Appendix A: Technical Expert Advisory Group and Expert Consultants

Technical Expert Advisory Group

Noel Bairey-Merz, MD	Cedars-Sinai Medical Center
Elizabeth Barrett-Connor, MD	University of California, San Diego
Robert Califf, MD	Duke University
Curt Furberg, MD	Wake Forest University
Lee Goldman, MD	University of California, San Francisco
Paul Heidenreich, MD	Stanford University
Mark Hlatky, MD	Stanford University
JoAnn Manson , MD, DrPH	Harvard Medical School, Brigham and Women's Hospital
Sally Shumaker, PhD	Wake Forest University
Marcia Stefanick, PhD	Stanford University
Nanette Wenger, MD	Emory University

Expert Consultants

Roger S. Blumenthal, MD, FACC	Johns Hopkins University
Lori Mosca, MD, MPH, PhD	Columbia University

Advice was also solicited from representatives of Partner Organizations, including:

Robert Christenson, PhD	American Association for Clinical Chemistry
Sharonne N. Hayes, M.D., F.A.C.C.	American College of Cardiology
Rosalind Fabunmi, Ph.D.	American Heart Association
Rose Marie Robertson, MD	American Heart Association
Mary Norine Walsh, MD	American College of Cardiology
Mary Winston, Ed.D.	American Heart Association

Appendix B: Literature Search Terms

The following terms were used to define the outcome for all questions.

	Search Terms
Outcome	cardiovascular diseases or heart diseases or heart or cardiovas* or cardiac* or coronary or myocardial
Publication Type	meta-analysis or meta-analy* or metaanaly* or metanaly* or review or overview and systematic
or	methodologic* or evidence* or Medline
Limits	publication date 1985 to 2002, English language, human

The following terms were used to define the predictor for each specific question.

Question	
1.01	exercise test* or stress test* or exercise electrocardio* or exercise tolerance test*
1.02	exercise echocardio* or coronary disease, ultrasonography or dobutamine, diagnostic or exercise test* or stress test*
1.03	coronary artery calcification or electron beam tomography or coronary arteriosclerosis, radiography or coronary disease, radionuclide imaging or heart radionuclide imaging or spect or tomography, x-ray computed
2.01	aspirin
2.02	adrenergic beta-antagonists or beta-blockers or beta blockers or B-blockers
2.03	angiotensin converting enzyme inhibitors or angiotensin-converting enzyme inhibitors or angiotensin receptor blockers
2.04	calcium channel blocker*

Appendix B: Literature SearchTerms (continued)

2.05	nitrate* or isosorbide mononitrate or isosorbide dinitrate
2.06	heparin or low molecular weight heparin
2.07	glycoprotein IIb-IIIa or glycoprotein IIb/IIIa or abciximab or tirofiban or eptifibatide
2.08	fibrinolytic agents or thrombolytics or thrombolysis or myocardial infarction, drug therapy or streptokinase or tissue plasminogen activator or myocardial reperfusion, methods
2.09	ticlopidine
2.10	clopidogrel
2.11	angioplasty, transluminal, percutaneous coronary or stent
2.12	coronary artery bypass graft surgery or CABG
3.01	hypertension or antihypertensive agents or vascular resistance
3.02	diabetes or diabetic*
3.03a	hyperlipidemia or cholesterol or LDL* or HDL* or VLDL or LPA or lipoprotein* or triglycerides or triglycerid*
3.03b	lipid lowering agents or anticholesteremic agents or antilipemic agents or hyperlipidemia, therapy
3.04	homocysteine or folic acid or pyridoxine
3.05	c-reactive
3.06	tobacco or smoking or nicotine
3.07	obesity or body weight or weight

Appendix B: Literature Search Terms (continued)

3.08	inactiv* or sedentary
3.09	aging or age factors or age or ageing or aging
3.10	menopause
3.11	racial stocks or ethnic groups or race
3.12	socioeconomic factors or income*
4.0	comparative study, male and female, sex factors or sex characteristics
5.01	troponin or troponin-t
5.02	creatine kinase or ck or ck-mb
5.03	myoglobin

Appendix C: Full Text Article Abstraction Form

Reviewer 1: **Reviewer 2:** **Question Code:** **Article:**

INCLUSION CRITERIA If answer is "NO" for any question 1-3 skip to #14.	**YES**	**NO**
1. Is the article a large randomized controlled trial, systematic review of the literature, a large prospective cohort (≥1000) with multivariable analysis, or X-sectional (for Key Q #1 & 4)?		
2. Does the review article address the evidence-based question?		
3. Does the article contain data on women that address the research question?		
SYSTEMATIC REVIEW	**YES**	**NO**
4. Was the information source appropriate?		
5. Was the information source adequately searched?		
6. Were the inclusion/exclusion criteria used to select articles clear and appropriate?		
7. Were the study assessments performed by at least 2 independent reviewers?		
8. Were the principal measures of effect and the methods of combining results appropriate? (summary effect size and CI)		
9. Was the methodological quality of the studies systematically assessed?		
10. Was the heterogeneity of the studies determined?		
11. Was there an assessment of publication bias?		
12. Was a sensitivity analysis included in the report?		
13. Years covered by review: ( ) to ( ) *(go to Question #14)*		
CLINICAL TRIAL	**YES**	**NO**
4. Was the intervention randomized?		
5. Was there a control group that received placebo?		
6. Were the participants and research staff blinded to the intervention?		
7. Were the inclusion/exclusion criteria clear and appropriate?		
8. Was there > 75% complete follow up? *(go to Question #14)*		
PROSPECTIVE COHORT	**YES**	**NO**
4. Were the inclusion/exclusion criteria clear and appropriate?		
5. Was there > 75% complete follow up?		
6. Did the analysis include multivariate adjustment for potential confounders?		
7. Was the outcome adjudicated blindly? *(go to Question #14)*		
ADDITIONAL INCLUSION CRITERIA (use for Key Question 1 only)	**YES**	**NO**
4. Was coronary angiography the "gold standard" for measuring the accuracy?		
5. Was data on the accuracy of these tests in women included?		
6. Were non-invasive tests performed exclusively in patients after myocardial infarction, percutaneous angioplasty, coronary artery surgery or hospitalization for an unstable coronary syndrome (yes-exclude)		
CROSS-SECTIONALQUALITY EVALUATION (use for Key Question 1 only)	**YES**	**NO**
7. Did all women who undergo the non-invasive test also undergo angiography?		
8. Was the diagnosis of coronary artery disease on angiography made by investigators blinded to results of the non-invasive test? *(go to Question #14)*		
CROSS-SECTIONALQUALITY EVALUATION (use for Key Question 4 only)	**YES**	**NO**
4. Were the inclusion/exclusion criteria clear and appropriate?		
5. Did the analysis include multivariate adjustment for potential confounders? *(go to Question #14)*		

14. Was this article a (check one only): *(required if Question 1-3 are 'yes')*

___ Systematic Review ___ Prospective cohort ___ Pooling project ___ Interesting other finding
___ Randomized controlled trial ___ Evidence-based guideline ___ Cost effectiveness analysis ___ Other

	YES	**NO**
15. Does this article contain data on women only? *(required if Question 1-3 are'yes')*		

16. Comments (continue on other side)

Appendix D: Articles Eligible for Full-Text Review by Key Question

1.01 Exercise tolerance testing

North of England evidence based guidelines development project: summary version of evidence based guideline for the primary care management angina. North of England Stable Angina Guideline Development Group. BMJ 1996;312(7034):827-32.

Alexander KP, Shaw LJ, Shaw LK, Delong ER, Mark DB, Peterson ED. Value of exercise treadmill testing in women. J Am Coll Cardiol 1998;32(6):1657-64.

Chiamvimonvat V, Sternberg L. Coronary artery disease in women. Can Fam Physician 1998;44:2709-17.

Detrano R, Gianrossi R, Froelicher V. The diagnostic accuracy of the exercise electrocardiogram: a meta-analysis of 22 years of research. Prog Cardiovasc Dis 1989;32(3):173-206.

Detrano R, Gianrossi R, Mulvihill D, Lehmann K, Dubach P, Colombo A, et al. Exercise-induced ST segment depression in the diagnosis of multivessel coronary disease: a meta analysis. J Am Coll Cardiol 1989;14(6):1501-8.

Detrano R, Janosi A, Lyons KP, Marcondes G, Abbassi N, Froelicher VF. Factors affecting sensitivity and specificity of a diagnostic test: the exercise thallium scintigram. Am J Med 1988;84(4):699-710.

Detrano R, Lyons KP, Marcondes G, Abbassi N, Froelicher VF, Janosi A. Methodologic problems in exercise testing research. Are we solving them? Arch Intern Med 1988;148(6):1289-95.

Detrano R. Variability in the accuracy of the exercise ST-segment in predicting the coronary angiogram: how good can we be? J Electrocardiol 1992;24(Suppl):54-61.

Fleischmann KE, Hunink MG, Kuntz KM, Douglas PS. Exercise echocardiography or exercise SPECT imaging? A meta-analysis of diagnostic test performance. JAMA 1998;280(10):913-20.

Garber AM, Solomon NA. Cost-effectiveness of alternative test strategies for the diagnosis of coronary artery disease. Ann Intern Med 1999;130(9):719-28.

Gianrossi R, Detrano R, Mulvihill D, Lehmann K, Dubach P, Colombo A, et al. Exercise-induced ST depression in the diagnosis of coronary artery disease. A meta-analysis. Circulation 1989;80(1):87-98.

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Gibbons RJ, Balady GJ, Beasley JW, Bricker JT, Duvernoy WF, Froelicher VF, et al. ACC/AHA Guidelines for Exercise Testing. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Exercise Testing). J Am Coll Cardiol 1997;30(1):260-311

Hlatky MA, Pryor DB, Harrell FE, Jr., Califf RM, Mark DB, Rosati RA. Factors affecting sensitivity and specificity of exercise electrocardiography. Multivariable analysis. Am J Med 1984;77(1):64-71.

Appendix D: Articles Eligible for Full-Text Review by Key Question (continued)

Iskandrian AE, Heo J, Nallamothu N. Detection of coronary artery disease in women with use of stress single-photon emission computed tomography myocardial perfusion imaging. J Nucl Cardiol 1997;4(4):329-35.

Jolliffe JA, Rees K, Taylor RS, Thompson D, Oldridge N, Ebrahim S. Exercise-based rehabilitation for coronary heart disease. Cochrane Database Syst Rev 2000;4.

Kotler TS, Diamond GA. Exercise thallium-201 scintigraphy in the diagnosis and prognosis of coronary artery disease. Ann Intern Med 1990;113(9):684-702.

Kuntz KM, Tsevat J, Weinstein MC, Goldman L. Expert panel vs decision-analysis recommendations for postdischarge coronary angiography after myocardial infarction. JAMA 1999;282(23):2246-51.

Kwok Y, Kim C, Grady D, Segal M, Redberg R. Meta-analysis of exercise testing to detect coronary artery disease in women. Am J Cardiol 1999;83(5):660-6.

Lau J, Ioannidis JP, Balk EM, Milch C, Terrin N, Chew PW, et al. Diagnosing acute cardiac ischemia in the emergency department: a systematic review of the accuracy and clinical effect of current technologies. Ann Emerg Med 2001;37(5):453-60.

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Miller TD, Roger VL, Milavetz JJ, Hopfenspirger MR, Milavetz DL, Hodge DO, et al. Assessment of the exercise electrocardiogram in women versus men using tomographic myocardial perfusion imaging as the reference standard. Am J Cardiol 2001;87(7):868-73.

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Selker HP, Zalenski RJ, Antman EM, Aufderheide TP, Bernard SA, Bonow RO, et al. An evaluation of technologies for identifying acute cardiac ischemia in the emergency department: a report from a National Heart Attack Alert Program Working Group. Ann Emerg Med 1997;29(1):13-87.

Shaw LJ, Hachamovitch R, Redberg RF. Current evidence on diagnostic testing in women with suspected coronary artery disease: choosing the appropriate test. Cardiol Rev 2000;8(1):65-74.

Williams SV, Fihn SD, Gibbons RJ. Guidelines for the management of patients with chronic stable angina: diagnosis and risk stratification. Ann Intern Med 2001;135(7):530-47.

1.02 Exercise echocardiogram

North of England evidence based guidelines development project: summary version of evidence based guideline for the primary care management angina. North of England Stable Angina Guideline Development Group. BMJ 1996;312(7034):827-32.

Appendix D: Articles Eligible for Full-Text Review by Key Question (continued)

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de Albuquerque Fonseca L, Picano E. Comparison of dipyridamole and exercise stress echocardiography for detection of coronary artery disease (a meta-analysis). Am J Cardiol 2001;87(10):1193-6; A4.

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Fleischmann KE, Hunink MG, Kuntz KM, Douglas PS. Exercise echocardiography or exercise SPECT imaging? A meta-analysis of diagnostic test performance. JAMA 1998;280(10):913-20.

Garber AM, Solomon NA. Cost-effectiveness of alternative test strategies for the diagnosis of coronary artery disease. Ann Intern Med 1999;130(9):719-28.

Garzon PP, Eisenberg MJ. Functional testing for the detection of restenosis after percutaneous transluminal coronary angioplasty: a meta-analysis. Can J Cardiol 2001;17(1):41-8.

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Appendix D: Articles Eligible for Full-Text Review by Key Question (continued)

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1.03 Coronary artery calcification score

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Budoff MJ, Diamond GA, Raggi P, Arad Y, Guerci AD, Callister TQ, et al. Continuous probabilistic prediction of angiographically significant coronary artery disease using electron beam tomography. Circulation 2002;105(15):1791-6.

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Doherty TM, Detrano RC, Mautner SL, Mautner GC, Shavelle RM. Coronary calcium: the good, the bad, and the uncertain. Am Heart J 1999;137(5):806-14.

Engman ML. An update on EBCT (Ultrafast CT) scans for coronary artery disease. J Insur Med 1998;30(3):175-9.

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Guerci AD, Spadaro LA, Goodman KJ, Lledo-Perez A, Newstein D, Lerner G, et al. Comparison of electron beam computed tomography scanning and conventional risk factor assessment for the prediction of angiographic coronary artery disease. J Am Coll Cardiol 1998;32(3):673-9.

Appendix D: Articles Eligible for Full-Text Review by Key Question (continued)

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Kennedy J, Shavelle R, Wang S, Budoff M, Detrano RC. Coronary calcium and standard risk factors in symptomatic patients referred for coronary angiography. Am Heart J 1998;135(4):696-702.

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Shavelle DM, Budoff MJ, LaMont DH, Shavelle RM, Kennedy JM, Brundage BH. Exercise testing and electron beam computed tomography in the evaluation of coronary artery disease. J Am Coll Cardiol 2000;36(1):32-8.

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2.01 Aspirin

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Appendix D: Articles Eligible for Full-Text Review by Key Question (continued)

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ISIS-3: a randomised comparison of streptokinase vs tissue plasminogen activator vs anistreplase and of aspirin plus heparin vs aspirin alone among 41,299 cases of suspected acute myocardial infarction. ISIS-3 (Third International Study of Infarct Survival) Collaborative Group. Lancet 1992;339(8796):753-70.

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Basinski A, Naylor CD. Aspirin and fibrinolysis in acute myocardial infarction: meta-analytic evidence for synergy. J Clin Epidemiol 1991;44(10):1085-96.

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Appendix D: Articles Eligible for Full-Text Review by Key Question (continued)

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Mehta RH, Bossone E, Eagle KA. Current concepts in secondary prevention after acute myocardial infarction. Herz 2000;25(1):47-60.

Oler A, Whooley MA, Oler J, Grady D. Adding heparin to aspirin reduces the incidence of myocardial infarction and death in patients with unstable angina. A meta-analysis. JAMA 1996;276(10):811-5.

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Appendix D: Articles Eligible for Full-Text Review by Key Question (continued)

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2.02 Beta-blockers

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Appendix D: Articles Eligible for Full-Text Review by Key Question (continued)

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Appendix E: Cost-effectiveness Analyses and Decision Analyses Articles (N = 21)

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Appendix F: Clinical Practice Guidelines (continued)

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Appendix F: Clinical Practice Guidelines (continued)

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Appendix F: Clinical Practice Guidelines (continued)

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Appendix G: Evidence Reports (N = 9)

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Appendix H: Abbreviations and Acronyms

ACE	angiotensin converting enzyme
AHRQ	Agency for Healthcare Research and Quality
β-blockers	beta-blockers
CABG	coronary artery bypass grafting
CHD	coronary heart disease
CKMB	creatinine kinase myocardial bands
CHF	congestive heart failure
CVD	cardiovascular disease
CI	confidence interval
DTS	Duke Treadmill Score
ECHO	echocardiography
EKG	electrocardiogram
EPC	Evidence-based Practice Center
ETT	exercise treadmill test
HDL	high density lipoprotein
HDL-C	high density lipoprotein cholesterol
LDL	low density lipoprotein
LDL-C	low density lipoprotein cholesterol
Lp(a)	lipoprotein a
Mg	milligrams
MI	myocardial infarction
Mmol	millimole
MRC/BHF	Medical Research Council/British Heart Foundation
N	number
NA	not available
NHLBI	National Heart Lung and Blood Institute
OR	odds ratio
PCI	percutaneous coronary intervention
PTCA	percutaneous coronary angioplasty
SES	socioeconomic status
SPECT	single photon emission computed tomography
RR	relative risk

Names of studies:

4S	Scandinavian Simvastatin Survival Study
AFCAPS/TEXCAPS	Air Force/Texas Coronary Artherosclerosis Prevention Study
AIRE	Acute Infarction Ramipril Efficacy
ARIC	Atherosclerosis Risk in Communities
BARI	Bypass Angioplasty Revascularization Investigation
BENESTENT	Belgian Netherlands Stent study
BBPP	Beta Blocker Pooling Project
CABRI	Coronary Angioplasty versus Bypass Revascularisation Investigation

Appendix H: Abbreviations and Acronyms (continued)

Names of studies (continued):

CARDIA	Coronary Artery Risk Development in Young Adults
CARE	Cholesterol and Recurrent Events trial
CCS	Chinese Cardiac Study
CHS	Cardiovascular Health Study
CIBIS, CIBIS II	Cardiac Insufficiency Bisoprolol Study
COPERNICUS	Carvedilol Prospective Randomized Cumulative Survival Study
CURE	Clopidogrel in Unstable Angina to Prevent Recurrent Events Study
Consensus	Cooperative New Scandinavian Enalapril Survival Study
DOM	Diagnostisch Onderzoek Mammacarcinoom (Diagnostic Investigation of Mammary Cancer) ???
EPIC	Evaluation of 7E3 for the Prevention of Ischemic Complications
EPILOG	Evaluation of Percutaneous Transluminal Coronary Angioplasty to Improve Long-Term Outcome with Abciximab Glycoprotein IIb/IIIa Blockade
EPISTENT	Evaluation of Platelet IIb/IIIa Inhibitor for Stenting
FHS	Framingham Heart Study;
FTT	Fibrinolytic Therapy Trialists' Collaborative Group
GISSI	Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico
GUSTO-I	Global Utilization of Strategies to Open Occluded Coronary Arteries Trial I
GUSTO-IV ACS	Global Utilization of Strategies to Open Occluded Coronary Arteries Trial IV in Acute Coronary Syndromes
HHP	Honolulu Heart Program
HOPE	Hypertension Optimal Treatment
INDANA	INdividual Data ANalysis of Antihypertensive Intervention Trials
ISIS-2	Second International Study of Infarct Survival
ISIS-4	Fourth International Study of Infarct Survival) Collaborative Group
LIPID	Long-term Intervention with Pravastatin in Ischaemic Disease
MERIT-HF	Metoprolol Extended-Release Randomized Intervention Trial in Heart Failure
MRFIT	Multiple Risk Factor Intervention Trial
MUSIC	Multicenter Ultrasound Stenting In Coronary study
NHANES	National Health and Examination Survey
NMRI	National Registry of Myocardial Infarction
OASIS	Organization to Assess Strategies for Ischemic Syndromes
PCI-CURE	Percutaneous Coronary Intervention Substudy of Clopidogrel in Unstable Angina to Prevent Recurrent Events Study
POSCH	Program on the Surgical Control of the Hyperlipidemias
PAMI	Primary Angioplasty in Myocardial Infarction
PARAGON	Platelet IIb/IIIa Antagonism for the Reduction of Acute Coronary Syndrome events in a Global Organization Network

Appendix H: Abbreviations and Acronyms (continued)

Names of studies (continued):

PHS	Physicians' Health Study
PR	Puerto Rico Heart Health Program
PRISM	Platelet Receptor Inhibition in Ischemic Syndrome Management
PRISM-PLUS	Platelet Receptor Inhibition in Ischemic Syndrome Management in Patients Limited by Unstable Signs and Symptoms
PURSUIT	Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression using Integrilin Therapy
RITA	Randomised Intervention Treatment of Angina
SAVE	Survival and Ventricular Enlargement
SHS	Strong Heart Study
SOLVD	Studies of Left Ventricular Dysfunction
Syst-China	Systolic Hypertension in China Study
TRACE	Trandolapril in Cardiac Evaluation
WOSCOPS	West of Scotland Coronary Prevention Study