, American Heart Association Task Force on Practice Guidelines, American Society of Echocardiography, American Society of Nuclear Cardiology, Society of Atherosclerosis Imaging and Prevention, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, Philip Greenland, Joseph S. Alpert, George A. Beller, Emelia J. Benjamin, Matthew J. Budoff, Zahi A. Fayad, Elyse Foster, Mark.A. Hlatky, John McB. Hodgson, Frederick G. Kushner, Michael S. Lauer, Leslee J. Shaw, Sidney C. Smith, Jr, Allen J. Taylor, William S. Weintraub, and Nanette K. Wenger J. Am. Coll. Cardiol. published online Nov 15, 2010; doi:10.1016/j.jacc.2010.09.002

## This information is current as of November 17, 2010

Updated Information & Services	including high-resolution figures, can be found at: http://content.onlinejacc.org/cgi/content/full/j.jacc.2010.09.00 2v1
Supplementary Material	Supplementary material can be found at: http://content.onlinejacc.org/cgi/content/full/j.jacc.2010.09.00 2/DC1
References	This article cites 62 articles, 42 of which you can access for free at: http://content.onlinejacc.org/cgi/content/full/j.jacc.2010.09.00 2v1#BIBL
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): <b>Guidelines</b> http://content.onlinejacc.org/cgi/collection/guidelines
Rights & Permissions	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://content.onlinejacc.org/misc/permissions.dtl
Reprints	Information about ordering reprints can be found online: http://content.onlinejacc.org/misc/reprints.dtl