Evidence Report/Technology Assessment
Number 80

Results of Systematic Review of Research on Diagnosis and Treatment of Coronary Heart Disease in Women

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AHRQ is the lead Federal agency charged with supporting research designed to improve the quality of health care, reduce its cost, address patient safety and medical errors, and broaden access to essential services. AHRQ sponsors and conducts research that provides evidence-based information on health care outcomes; quality; and cost, use, and access. The information helps health care decisionmakers—patients and clinicians, health system leaders, and policymakers—make more informed decisions and improve the quality of health care services.

Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-Based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review prior to their release.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome written comments on this evidence report. They may be sent to: Director, Center for Practice and Technology Assessment, Agency for Healthcare Research and Quality, 6010 Executive Blvd., Suite 300, Rockville, MD 20852.

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Structured Abstract

Objectives. The Agency for Healthcare Research and Quality and several partner organizations charged the University of California, San Francisco-Stanford Evidence-based Practice Center to review the evidence on five key topics related to coronary heart disease (CHD) in women: (1) accuracy of noninvasive testing for diagnosis of CHD; (2) efficacy of treatments; (3) strength of risk factors and efficacy of risk factor reduction; (4) utilization of tests and treatments in men compared to women, and (5) accuracy of biomarkers for diagnosis of myocardial infarction. These five key questions included 42 discrete subtopics. We used standard methods to systematically review the medical literature to address each subtopic. The evidence identified was reviewed, graded and summarized for each subtopic and further research was recommended as appropriate.

Search Strategy. We identified 6,403 citations from searching electronic databases from 1985 through July 2001, reviewing bibliographies, and by recommendation from our peer reviewers.

Selection Criteria. After the titles were screened, abstracts were reviewed independently by two investigators who coded each abstract for eligibility for full text review. In order to be categorized as providing evidence regarding a research question, the article had to address the predictor variable and the clinical outcome and contain data to address the question specifically in women. Articles meeting inclusion criteria were abstracted independently on a standardized form by two investigators, and received a quality score based on predefined criteria. All studies rated good or fair were included in this review.

Data Collection and Analysis. The titles and abstracts were entered and coded in EndNote® files. Data from the standardized review form was entered into a Microsoft® Access database, which allowed tracking of the eligibility, quality and type of study of each article reviewed.

Main Results. We reviewed the full text of 819 articles and found 162 that provided evidence in women. We found no data in women to address 13 of the subtopics, weak data to address 15, fair data for eight and good data to address six.

- Fair evidence suggests that the accuracy of exercise EKG and exercise thallium testing for CHD in women is low. The accuracy of exercise echocardiography appears to be higher, but data are limited.
- Fair or good evidence suggests that beta-blockers, aspirin and angiotensin converting enzyme inhibitors reduce risk for CHD events and that nitrates are ineffective in women with known heart disease.
- Fair evidence suggests that glycoprotein IIb/IIIa inhibitor drugs given to women undergoing percutaneous revascularization result in a reduced risk of CHD events and need for revascularization, but treatment of women suffering acute coronary syndromes may result in increased mortality. This was the only treatment for which there was evidence of a possible interaction by gender: men treated with IIb/IIIa drugs during acute coronary syndromes appear to benefit.

- Fair or good evidence suggests that hyperlipidemia, diabetes, and hyperhomocysteinemia are risk factors for CHD in women.
- Fair or good evidence suggests that smoking cessation after MI and treatment of hypertension and hyperlipidemia lower risk for CHD events in women.
- We found little evidence to address the key questions in women of different races or ethnicities. The only evidence regarding differences by ethnicity suggests that African-American women may benefit more from treatment of hypertension than white women.

Conclusions. New or updated systematic reviews of the literature appear to be feasible and would likely provide clinically important information for 14 of the subtopics. The major limitation in performing these systematic reviews is that data stratified by gender and race/ethnicity from completed studies may not available. We recommend that, in addition to requiring participation of women and minorities in research, the National Institutes of Health, U.S. Food and Drug Administration and other funding and regulatory agencies insist that outcome data by subgroup be published or archived.

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Overview

Coronary heart disease (CHD) is the most common disease and cause of death in women, accounting for over 250,000 deaths in women per year. Over the last two decades, multiple important studies have helped define accurate clinical tests, risk factors, preventive interventions, and effective therapies for CHD. Unfortunately, many of these studies have either excluded women entirely or included only limited numbers of women and minorities. Thus, much of the evidence supporting contemporary recommendations for testing, prevention, and treatment of coronary disease in women is extrapolated from studies conducted predominantly in middle-aged men. The two best approaches to obtain additional evidence on diagnosis and treatment of CHD in women are to conduct large studies that include adequate numbers of women and minorities to answer the research question or to perform systematic reviews and meta-analyses summarizing effect estimates by subgroup.

The Agency for Healthcare Research and Quality (AHRQ) and several partner organizations charged the University of California, San Francisco (UCSF)-Stanford Evidence-based Practice Center (EPC) with the development of an initial review of evidence-based research on five key topics, including 42 subtopic areas related to the diagnosis and management of coronary heart disease in women and minority race/ethnic groups.

The three major aims of this project were to (1) determine whether any of the 42 specific subtopic areas have been adequately addressed in systematic reviews or definitive individual studies, (2) summarize the information from the evidence-based studies identified that address the subtopics, and (3) describe the feasibility of further research for each subtopic.

Key Questions

1. **Are there accurate non-invasive approaches to evaluating suspected coronary disease in women? (3 subtopics, 1.01-1.03)**
   - 1.01 exercise tolerance testing, with and without perfusion imaging
   - 1.02 exercise echocardiogram
   - 1.03 coronary artery calcification score
2. **Are there effective treatments for women with coronary heart disease? (15 subtopics 2.01-2.12 with secondary and primary prevention considered separately as appropriate)**
   - 2.01 aspirin
     - a. secondary prevention
     - b. primary prevention
   - 2.02 beta-blockers
     - a. secondary prevention
     - b. primary prevention
   - 2.03 angiotensin converting enzyme inhibitors
     - a. secondary prevention
     - b. primary prevention
   - 2.04 calcium channel blockers
   - 2.05 nitrates
   - 2.06 heparin, including low molecular weight heparin
   - 2.07 glycoprotein IIb/IIIa inhibitor drugs
   - 2.08 thrombolysis
   - 2.09 ticlopidine
   - 2.10 clopidogrel

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2.11 angioplasty or stenting
2.12 coronary artery bypass surgery

3. **What are the risk factors for coronary heart disease in women and does modifying these risk factors result in reduced risk for coronary heart disease events? (20 subtopics labeled 3.01-3.12 with subtopic as a risk factor for CHD or treatment/modification of a risk factor for CHD prevention considered separately where appropriate)**
   - 3.01 hypertension
     - a. as a risk factor
     - b. treatment
   - 3.02 diabetes
     - a. as a risk factor
     - b. treatment
   - 3.03 hyperlipidemia (LDL-, HDL-cholesterol, triglycerides, lipoprotein (a))
     - a. as a risk factor
     - b. treatment
   - 3.04 elevated homocysteine
     - a. as a risk factor
     - b. treatment
   - 3.05 C-reactive protein
     - a. as a risk factor
     - b. treatment
   - 3.06 cigarette smoking
     - a. as a risk factor
     - b. smoking cessation
   - 3.07 obesity
     - a. as a risk factor
     - b. weight reduction
   - 3.08 inactivity
     - a. as a risk factor
     - b. exercise
   - 3.09 age
   - 3.10 age at menopause
   - 3.11 ethnicity
   - 3.12 socioeconomic status
4. **Are accurate tests (defined in #1), effective treatments (defined in #2), or risk factor modifications (defined in #3) underutilized in women (or among women of various race/ethnic populations) compared to men?**
5. **What is the prognostic value of biochemical markers for diagnosis of acute myocardial infarction or unstable angina in women? (3 subtopics labeled 5.01-5.02)**
   - 5.01 troponin
   - 5.02 creatinine kinase myocardial bands including isoforms
   - 5.03 myoglobin

Methodology

Data Sources

To assemble a bibliographic database of systematic reviews and articles that might provide definitive primary data, we searched MEDLINE®, the Cochrane Database and DARE from 1985 to July 2001, reviewed the bibliographies of retrieved articles and sought suggestions for additional articles from an expert Advisory Board and Peer Reviewers.

Inclusion Criteria

To be categorized as an article that provided evidence regarding a key question, the article had to address the subtopic and contain data specific to women. For subtopics with CHD events as the outcome (effects of risk factors, risk factor modification, and treatment), we required that the outcome be CHD events or mortality. For key question 1, the gold standard test to which noninvasive test results were compared was required to be angiographic evidence of coronary disease. When systematic reviews were not available to address the subtopic, we also searched for clinical trials, prospective cohort, and cross-sectional studies as appropriate.

Search Terms

We conducted a separate search for evidence regarding each of the 42 subtopics using the same search terms for CHD outcomes (i.e., cardiovascular diseases or heart diseases or heart or cardiovas* or cardiac* or coronary or myocardial) and for systematic reviews (i.e., publication type: meta-analysis or meta-analy* or metaanaly* or metanaly* or review or overview and systematic or methodologic* or evidence*) and added terms specific to each subtopic.

Data Abstraction

One UCSF-Stanford EPC physician investigator reviewed all identified titles and excluded those that clearly did not meet inclusion criteria. The abstracts of remaining articles were reviewed by two UCSF-Stanford EPC physician investigators, who independently classified eligibility. The full text of remaining eligible articles was reviewed independently by two UCSF-Stanford EPC physician investigators using a standardized abstraction form to classify eligibility and rate quality as fair or good based on predefined criteria.

Evaluation of Evidence Provided by Identified Articles

We reviewed and summarized in detail the findings of each systematic review and clinical trial identified. A general summary of the overall findings from prospective cohort and cross-sectional studies pertinent to each subtopic is also

provided. Finally, we summarized the answer to each subtopic question, graded the evidence as none, weak, fair or good, compared results in women and men and recommended a new or updated systematic review if feasible.

Results of Literature Searches

The searches identified 6,403 citations. After review of titles and abstracts, 810 articles were retrieved and reviewed in full text. The 162 articles that provided evidence in women are characterized with regard to study design and quality as follows:

	Total	Good Quality	Fair Quality
Systematic review	32	17	15
Randomized trial	25	17	8
Prospective cohort	66	59	7
Cross-sectional	39	25	14
Total	162	118	44

In total, we reviewed the full text of 272 systematic reviews and 55 randomized trials; only 32 systematic reviews and 25 randomized trials contained evidence on the key question in women. In general, most authors of systematic reviews and randomized trials that we identified did not perform subgroup analyses in women or ethnic minorities, even though a substantial proportion of participants were women or minorities.

Of the articles that provide evidence to address one of the key questions in women, only 35 percent are systematic reviews or randomized trials. The remaining cohort and cross-sectional studies provide some evidence, but the study designs are susceptible to bias due to confounding.

Findings

General

- We found no data in women to address 13 of the subtopic questions, weak data to address 15, fair data for eight, and good data to address six.
- In general, no evidence addressed differences in the accuracy of diagnostic tests, strength of risk factors, effects of treatment, and prognostic value of markers for ischemia in women of different races or ethnicity. The only evidence regarding differences by ethnicity suggests that African-American women may benefit more from treatment of hypertension than white women.

Non-invasive diagnostic testing

Fair evidence suggests that the accuracy of exercise EKG and exercise thallium testing for CHD in women is low. The accuracy of exercise echocardiography appears to be higher, but data are limited.

Weak evidence suggests that the absence of coronary calcification may be useful for ruling out disease in both men and women.

Treatments

- Fair or good evidence suggests that beta-blockers, aspirin, and angiotensin converting enzyme inhibitors reduce risk for CHD events in women with known heart disease.
- Good evidence suggests that nitrates do not reduce risk for CHD events in women with known heart disease.
- Fair evidence suggests that glycoprotein IIb/IIIa inhibitor drugs given to women undergoing percutaneous revascularization result in a reduced risk of CHD events and need for revascularization, but treatment in women suffering acute coronary syndromes may result in increased mortality. This was the only treatment for which there was evidence of a possible interaction by gender: men treated with IIb/IIIa drugs during acute coronary syndromes appear to benefit.
- Evidence regarding the efficacy of important treatments such as calcium channel blockers, heparin, ticlopidine, clopidogrel, coronary artery bypass surgery, percutaneous angioplasty and coronary stenting in women is weak.

Risk factors and risk factor modification

- Fair or good evidence suggests that hyperlipidemia, diabetes and hyperhomocysteinemia are risk factors for CHD in women.
- Only weak evidence links most of the risk factors of interest and CHD risk in women. This is primarily because all of the studies addressing the strength of risk factors are observational and very few good-quality systematic reviews have been completed.
- Risk factors for CHD seem to be equally strong in men and women with the possible exceptions of age, diabetes, and certain lipoproteins.
- Fair or good evidence suggests that smoking cessation after MI and treatment of hypertension and of hyperlipidemia lower risk for CHD events in women.
- No evidence was found for the effectiveness of other interventions to modify risk factors in women.

Differences in utilization

- Weak evidence suggests that men are more likely than women to undergo diagnostic testing and treatment for CHD, but that women are more likely than men to be treated for hypertension.

- Differences in utilization of tests and treatment might be explained by differences in severity of disease or comorbidities between men and women or by overuse of tests and treatments in men.

Biochemical Markers

- No evidence was found to address the diagnostic value of troponins, creatine kinase or myoglobin in women with ischemia.

Future Research

We believe that a new or updated systematic review is feasible and would be provide clinically important information for the following subtopics:

- Exercise tolerance testing
- Exercise echocardiogram
- Aspirin for secondary prevention
- Beta-blockers for secondary prevention
- Hypertension as a risk factor
- Diabetes as a risk factor
- Hyperlipidemia as a risk factor
- Hyperlipidemia treatment
- Homocysteine as a risk factor
- Smoking as a risk factor
- Smoking cessation
- Obesity as a risk factor
- Age as a risk factor
- Differences in utilization between men and women

The major limitation in performing these systematic reviews will be the availability of data on women and minority populations. Women typically comprise 20 to 30 percent of participants in randomized trials, but risk estimates for women are infrequently published. Thus, investigators attempting to systematically review the medical literature must attempt to contact investigators and obtain unpublished risk estimates. For a variety of reasons, these subgroup analyses are often not available. Thus, even though the National Institutes of Health and other funding agencies appear to have succeeded in assuring that some proportion of women and minorities are included in randomized trials, data from such participation are not generally available. We recommend that, in addition to demanding participation of women and minorities in research, the National Institutes of Health, U.S. Food and Drug Administration and other funding and regulatory agencies insist that primary and secondary outcome data by subgroup be published or archived. Similarly, we recommend that funding agencies that support systematic reviews require inclusion of subgroup estimates in women and minorities whenever possible.

Availability of the Full Report

The full evidence report from which this summary was taken was prepared for the Agency for Healthcare Research and Quality (AHRQ) by the University of California, San Francisco-Stanford Evidence-based Practice Center, under Contract No. 290-97-0013. It is expected to be available in May 2003. At that time, printed copies may be obtained free of charge from the AHRQ Publications Clearinghouse by calling 800-358-9295. Requesters should ask for Evidence Report/Technology Assessment No. 80, *Results of Systematic Review of Research on Diagnosis and Treatment of Coronary Heart Disease in Women*. In addition, Internet users will be able to access the report and this summary online through AHRQ's Web site at www.ahrq.gov.

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Chapter 1: Introduction

Coronary Heart Disease in Women

Coronary heart disease (CHD) is the most common disease and the most common cause of death in women. Approximately one in two women develop CHD and one in three die from it,[1] accounting for over 250,000 deaths in women per year.[2] Despite the very high prevalence of CHD in women, it has traditionally been thought of as a disease of middle-aged men, perhaps because women tend to develop CHD about a decade later in life than men.[3] Over the last two decades, multiple important studies have helped define accurate clinical tests, important risk factors, preventive interventions, and effective therapies for CHD. Unfortunately, many of these studies have either excluded women entirely or included only limited numbers of women.[4] Thus, much of the evidence that supports contemporary recommendations for testing, prevention, and treatment of coronary disease in women is extrapolated from studies conducted predominantly in middle-aged men. Applying the findings of studies in men to management of CHD in women may not be appropriate, since the symptoms of CHD, natural history, and response to therapy differ in men and women.[2]

The first symptoms of CHD in women are often atypical, and angina is less predictive of CHD in women than in men.[5] Compared to men, early mortality following myocardial infarction is higher in women,[6] perioperative complications and mortality after percutaneous angioplasty and coronary artery bypass surgery are higher,[7, 8] and long-term prognosis is worse.[9-11] Mortality rates for CHD among African-American women are about double those in white women.[11] It is uncertain if these unfavorable clinical outcomes are gender-specific, reflecting more advanced age, smaller body size, or more frequent and severe risk factors and comorbid illnesses in women, or whether it is the result of late diagnosis and less optimal care.

Some studies suggest that women and nonwhites are less likely to undergo intensive and invasive evaluation and treatment for cardiac disease than white men with similar symptoms.[12-14] These differences might be the result of overuse of tests and treatments in men, older age and more comorbid illnesses in women, or gender and race bias among health care providers.

Approaches to Improving Evidence on Diagnosis and Treatment of CHD in Women

Because many studies of diagnosis and treatment for CHD have excluded women or included only a small proportion of women, clinicians have typically been forced to generalize the findings of studies conducted predominantly in middle-aged white men to women and minorities. There are three basic approaches to obtain better evidence regarding diagnosis and treatment of CHD in women and minority populations: 1) perform clinical studies that include adequate numbers of women and minorities to determine outcomes for these subgroups separately; 2) perform systematic reviews and meta-analyses using subgroup estimates by gender and ethnicity to calculate summary estimates of effect and determine if there are interactions by gender; 3) perform systematic reviews and multivariate meta-analyses to determine if gender and ethnicity are predictors of outcome. The first option may be feasible or even required in some cases, such as the role of postmenopausal hormone therapy to prevent CHD in women.[15, 16] In general, however, this approach is not feasible because it is too expensive to study adequate numbers of women and minorities to answer each clinical question. Given this, the next best option is to conduct systematic reviews and meta-analyses to calculate summary estimates of outcome in women and minorities. This approach is limited because studies that include a substantial proportion of women often do not publish subgroup estimates of effect in women and minorities. Thus, performing a meta-analysis typically requires contacting the authors of studies and requesting estimates of the outcomes by subgroup. Authors are sometimes unable or unwilling to provide such subgroup estimates, limiting the completeness of meta-analyses. Performing multivariate meta-analysis to determine if gender or ethnicity is a predictor of outcome can yield information on whether the outcome differs by gender or ethnicity, however, it is often under-powered (because the sample size is equal to the number of studies in the meta-analysis) and does not provide specific estimates of the effects in women.

Key Questions

Recognizing the importance of the issues raised above, multiple groups have requested evidence-based research pertinent to diagnosis and management of CHD in women and minorities. The groups include an ad hoc women's health coalition (American Heart Association, American College of Cardiology, American College of Obstetricians and Gynecologists, American Society of Echocardiography, Association of Black Cardiologists, Jacobs Institute of Women's Health, Mayo Clinic Women's Heart Clinic, Society for Women's Health Research, and WomenHeart: National Coalition for Women with Heart Disease), the American Association for Clinical Chemistry and the NIH Office of Research in Women's Health. The Centers for Medicare and Medicaid Services and Harvard Pilgrim Health Services have also expressed interest. Concern about sex and gender-based differences in diagnosis and treatment of CHD was also noted in the Senate

Appropriations Committee's report accompanying the FY 2000 Departments of Labor, Health and Human Services, and Education and Related Agencies Appropriations bill. Specifically, these groups have requested evidence related to: 1) the accuracy of noninvasive tests for diagnosis of CHD in women; 2) the value of traditional treatments for CHD in women; 3) the importance of risk factors for CHD in women; 4) appropriate utilization of tests, treatments and risk factor modification in women, and 5) the prognostic value of biologic markers for diagnosis of acute coronary syndromes in women.

The University of California, San Francisco (UCSF)-Stanford Evidence-based Practice Center (EPC) worked with staff at the Agency for Healthcare Research and Quality to refine these five areas of interest to include the specific questions listed in Table 1. Of note, these questions include 42 separate topic areas (e.g., the accuracy of *exercise tolerance testing*; the effect of treatment with *aspirin*, the strength of *hypertension* as a risk factor, the prognostic value of *troponins*) and multiple questions concerning each (what is the accuracy of *exercise tolerance testing* in women? does the accuracy of *exercise tolerance testing* differ in men and women? does the accuracy of *exercise tolerance testing* differ by ethnicity?). We assessed the strength of risk factors separately from the effect of modifying the same risk factor, and assessed the effect of treatments in primary and secondary prevention separately. Thus, the total number of specific questions is large, although many are related.

The major aim of this report is to determine if any of these specific questions have been adequately addressed in systematic reviews or in methodologically sound individual studies with adequate numbers of women and minorities**.** We identified evidence-based studies that address the key questions, assessed their quality, and described and summarized their findings.

Chapter 2: Methodology

Identification of Evidence

Data Sources

We searched MEDLINE®, the Cochrane Database and DARE from 1985 through July 2001. We also reviewed the bibliographies of articles fitting our inclusion criteria and asked our expert Technical Expert Advisory Board and Peer Reviewers (Appendix A) to notify us of articles that provide evidence to address the key questions. Articles outside of the above date parameters were included if recommended by our advisors or reviewers.

Search Terms

We developed search terms to identify the outcome variable (i.e., mortality and coronary disease events), the predictors (defined by the individual key questions), and the study design (systematic reviews, Appendix B). We defined coronary disease events as nonfatal myocardial infarction and CHD death. We conducted a separate search for evidence regarding each predictor using the specific search terms listed in Appendix B. Each search used the same search terms for the outcome variable and for systematic review.

For each topic, we searched the databases above for evidence from systematic reviews. To identify evidence regarding the accuracy of diagnostic tests for CHD in women (questions 1.01-1.03), we additionally reviewed large cross-sectional studies. To identify evidence regarding the efficacy of treatments for CHD in women (questions 2.01-2.12), we also sought large randomized clinical trials that provided data on outcomes in women. To identify evidence regarding the strength of the association of traditional risk factors and CHD in women (questions 3.01-3.12), we also sought large prospective cohort studies with multivariate adjustment for potential confounders. To identify evidence regarding the utilization of accurate tests, effective treatments, and risk factor modifications in women compared to men (question 4.0); we also reviewed large prospective cohort and cross-sectional studies with multivariate adjustment for potential confounders. To identify evidence regarding the prognostic value of troponins, creatine kinase myocardial bands, and myoglobin (questions 5.01-5.03); we also sought large prospective cohort studies with multivariate adjustment for potential confounders.

Inclusion Criteria

To be categorized as an article that provides evidence regarding a key question, the article had to address the predictor variable (as defined by the key questions and search terms listed in Appendix B) and the outcome of CHD events or mortality (with the exception of angiographic evidence of atherosclerosis for question 1) and contain data to address the question specifically in women.

Article Identification

An initial search using the terms listed in Appendix B identified articles that potentially provided evidence regarding the key questions. One UCSF-Stanford EPC physician investigator reviewed the titles and excluded those that clearly did not provide data on humans or clearly did not address the key question.

The abstracts of all remaining articles were reviewed independently by two UCSF-Stanford EPC physician investigators, who classified each article using the codes listed below. The two abstractors discussed each abstract and decided by consensus on the code that was entered into the database.

PV – the article clearly does not address the correct predictor variable (as defined by the key question)
OV - the article clearly does not address the correct outcome variable (CHD events or mortality, or for question 1, angiographic evidence of coronary atherosclerosis)
NSR – the article is a review that is clearly not systematic
NH - the article clearly does not include data on humans
NW – the article clearly does not include data on women
E – the article may contain evidence regarding the key question in women

All articles coded E were retrieved and the full text was reviewed independently by two UCSF-Stanford EPC physician investigators using a standardized abstraction form (Appendix C). If the article did not address the key question, did not include data to answer the question in women, or was a review that was not systematic, it was eliminated from further consideration. Articles that addressed a key question in women *and* were a systematic review, large prospective cohort or cross-sectional study with multivariate analysis, or a large randomized trial were classified as eligible for review. Large cohort studies, cross-sectional studies, and randomized trials were those that included 1000 or more participants.

Quality Assessment

We considered any article that addressed a key question in women *and* were a systematic review, large prospective cohort or cross-sectional study with multivariate analysis, or large randomized trial to be *fair quality.*

To be categorized as *good quality,* articles were required to meet the following additional parameters:

Systematic Reviews (questions 4-8 on the abstraction sheet in Appendix C)

- information source appropriate
- information source adequately searched
- inclusion/exclusion criteria clear and appropriate
- data abstraction performed by at least 2 independent reviewers

- principal measures of effect and the methods of combining results appropriate

Randomized Trials (questions 4-8 on the abstraction sheet in Appendix C)

- intervention randomized
- control group received placebo
- participants and research staff blinded to the intervention
- inclusion/exclusion criteria clear and appropriate
- more than 75 percent complete follow-up

Prospective Cohort Studies (questions 4-7 on the abstraction sheet in Appendix C)

- inclusion/exclusion criteria clear and appropriate
- more than 75 percent complete follow-up
- analysis includes multivariate adjustment for potential confounders
- outcome adjudicated blindly

Cross-sectional Studies

For Question 1: Non-invasive diagnostic tests (questions 7-8 on the abstraction sheet in Appendix C)):

- all women who underwent the non-invasive test also underwent angiography
- diagnosis of CAD on angiography made by investigators blinded to results of the non-invasive test

For Question 4: Utilization differences in women and men (questions 4-5 on the abstraction sheet in Appendix C)):

- inclusion/exclusion criteria clear and appropriate
- analysis includes multivariate adjustment for potential confounders

Our searches identified several articles that presented the pooled results of individual level data from multiple randomized trials or cohort studies. We treated these articles as fair quality systematic reviews. We did not rate the quality of cost-effectiveness analyses, decision analyses, evidence reports, or clinical practice guidelines.

Completeness

Determining whether evidence-based reports are complete and up-to-date is difficult. For example, if a good systematic review of randomized trials was completed in 1994 and no additional important randomized trial has been completed, the systematic review can be considered complete. However, if the results of several new trials have been published

and could alter the results of the systematic review, the review may be out-dated. Determination of completeness can only be definitively decided by a formal update of the systematic review.

Data Management and Archive

The titles and abstracts identified by each search were electronically transferred into separate EndNote[17] files identified by key question. The code assigned to each article after review of the abstract was entered in the EndNote file as a keyword. Using the EndNote keyword, articles can be classified by reason for exclusion. Lists of excluded articles categorized by reason for exclusion can be provided on request.

We also constructed a Microsoft Access[18] database that was used to enter data from the abstraction forms completed at review of the full text of articles. This database allows us to track and report the reasons for exclusion of each article for which the full text was reviewed, the type of study (systematic review, randomized trial, cohort, cross-sectional, cost-effectiveness or decision analysis, evidence report and clinical practice guideline), and the number or proportion of eligible articles that were judged good quality.

The full-text articles that were retrieved, along with the completed abstraction sheet and names of the two reviewers for each article are filed by key question in Dr. Grady's offices at the Women's Health Clinical Research Center at UCSF.

Results of Literature Searches

Our systematic reviews identified 6,403 articles that potentially addressed a key question (Figure 1). In addition, we reviewed articles that were recommended by our Technical Expert Advisory Group and Peer Reviewers (Appendix A) or were identified by review of the bibliographies of articles eligible for full text review. We searched the websites of large clinical trials and large cohort studies for additional publications. After review of the titles and abstracts of these articles, we eliminated 5,520 that did not address a key question, did not contain data on women or were a review that was not systematic Thus, we reviewed the full text of 810 articles (Appendix D). Of these, 648 did not address the key question, did not include data to answer the question in women, or were reviews that were not systematic, leaving 162 articles that provide evidence to address the key questions (Evidence Table 1).

The 162 articles that provided evidence in women are characterized with regard to study design and quality as follows:

	Total	Good Quality	Fair Quality
Systematic review	32	17	15
Randomized trial	25	17	8
Prospective cohort	66	59	7
Cross-sectional	39	25	14
Total	162	118	44

Good quality articles are denoted with the superscript "a" in Evidence Table 1. Our searches also identified 21 cost-effectiveness or decision analyses (Appendix E), 43 clinical practice guidelines (Appendix F) and nine evidence reports (Appendix G) which were not rated for quality or reviewed in detail.

Table 2 displays the key question number, the topic of the question, the total number of articles identified, the number of articles for which the full-text was reviewed, the number of articles that provide evidence regarding the key question in women and the number of good quality articles that provide evidence regarding the key question in women.

In total, we reviewed the full text of 272 systematic reviews and 55 randomized trials; only 32 systematic reviews and 25 randomized trials contained evidence on the key question in women. In general, most of authors of systematic reviews and randomized trials that we identified did not perform subgroup analyses in women or ethnic minorities, even though a substantial proportion of participants were women or minorities.

Of the articles that provide evidence to address one of the key questions in women, only 35 percent are systematic reviews or randomized trials. The remaining cohort and cross-sectional studies provide some evidence, but the study designs are susceptible to bias due to confounding.

Summary of Evidence

Hierarchy of Evidence and Completeness of Searches

We assumed that a systematic review of the literature provided the most evidence-based data to address a key question. Thus, we focused our searches by including terms to identify systematic reviews and are confident that we identified all systematic reviews published in English that provide data on any of the five key questions in women.

When systematic reviews were not available, we relied on the findings of individual large randomized trials to address key questions related to treatment (question 2.01-2.12) and risk factor modification (question 3.01b-3.08b). We reviewed articles that were recommended by our Technical Expert Advisory Board and Peer Reviewers (Appendix

A) or were identified by review of the bibliographies of articles eligible for full text review. We additionally searched the websites from large clinical trials for publications.

Key questions concerning the accuracy of non-invasive testing (1.01-1.03), the strength of CHD risk factors (3.01a-3.08a, 3.09-3.12), comparative utilization of diagnostic tests and treatments in men and women (4.0) and the prognostic value of biochemical markers (5.01-5.03) cannot be addressed by randomized trials. When systematic reviews were not available for these key questions, we relied on the findings of individual cohort or cross-sectional studies. We reviewed articles that were recommended by our Technical Expert Advisory Board and Peer Reviewers (Appendix A) or were identified by review of the bibliographies of articles eligible for full text review. We additionally searched the websites from large prospective cohort studies for publications.

For the question concerning utilization of tests and treatments (Question 4), we searched for systematic reviews. When these were not available, we relied on the findings of individual cohort or cross-sectional studies, which were identified during our database searches (Appendix B). We also consulted with our Technical Expert Advisory Board (Appendix A) to identify studies that our searches may have missed.

We tracked all decision and cost-effectiveness analyses (Appendix E), clinical practice guidelines (Appendix F) and evidence reports (Appendix G), that were identified by our searches and advisors, but we did not search specifically for these publication types and did not review these publications to determine if they address a key question in women or include evidence-based recommendations.

Summary of Studies

All good and fair quality studies are summarized. Each reference is preceded by either a "G", indicating a good quality study, or "F", indicating a fair quality study. The reasons that a study is rated only fair quality are stated at the end of each review.

If a randomized trial, prospective cohort study or cross-sectional study was summarized in a systematic review that was included in our analysis, we did not independently report the findings from the primary study.

For each systematic review and randomized trial, we describe the study design, participants, predictor and outcome variables, and the main findings. When possible, we present the findings as odds ratios (OR) or relative risks (RR) with 95 percent confidence intervals (CI) and p-values for all participants combined and for women separately. The general format for presenting the results is demonstrated in the following table:

	All Participants (N=x)			Women (N=x; y% women)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
CHD Event	x.x	x.x-y.y	.xx	x.x	x.x-y.y	.xx

We elected to present data for all participants rather than for men. If there is no evidence of an interaction by gender, the outcome estimate for all participants is the most precise and accurate estimate for all subgroups, including women. When there was evidence of an interaction by gender, or when the manuscript presented only data for men and women separately, we included estimates in the tables for men rather than for all participants.

All identified good and fair quality prospective cohort and cross-sectional studies are listed by key question. The number of cohort studies was large, multiple publications from the same cohort were identified, definitions of the predictor variable were not uniform (i.e., socioeconomic status defined as level of income, education, postal code, etc), duration of observation varied markedly, definition of the outcomes were not uniform and the quality of the studies was much more variable than for randomized trials. Given these problems, we did not describe each cohort study individually, but present a general summary of the overall findings of the cohort studies. For most of the key questions where the evidence comes entirely from cohort studies, the number and size of the studies identified allows us to make clear recommendations concerning the feasibility of conducting a systematic review. Decision analyses and cost-effectiveness analyses, evidence reports and clinical practice guidelines were not reviewed or summarized, but are listed in Appendices E, F and G.

Evidence by Ethnicity

We found very little evidence to address the five key questions in minority populations of women. Where this information is available, it is included in the description of each study and in the summaries of the evidence for each key question.

Abbreviations

The abbreviations and acronyms that were used throughout the review are listed in Appendix H.

Chapter 3: Results

Results by Key Question

QUESTION 1

1. Are there accurate non-invasive approaches to evaluating suspected coronary disease in women? (3 subtopics, labeled 1.01-1.03)

Specifically, what are the summary estimates of sensitivity, specificity, and positive and negative likelihood ratios (using angiographic diagnosis of coronary artery disease as the gold standard) for the following tests, calculated separately for women, for men, and for women restricted to major ethnic groups (Caucasian, African-American, Hispanic, Asian):

1.01 exercise tolerance testing, with and without perfusion imaging (thallium)
1.02 exercise echocardiogram (ECHO)
1.03 coronary artery calcification score

1.01 Exercise testing

G.1. 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.[19]

This is a systematic review of the English language literature published from 1966 to 1995 that provided separate estimates of the accuracy of exercise EKG and exercise thallium using planar or tomographic imaging for diagnosis of coronary atherosclerosis in women. Mean weighted estimates of accuracy are given below.

	N Studies	N Women	Sensitivity	Specificity	Likelihood Ratio+	Likelihood Ratio-
Exercise EKG	19	3,721	.61	.70	2.3	0.55
Exercise thallium	5	842	.78	.64	2.9	0.36

These non-invasive tests appear to be only moderately accurate for diagnosis of CHD in women. Exercise thallium appears to be more sensitive but less specific than exercise EKG, resulting in similar likelihood ratios.

From the ten studies that provided data on men, Kwok et al. also calculated the accuracy of exercise EKG in men and found a mean weighted sensitivity of 0.70 and specificity of 0.77, suggesting that exercise EKG is somewhat more accurate in men than in women. A prior meta-analysis,[20] using similar selection criteria, identified 147 studies including 24,074 participants, most of whom were men, and calculated a mean weighted sensitivity and specificity for exercise EKG of 0.68 and 0.77, very similar to that calculated by Kwok, et al. These studies would suggest that the positive likelihood ratio for an abnormal exercise EKG in men is about 3, somewhat higher than the summary estimate of 2.3 reported from the Kwok et al. meta-analysis in women.

Kwok et al. did not calculate a summary estimate for the accuracy of exercise thallium in men, because only two studies included in their meta-analysis included men. A prior meta-analysis using similar inclusion criteria, that identified 56 studies with 6,038 mostly male participants, found a mean weighted sensitivity of exercise thallium of 0.85 and sensitivity of 0.85.[21] Based on these findings, the positive likelihood ratio for an abnormal exercise thallium test in men is 5.7, substantially higher than the summary estimate of 2.9 reported from the Kwok et al. meta-analysis in women.

G.2. 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.[22]

The systematic review by Fleischmann et al. reviewed the accuracy of exercise single photon emission computed tomography (SPECT) and exercise echocardiography (see 1.02). The authors searched Medline for English language articles published from 1990 to 1997. The main results are given below (likelihood ratios were calculated from the summary weighted sensitivity and specificity). The sensitivity was high, but the specificity of exercise SPECT was low, resulting in a low positive likelihood ratio.

	N Studies	N Subjects	% Women	Sensitivity	Specificity	Likelihood Ratio+	Likelihood Ratio-
Exercise SPECT	27	3237	30	.87	.64	1.9	0.20

Unfortunately, the analysis does not provide separate estimates of the accuracy of these tests among women. Multivariate analyses suggested that fewer men (more women) in a study was associated with lower accuracy for exercise SPECT.

F.3. 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;4:329-35.[23]

This cross-sectional study provides data on the accuracy of exercise single-photon emission computed tomography (SPECT) imaging with thallium-201 in 727 men (87 percent with CHD) and 266 women (81 percent with CHD). The definition of an abnormal exercise test was not provided. Coronary artery disease was defined as 50 percent or greater narrowing of one or more of the major coronary arteries.

Exercise thallium SPECT	N	Sensitivity	Specificity	Likelihood Ratio+*	Likelihood Ratio-*
Women	266	.72	.69	2.3	.41
Men	727	.92	.70	3.1	.11

*calculated from sensitivity and specificity

The sensitivity of exercise thallium SPECT imaging was lower in women than in men, while the specificity was similar. This resulted in both a lower positive likelihood ratio and a lower negative likelihood ratio for women than for men.

This study was rated fair quality because not all persons who underwent the stress tests had coronary angiography and the manuscript does not state that the angiographers were blinded to the results of the stress tests.

F.4. Miller TD, Roger VL, Milavetz JJ, Hopfenspirger MR, Milavetz DL, Hodge DO, et al. Assessment of the exercise electrocardiogram in women versus men using tomogrphic myocardial perfusion imaging as the reference standard. Am J Cardiol 2001;87:868-73.[24]

This cross-sectional study provides data on the accuracy of exercise EKG testing in 838 men (75 percent with CHD) and 205 women (60 percent with CHD). Patients exercised according to the Bruce or Naughton protocol to severe fatigue, moderate angina or ≥2 mm ST depression. An abnormal exercise test was defined as ≥1mm horizontal or down-sloping ST depression. Coronary artery disease was defined as 50 percent or greater narrowing of one or more of the major coronary arteries.

Exercise EKG	N	Sensitivity	Specificity	Likelihood Ratio+*	Likelihood Ratio-*
Women	205	.53	.69	1.7	.68
Men	838	.63	.74	2.4	.50

*calculated from sensitivity and specificity

The sensitivity of exercise EKG was lower in women than in men, while the specificity was similar. This resulted in a lower positive likelihood ratio for women than for men.

This study was rated fair quality because not all persons who underwent the stress tests had coronary angiography and the manuscript does not state that the angiographers were blinded to the results of the stress tests.

Summary

The accuracy of exercise EKG and exercise thallium (with either conventional or SPECT imaging) for the diagnosis of CHD is lower in women than in men. The accuracy of these tests in women appears to be low due to both poor sensitivity and specificity with positive likelihood ratios ranging from 2 to 3 and negative likelihood ratios of .35 to .70.

1.02 Exercise echocardiogram

G.1. 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.[22]

Summary estimates of the accuracy of exercise echocardiogram *in men and women* from the systematic review by Fleischmann et al. (also described in section 1.01) are given below.

	N Studies	N Subjects	% Women	Sensitivity	Specificity	Likelihood Ratio+	Likelihood Ratio-
Exercise ECHO	24	2637	31	.85	.77	3.7	0.19

Unfortunately, the analysis does not provide separate estimates of the accuracy of these tests among women. Multivariate analyses suggested that the average proportion of men in the study did not affect the summary accuracy estimates for exercise echocardiogram.

G.2. 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.[19]

Summary estimates of the accuracy of exercise echocardiogram *in women* from the systematic review by Kwok et al. (also described in section 1.01) are given below.

	N Studies	N Women	Sensitivity	Specificity	Likelihood Ratio+	Likelihood Ratio-
Exercise ECHO	3	296	.86	.79	4.29	0.18

Summary

The accuracy of exercise echocardiogram in women appears to be better than either exercise EKG or exercise thallium, but this finding is based on limited data (3 studies including only 296 women). Estimates of the accuracy of exercise echocardiogram among both men and women from the systematic review by Fleischmann et al.[22] are very similar to the estimates among women from the systematic review by Kwok et al.[19] and Fleischmann et al.[22] found no evidence of lower accuracy of exercise echocardiogram in studies that included a higher proportion of women.

1.03 Coronary artery calcification score

G.1. Detrano R, Hsiai T, Wang S, Puentes G, Fallovollita J, Shields P, et al. Prognostic value of coronary calcification and angiographic stenoses in patients undergoing coronary angiography. J Am Coll Cardiol 1996;27:285-90.[25]

This cross-sectional study provides data on the accuracy of measures of coronary calcification in 280 symptomatic men and 211 symptomatic women. All participants underwent computed tomographic measures of coronary calcium (method for computing score and range not given) and coronary angiography. Abnormal coronary calcium was defined as a coronary calcium score >0 or <100. Coronary artery disease was defined as 50 percent or greater narrowing of one or more of the major coronary arteries.

Calicum score >0	Sensitivity	Specificity	Likelihood Ratio+*	Likelihood Ratio-*
Women				
>55 years old	.98	.31	1.4	.06
≤55 years old	.93	.46	1.7	.15
Men				
>55 years old	.97	.13	1.1	.03
≤55 years old	.92	.30	1.3	.27
Calicum score >100				
Women				
>55 years old	.77	.65	2.2	.35
≤55 years old	.60	.88	5.0	.45
Men				
>55 years old	.86	.51	1.8	.27
≤55 years old	.49	.73	1.8	.70

*calculated from sensitivity and specificity

The overall accuracy of computed tomographic calcium score >0 was low in both men and women. Given the high sensitivity and low negative likelihood ratio of no calcium on computed tomography, a negative test might be useful to rule out CHD in both women and men. The accuracy of a calcium score greater than 100 appears to be low in both men and women. The positive likelihood ratio of a high calcium score in women under 55 appears to be higher than in any other group of men or women, but this probably occurred by chance or due to multiple comparisons.

G.2. Budoff MJ, Shokooh S, Shavelle RM, Kim HT, French WJ. Electron beam tomography and angiography: sex differences. Am Heart J 2002;143:877-82.[26]

This cross-sectional study provides data on the accuracy of measures of coronary calcification in 733 symptomatic men (70 percent with CHD) and 387 women (41 percent with CHD). All participants underwent computed tomographic measures of coronary calcium (method for computing score and range not given) and coronary angiography. Abnormal coronary calcium was defined as a coronary calcium score >0. Coronary artery disease was defined as 50 percent or greater narrowing of one or more of the major coronary arteries.

	Sensitivity	Specificity	Likelihood Ratio+*	Likelihood Ratio-*
Women	.96	.57	2.2	.09
Men	.96	.46	1.8	.07

*calculated from sensitivity and specificity

The overall accuracy of computed tomographic calcium score is low in both men and women. Among women, 64 percent had a coronary calcium score of 0 compared to 44 percent of men. Given the high sensitivity and low negative likelihood ratio of a calcium score of 0, a negative test might be useful to rule out CHD in women.

Summary

The overall accuracy of computed tomographic calcium score is low in both men and women. For a calcium score of 0, the sensitivity is high and the negative likelihood ratio is low. Thus, a calcium score of 0 might be useful to rule out CHD in both women and men.

Overall Summary and Recommendations for Question 1

The accuracy of exercise EKG and exercise thallium for the diagnosis of coronary atherosclerosis in women appears to be low with positive likelihood ratios of 2 to 3 and negative likelihood ratios of .35 to .70. The accuracy of exercise echocardiogram appears to be higher than exercise EKG or exercise thallium imaging with a positive likelihood ratio of 4 and a negative likelihood ratio of .2. Based on the review of Fleischmann et al.,[22] exercise echocardiogram also seems to be superior to exercise SPECT.

Two good-quality studies[25, 26] of the accuracy of computed tomographic measures of coronary calcium suggest that a score of 0 has a high sensitivity and low negative likelihood ratio for angiographic coronary disease. Thus, while this test has a low positive likelihood ratio, it might be useful for ruling out disease in both men and women.

While we found two good quality systematic reviews, each is limited. The review by Kwok et al.[19] included only studies published until 1995 using exercise EKG or exercise thallium with planar imaging and the review by Fleischmann, et al.[22] did not estimate the accuracy of noninvasive tests separately for women. Importantly, the systematic reviews do not address the accuracy of current myocardial perfusion imaging technology using thallium and/or technetium agents with SPECT or gated SPECT imaging in women. A

systematic review of the accuracy of current myocardial perfusion imaging for the diagnosis of CHD in women is feasible and could contribute important clinical information.

QUESTION 2

2. Are there effective treatments for women with coronary heart disease? (15 subtopics labeled 2.01-2.12 with secondary and primary prevention considered separately where appropriate)

Specifically, what are the summary estimates of the relative risk or risk reduction for mortality or CHD events for the following potential treatments, calculated separately for women and for women restricted to major ethnic groups (Caucasian, African-American, Hispanic, Asian):

2.01 aspirin
  a. secondary prevention
  b. primary prevention
2.02 beta-blockers
  a. secondary prevention
  b. primary prevention
2.03 angiotensin converting enzyme (ACE) inhibitors
  a. secondary prevention
  b. primary prevention
2.04 calcium channel blockers
2.05 nitrates
2.06 heparin, including low molecular weight heparin
2.07 IIb/IIIa drugs
2.08 thrombolysis
2.09 ticlopidine
2.10 clopidogrel
2.11 angioplasty or stenting (PTCA)
2.12 coronary bypass surgery (CABG)

2.01a Aspirin: secondary prevention

G.1. Collaborative overview of randomised trials of antiplatelet therapy--I: Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. Antiplatelet Trialists' Collaboration. BMJ 1994;308(6921):81-106.[27]

The Antiplatelet Trialists' Collaboration provides a systematic review of 145 randomized controlled trials published prior to 1990. Trial selection required that participants were randomized to aspirin and/or dipyridamole or sulphinpyrazone for at least one-month.

The primary outcome was defined as vascular events, including non-fatal MI, nonfatal stroke, and vascular death.

While the systematic review included both primary and secondary prevention trials, gender stratified results for vascular events are only available for high-risk women, defined as those with unstable angina, acute myocardial infarction, prior MI, stroke, transient ischemic attack, or other high risk conditions.

	Men (N=39,417)			Women (N=9,962; 20%)		
Outcome	RR	95% CI	p-value	RR	95% CI	p-value
Vascular events	.78	NA	<.0001	.81	NA<.0001	

There was a similar 20 percent reduction in risk of vascular events among both men and women. Compared to high dose therapy (500 – 1500 mg daily), low and intermediate doses of aspirin (< 160 mg/day and 160 –325 mg) were slightly more beneficial, but the 95 percent confidence intervals overlap. In the entire high-risk population (approximately 50,000 individuals), there was no evidence that aspirin increased the risk of non-vascular death or fatal stroke. Evidence on the risks associated with aspirin therapy was not provided separately for women.

G.2. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Lancet 1988;2(8607):349-60.[28]

The Second International Study of Infarct Survival (ISIS-2) was a randomized trial of the effect of low-dose aspirin and streptokinase on cardiovascular outcomes following acute myocardial infarction. Between 1985 and 1987, 17,187 hospitalized patients in 16 countries were randomized to receive either one hour of intravenous streptokinase or identical placebo. Participants were also randomized to aspirin (162.5 mg daily) or identical placebo (2x2 factorial design); thus, there were four treatment groups: streptokinase alone, aspirin alone, both, or neither. Randomization occurred within 24-hours after the onset of symptoms of an acute MI. The main outcome was vascular death (cardiac, cerebral, hemorrhagic and other vascular deaths) during 5 weeks of follow-up.

	All Participants (N=17,187)			Women (N=3,945; 23%)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
Vascular death	.77	.70-.85	<.00001	.83	NA*	NA

*figure demonstrates that the 95 percent confidence interval does not cross 1.0.

There appeared to be about a 20 percent reduction in risk of vascular events in women that was similar to the benefit observed in all participants. There were no statistically significant differences in the odds ratios for vascular death among men and women. For both genders combined, the risks of major bleeding and hemorrhagic stroke were not increased with aspirin use. There was a small excess risk of minor bleeding (0.6 percent).

2.01b Aspirin: primary prevention

G.1. de Gaetano G. Low-dose aspirin and vitamin E in people at cardiovascular risk: a randomised trial in general practice. Collaborative Group of the Primary Prevention Project. Lancet 2001;357(9250):89-95.[29]

The Primary Prevention Project was a randomized trial of the effect of low-dose aspirin (100 mg/day) on cardiovascular risk (nonfatal MI, nonfatal stroke and cardiovascular death). All participants were over age 50 years and had at least one major cardiovascular risk factor (hypertension, hypercholesterolemia, diabetes, obesity, family history of premature MI or age ≥ 65 years). The trial was prematurely concluded after 3.6 years due to new information from other studies on the benefits of aspirin therapy, primarily in men.

	All Participants (N=3,012 men; 2,583 women)		
Outcome	RR	95% CI	p-value
Cardiovascular death	.56	.31-.99	NA
Combined endpoint*	.71	.48-1.04	NA
MI	.69	.38-1.23	NA

*cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke

The results included in the report were not stratified by gender, but the authors state that the direction and size of the effects were similar in men and women. None of the findings were statistically significant, likely due to early termination of the trial. Participants in the aspirin group were more likely to report major bleeding (1.1 percent vs. 0.3 percent; $p < .001$).

G.2. Hansson L, Zanchetti A, Carruthers SG, Dahlof B, Elmfeldt D, Julius S, et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. Lancet 1998;351(9118):1755-62.[30]
G.3. Kjeldsen SE, Kolloch RE, Leonetti G, Mallion JM, Zanchetti A, Elmfeldt D, et al. Influence of gender and age on preventing cardiovascular disease by antihypertensive treatment and acetylsalicylic acid. The HOT study. Hypertension Optimal Treatment. J Hypertens 2000;18(5):629-42.[31]

The Hypertension Optimal Treatment (HOT) trial was a randomized trial among 18,790 persons with hypertension (8,883 women) aged 50-80 years, who were randomized to 75 mg/day of aspirin or placebo and followed for 3.8 years. The main outcome was major cardiovascular events (fatal and nonfatal stroke, MI and all other cardiovascular deaths).

	All Participants (N=18,790)			Women (N=8,883; 47%)		
Outcome	RR	95% CI	p-value	RR	95% CI	p-value
Mortality	.93	.79-1.09	.36	1.12	.86-1.47	.41
Cardiovascular events	.85	.73-.99	.03	.81	.63-1.04	.10
MI	.64	.49-.85	.0002	.81	.49-1.31	.38

There was a 15 percent reduction in risk of cardiovascular events and a 35 percent reduction in risk of MI in all participants. Risk of death was reduced 7 percent, but this finding was not statistically significant. Among women, mortality was not decreased. Risk of cardiovascular events and of MI was reduced about 20 percent, but these findings were not statistically significant. The risk of fatal bleeding was not increased by aspirin therapy in men or women, but the risk of non-fatal major bleeding was increased in both genders (RR in men 1.6, p-value .01; RR in women 2.1, p-value .006).

G.4. Manson JE, Stampfer MJ, Colditz GA, Willett WC, Rosner B, Speizer FE, et al. A prospective study of aspirin use and primary prevention of cardiovascular disease in women. JAMA 1991;266(4):521-7.[32]

The Nurses Health Study is a prospective cohort study of risk factors for various diseases. Between 1980 and 1986, 87,678 women aged 34 to 65 years were followed prospectively to determine the association between aspirin therapy (assumed dose 325 mg) and the risk of a cardiovascular event. The primary outcomes were nonfatal MI and CHD death.

The multivariate adjusted relative risks (RR) for cardiovascular events among women taking various numbers of aspirin per week compared to nonusers are as follows:

	Number of Aspirin per Week		
	1-6	7-14	>15
Outcome	RR (95% CI)	RR (95% CI)	RR (95% CI)
Mortality	.86 (.72-1.03)	1.14 (.89-1.47)	.97 (.76-1.23)
Nonfatal MI and CHD Death	.75 (.58-.99)	1.20 (.84-1.69)	.89 (.63-1.27)
Stroke	.99 (.71-1.36)	.83 (.49-1.42)	1.20 (.79-1.83)

Low-dose aspirin (1 to 6 aspirin/week) reduced risk of CHD events about 25 percent and mortality about 15 percent, but higher doses were not associated with benefit and there was no reduction in risk of stroke.

Summary and Recommendations

For secondary prevention, there is good evidence from a systematic review of randomized trials[27] that aspirin therapy reduces risk of cardiovascular events about 20 percent in women with coronary disease or women at high risk for CHD and that the reduction in risk appears to be similar in men and women. This result is supported by the findings of one clinical trial that included a large number of women[28] and found about a 20 percent reduction in risk of cardiovascular events among women admitted to the hospital for suspected MI. However, the systematic review[27] searched the literature only up to 1990, and the authors did not provide detailed information on dose, duration of treatment, subgroups of women (those with prior acute MI, distant MI, unstable angina, etc), specific outcomes in women (MI, stroke, cardiac death, etc) or on the effect of aspirin in low-risk women (primary prevention). The clinical trial[28] provides evidence only for women admitted to the hospital with suspected MI. A more detailed and current systematic review of the data in women is feasible and might provide clinically important information.

Evidence that aspirin is beneficial for primary prevention of cardiovascular disease among women is weak. The systematic review by the Antiplatelet Trialists' Collaboration[27] identified multiple small trials that included about 20,000 persons at "low risk" for vascular events for whom aspirin would be considered primary preventive therapy. However, no information on the number of women in the low risk group or the effect of aspirin in low-risk women was provided. Evidence from the Hypertension Optimal Treatment trial[31] among men and women with hypertension suggests that risk for cardiovascular events was reduced about 20 percent in women taking aspirin but total mortality was not reduced. A second large randomized trial included over 2,500 women,[29] but the results were not stratified by gender and the trial was stopped prematurely providing inadequate power. A large, well-conducted prospective cohort study among women[32] found that aspirin therapy reduced risk of CHD events about 25 percent, but the findings of this study are susceptible to bias due to the observational design. Definitive evidence may be available from the Women's Health Study, a clinical trial that is currently on-going among 40,000 postmenopausal women randomized to 100 mg daily of aspirin versus placebo.

A systematic review of aspirin for primary prevention could provide important evidence, assuming that data stratified by gender could be obtained from earlier small trials, the Primary Prevention Project[29] and the Hypertension Optimal Treatment trial.[31] However, a systematic review should likely await the results of the on-going Women's Health Study, a randomized trial of aspirin therapy among women that may be definitive.

2.02a Beta-blockers: secondary prevention

Outpatient Treatment in Patients with Congestive Heart Failure (CHF)

F.1. Leizorovicz A, Lechat P, Cucherat M, Bugnard F. Bisoprolol for the treatment of chronic heart failure: a meta-analysis on individual data of two placebo-controlled studies--CIBIS and CIBIS II. Cardiac Insufficiency Bisoprolol Study. Am Heart J 2002;143(2):301-7.[33]

This systematic review summarized the results of two randomized controlled trials of the effect of beta-blockers on risk for mortality in persons with CHF. All participants in the Cardiac Insufficiency Bisoprolol Study (CIBIS) and CIBIS II had symptomatic heart failure (New York Heart Association class III or IV) and ejection fraction of less than 40 percent. Participants were randomized to receive up to 10 mg of bisoprolol or identical placebo. The primary outcome was mortality during a mean follow-up of 1.9 years (CIBIS) and 1.3 years (CIBIS II).

	All Participants (N=3,288)			Women (N=627; 19%)		
Outcome	RR	95% CI	p-value	RR	95% CI	p-value
Mortality	.71	.60-.83	.00003	.62	.40-.97	NA

There was a 30 percent reduction in risk of death among all participants assigned to beta-blockers compared to those assigned to placebo and a similar reduction in risk of death among women.

This study was rated fair quality because there was no systematic review of the literature and inclusion and exclusion criteria were not described.

F.2. Ghali JK, Pina IL, Gottlieb SS, Deedwania PC, Wikstrand JC. Metoprolol CR/XL in female patients with heart failure: analysis of the experience in Metoprolol Extended-Release Randomized Intervention Trial in Heart Failure (MERIT-HF). Circulation 2002;105(13):1585-91.[34]

The Metoprolol Extended-Release Randomized Intervention Trial in Heart Failure (MERIT-HF) was a randomized trial that assessed the effect of metoprolol on CHF mortality. Participants had New York Heart Association class II-IV heart failure with ejection fraction 40 percent or lower and all received diuretics and ACE inhibitors. Participants were randomized to controlled release/extended release metoprolol (12.5 mg or 25 mg daily) or identical placebo. The primary outcome was mortality during a mean follow-up of one year.

	Men (N=3,093)			Women (N=898; 22%)		
Outcome	RR	95% CI	p-value	RR	95% CI	p-value
Mortality	.66	.53-.81	.0001	.93	NA*	NS
Mortality or hospitalization	.82	.73-.92	.001	.79	NA	.04

Women appeared to have a smaller reduction in mortality associated with beta-blocker treatment compared to men, but a similar reduction in mortality or hospitalization.

This manuscript also presents a systematic review of data from 3 large randomized trials of beta-blocker therapy for CHF: MERIT-HF (described above in F.2), CIBIS II (described in F.1) and the Carvedilol Prospective Randomized Cumulative Survival Study (COPERNICUS). COPERNICUS randomized 2,289 participants with symptomatic heart failure and an ejection fraction of less than 25 percent to carvedilol or placebo. Carvedilol dose was titrated from 3.125 mg to 25 mg twice daily and placebo was similarly titrated. Most participants were also taking diuretics, digoxin and angiotensin converting enzyme inhibitors. The average length of follow-up was 10.4 months.

	Men (N=7,044)			Women (N=1,883)		
Outcome	RR	95% CI	p-value	RR	95% CI	p-value
Mortality	.66	.58-.75	NA	.69	.51-.93	NA

In these three trials, there was a statistically significant 30 percent reduction in the risk of mortality associated with beta-blocker treatment in both men and women with CHF. Although the types of beta-blockers used differed in the three trials, there was little evidence of an effect on outcome.

This manuscript was rated fair quality because there was no systematic review of the literature, inclusion and exclusion criteria were not defined and the statistical methods were inadequately described.

Treatment in the Setting of Acute MI

F.3. The Beta-Blocker Pooling Project (BBPP): subgroup findings from randomized trials in post infarction patients. The Beta-Blocker Pooling Project Research Group. Eur Heart J 1988;9(1):8-16.[35]

The Beta-Blocker Pooling Project is a systematic review that included double-blinded, placebo-controlled trials with 200 or more participants who were randomized to beta-blockers within 1 to 45 days after acute MI and followed for at least one year. Nine eligible trials were identified. Beta-blockers differed by trial, and drug doses were within the range for treatment of angina or hypertension. All trials were published by the end of 1983.

	All Participants (N=13,679)			Women (N=2,281; 17%)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
Mortality	.76	.66-.87	<.0001	.81	NA	.17

Treatment with beta-blockers after MI reduced risk of death by about 25 percent in all participants. The risk reduction was similar in women, but the findings were not statistically significant, likely due to the small number of women included. The test for homogeneity of outcomes indicated that the results of the trials were not consistent (p = .05), possibly due to differences in the beta-blockers studied.

This systematic review was categorized as fair quality based on the lack of information regarding the methods used, including inclusion criteria, search strategy and data abstraction.

F.4. Olsson G, Wikstrand J, Warnold I, Manger Cats V, McBoyle D, Herlitz J, et al. Metoprolol-induced reduction in postinfarction mortality: pooled results from five double-blind randomized trials. Eur Heart J 1992;13(1):28-32.[36]

This is a systematic review that includes outcomes from five large double-blind, placebo controlled randomized trials to assess the effect of treatment with metoprolol on mortality after MI. Randomization occurred 1 to 14 days after MI, with follow-up between 3 months and 3 years.

	All Participants (N=5,474)			Women (N=1,121; 20%)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
Mortality	.81	NA	.04	.77	NA	NA

Mortality was reduced about 20 percent in all participants. The reduction in mortality was similar among women, but the finding was not statistically significant, likely due to the small number of women included. The ORs were not significantly different in men and women.

This systematic review was categorized as fair quality based on the lack of information regarding the methods used, including inclusion criteria, search strategy and data abstraction.

2.02b Beta-blockers: primary prevention

No systematic reviews or randomized trial that addressed the value of beta-blockers for primary prevention of CHD in women were identified.

Summary and Recommendations

Two small meta-analyses[33] that included data from 4 large randomized trials found that treatment with beta-blockers reduced the risk of mortality by about 30 percent in both men and women with heart failure. There have been approximately 20 randomized trials of the effect of beta-blockers in persons with CHF. Many of these included a small proportion of women, but did not report results specific to women. Since 1996 there have been approximately eleven other systematic reviews of the effect of treatment with beta-blockers in persons with CHF; however, none has presented data specific to women. A systematic review of the CHF literature is feasible and could provide a more accurate estimate of the effect on mortality, assess other outcomes such as hospitalizations and adverse effects, and evaluate outcomes in subgroups of women, such as those with severe CHF.

Based on evidence from two systematic reviews,[35, 36] treatment with beta-blockers shortly after MI in women appears to decrease mortality 20 to 25 percent. However, neither of these reviews was good quality. Both are over 10 years old and provide no data on long-term beta-blocker treatment after MI. It would be useful to update these systematic reviews using currently accepted methodologic standards.

No data addressed the value of beta-blockers for primary prevention of CHD in women.

2.03a Angiotensin converting enzyme (ACE) inhibitors: secondary prevention

Outpatient Treatment in Patients with Congestive Heart Failure (CHF)

G.1. Garg R, Yusuf S. Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. Collaborative Group on ACE Inhibitor Trials. JAMA 1995;273(18):1450-6.[37]

The Collaborative Group on ACE Inhibitor Trials is a systematic review of findings from 32 trials (1985-1994) evaluating the effect of angiotensin-converting enzyme (ACE) inhibitors on CHD mortality. All study participants had New York Heart Association class II or greater CHF. The minimum length of follow-up was eight weeks. Twelve trials followed participants for greater than three months.

	Men (N=5,399)			Women (N=1,587; 23%)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
Mortality	.76	.65-.88	NA	.79	.59-1.06	NA
Combined endpoint*	.63	.55-.73	NA	.78	.59-1.04	NA

*mortality or hospitalization for CHF

Risk for mortality was reduced about 20 percent in both men and women and risk for mortality or hospitalization was reduced about 30 to 40 percent. However, the results in women were not statistically significant, likely due to the small sample size. The analyses were primarily based on trials with the ACE inhibitor enalapril, although studies with captopril, lisinopril, quinapril, and ramipril were also represented in this review.

G.2. Flather MD, Yusuf S, Kober L, Pfeffer M, Hall A, Murray G, et al. Long-term ACE-inhibitor therapy in patients with heart failure or left-ventricular dysfunction: a systematic overview of data from individual patients. ACE-Inhibitor Myocardial Infarction Collaborative Group. Lancet 2000;355(9215):1575-81.[38]

The ACE-inhibitor Myocardial Infarction Collaborative Group provides a systematic review of randomized trials with 1,000 or more participants with left ventricular dysfunction or heart failure after acute myocardial infarction. The five trials included in the pooled analyses are Survival and Ventricular Enlargement (SAVE), Acute Infarction Ramipril Efficacy (AIRE), Tandolapril in Patients with Reduced Left-ventricular Function after Acute Myocardial Infarction (TRACE), Studies of Left Ventricular Dysfunction (SOLVD) treatment and SOLVD prevention. The trial outcomes were mortality, readmission for CHF, and reinfarction.

	Men (N=10,367)			Women (N=2,396; 19%)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
Mortality	.79	.72-.87	NA	.85	.71-1.02	NA
Combined endpoint*	.71	.65-.77	NA	.79	.67-.93	NA

*mortality, readmission for CHF or MI

Risk for mortality was reduced about 20 percent in both men and women. The estimate in men was highly statistically significant, while the estimate in women was only borderline significant, likely due to the smaller sample size. Women also had a statistically significant 20 percent reduction in risk of the combined endpoint.

Outpatient Treatment in Persons at High Risk for Coronary Events

G.3. Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. N Engl J Med 2000;342(3):145-53.[39]

G.4. Dagenais GR, Yusuf S, Bourassa MG, Yi Q, Bosch J, Lonn EM, et al. Effects of ramipril on coronary events in high-risk persons: results of the Heart Outcomes Prevention Evaluation Study. Circulation 2001;104(5):522-6.[40]

G.5. Lonn E, Roccafort R, Yi Q, Dagenais G, Sleight P, et al. Effect of long-term therapy with ramipril in high-risk women. J Am Coll Cardiol 2002;40:693.[41]

All three of these manuscripts are based on findings from the Heart Outcomes Prevention Evaluation (HOPE) trial, a randomized trial to evaluate the effects of ramipril 10 mg/day and vitamin E on cardiovascular outcomes (2x2 factorial design). The first manuscript (Yusuf, et al.) focuses on the main findings, the second (Dagenais et al.) on findings in subgroups at high risk and the third (Lonn et al.) on the results in women. All participants were older than age 55 years, and had vascular disease or diabetes plus one other cardiovascular risk factor, but not congestive heart failure. The trial was terminated after 4.5 years of follow-up due to a beneficial effect of ramipril on CHD outcomes.

	All Participants (N=9,297)			Women (N=2,480; 27%)		
Outcomes	RR	95% CI	p-value	RR	95% CI	p-value
Combined endpoint*	.78	.70-.86	<.001	.77	.62-.96	<.05
MI	.80	.70-.90	<.001	.89	.69-1.17	NA

*cardiovascular mortality, MI, or stroke

Risk for the combined endpoint of cardiovascular mortality, MI or stroke was statistically significantly reduced about 20 percent in all participants and in women. Risk for MI was also about 20 percent lower in all participants and 10 percent lower in women. This finding in women was not statistically significant, likely due to the smaller sample size and lower rate of MI in women (9.4 percent among women in the placebo group vs. 13.2 percent among men).

Inpatient Treatment in the Setting of Probable Acute MI

G.6. Indications for ACE inhibitors in the early treatment of acute myocardial infarction: systematic overview of individual data from 100,000 patients in randomized trials. ACE Inhibitor Myocardial Infarction Collaborative Group. Circulation 1998;97(22):2202-12.[42]

The ACE Inhibitor Myocardial Infarction Collaborative Group analysis provides a systematic review of four randomized trials (Cooperative New Scandinavian Enalapril Survival Study (Consensus-II), Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI-3), Second International Study of Infarct Survival (ISIS-4), Chinese Cardiac Study (CCS-1)) in which ACE inhibitor treatment was initiated within 36 hours after onset of symptoms of MI. The primary outcome was mortality after 30 days of therapy. All of the trials were conducted between 1990 and 1995. The four included trials studied the ACE inhibitors captopril, enalapril, and lisinopril.

	All Participants (N= 98,496)			Women (N=24,834; 25%)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
Mortality at 30-days	.93	.89-.98	NA	.95	NA*	NA

*Figure demonstrates that the 95 percent CI overlaps 1.0.

There was a statistically significant but small (7%) reduction in risk of 30-day mortality among all participants. The reduction in risk among women was similar, but not statistically significant, likely due to the smaller number of women studied. Two known side effects of ACE inhibitors, persistent hypotension and renal dysfunction, were also evaluated by gender.

	Men (N=73,637)			Women (N=24,826; 25%)		
Outcome	OR	99% CI	p-value	OR	99% CI	p-value
Hypotension	2.11	1.99-2.23	NA	1.97	1.80-2.15	NA
Renal Dysfunction	2.11	1.73-2.57	NA	1.57	1.14-2.17	NA

Risk for hypotension and for renal dysfunction was increased about 2-fold in both men and women.

Randomized trials not included in the systematic reviews

F.7. GISSI-3: effects of lisinopril and transdermal glyceryl trinitrate singly and together on 6-week mortality and ventricular function after acute myocardial infarction. Gruppo Italiano per lo Studio della Sopravvivenza nell'infarto Miocardico. Lancet 1994;343(8906):1115-22.[43]

Between 1991 and 1993, the GISSI-3 randomized trial enrolled 19,394 patients from 200 Italian hospitals. Participants were randomized to lisinopril, nitrates, or open control (2x2 factorial design) within 24-hours after the onset of symptoms of acute MI. Participants assigned to lisinopril received an initial 5 mg dose, which was titrated to 10 mg daily for 6 weeks. The primary outcomes were assessed after 6 weeks and 6 months of follow-up. The short-term results were included in the systematic review described above. This manuscript presents the 6-month findings.

	All Participants (N=19,318)			Women (N=4,276; 22%)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
Mortality	.95	NA	NA	.89	NA	NA
Combined endpoint*	.92	.86-.99	NA	.87	.76-1.00	.05

* mortality and clinical CHF

At 6 months, there was no reduction in risk of mortality among all participants or in women. There was a statistically significant 10 percent reduction in risk of mortality and clinical CHF among all participants and among women. Among all participants, persistent hypotension and renal dysfunction were significantly more likely to occur on ACE inhibitor therapy compared to controls (OR for hypotension = 2.48: 95 percent CI , 2.09 – 2.93; OR for renal dysfunction = 2.15; 95 percent CI, 1.58 – 2.92).

This study was given a fair quality rating based on the lack of a placebo control group.

2.03b Angiotensin converting enzyme (ACE) inhibitors: primary prevention

No systematic review or randomized trial that addressed the value of ACE inhibitors for primary prevention of CHD in women was identified.

Summary and Recommendations

Among women with documented CHF, two good systematic reviews[37, 38] suggest that outpatient treatment with ACE inhibitors reduces the risk of mortality 15 to 20 percent.

Results of the HOPE trial[39-41] suggest that outpatient treatment of women with cardiovascular disease or with multiple risk factors results in about a 20 percent reduction in risk of cardiovascular events.

Based on the results of 4 large randomized trials, treatment with ACE inhibitors within 36 hours of acute MI is probably associated with about a 7 percent reduction in risk of mortality in the 30 days after MI, but this small benefit is associated with about a 2-fold increased risk of both hypotension and renal dysfunction.

New systematic reviews of these topics are feasible, but unlikely to provide additional information on use of ACE inhibitors in women.

No data addressed the value of ACE inhibitors for primary prevention of CHD in women.

2.04 Calcium channel blockers

There were no systematic reviews, randomized trials, or cohort studies identified for this topic.

2.05 Nitrates

Inpatient Treatment for Probable Acute MI

F.1. GISSI-3: effects of lisinopril and transdermal glyceryl trinitrate singly and together on 6-week mortality and ventricular function after acute myocardial infarction. Gruppo Italiano per lo Studio della Sopravvivenza nell'infarto Miocardico. Lancet 1994;343(8906):1115-22.[43]

Between 1991 and 1993, 19,394 patients (4,191 women) from 200 Italian hospitals were enrolled in the GISSI-3 randomized trial. Participants were randomized to lisinopril or nitrates or open control (2x2 factorial design) within 24 hours of the onset of acute MI symptoms. Participants assigned to nitrates received an intravenous infusion (glyceryl trinitrates) for 24 hours, followed by a transdermal patch (10 mg daily) or isosorbide

mononitrate (50 mg daily). Tolerance to the drug was minimized by removal of the transdermal patch for 10 hours each day. The primary outcomes measured after 6 weeks of therapy included all cause mortality and development of clinical CHF.

	All Participants (N=19,394)			Women (N=4,191; 22%)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
Mortality	.94	.84-1.05	.28	.86	NA	NA
Mortality and CHF	.94	.87-1.02	.12	.87	.75-1.01	NA

Among all participants, treatment with nitrates did not result in lower risk for mortality or mortality and CHF. Among women, there appeared to be a trend to reduced risk, but differences in the outcomes between women and all participants are small, suggesting that the effect of treatment with nitrates in women is no different from the overall effect. Women assigned to nitrates were not at a significantly increased risk for persistent hypotension (OR = 1.07; 95% CI, .95 – 1.20).

This study was given a fair quality rating based on the lack of a placebo control group.

G.2. ISIS-4: a randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. Lancet 1995;345(8951):669-85.[44]

Between 1991 and 1993, 58,050 patients were enrolled in the ISIS-4 randomized trial within 24 hours of the onset of symptoms of an acute MI. Treatment interventions included oral captopril, oral mononitrates, and IV magnesium sulfate (2x2x2 factorial design). Participants were assigned to one month of oral controlled-release mononitrate therapy (30 mg initial dose titrated to 60 mg daily) or placebo. Total mortality was assessed after 5 weeks of therapy.

	All Participants (N=58,050)			Women* (N=14,990; 26%)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
Mortality	.97	.91-1.03	NS	.90	NA	NS

*RR and 95 percent CIs for the main outcome stratified by gender are presented only in a figure and are thus estimated for women.

Nitrate therapy did not reduce risk for mortality among all patients or among women. Differences in the outcomes in all participants compared to women are small, suggesting that the effect of treatment with nitrates in women is no different from the overall effect.

Participants receiving mononitrate therapy were at increased risk for profound hypotension, requiring termination of study treatment (8.1 percent for treatment versus 6.7 percent for placebo; $p < .0001$).

F.3. Six-month effects of early treatment with lisinopril and transdermal glyceryl trinitrate singly and together withdrawn six weeks after acute myocardial infarction: the GISSI-3 trial. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico. J Am Coll Cardiol 1996;27(2):337-44.[45]

This follow-up report from the GISSI-3 randomized trial[43] indicates that there were no additional benefits associated with nitrate therapy in all participants or in women after six months of follow-up.

	All Participants (N=19,394)			Women (N=4,191; 22%)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
Mortality	.98	NA	NA	.90	NA	NA
Mortality and CHF	.97	.90-1.04	.39	.92	.80-1.05	.22

This study was given a fair quality rating based on the lack of a placebo control group.

Summary and Recommendations

Good evidence from two randomized trials suggests that mortality in women is not reduced after MI by early treatment with nitrates. Further systematic review of the literature related to this question is unlikely to provide clinically useful information.

2.06 Heparin

There were no systematic reviews, randomized trials, or cohort studies identified for this topic.

2.07. Glycoprotein IIb/IIIa Drugs

To Reduce Risk of Coronary Events in Patients Undergoing Percutaneous Coronary Intervention

F.1. Cho L, Topol EJ, Balog C, Foody JM, Booth JE, Cabot C, et al. Clinical benefit of glycoprotein IIb/IIIa blockade with Abciximab is independent of gender: pooled analysis from EPIC, EPILOG and EPISTENT trials. Evaluation of 7E3 for the Prevention of Ischemic Complications. Evaluation in Percutaneous Transluminal Coronary Angioplasty to Improve Long-Term Outcome with Abciximab GP IIb/IIIa blockade. Evaluation of Platelet IIb/IIIa Inhibitor for Stent. J Am Coll Cardiol 2000;36(2):381-6.[46]

In this systematic review, results from three trials, Evaluation of 7E3 for the Prevention of Ischemic Complications (EPIC), Evaluation of Percutaneous Transluminal Coronary Angioplasty to Improve Long-Term Outcome with Abciximab Glycoprotein IIb/IIIa Blockade (EPILOG), Evaluation of Platelet IIb/IIIa Inhibitor for Stenting (EPISTENT) were pooled to assess the effect of treatment with abciximab on CHD outcomes. Between 1994 and 1998, 1,701 women and 4,824 men were randomized to abciximab or placebo. All participants were undergoing elective or urgent percutaneous coronary intervention. The maximum duration of treatment with abciximab was 12 hours. All participants received aspirin and heparin (either weight-adjusted standard dose or low dose heparin). The primary endpoint was a composite of death, MI and urgent revascularization at 6 weeks and 6 months. The main results are listed below:

	Men (N=4,824)			Women (N=1,771; 37%)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
Mortality, 1 year	.70	NA	.06	.62	NA	.03
Combined endpoint*						
6 weeks	.51	NA	.001	.51	NA	.001
6 months	.59	NA	<.001	.62	NA	.01

*death, MI and urgent revascularization

Mortality was about 40 percent in women who received IIb/IIIa inhibitors compared to those who received placebo. Risk for coronary events was reduced about 50 percent six weeks after treatment and about 40 percent six months after treatment. There were no statistical differences in the RRs for men and women.

The incidence of major bleeding was not higher in women or men treated with abciximab compared to those treated with placebo.

Our reviewers classified this systematic review as fair because it lacked information regarding inclusion criteria, search strategy, and data abstraction.

To Reduce Risk of Coronary Events in Persons with Acute Coronary Syndromes

G.2. Boersma E, Harrington RA, Moliterno DJ, White H, Theroux P, Van de Werf F, et al. Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: a meta-analysis of all major randomised clinical trials. Lancet 2002;359(9302):189-98.[47]

This systematic review included all randomized trials that: 1) included persons admitted to the hospital with acute coronary syndromes but without persistent ST elevation on EKG; 2) compared a glycoprotein IIb/IIIa inhibitor with placebo or control; 3) recommended against early coronary revascularization during study drug infusion and 4) enrolled at least 1000 patients. Six trials were identified that fit the inclusion criteria (PRISM, PRISM-PLUS, PARAGON-A, PARAGON-B, PURSUIT, GUSTO-IV ACS)

and individual patient data were obtained from each. The six trials enrolled 31,402 participants (10,991 women) from 41 countries and used 4 different glycoprotein IIb/IIIa inhibitors. In all trials, glycoprotein IIb/IIIa inhibitors were started within 12 to 24 hours of onset of symptoms and continued for 48 to 120 hours. In most of the trials, all participants were treated with aspirin and standard dose heparin. Outcomes at 30 days are given below:

	Men (N=20,388)			Women (N=11,013; 35%)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
Mortality	.83	.71-.96	NA	1.08	.89-1.33	NA
Death or MI	.81	.75-.89	NA	1.15	1.01-1.30	NA
Major bleeding	1.6	1.3-2.0	NA	2.2	1.6-2.9	NA

Among treated men, mortality was reduced 17 percent and death or MI 19 percent at 30 days. Among women, risk for death or MI was increased 15 percent. Risk for major bleeding was increased about 2-fold in both genders. The difference in ORs for mortality and death or MI between men and women was highly statistically significant. There were multiple differences between men and women participants at baseline: on average, women were older, more likely to have diabetes, heart failure and ST depression on admission, less likely to have elevated CKMB concentrations and less likely to have had coronary revascularization or MI. However, sex differences in the effect of glycoprotein IIb/IIIa inhibitors remained after adjusting for these baseline differences. There was no interaction with level of CKMB, but both men and women with elevated baseline troponins (measured on only 34 percent of men and 37 percent of women) appeared to benefit from treatment with glycoprotein IIb/IIIa inhibitors while those without elevated troponins did not.

	Participants with elevated troponins (T or I $\geq$ 1 µg/L)					
	Men (N=7,002)			Women (N=4,057; 37%)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
Mortality	.75	.55-1.04	NA	.80	.53-1.21	NA
Death or MI	.82	.65-1.03	NA	.93	.68-1.28	NA

Glycoprotein IIb/IIIa inhibitors increased major bleeding complications, and this increased risk appeared to be higher in women than in men. There was no increased risk for intracranial hemorrhage or stroke.

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; PARAGON = Platelet IIb/IIIa Antagonism for the Reduction of Acute Coronary Syndrome events in a Global Organization Network; PURSUIT = Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression using Integrilin Therapy; GUSTO-IV ACS = Global Utilization of Strategies to Open Occluded Coronary Arteries Trial IV in Acute Coronary Syndromes

Summary and Recommendations

A fair-quality, relatively recent systematic review[46] that included data from 3 large randomized trials of the effect of glycoprotein IIb/IIIa inhibitors in women undergoing percutaneous coronary interventions found a 40 to 50 percent reduction in risk of death, MI and urgent revascularization at 6 weeks to 6 months, and a 40 percent reduction in mortality at one year. There appears to be no difference in the effect of these drugs in men and women who are undergoing percutaneous coronary intervention.

Among women admitted to the hospital for acute coronary syndromes, the effect of glycoprotein IIb/IIIa inhibitor treatment is not clear. A good quality, recent systematic review[47] that included data from 6 large randomized trials of the effect of glycoprotein IIb/IIIa inhibitors in women admitted to the hospital with acute coronary syndromes found that women did not benefit from treatment. The risk of mortality or MI was statistically significantly increased by 15 percent at 30 days of follow-up and there was a highly statistically significant interaction between gender and the effect of glycoprotein IIb/IIIa inhibitors. In a subset of about 1/3 of both men and women in whom troponins were elevated, treatment appeared to reduce risk of mortality about 20 to 25 percent in both men and women. However, these findings are not statistically significant, are based on subset analyses in women with elevated troponins, and there does not appear to be a similar benefit in women with elevated CPKs.

New systematic reviews of these topics are feasible, but are unlikely to add important clinical information.

2.08 Thrombolysis

Thrombolysis compared to placebo or control

G.1. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Lancet 1994;343(8893):311-22.[48]

This systematic review includes pooled data from nine trials including 58,600 patients (13,855 women) hospitalized for suspected myocardial infarction or unstable angina. The trials included in this analysis were published between 1986 and 1993. Participants were randomized to receive fibrininolytic therapy with streptokinase, anistreplase, tissue plasminogen activator or urokinase versus open control or placebo. In most trials participants received both aspirin and heparin. The primary outcome was mortality during the first 35 days after treatment.

	All Participants (N=58,600)			Women (N=13,855; 24%)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
Mortality						
day 1	1.26	1.13-1.38	NA	1.13	NA	NA
day 35	.82	. 77-.87	NA	.88	NA*	NA
Stroke, day 35	1.5	NA	NA	1.6	NA	NA
Major bleed, day 35	2.75	NA	NA	2.8	NA	NA

* figure shows that 95 percent CI did not cross 1.0

In both women and men, thrombolysis was associated with excess mortality on the first day of treatment, but a statistically significant 20 percent reduction in risk of mortality by 35 days after treatment. There were no statistically significant differences between the risk reductions observed for women and men. Because the absolute risk of mortality was higher for women than for men (5.5 percent vs. 3.2 percent in the control group on the first day of treatment and 16.0 percent vs. 10.1 percent by 35 days after treatment), the absolute risk during the first day was higher in women (7 vs. 1 per 1000) and the absolute benefit by 35 days greater than in men (27 vs. 20 per 1000). Mortality may have been higher in women than in men because the women were older and were more likely to have experienced a delay in treatment, both major risk factors for mortality.

The overall risks of stroke and major bleeding were increased similarly in both men and women and were highest during the first day of therapy.

Thrombolysis compared to PTCA for acute MI

F.2. Stone GW, Grines CL, Browne KF, Marco J, Rothbaum D, O'Keefe J, et al. Comparison of in-hospital outcome in men versus women treated by either thrombolytic therapy or primary coronary angioplasty for acute myocardial infarction. Am J Cardiol 1995;75(15):987-92.[49]

The Primary Angioplasty in Myocardial Infarction (PAMI) trial was a randomized trial to compare CHD outcomes in participants with acute MI randomized to tissue plasminogen activator (100 mg) and subsequent conservative therapy or immediate PTCA. Between 1990 and 1992, 395 participants (107 women) were enrolled within 12 hours of onset of anginal symptoms. The primary outcome was in-hospital mortality and acute MI. Major findings comparing immediate PTCA to thrombolysis are as follows:

	Men (N=288)			Women (N=107; 27%)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
In-hospital mortality	.60	NA	.46	.29	NA	.07
MI	.36	NA	.06	.57	NA	.64

Mortality and risk of MI were lower among both men and women with symptoms of acute MI treated with immediate PTCA compared to those treated with tissue plasminogen activator. However, none of the outcomes were statistically significant, probably because the trial was too small.

No strokes occurred among either men or women in the PTCA group, while 2.8 percent of men and 5.3 percent of women experienced a stroke in the tissue plasminogen activator group. All of the strokes in women were hemorrhagic. Among patients assigned to tissue plasminogen activator, mortality in women was higher than in men (14.0 vs. 4 percent); there was no difference in mortality rates among women and men assigned to PTCA. At baseline, women were, on average, 8 years older than men and more likely to have diabetes, hypertension, history of CHF and had a longer interval of time between onset of symptoms and randomization. After multivariate adjustment for these risk factors, gender was no longer predictive of mortality with tissue plasminogen activator ($p = .25$).

This trial was rated fair quality because it was not blinded.

Summary and Recommendations

A systematic review of 9 large randomized trials[48] demonstrates that thrombolysis reduces the risk of 5-week mortality in women and men hospitalized with suspected acute MI about 15 percent. Thrombolysis resulted in about a 50 percent increased risk of stroke and a nearly 3-fold increased risk of major bleeding in both men and women.

One small trial suggested that PTCA may be more effective than thrombolysis for reducing in-hospital mortality in women and much less likely to cause hemorrhagic stroke,[49] but none of the relative risk estimates were statistically significant.
The systematic review is somewhat out of date. An updated review might be useful by providing more complete estimates for the effects of thrombolysis in women, but is unlikely to alter the major findings.

2.09 Ticlopidine

There were no systematic reviews, randomized trials, or cohort studies identified for this topic.

2.10 Clopidogrel

To Reduce Risk of Coronary Events in Persons with Acute Coronary Syndrome

G.1. Yusuf S, Zhao F, Mehta SR, et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. N Engl J Med 2001;345(7):494-502.[50]

The Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) study was a randomized trial to assess the effect of clopidogrel among persons with acute coronary syndromes (hospitalization for ischemic symptoms without ST-elevation). Between 1998 and 2000 12,562 patients (38 percent women) were randomized to clopidogrel (300mg loading dose, followed by 75mg/day) or placebo within 24-hours of the onset of acute coronary symptoms. Treatment continued for 3 to 12 months. All participants also received daily treatment with aspirin (75-325 mg). The primary outcome was death from cardiovascular causes, nonfatal MI, or stroke.

	All (N=12,562)			Women (N= 4,836; 38%)		
Outcome	RR	95% CI	p-value	RR	95% CI	p-value
Primary Events*	.80	.72-.90	<.001	.89	.NA	NA**

*Death from cardiovascular causes, nonfatal MI, or stroke
**figure demonstrates that 95 percent CI crosses 1.0.

Among all participants, there was a highly statistically significant 20 percent reduction in risk of cardiovascular death, nonfatal MI or stroke among those assigned to clopidogrel. The reduction in risk was about 10 percent in women and was not statistically significant. The risk of a major bleeding was 38 percent higher for participants receiving clopidogrel (p = .001); however risks for life-threatening bleeding complications and hemorrhagic strokes were not increased.

To Reduce Risk of Coronary Events in Patients Undergoing Percutaneous Coronary Intervention

G.2. Mehta SR, Yusuf S, Peters RJ, et al. Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study. Lancet 2001;358(9281):527-33.[51]

PCI-CURE is a randomized trial comparing the effect of extended treatment with clopidogrel among a subset of CURE participants who underwent percutaneous coronary intervention (PCI). All participants received open-label treatment with aspirin (75-325 mg/day) and were randomized to clopidogrel (300mg loading dose, followed by

75mg/day) or placebo within 24-hours of the onset of acute coronary symptoms. Those who underwent PCI had blinded study medication stopped and received 2-4 weeks of open label treatment after PCI with either clopidogrel or ticlopidine. They were then restarted on blinded study medication that continued for 3 to 12 months. Thus, the main comparison is between short-term treatment with clopidogrel or ticlopidine (2 to 4 weeks) after PCI compared to long-term treatment (3 to 12 months). The risk of death from cardiovascular causes, nonfatal MI, or stroke was assessed among 2,658 participants (30 percent women) who underwent PCI.

	All (N=2,658)			Women (N=804; 30%)		
Outcome	RR	95% CI	p-value	RR	95% CI	p-value
Primary Event*	.70	.50-.97	.03	.77	.52-1.15	NA**

*Death from cardiovascular causes, nonfatal MI, or stroke
**figure demonstrates that 95 percent CI crosses 1.0.

In this subgroup analysis, risk for death from cardiovascular causes, nonfatal MI or stroke was statistically significantly reduced 30 percent among all participants. Among women, the risk reduction was about 20 percent and was not statistically significant. The risk of bleeding following PTCA was not increased by treatment with clopidogrel.

Summary and Recommendations

Results from the CURE trial [50] suggest that 2 to 4 weeks of treatment with clopidogrel among women with acute coronary syndromes probably reduces risk of cardiovascular events and death about 10 to 20 percent. This benefit was associated with about a 40 percent increased risk of major bleeding, but risks for life-threatening bleeding complications and hemorrhagic stroke were not increased. Prolonged treatment (3 to 12 months) with clopidogrel among women undergoing percutaneous coronary intervention[51] also appears to reduce risk of cardiovascular events and death about 20 to 30 percnet more than brief treatment (2 to 4 weeks). However, these estimates of benefit are based only on the results of one trial, the effects in women were uniformly lower than in men, and the results were not statistically significant. Treatment with clopidogrel among persons undergoing PCI was not associated with serious adverse side effects.

A systematic review of the effect of clopidogrel on CHD outcomes in women is not feasible given that only one major randomized trial has been published.

2.11 Percutaneous transluminal coronary angioplasty (PTCA) and stenting

Angioplasty compared to medical management in patients with CHD

F.1. Coronary angioplasty versus medical therapy for angina: the second Randomised Intervention Treatment of Angina (RITA-2) trial. RITA-2 trial participants. Lancet 1997;350(9076):461-8.[52]

RITA-2 was a randomized trial to compare long-term CHD outcomes following PTCA to medical management in patients with CHD. Patients were required to have coronary disease that was suitable for either PTCA or medical management and a significant stenosis of at least one major coronary vessel that appeared technically amenable to PTCA. Participants were not required to have symptoms of angina. Between 1992 and 1996, 1,018 participants (183 women) were enrolled. The primary outcome was death plus nonfatal MI after an average of 2.7 years of follow-up. Major findings, comparing PTCA to medical management are presented below:

	All (N=1,018)			Women (N=183; 18%)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
Mortality	1.6	NA	.32	NA		
Death + nonfatal MI	1.9	1.08-3.41	.02	NA		
CABG	1.4	NA	NA	NA		

Among all patients, risk of death or nonfatal MI was 90 percent higher among those randomized to PTCA compared to those randomized to medical therapy. The authors state that there were no differences in the primary outcome by gender, but no quantitative estimates are given. Both men and women were less likely to experience grade 2 or worse angina (Canadian Cardiovascular Society) during the first six months following PTCA (in women: 22.8 percent PTCA versus 39.8 percent medical management, in men: 20.5 percent PTCA versus 31.4 percent medical management). However, these differences in prevalence of angina in the treatment groups were markedly attenuated over time such that there was no difference in prevalence of angina by 3 years of follow-up.

This trial was rated fair quality because it was not blinded.

Angioplasty compared to CABG for treatment of symptomatic multivessel coronary disease

G.2. First-year results of CABRI (Coronary Angioplasty versus Bypass Revascularisation Investigation). CABRI Trial Participants. Lancet 1995;346(8984):1179-84.[53]

The Coronary Angioplasty versus Bypass Revascularisation Investigation (CABRI) was an international randomized trial comparing CABG and PTCA for 1,054 patients with symptomatic multivessel coronary disease. Recruitment began in 1988 and continued for 53 months. The primary outcomes were angina (Canadian Cardiovascular Society class >1) and mortality after one year of follow-up. Major findings comparing PTCA to CABG are presented below:

	All (N=1,054)			Women (N=234; 22%)		
Outcome	RR	95% CI	p-value	RR	95% CI	p-value
Mortality	1.42	.73-2.76	.30	NA	NA	NA
Nonfatal MI	1.42	.80-2.54	.23	NA	NA	NA
Angina	1.54	1.09-2.16	.01	3.12	1.4-6.5	.002
Revascularization	5.23	3.9-7.0	<.001	NA	NA	NA

For both genders combined there were no significant differences in risk of death or nonfatal MI between the CABG and PTCA groups. Overall, PTCA was associated with an increased risk for clinically significant angina and with a marked increased risk of undergoing another revascularization procedure within one year. Among women, the prevalence of angina after 1 year was 3-fold higher with PTCA compared to CABG. In contrast, men were about 50 percent more likely to experience angina after PTCA compared to CABG but this difference between men and women was not statistically significant (p for interaction = .052). Other risk estimates for women were not presented.

Angioplasty compared to thrombolysis for acute MI

F.3. Stone GW, Grines CL, Browne KF, Marco J, Rothbaum D, O'Keefe J, et al. Comparison of in-hospital outcome in men versus women treated by either thrombolytic therapy or primary coronary angioplasty for acute myocardial infarction. Am J Cardiol 1995;75(15):987-92.[49]

The Primary Angioplasty in Myocardial Infarction (PAMI) trial was a randomized trial to compare CHD outcomes in participants with acute MI randomized to tissue plasminogen activator (100 mg) and subsequent conservative therapy or immediate PTCA. Between 1990 and 1992, 395 participants (107 women) were enrolled within 12 hours of the onset of anginal symptoms. The primary outcome was in-hospital mortality and acute MI. Major findings comparing immediate PTCA to thrombolyis are as follows:

	Men (N=288)			Women (N=107; 27%)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
In-hospital mortality	.60	NA	.46	.29	NA	.07
MI	.36	NA	.06	.57	NA	.64

Mortality and risk of MI were lower among both men and women with symptoms of acute MI treated with immediate PTCA compared to those treated with tissue plasminogen activator. However, none of the outcomes were statistically significant, probably because the trial was too small.

No strokes occurred among either men or women in the PTCA group, while 2.8 percent of men and 5.3 percent of women experienced a stroke in the tissue plasminogen activator group. All of the strokes in women were hemorrhagic. Among patients assigned to tissue plasminogen activator, mortality in women was higher than in men (14.0 vs. 4 percent); there was no difference in mortality rates among women and men assigned to PTCA. At baseline women were, on average, 8 years older than men and more likely to have diabetes, hypertension, history of CHF, and had a longer interval of time between onset of symptoms and randomization. After multivariate adjustment for these risk factors, gender was no longer predictive of mortality with tissue plasminogen activator ($p = .25$).

This trial was rated fair quality because it was not blinded.

Prospective Cohort Studies

We reviewed eight prospective cohort studies that assessed the association between PTCA and CHD outcomes. The findings from these studies indicate that women are at higher risk than men for in-hospital mortality following PTCA.[7, 54-58] Possible explanations for this observation include older age, more severe underlying disease and anatomical differences, such as smaller vessel size and decreased body surface area, which may predispose women to an increased risk of death in the post-procedure period.[58] Longer term clinical success rates following PTCA were also measured in several cohorts.[7, 55, 56, 59] In these studies, the main measure of clinical success was the probability of survival following PTCA (1 year to 10 years). Between 70 and 90 percent of all patients survived during this time interval. Survival rates did not differ by gender; however, women were as much as 78 percent more likely than men to experience symptoms of angina during long-term follow-up.[7]

G.4. Holmes DR, Jr., Holubkov R, Vlietstra RE, Kelsey SF, Reeder GS, Dorros G, et al. Comparison of complications during percutaneous transluminal coronary angioplasty from 1977 to 1981 and from 1985 to 1986: the National Heart, Lung, and Blood Institute Percutaneous Transluminal Coronary Angioplasty Registry. J Am Coll Cardiol 1988;12(5):1149-55.[54]

G.5. Kelsey SF, James M, Holubkov AL, Holubkov R, Cowley MJ, Detre KM. Results of percutaneous transluminal coronary angioplasty in women. 1985-1986 National Heart, Lung, and Blood Institute's Coronary Angioplasty Registry. Circulation 1993;87(3):720-7.[7]

G.6. Weintraub WS, Wenger NK, Kosinski AS, Douglas JS, Jr., Liberman HA, Morris DC, et al. Percutaneous transluminal coronary angioplasty in women compared with men. J Am Coll Cardiol 1994;24(1):81-90.[55]

G.7. Mehilli J, Kastrati A, Dirschinger J, Bollwein H, Neumann FJ, Schomig A. Differences in prognostic factors and outcomes between women and men undergoing coronary artery stenting. JAMA 2000;284(14):1799-805.[56]

F.8. Bell MR, Holmes DR, Jr., Berger PB, Garratt KN, Bailey KR, Gersh BJ. The changing in-hospital mortality of women undergoing percutaneous transluminal coronary angioplasty. JAMA 1993;269(16):2091-5.[57]

G.9. Ellis SG, Roubin GS, King SB, 3rd, Douglas JS, Jr., Shaw RE, Stertzer SH, et al. In-hospital cardiac mortality after acute closure after coronary angioplasty: analysis of risk factors from 8,207 procedures. J Am Coll Cardiol 1988;11(2):211-6.[58]

F.10. Shaw LJ, Miller DD, Romeis JC, Kargl D, Younis LT, Chaitman BR. Gender differences in the noninvasive evaluation and management of patients with suspected coronary artery disease. Ann Intern Med 1994;120(7):559-66.[14]

F.11. Bell MR, Grill DE, Garratt KN, Berger PB, Gersh BJ, Holmes DR, Jr. Long-term outcome of women compared with men after successful coronary angioplasty. Circulation 1995;91(12):2876-81.[59]

Coronary stenting

No studies were identified that provided data on the efficacy of coronary stenting to reduce risk of CHD events in women.

Summary and Recommendations

Evidence regarding the efficacy of PTCA to reduce the risk of CHD events in women is weak. For treatment of patients with symptomatic coronary artery disease who are suitable for PTCA or medical therapy, one small trial including only 183 women suggests that PTCA is more likely to result in death or nonfatal MI at 3 years than medical management, but no specific estimates were given for women.[52] PTCA did appear to be superior to medical management for relief of angina in the first 6 months, but there was no difference in symptoms after 3 years of follow-up.

One trial,[53] including only 234 women, suggested that CABG and PTCA have similar effects on risk for CHD events at one year after the procedure among women with symptomatic multivessel coronary disease. In women, PTCA was associated with 3-fold higher rates of angina at one year compared to CABG, but quantitative estimates among women for other outcomes were not given.[53]

For treatment of patients during acute MI, one small trial including only 107 women suggested that PTCA may be more effective than thrombolysis for reducing in-hospital mortality in women (70 percent reduction) than in men (40 percent reduction), and much less likely to cause hemorrhagic stroke,[49] but none of the relative risk estimates were statistically significant.

Whether PTCA is superior to medical management or CABG for management of CHD in women is very important and currently unanswered. However, there appears to be insufficient data to conduct a definitive systematic review of these questions.

2.12 Coronary artery bypass graft surgery

CABG surgery compared to medical therapy for treatment of symptomatic coronary disease

G.1. Davis KB, Chaitman B, Ryan T, Bittner V, Kennedy JW. Comparison of 15-year survival for men and women after initial medical or surgical treatment for coronary artery disease: a CASS registry study. Coronary Artery Surgery Study. J Am Coll Cardiol 1995;25(5):1000-9.[60]

This is a prospective cohort study based on the Coronary Artery Surgery Study Registry of men and women with operable symptomatic coronary disease who were treated with either medical therapy or CABG surgery at one of 15 medical centers in the US between 1974 and 1979. The main outcomes were 8 and 15-year survival, based on 6,018 men and 1,095 women who were initially managed medically, and 6,922 men and 1,291 women who were initially managed surgically. Operative mortality was 2.5 percent among men and 5.3 percent among women (P<.0001). Multivariate adjusted relative risks for 8-year survival comparing medical management to CABG surgery are given below:

	Men (N=12,940)			Women (N=2,386; 16%)		
Outcome	RR	95% CI	p-value	RR	95% CI	p-value
8-year survival						
single vessel disease	1.07	NA	<.05	1.05	NA	>.05
double vessel disease	1.17	NA	<.05	1.13	N A	<.05
triple vessel disease	1.41	NA	>.05	1.56	NA	<.05

At 8 years, both men and women with double or triple vessel CHD appear to have improved survival, with the largest benefit in those with triple vessel disease. At 15 years, there were no differences between survival rates for medical and surgical management in either men or women, but 75 percent of all of the men and 72 percent of the women had undergone CABG surgery at 15 years.

CABG surgery compared to angioplasty for treatment of symptomatic multivessel coronary disease

G.2. First-year results of CABRI (Coronary Angioplasty versus Bypass Revascularisation Investigation). CABRI Trial Participants. Lancet 1995;346(8984):1179-84.[53]

The Coronary Angioplasty versus Bypass Revascularisation Investigation (CABRI) was an international randomized trial comparing CABG surgery and PTCA for 1,054 patients with symptomatic multivessel coronary disease. Participant recruitment began in 1988 and continued for 53 months. The primary outcomes were angina (Canadian Cardiovascular Society class >1) and mortality after one year of follow-up. Major findings comparing PTCA to CABG surgery are presented below:

	All (N=1,054)			Women (N=234; 22%)		
Outcome	RR	95% CI	p-value	RR	95% CI	p-value
Mortality	1.42	.73-2.76	.30	NA	NA	NA
Nonfatal MI	1.42	.80-2.54	.23	NA	NA	NA
Angina	1.54	1.09-2.16	.01	3.12	1.4-6.5	.002
Revascularization	5.23	3.9-7.0	<.001	NA	NA	NA

For both genders combined there were no significant differences in risk of death or nonfatal MI between the CABG surgery and PTCA groups. Overall, PTCA was associated with an increased risk for clinically significant angina and with a marked increased risk of undergoing another revascularization procedure within one year. Among women, the prevalence of angina after 1 year was 3-fold higher with PTCA compared to CABG surgery. In contrast, men were about 50 percent more likely to experience angina after PTCA compared to CABG surgery, but this difference between men and women in effect of the procedures on angina was not statistically significant (p for interaction = .052). Other risk estimates were for women were not presented.

G.3. Jacobs AK, Kelsey SF, Brooks MM, Faxon DP, Chaitman BR, Bittner V, et al. Better outcome for women compared with men undergoing coronary revascularization: a report from the bypass angioplasty revascularization investigation (BARI). Circulation 1998;98(13):1279-85.[61]

The Bypass Angioplasty Revascularization Investigation (BARI) was a randomized trial to assess the effect of CABG surgery compared to PTCA among 1,829 participants (489 women; 27 percent) with angina or myocardial ischemia and multivessel coronary disease amenable to both CABG surgery and PTCA. The average length of follow-up was 5 years.

Data from this article are difficult to interpret because only crude rates are presented. Relative risk estimates, confidence intervals and p-values were not provided. The authors note that the risk for in-hospital MI was significantly reduced among women who underwent PTCA compared to CABG surgery (4.8 vs. 9.8 percent; p=.03). In men, rates of in-hospital MI were also lower among those randomized to PTCA compared to CABG surgery (2.4 vs. 4.6 percent), but this comparison was presumably not statistically significant, as no p-value was given. No information on 5-year outcomes among women is presented.

Summary and Recommendations

Evidence regarding the efficacy of CABG surgery to reduce the risk of CHD events and death in women is limited. One large cohort study[60] suggests that despite a high perioperative mortality rate (5.3 percent), 8-year survival is improved in women with double or triple vessel coronary disease who undergo CABG surgery compared to initial medical management. By 15 years of observation, the majority of women (72 percent) had undergone CABG surgery and there was no difference in long-term survival among those initially treated surgically compared to those initially treated medically. The results of this study may be biased by differences in risk between patients who are chosen to undergo CABG surgery compared to those chosen to receive medical therapy.

Randomized trials to compare the effectiveness of CABG surgery and PTCA provide little evidence regarding the relative effectiveness of these procedures in women. The Coronary Angioplasty versus Bypass Revascularisation Investigation[53] suggests that neither revascularization procedure is superior with regard to mortality or CHD outcomes in women, but that CABG surgery is more effective than PTCA in relieving angina and is less likely to be followed by additional revascularization procedures.

Coronary artery bypass surgery is a major procedure that is associated with substantial perioperative morbidity, mortality and expense. It is not clear that a systematic review of the data regarding the efficacy of this procedure for preventing CHD events in women is feasible. However, this topic is very important given the potential benefits and risks of bypass surgery in women. Given this, we recommend that a systematic review be attempted. If data are inadequate to provide definitive answers, additional research should be conducted.

QUESTION 3

3. What are the risk factors for coronary heart disease in women, does modifying these risk factors result in reduced risk for coronary heart disease events, and what are the most effective methods for modifying these risk factors? (20 subtopics labeled 3.01-3.12 with subtopic as a risk factor for CHD or treatment/modification of a risk factor for CHD prevention considered separately where appropriate)

3.01 hypertension:
- a. as a risk factor
- b. treatment

3.02 diabetes
- a. as a risk factor
- b. treatment

3.03 hyperlipidemia (high LDL, triglycerides, Lp(a), low HDL)
- a. as a risk factor
- b. treatment

3.04 homocysteine
- a. as a risk factor
- b. treatment

3.05 C-reactive protein
- a. as a risk factor
- b. treatment

3.06 cigarette smoking
- a. as a risk factor
- b. smoking cessation

3.07 obesity
- a. as a risk factor
- b. weight reduction to reduce risk

3.08 inactivity
- a. as a risk factor
- b. exercise

3.09 age

3.10 age at menopause

3.11 ethnicity

3.12 socioeconomic status

3.01a Hypertension as a risk factor for CHD in women

We identified no systematic reviews that addressed the strength of hypertension as a risk factor for CHD outcomes in women.

Prospective Cohort Studies

Data from the Nurses' Health Study[62] and from the Framingham Heart Study[63] suggest a 2 to 3-fold increased risk of coronary heart disease events among women with hypertension, after adjustment for other CHD risk factors. However, the evidence from these two studies is not convincing. In the Nurses' Health Study,[62] hypertension was self-reported and blood pressure was not measured. The report from the Framingham Heart Study[63] provides no definition of hypertension and no confidence intervals or p-values for the reported risk estimates. Among women in the Copenhagen City Heart Study, [64], isolated systolic hypertension (SBP $\geq$ 160 mm Hg and DBP < 90 mm Hg) was not associated with an increased risk of MI (RR = 0.8; 95 % CI, 0.3 – 2.0), but women with diastolic hypertension (DBP > 90 mm Hg) were 1.7 times more likely than normotensive women to have a MI (95 % CI, 1.1 – 2.8). In the Walnut Creek Cohort, [65] the risk all-cause mortality (excluding accidental death) was 1.6 times higher among premenopausal women with high blood pressure compared to those without. The risk of all-cause mortality was not significantly higher among postmenopausal women with high blood pressure compared to those without.

G.1. Fiebach NH, Hebert PR, Stampfer MJ, Colditz GA, Willett WC, Rosner B, et al. A prospective study of high blood pressure and cardiovascular disease in women. Am J Epidemiol 1989;130(4):646-54.[62]
G.2. Kannel WB. Blood pressure as a cardiovascular risk factor: prevention and treatment. JAMA 1996;275(20):1571-6.[63]
F.3. Nielsen WB, Vestbo J, Jensen GB. Isolated systolic hypertension as a major risk factor for stroke and myocardial infarction and an unexploited source of cardiovascular prevention: a prospective population-based study. J Hum Hypertens 1995;9:175-80.[64]
F.4. Perlman JA, Wolf PH, Ray R, Lieberknecht G. Cardiovascular risk factors, premature heart disease, and all-cause mortality in a cohort of Northern California women. Am J Obstet Gynecol. 1988;158:1568-74.[65]

3.01b Treatment of hypertension to reduce risk of CHD events in women

Systematic Reviews

F.1. Gueyffier F, Boutitie F, Boissel JP, Pocock S, Coope J, Cutler J, et al. Effect of antihypertensive drug treatment on cardiovascular outcomes in women and men. A meta-analysis of individual patient data from randomized, controlled trials. The INDANA Investigators. Ann Intern Med 1997;126(10):761-7.[66]

This systematic review from the Individual Data Analysis of Antihypertensive intervention trials (INDANA) pooled data from seven large randomized trials that studied the effect of treatment for hypertension on CVD outcomes. All trials were conducted between 1972 and 1990. Only trials that enrolled both men and women were included. Results from only 7 of 15 published clinical trials were included in this review, but these 7 trials represent 97 percent of all participants in the 15 trials. Drug interventions included thiazide diuretics and/or beta-blockers. The primary outcomes were fatal and nonfatal cardiovascular events among hypertensive men and women aged 30 to 84 years.

	Men (N=19,975)			Women (N=20,802; 68%)		
Outcome	RR	95% CI	*P*-value	RR	95% CI	*P*-value
Mortality	.88	.80-.97	.01	.91	.81-1.01	.09
Fatal CHD events	.83	.71-.97	.02	.92	.74-1.16	.48
Major CHD events	.82	.73-.92	<.001	.85	.72-1.01	.06

Among treated hypertensive men, there was a statistically significant 12 percent reduction in risk of mortality, a 17 percent reduction in risk of fatal CHD events, and an 18 percent reduction in risk of major coronary events. While none of the risk estimates in women were statistically significant, there were strong statistical trends suggesting that the patterns of risk reduction for mortality (9 percent reduction) and major coronary events (15 percent reduction) were similar to those in men. There was no evidence of an interaction between treatment effect and gender (p >.10).

This manuscript was given a fair quality rating because it did not describe the search or data abstraction methods.

G.2. Quan A, Kerlikowske K, Gueyffier F, Boissel JP. Efficacy of treating hypertension in women. J Gen Intern Med 1999;14(12):718-29.[67]
Quan A, Kerlikowske K, Gueyffier F, Boissel JP. Pharmacotherapy for hypertension in women of different races. Cochrane Database Syst Rev 2000(3):CD002146.[68]

This is a systematic review of the findings of 11 randomized trials that studied the effect of treatment for hypertension on risk for CVD events in women. Clinical trials were included if they met the following criteria: publication between 1966 and 1998, more than 100 women, hypertension was defined, the intervention was a drug, the control group received a placebo or standard care, and the outcomes included CVD events. CHD outcomes included all cause mortality, fatal CHD events and all CHD events (fatal and nonfatal). Interventions included diuretics, beta-blockers, calcium channel blockers, and clonidine. After adjustment for baseline risk factors, the findings were as follows.

	Women 30-54 years (N=8,565)			Women ≥ 55 years (N=17,604)		
Outcome	RR	95% CI	*P*-value	RR	95% CI	*P*-value
Mortality	.92	.68-2.79	NA	.89	.77-1.02	NA
Fatal CHD	1.47	.78-4.76	NA	.84	.65-1.08	NA
CHD events*	.80	.56-2.86	NA	.82	.67-1.01	NA

*fatal and nonfatal events

None of the effects of treatment were statistically significant. However, there were strong trends to reduced risk of mortality, fatal CHD and CHD events in older women. Among younger women, the pattern of risk reduction for mortality and CHD events was similar to that among women 55 or older, but the confidence intervals were much wider. There was no statistical evidence of an interaction between treatment effect and age.

	White Women (N=22,963)			African-American Women (N=3,206)		
Outcome	RR	95% CI	*P*-value	RR	95% CI	*P*-value
Mortality	.98	.85-1.13	NA	.59	.44-80	NA
Fatal CHD	.95	.73-1.23	NA	.71	.40-1.25	NA
CHD events	.88	.72-1.08	NA	.61	.42-.89	NA

Among white women, there was no evidence that treatment reduced risk. In contrast, treatment was associated with a 30 to 40 percent reduction in the risk of mortality and CHD events among African-American women. These risk reductions were statistically significant among African-American women, despite the relatively small number included in the trials. There was statistical evidence of interaction of the effects of treatment and race on total mortality (p =.003).

Randomized Trials Not Included in the Systematic Reviews

F.3. Wang J, Staessen JA, Gong L, Liu L. Chinese trial on isolated systolic hypertension in the elderly. The Systolic Hypertension in China (Syst-China) Collaborative Group. Arch Intern Med 2000;160:211-20.[69]

Syst-China was a randomized trial to test the effect of treatment for isolated systolic hypertension on CVD outcomes. Between 1988 and 1991, 2,394 persons age 60 or older (36 percent women) with systolic blood pressures between 160 and 219 mm Hg, were randomized to active treatment (nitrendipine plus captopril, and/or hyrochlorothiazide) or placebo. The median follow-up time was 3 years.

	Men (N=1,541)			Women N=853)		
Outcome	RR	95% CI	*P*-value	RR	95% CI	*P*-value
Mortality	.74	.50-1.09	.12	.34	.16-.72	.005

The treatment-by-sex interaction approached statistical significance (p = .06), indicating that the mortality benefit associated with treatment of isolated systolic hypertension may be greater in women than in men.

Summary and Recommendations

Hypertension as a Risk Factor for CHD in Women

Results of four large cohort studies[62-65] suggest that hypertension, especially diastolic hypertension, is associated with a 1.6 to 3-fold increased risk for coronary heart disease events in women. Substantial additional data regarding the association of high blood pressure and CHD outcomes in women could likely be obtained from the placebo groups followed in large clinical trials of treatment for hypertension. Based on these data, a systematic review and meta-analysis would likely be feasible. Summary estimates of the effect of blood pressure on CHD risk could be important in helping to identify the women who are most likely to benefit from therapy.

Treatment of Hypertension to Reduce Risk of CHD Events in Women

The best evidence regarding the effect of treatment of hypertension on risk for CHD events among women comes from two systematic reviews. The systematic review by the INDANA investigators[66] suggests that treatment of hypertension in women results in small reductions in risk of mortality (9 percent) and CHD events (15 percent), but the findings were not statistically significant. The systematic review by Quan et al.[67] found

strong statistical trends to reduced risk of mortality (11 percent), fatal CHD events (16 percent) and all CHD events (18 percent) among women over age 55 years, but not among younger women. These differences between younger and older women may be due to the small number of events that occurred in younger women. The systematic review by Quan et al.[67] also provides the only evidence regarding treatment of hypertension in women by race. Although relatively few black women were included in the trials, they experienced a statistically significant reduction in risk of mortality (41 percent) and of CHD events (39 percent). There was no evidence of benefit among white women, and there was statistical evidence that the effect of treatment on mortality differed in white and black women. The findings of the Syst-China trial[69] suggest that treatment of isolated systolic hypertension may reduce the risk of mortality by as much as 65 percent in elderly Chinese women. The reason for this difference in the effect of treatment of hypertension between races is not clear.

Repeating the two relatively recent systematic reviews is unlikely to add additional clinical information.

3.02a Diabetes as a risk factor for CHD in women

Systematic Reviews

F.1. Orchard TJ. The impact of gender and general risk factors on the occurrence of atherosclerotic vascular disease in non-insulin-dependent diabetes mellitus. Ann Med 1996;28(4):323-33.[70]

This is a systematic review of the results from 12 prospective cohort studies published between 1980 and 1993 that address the association between non-insulin dependent diabetes and CHD events in men and women. Diabetes was defined by glucose tolerance testing, medication use, or medical history. The main outcomes were CHD death and MI. Follow-up ranged from 2 to 30 years. The authors did not calculate summary estimates comparing risk for CHD death among diabetic and nondiabetic men and women. Instead, they calculated a summary relative risk comparing the risk for CHD events among women to that among men.

	RR	95% CI
CHD death		
Diabetics	1.47	1.09-1.99
Nondiabetics	2.52	1.91-3.34
MI		
Diabetics	1.75	1.23-2.49
Nondiabetics	1.92	1.36-2.79

The findings suggest that men diabetics and non-diabetics have a higher risk for CHD events than women. The increased risk associated with male sex is about 2 to 2.5-fold for nondiabetics, but only 1.5 to 2-fold for diabetics. The narrowing of the male disadvantage with respect to CHD risk suggests that diabetes is a stronger risk factor for CHD in women than in men. These findings are limited because the outcomes of the individual studies were not adjusted for other predictors of CHD events, and there was significant between-study heterogeneity of the findings.

This study was rated fair quality based on the lack of a systematic literature search.

G.2. Lee WL, Cheung AM, Cape D, Zinman B. Impact of diabetes on coronary artery disease in women and men: a meta-analysis of prospective studies. Diabetes Care 2000;23(7):962-8.[71]

This is a systematic review of 10 prospective cohort studies published between 1966 and 1999 evaluating the association between diabetes and CHD risk. The criteria for inclusion were prospective cohort studies that provided data on the risk of CHD events in both men and women with diabetes. Diabetes was diagnosed by self-report, physician diagnosis, treatment with insulin or oral hypoglycemic agents, or random or fasting glucose measures. The primary outcome was CHD mortality. Follow-up time ranged from 4 to 36 years.

	Men			Women		
	RR*	95% CI	p-value	RR*	95% CI	p-value
CHD death	1.85	1.47-2.33	NA	2.58	2.05-3.26	NA

*summary RR comparing risk for CHD death among diabetics to nondiabetics

These results suggest that risk for CHD death is increased 2.6-fold in diabetic women compared to nondiabetic women and 1.8-fold in diabetic men compared to nondiabetic men. While many of the individual studies provided outcomes adjusted for other predictors of CHD risk, the meta-analytic techniques used to calculate summary estimates included only unadjusted estimates.

Cohort Studies Not Included in the Systematic Reviews

We reviewed data from four cohort studies, including the Framingham Heart Study[72-74] and the Nurses Health Study.[75, 76] The findings suggest that diabetes is associated with a 1.5 to 3-fold increased risk of CHD events in women after adjustment for other risk factors. The relative risk of CHD events among women with diabetes appears to be almost twice that of men with diabetes.[72, 74] However, there is considerable variation in the levels of other CHD risk factors among men and women in these studies making evaluations of gender differences difficult.

G.3. Abbott RD, Donahue RP, Kannel WB, Wilson PW. The impact of diabetes on survival following myocardial infarction in men vs women. The Framingham Study. JAMA 1988;260(23):3456-60.[72]
G.4. Brand FN, Abbott RD, Kannel WB. Diabetes, intermittent claudication, and risk of cardiovascular events. The Framingham Study. Diabetes 1989;38(4):504-9.[73]
G.5. Kannel WB, D'Agostino RB, Wilson PW, Belanger AJ, Gagnon DR. Diabetes, fibrinogen, and risk of cardiovascular disease: the Framingham experience. Am Heart J 1990;120(3):672-6.[74]
G.6. Manson JE, Colditz GA, Stampfer MJ, Willett WC, Krolewski AS, Rosner B, et al. A prospective study of maturity-onset diabetes mellitus and risk of coronary heart disease and stroke in women. Arch Intern Med 1991;151(6):1141-7.[75]
G.7. Donahue RP, Goldberg RJ, Chen Z, Gore JM, Alpert JS. The influence of sex and diabetes mellitus on survival following acute myocardial infarction: a community-wide perspective. J Clin Epidemiol 1993;46(3):245-52.[77]
G.8. Malmberg K, Yusuf S, Gerstein HC, Brown J, Zhao F, Hunt D, et al. Impact of diabetes on long-term prognosis in patients with unstable angina and non-Q-wave myocardial infarction: results of the OASIS (Organization to Assess Strategies for Ischemic Syndromes) Registry. Circulation 2000;102(9):1014-9.[78]
G.9. Hu FB, Stampfer MJ, Solomon CG, Liu S, Willett WC, Speizer FE, et al. The impact of diabetes mellitus on mortality from all causes and coronary heart disease in women: 20 years of follow-up. Arch Intern Med 2001;161(14):1717-23.[76]

3.02b Treatment of diabetes to reduce risk of CHD events in women

There were no systematic reviews or randomized trials identified that addressed the effectiveness of treatment of diabetes to reduce risk of CHD events in women.

Summary and Recommendations

Diabetes as a Risk Factor for CHD in Women

The systematic review by Orchard et al.[70] suggests that the relative risk for CHD events is higher among women than among men diabetics, but does not provide an estimate of the summary relative risk in women. The systematic review by Lee et al.[71] reported that risk for CHD death was about 2.6-fold higher among women diabetics compared to non-diabetics. This increase in risk appears to be higher than that associated with diabetes in men (1.8-fold increased risk). One explanation for the higher risk among women than among men diabetics is that diabetes is, by mechanisms that are not clear, more harmful in women than in men. Alternatively, women diabetics may be more likely to have other CHD risk factors, or more severe CHD risk factors than men diabetics. The summary estimates calculated by Lee et al.[71] were based on unadjusted findings and do not address this issue. In addition, the systematic review by Lee et al.[71] does not include the results

from several studies that were analyzed in the earlier systematic review by Orchard et al.[70] It is feasible to update these systematic reviews and to calculate comparable, adjusted relative risk estimates in men and women diabetics. An adjusted analysis may provide clinically and scientifically important evidence to determine if diabetes has more harmful effects on CHD risk in women or is more likely to be associated with other risk factors in women.

Treatment of Diabetes to Reduce Risk of CHD Events in Women

There was no evidence regarding the efficacy of treatment of diabetes to reduce the risk of CHD events in women.

3.03.a Hyperlipidemia as a risk factor for CHD in women

Total, LDL- and HDL-cholesterol, and triglycerides

F.1. Manolio TA, Pearson TA, Wenger NK, Barrett-Connor E, Payne GH, Harlan WR. Cholesterol and heart disease in older persons and women. Review of an NHLBI workshop. Ann Epidemiol 1992;2(1-2):161-76.[79]

This systematic review includes the findings of 22 United States (US) and international cohort studies presented at a workshop at the National Heart Lung and Blood Institute in 1991. Inclusion criteria were measurement of serum cholesterol, follow-up for CHD events, explicit criteria for CHD outcomes and availability of results stratified by gender, age and ethnicity. The review includes 90,349 women, 891,882 men, and data stratified by ethnicity among approximately 348,600 men who were screened for the Multiple Risk Factor Intervention Trial (MRFIT) (316,000 white, 22,000 black, 6,600 Hispanic and 4,000 Asian men). Findings were summarized separately by gender, age at the time of lipid measurements (less than 65 years versus 65 years and older) and, where possible, ethnicity. The majority of the participants in these studies did not have CHD at the beginning of the study, but had either elevated cholesterol or other risk factors for CHD. Unadjusted relative risks for CHD mortality were summarized.

	Summary Relative Risk (95% CI)			
Sex and Age	Total Cholesterol*	LDL-C*	HDL-C*	Triglycerides*
Women				
<65 years	2.44†	3.27†	2.13†	1.98†
≥65 years	1.12	1.13	1.75†	1.39†
Men				
<65 years	1.73†	1.92†	2.31†	1.16†
≥65 years	1.32†	1.51†	1.09	1.24†

*RR compares those with total cholesterol <200 to ≥ 240 mg/dL; those with LDL-cholesterol <140 to ≥ 160 mg/dL , those with HDL-cholesterol ≥ 60mg/dL to < 50, and those with triglycerides < 100 mg/dL to ≥ 130 mg/dL.
† p<.05 for unadjusted comparisons

For women less than 65 years old, risk for CHD death increased with higher total cholesterol, LDL-C and triglycerides and with lower HDL-C. For women and men less than 65 years old, the increased relative risk associated with elevated total cholesterol, LDL-C and triglycerides was higher for women than for men, while the increased risk associated with low HDL-C was similar. Among older men, CHD mortality was increased with higher total cholesterol, LDL-C and triglycerides, but not with lower HDL-C. Among older women, only low HDL-C and high triglycerides were associated with increased risk.

No specific risk estimates were given for minority populations, but relative risks associated with elevated total cholesterol were said to be similar for white, black, Hispanic and Asian middle-aged and older men based on data from the MRFIT screenees.

This study was rated as fair because it did not provide information on how the cohorts included were identified or selected for inclusion. In addition, the summary estimates may be biased because the comparisons are not adjusted for potential confounding factors.

F.2. Jacobs D, Blackburn H, Higgins M, Reed D, Iso H, McMillan G, et al. Report of the Conference on Low Blood Cholesterol: Mortality Associations. Circulation 1992;86(3):1046-60.[80]

This systematic review includes the findings of 11 US and international cohort studies presented at a workshop at the National Heart Lung and Blood Institute in 1992. The purpose of this workshop was to investigate the association of low blood cholesterol and risk for non-cardiovascular death. Inclusion criteria were not stated. The review includes 124,814 women and 523,737 men, most of whom did not have CVD at the start of the studies. The main outcomes were death, CVD death, cancer death, and non-CVD, non-cancer death. When possible, adjusted outcomes from each individual cohort were used

to calculate the summary estimates. Results for the men included in the MRFIT screenees were presented separately because they constituted 67 percent of the population.

Total Cholesterol (mg/dL)	Relative Risk*			
	All death	CVD death	Cancer death	Non-CVD, non-cancer
MEN				
<160	1.17†	1.04	1.18†	1.32†
160-199	1.00	1.00	1.00	1.00
200-239	1.00	1.16†	.95	0.89†
≥240	1.14†	1.48†	.95	0.87†
MRFIT MEN				
<160	1.17†	0.89	1.23†	1.48†
160-199	1.00	1.00	1.00	1.00
200-239	1.05†	1.31†	.95	0.87†
≥240	1.22†	1.86†	.91†	0.84†
WOMEN				
<160	1.10	0.96	1.05	1.41†
160-199	1.00	1.00	1.00	1.00
200-239	0.94	0.95	1.01	0.92
≥240	0.97	1.09	0.97	0.82†

*comparing total cholesterol of 160-199 mg/dL to the other categories and excluding deaths that occurred in the first 5 years of follow-up
†p-value less than .05

Among men, risk for death was increased 15 to 20 percent and risk for CVD death was increased 50 to 80 percent among those with total cholesterol ≥240 mg/dL. Among men with cholesterol <160 mg/dL, risk for cancer death was increased about 20 percent and risk for non-CVD, non-cancer death was increased 30 to 50 percent. There were no statistically significant associations between total cholesterol levels and any cause of death among women, except that risk for non-CVD, non-cancer death was increased among women with cholesterol levels <160mg/dL.

This study was rated as fair because it did not provide information on how the cohorts included were identified or selected for inclusion.

G.3. Hokanson JE, Austin MA. Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population-based prospective studies. J Cardiovasc Risk 1996;3(2):213-9.[81]
G.4. Austin MA, Hokanson JE, Edwards KL. Hypertriglyceridemia as a cardiovascular risk factor. Am J Cardiol 1998;81(4A):7B-12B.[82]

These two manuscripts report the results of a systematic review of population-based international studies, published between 1965 and 1994, that assessed the correlation between triglyceride levels and risk for CVD (CVD death, CHD death, and MI). Inclusion criteria were prospective cohort design, population-based sampling, and a fasting triglyceride measurement. Seventeen studies provided data on men (N=46,413), with an average duration of follow-up of 8.4 years. Five studies provided data on women (N=10,864), with average duration of follow-up of 11.4 years. Six studies with men (N= 22,293) and two studies with women (N = 6,345) provided risk estimates adjusted for other potential confounders, including HDL-cholesterol level. Most participants in these studies did not have CVD at the start of the studies.

	Men (N=46,413/22,293)			Women (N=10,864; 19%/6,345; 22%)		
Outcome	OR*	95% CI	p-value	OR*	95% CI	p-value
CVD events						
unadjusted	1.32	1.26-1.39	NA	1.76	1.50-2.07	NA
adjusted	1.14	1.05-1.28	NA	1.37	1.13-1.66	NA

*per 1 mmol/L increase in triglyceride level

Risk of CVD events among men and women was correlated with triglyceride levels. The increased cardiovascular risk associated with elevated triglycerides appeared to be higher in women (about 40 percent increase in CVD risk per 1 mmol/L increase in triglyceride level) compared to men (about 15 percent increase per 1 mmol/L increase in triglyceride level).

Lipoprotein (a)

F.5. Craig WY, Neveux LM, Palomaki GE, Cleveland MM, Haddow JE. Lipoprotein(a) as a risk factor for ischemic heart disease: meat-analysis of prospective studies. Clin Chem 1998;44(11):2301-6.[83]

This is a systematic review of observational studies on the association between lipoprotein a (Lp(a)) and risk for CHD. The articles in this review were published between 1991 and 1997, and included persons without known CHD. The average length of follow-up was between 1 and 15 years. The outcomes were fatal and nonfatal CHD. The 12 cohort and nested case-control studies included in this review included 11,105 men. Three studies provided data on women (N = 547). The summary outcome was expressed as the ratio of Lp(a) level in mg/dL among cases and controls.

The overall association between Lp(a) and risk of ischemic heart disease was similar for males and females (case:control ratio = 1.42; 95% CI 1.21 – 1.63 in men, and case:control ratio = 1.32; 95% CI 1.19 – 1.45 in women). Adjustment for age, blood pressure, body mass index, smoking, and lipoprotein-related variables did not modify the significance of this relation. However, there was considerable between-study variability

in Lp(a) case:control ratios (p for heterogeneity < .001). Among women, the dose response relation between Lp(a) and ischemic heart disease was equivocal.

This study was rated fair quality because it did not describe the inclusion criteria or methods for independent data abstraction.

3.03b Treatment of hyperlipidemia to reduce risk of CHD events in women

F.1. Walsh JM, Grady D. Treatment of hyperlipidemia in women. JAMA 1995;274(14):1152-8.[84]

Primary and secondary prevention trials published between 1971 and 1994 were included in this systematic review of the effectiveness of interventions to lower cholesterol in women. The outcomes were total and CHD mortality. The authors identified three primary prevention trials and six secondary prevention trials. However, only two of the primary prevention trials, and three of the secondary prevention trials, included adequate data for inclusion in the meta-analyses. Interventions studied in the two primary prevention trials included low-saturated fat diet and colestipol. The interventions included in the three secondary prevention trials included clofibrate and simvastatin. Summary estimates of relative risks were calculated using standard meta-analytic methods.

	Primary Prevention (N=5,848)			Secondary Prevention (N=1,048)		
Outcome	RR	95% CI	p-value	RR	95% CI	p-value
Mortality	1.15	.90-1.46	NA	1.17	.70-1.96	NA
CHD Mortality	1.03	.62-1.70	NA	.36	.25-.52	NA

For primary prevention, there was no effect of treatment on CHD or total mortality. Given the small number of outcome events, there may have been inadequate power to detect differences. Also, two of the primary prevention trials were conducted in institutionalized populations that may not be representative of healthy women. For secondary prevention, there was a statistically significant 64 percent reduction in risk of CHD mortality among treated women, but no reduction in overall mortality.

This study was rated fair quality because it did not describe inclusion criteria or a blinded review of the findings.

F.2. Byington RP, Jukema JW, Salonen JT, Pitt B, Bruschke AV, Hoen H, et al. Reduction in cardiovascular events during pravastatin therapy. Pooled analysis of clinical events of the Pravastatin Atherosclerosis Intervention Program. Circulation 1995;92(9):2419-25.[85]

This is a systematic review of the data from four randomized, blinded, placebo controlled trials using pravastatin for reduction of cholesterol among persons with CHD and mildly to moderately elevated cholesterol. Outcomes were mortality and MI.

	All (N=1,891)			Women (N=67)		
Outcome	RR	95% CI	p-value	RR	95% CI	p-value
Mortality	.54	.25-1.09	.17	NA	NANA	
MI	.48	.20-.63	.001	NA	NA.04	

Only 4 MIs occurred among the women assigned to pravastatin and none in the placebo group. Thus, these 4 randomized trials of pravastatin provide no information on the effect of lipid-lowering in women.

This review was rated fair quality because it did not provide a clear description of search methods, inclusion criteria or methods for extracting data.

F.3. Buchwald H, Campos CT, Boen JR, Nguyen P, Williams SE, Lau J, et al. Gender-based mortality follow-up from the Program on the Surgical Control of the Hyperlipidemias (POSCH) and meta-analysis of lipid intervention trials. Women in POSCH and other lipid trials. Ann Surg 1996;224(4):486-98; discussion 498-500.[86]

This is a systematic review of lipid intervention trials. All trials were published between 1971 and 1994. Among the seven primary and secondary prevention trials included in the review, interventions were diet, clofibrate, colestipol, simvastatin, pravastatin, and ileal bypass surgery. Primary and secondary prevention trials were not analyzed separately.

	Men (N=11,173)			Women (N=7,077)		
Outcome	RR	95% CI	p-value	RR	95% CI	p-value
Mortality	.81	.67-.98	.03	.89	.60-1.32	.56

The findings suggested a 20 percent reduction in risk of mortality among men treated with cholesterol-lowering interventions, but no benefit in women.

The results from the Program On Surgical Control of the Hyperlipidemias (POSCH) were also presented in this report. Treatment with partial ileal bypass surgery in women did not reduce the risk of overall mortality, CHD mortality, or CHD events (CHD mortality or

nonfatal MI). In contrast, risk of CHD death and CHD death or nonfatal MI were significantly reduced among men in the surgical intervention group.

This review was rated fair quality because it did not provide a clear description of methods for searching or extracting data from identified studies.

G.4. LaRosa JC, He J, Vupputuri S. Effect of statins on risk of coronary disease: a meta-analysis of randomized controlled trials. JAMA 1999;282(24):2340-6.[87]

This is a systematic review of five clinical trials published between 1966 and 1998 on the effect of statin therapy on CHD risk. The criteria for inclusion were: treatment with statin drugs or placebo, at least 4 years of follow-up and clinical disease or death as the primary endpoint. The review included three secondary prevention trials (4S, CARE, LIPID) and two primary prevention trials (WOSCOPS and AFCAPS/TEXCAPS). Standard meta-analytic methods were used to calculate the following summary estimates.

	All (N=30,817)			Women (N=3,916;13%)		
Outcome	RR	95% CI	p-value	RR	95% CI	p-value
Mortality	.79	.72-.86	NA	NA	NA	NA
Major CHD events	.69	.64-.74	<.001	.71	.58-.87	<.001

Results were not stratified by primary and secondary prevention. There was about a 30 percent reduction in risk of major CHD events in all participants and in women treated with statins. Risk for total mortality was decreased in men treated with statins, but no data regarding total mortality in women was provided, probably because the number of women studied was relatively small.

4S = Scandinavian Simvastatin Survival Study; CARE = Cholesterol and Recurrent Events trial; LIPID = Long-term Intervention with Pravastatin in Ischaemic Disease; WOSCOPS = West of Scotland Coronary Prevention Study; AFCAPS/TEXCAPS = Air Force/Texas Coronary Artherosclerosis Prevention Study

Clinical Trials Not Included in the Systematic Reviews

G.5. Miettinen TA, Pyorala K, Olsson AG, Musliner TA, Cook TJ, Faergeman O, et al. Cholesterol-lowering therapy in women and elderly patients with myocardial infarction or angina pectoris: findings from the Scandinavian Simvastatin Survival Study (4S). Circulation 1997;96(12):4211-8.[88]

This manuscript provides additional data on women included in the Scandinavian Simvastatin Survival Study (4S). Main findings of the 4S were included in each of the three systematic reviews described above. 4S was a randomized trial that studied the effect of treatment with simvastatin on the risk of coronary events in persons with CHD. Between 1988 and 1989, 4,444 high-risk patients (827 women) from 94 clinical centers were randomized to simvastatin or placebo. All participants (age 35 – 70 years) had a

history of angina pectoris or myocardial infarction, and elevated serum cholesterol. The treatments were titrated between 10 mg and 40 mg, to achieve the goal LDL-cholesterol levels of 115-200 mg/dL. Outcomes were total mortality and major coronary events (coronary death, nonfatal definite or probable MI, silent MI or resuscitated cardiac arrest). The trial was stopped prematurely after a mean follow-up of 5.4 years, due to evidence of benefit with treatment.

	Men (N=3,617)			Women (N=827; 19%)		
Outcome	RR*	95% CI	p-value	RR*	95% CI	p-value
Mortality	.65	.53-.80	<.001	1.16	.68-1.99	.58
CHD death	.55	.43-.71	<.001	.86	.42-1.74	.67
Major CHD events	.66	.58-.75	<.001	.66	.48-.91	.01

Both men and women had a statistically significant 34 percent reduction in risk of major CHD events. However, men also had a statistically significant 35 to 45 percent reduction in risk of CHD death and total mortality. Similar benefits were not observed in women. The interaction between treatment and gender for the mortality outcome was not statistically significant. Overall, there was no difference between the treatment groups in other causes of death or side effects.

G.6. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,538 high-risk individuals: a randomized placebo controlled trial. Heart Protection Study Collaborative Group. Lancet 2002; 360:7-22.[89]

The MRC/BHF Heart Protection Study was a randomized trial to assess the effect of cholesterol-lowering on CHD outcomes. Between 1994 and 1997, 20,536 participants (5082 women) with known CHD, other occlusive arterial disease or diabetes were randomly assigned to simvastatin (40 mg daily) or identical placebo. The average length of follow-up was 5 years.

	All (N=20,536)			Women (N=5,082; 25%)		
Outcome	RR	95% CI	*P*-Value	RR	95% CI	*P*-Value
Mortality	.87	.81-.94	.0003			
Major vascular event*	.76	.72-.81	<.001	.81	NA	NA**

*Coronary death, nonfatal MI, stroke, coronary or non-coronary revascularization
**figure demonstrates that 95% CI does not cross 1.0.

The findings from this study indicate that, among men and women with known CHD or at high risk for CHD, treatment with simvastatin significantly lowers cardiovascular event rates by approximately 25 percent, regardless of pretreatment cholesterol levels. The risk of myopathy associated with treatment was about 0.01 percent.

Summary and Recommendations

Hyperlipidemia as a Risk Factor for CHD in Women

Evidence regarding the association of abnormal lipoprotein levels and CHD risk in women is inconclusive. The systematic review by Manolio et al.[79] suggests that the pattern of risk associated with hyperlipidemia in middle-aged women is similar to that for middle-aged men (increased risk for CHD mortality with higher total cholesterol, LDL-C and triglycerides, and with lower HDL-C). However, the pattern of risk among older women appears to be different than in men (i.e., CHD risk was increased among older men with higher total cholesterol and LDL-C, but not in older women). In addition, CHD risk was increased among older women with low HDL-C and high triglycerides, but not among older men with these lipid abnormalities. There are several limitations to the review by Manolio et al.,[79] including an outdated and incomplete literature search and the lack of adjusted results. Evidence provided by the systematic review by Jacobs et al.[80] is not very helpful, as summary data was provided only for total cholesterol levels. The systematic review by Hokanson, et al.[81] and Austin et al.[82] strongly suggests that elevated triglyceride level is a risk factor for CVD, and that this elevated risk is higher in women than in men.

The suggestion that the pattern of risk associated with lipoprotein abnormalities in women is different than in men could be clinically important. This is especially true because statins, which are the most widely used lipid-lowering drugs, primarily reduce LDL-cholesterol. If elevated LDL-C is a weaker risk factor in women than low HDL-C, these drugs may be less effective for lowering risk in women than in men. A systematic review of the literature to address the association of lipoproteins and risk for CHD in women is feasible and would likely contribute important clinical information.

Treatment of Hyperlipidemia to Reduce Risk of CHD Events in Women

The best evidence concerning the effect of lipid-lowering on CHD risk in women is provided by the systematic review by LaRosa et al.[87] Both women and men with hypercholesterolemia had a 30 percent reduction in risk of major CHD events. Men also experienced a 20 percent reduction in total mortality. The effect on total mortality in women was not provided, perhaps because only 13 percent of the participants in the five trials reviewed were women. A recent large randomized trial[89] among persons with CHD or at high risk for CHD found that treatment with simvastatin reduced risk of major vascular events about 25 percent in both men and women, regardless of cholesterol level.

The review by LaRosa et al.[87] included only clinical trials of statin drugs for lipid-lowering, only one quantitative estimate of the effect of lipid lowering on risk for CHD events in women and no separate assessments of the effectiveness for primary and secondary prevention. A systematic review focused on the effects of lipid-lowering in women could provide important clinical information.

3.04a Homocysteine as a risk factor for CHD in women

Systematic Reviews

F.1. Boushey CJ, Beresford SA, Omenn GS, Motulsky AG. A quantitative assessment of plasma homocysteine as a risk factor for vascular disease. Probable benefits of increasing folic acid intakes. JAMA 1995;274(13):1049-57.[90]

In this systematic review, standard methods were used to determine the association between homocysteine and risk for CVD events. Overall, 27 observational studies were identified that fulfilled the inclusion criteria of providing data on the association of serum homocysteine level and risk for vascular disease. Nine of the 27 included studies were considered high quality because they were prospective cohorts or population-based case-control studies. Coronary disease was defined as fatal and nonfatal MI and angiographically confirmed occlusion of at least one major coronary artery. Only three studies provided data on women. Assuming a linear relation between homocysteine and outcomes, the summary odds ratios, based on a 5 µmol/L increase in homocysteine are given below:

	All (N=NA)			Women (N=NA)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
CHD events	1.7	1.5-1.9	NA	1.8	1.4-2.3	NA

Each 5 µmol/L increase in serum homocysteine level was associated with a 70 percent increased risk of CHD events among all participants and an 80 percent increased risk of CHD events in women.

This article was rated fair quality based on lack of information regarding analysis methods.

3.04b Treatment to reduce homocysteine levels to reduce risk of CHD events in women

There were no systematic reviews identified for this topic. Folate supplementation is known to reduce serum homocysteine levels in men.[91] Whether reductions in homocysteine lead to a decreased risk of CHD events has not been tested in a randomized controlled trial.

Summary and Recommendations

Homocysteine as a Risk Factor for CHD in Women

A systematic review of observational studies suggests that higher serum homocysteine levels are strongly associated with higher risk for CHD events in both men and women.[90] Each 5 µmol/L increase in serum homocysteine level was associated with a 70 percent higher risk of CHD events among both men and women. This systematic review is relatively old and did not rate studies by degree of statistical adjustment for potential confounding variables. An updated systematic review of this topic is feasible and could provide important evidence.

Treatment to Lower Homocysteine Levels to Reduce Risk of CHD Events in Women

There is insufficient evidence in women to address this question.

3.05a C-reactive protein as a risk factor for CHD events in women

There were no systematic reviews identified for this topic.

Prospective Cohort Studies

We reviewed two reports from the Women's Health Study that evaluated the association between C-reactive protein and the risk of CVD events in 28,263 healthy postmenopausal women.[92, 93] After adjustment for markers of inflammation, lipoprotein measures and other coronary heart disease risk factors, the relative risk of a CVD event associated with a one-quartile increase in the concentration of C-reactive protein levels was 1.5 (95% CI, 1.1-2.1; p = .02).

G.1. Ridker PM, Buring JE, Shih J, Matias M, Hennekens CH. Prospective study of C-reactive protein and the risk of future cardiovascular events among apparently healthy women. Circulation 1998;98(8):731-3.[92]
G.2. Ridker PM, Hennekens CH, Buring JE, Rifai N. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. N Engl J Med 2000;342(12):836-43.[93]

3.05b Treatment to reduce C-reactive protein levels to reduce risk of CHD events in women

There were no systematic reviews, randomized trials, or cohort studies identified for this topic.

Summary and Recommendations

C-Reactive Protein as a Risk Factor for CHD Events in Women

One large cohort study[93] suggests that higher C-reactive protein levels are associated with increased risk for CVD events in women. A systematic review of this topic is not feasible due to lack of data.

3.06a Smoking as a risk factor for CHD in women

There were no systematic reviews identified for this topic.

Prospective Cohort Studies

We identified six prospective cohort studies evaluating the relation between cigarette smoking and risk of CHD in women. Four studies reported that smoking was independently associated with increased risk of fatal or nonfatal CHD events with a RR of about 2.[94-98] Smoking was associated with increased CHD risk in the Framingham Heart Study[99, 100] and in a study of three communities,[101] but the findings in these two cohorts were not statistically significant in women.

G.1. Willett WC, Green A, Stampfer MJ, Speizer FE, Colditz GA, Rosner B, et al. Relative and absolute excess risks of coronary heart disease among women who smoke cigarettes. N Engl J Med 1987;317(21):1303-9.[94]
G.2. Kannel WB, D'Agostino RB, Belanger AJ. Fibrinogen, cigarette smoking, and risk of cardiovascular disease: insights from the Framingham Study. Am Heart J 1987;113(4):1006-10.[99]
G.3. Freund KM, Belanger AJ, D'Agostino RB, Kannel WB. The health risks of smoking. The Framingham Study: 34 years of follow-up. Ann Epidemiol 1993;3(4):417-24.[100]
G.4. LaCroix AZ, Lang J, Scherr P, Wallace RB, Cornoni-Huntley J, Berkman L, et al. Smoking and mortality among older men and women in three communities. N Engl J Med 1991;324(23):1619-25.[101]
G.5. Kawachi I, Colditz GA, Stampfer MJ, Willett WC, Manson JE, Rosner B, et al. Smoking cessation and time course of decreased risks of coronary heart disease in middle-aged women. Arch Intern Med 1994;154(2):169-75.[95]
G.6. Paganini-Hill A, Hsu G. Smoking and mortality among residents of a California retirement community. Am J Public Health 1994;84(6):992-5.[96]
G.7. Njolstad I, Arnesen E, Lund-Larsen PG. Smoking, serum lipids, blood pressure, and sex differences in myocardial infarction. A 12-year follow-up of the Finnmark Study. Circulation 1996;93(3):450-6.[97]
G.8. Prescott E, Hippe M, Schnohr P, Hein HO, Vestbo J. Smoking and risk of myocardial infarction in women and men: longitudinal population study. BMJ 1998;316(7137):1043-7.[98]

3.06b Smoking cessation to reduce risk of CHD in women

Systematic Reviews

G.1. Wilson K, Gibson N, Willan A, Cook D. Effect of smoking cessation on mortality after myocardial infarction: meta-analysis of cohort studies. Arch Intern Med 2000;160(7):939-44.[102]

This systematic review of observational studies evaluated the association between smoking cessation after MI and subsequent overall mortality. The twelve international studies included in this meta-analysis were published between 1966 and 1996 and included at total of 5,878 participants. Two of the studies provided data on 185 women. Smoking status was evaluated by self-report during the first year after MI. The duration of follow-up ranged from 2 to 10 years.

	All (N=5,878)			Women (N=185; 3.1%)		
Outcome	OR	95% CI	p-value	OR	95% CI	p-value
Mortality	.54	.46-.62	NA	.36	.23-.54	NA

Mortality was reduced by 50 percent among all participants and about 65 percent among women who stopped smoking after their MI, compared to persons who continued to smoke. The findings from some of the individual studies included in this meta-analysis were not adjusted for differences in CHD risk factors between persons who quit and those who continued to smoke.

Prospective Cohort Studies Not Included in the Systematic Review

We reviewed eight manuscripts based on six prospective cohort studies. Compared to women who had never smoked cigarettes, women who were former smokers had as much as a 50 percent increased risk of fatal and nonfatal coronary heart disease events, although this finding was not significant.[94, 97, 98] Among former smokers, CHD event rates approach that of non-smokers 10 to 20 years after cessation of smoking.[95, 96, 101, 103, 104]

G.2. Willett WC, Green A, Stampfer MJ, Speizer FE, Colditz GA, Rosner B, et al. Relative and absolute excess risks of coronary heart disease among women who smoke cigarettes. N Engl J Med 1987;317(21):1303-9.[94]

G.3. Omenn GS, Anderson KW, Kronmal RA, Vlietstra RE. The temporal pattern of reduction of mortality risk after smoking cessation. Am J Prev Med 1990;6(5):251-7.[103]

G.4. LaCroix AZ, Lang J, Scherr P, Wallace RB, Cornoni-Huntley J, Berkman L, et al. Smoking and mortality among older men and women in three communities. N Engl J Med 1991;324(23):1619-25.[101]

G.5. Kawachi I, Colditz GA, Stampfer MJ, Willett WC, Manson JE, Rosner B, et al. Smoking cessation in relation to total mortality rates in women. A prospective cohort study. Ann Intern Med 1993;119(10):992-1000.[104]
G.6. Kawachi I, Colditz GA, Stampfer MJ, Willett WC, Manson JE, Rosner B, et al. Smoking cessation and time course of decreased risks of coronary heart disease in middle-aged women. Arch Intern Med 1994;154(2):169-75.[95]
G.7. Paganini-Hill A, Hsu G. Smoking and mortality among residents of a California retirement community. Am J Public Health 1994;84(6):992-5.[96]
G.8. Njolstad I, Arnesen E, Lund-Larsen PG. Smoking, serum lipids, blood pressure, and sex differences in myocardial infarction. A 12-year follow-up of the Finnmark Study. Circulation 1996;93(3):450-6.[97]
G.9. Prescott E, Hippe M, Schnohr P, Hein HO, Vestbo J. Smoking and risk of myocardial infarction in women and men: longitudinal population study. BMJ 1998;316(7137):1043-7.[98]

Summary and Recommendations

Smoking and Risk for CHD among Women

Based on the findings of six cohort studies,[94-101] smoking appears to be associated with an approximate 2-fold increased risk of CHD events in women, but no systematic review has quantified this increased risk or compared it to the increased risk among male smokers. A systematic review appears to be feasible and could provide important information.

Smoking Cessation to Reduce Risk of CHD Events among Women

A systematic review of prospective cohort studies found that smoking cessation after MI was associated with about a 50 percent lower risk of death during 2 to 10 years of observation.[102] This evidence is observational and subject to the biases associated with this study design. Of particular concern, it is not clear that the results of the studies included in the systematic review were adjusted for differences in CHD risk factors between smokers who quit and those who continued to smoke. This systematic review, though published in 2000, included only studies published before 1996. Given that the systematic review is relatively old, and the fact that only 185 women are represented in the review, we recommend a systematic review of the literature to update this topic.

3.07a Obesity as a risk factor for CHD in women

There were no systematic reviews identified for this topic.

Prospective Cohort Studies

We reviewed data from five cohort studies. Among women in the Framingham Heart Study,[105, 106] the Nurses' Health Study,[107-111], Atherosclerosis Risk in Communities (ARIC),[116] and the Atherosclerosis Risk in Communities (ARIC) and Cardiovascular Risk Development in Young Adults (CARDIA) studies,[112] increased weight or body mass index were associated with 1.5 to 3-fold increases in the risk of fatal and nonfatal CHD events. Fluctuating weight patterns and increased waist-hip ratios were associated with a 1.5 to 2-fold increased risk for CHD events and mortality among participants in the Iowa Women's Health Study[113-115] and the Nurses' Health Study.[109] Compared to BMI and skinfold measurements, waist-hip ratio was a better predictor of CHD among African-American women in the ARIC and CARDIA studies.[112, 116]

G.1. Harris T, Cook EF, Garrison R, Higgins M, Kannel W, Goldman L. Body mass index and mortality among nonsmoking older persons. The Framingham Heart Study. JAMA 1988;259(10):1520-4.[105]
G.2. Manson JE, Colditz GA, Stampfer MJ, Willett WC, Rosner B, Monson RR, et al. A prospective study of obesity and risk of coronary heart disease in women. N Engl J Med 1990;322(13):882-9.[107]
G.3. Folsom AR, Burke GL, Byers CL, Hutchinson RG, Heiss G, Flack JM, et al. Implications of obesity for cardiovascular disease in blacks: the CARDIA and ARIC studies. Am J Clin Nutr 1991;53(6 Suppl):1604S-1611S.[112]
G.4. Kannel WB, Cupples LA, Ramaswami R, Stokes J, 3rd, Kreger BE, Higgins M. Regional obesity and risk of cardiovascular disease; the Framingham Study. J Clin Epidemiol 1991;44(2):183-90.[106]
G.5. Manson JE, Willett WC, Stampfer MJ, Colditz GA, Hunter DJ, Hankinson SE, et al. Body weight and mortality among women. N Engl J Med 1995;333(11):677-85.[108]
G.6. Willett WC, Manson JE, Stampfer MJ, Colditz GA, Rosner B, Speizer FE, et al. Weight, weight change, and coronary heart disease in women. Risk within the 'normal' weight range. JAMA 1995;273(6):461-5.[109]
G.7. Folsom AR, French SA, Zheng W, Baxter JE, Jeffery RW. Weight variability and mortality: the Iowa Women's Health Study. Int J Obes Relat Metab Disord 1996;20(8):704-9.[113]
G.8. French SA, Folsom AR, Jeffery RW, Zheng W, Mink PJ, Baxter JE. Weight variability and incident disease in older women: the Iowa Women's Health Study. Int J Obes Relat Metab Disord 1997;21(3):217-23.[114]
G.9. Folsom AR, Stevens J, Schreiner PJ, McGovern PG. Body mass index, waist/hip ratio, and coronary heart disease incidence in African Americans and whites. Atherosclerosis Risk in Communities Study Investigators. Am J Epidemiol 1998;148(12):1187-94.[116]
G.10. Rexrode KM, Carey VJ, Hennekens CH, Walters EE, Colditz GA, Stampfer MJ, et al. Abdominal adiposity and coronary heart disease in women. JAMA 1998;280(21):1843-8.[110]

G.11. Folsom AR, Kushi LH, Anderson KE, Mink PJ, Olson JE, Hong CP, et al. Associations of general and abdominal obesity with multiple health outcomes in older women: the Iowa Women's Health Study. Arch Intern Med 2000;160(14):2117-28.[115]
G.12. Field AE, Coakley EH, Must A, Spadano JL, Laird N, Dietz WH, et al. Impact of overweight on the risk of developing common chronic diseases during a 10-year period. Arch Intern Med 2001;161(13):1581-6.[111]

3.07b Weight reduction to reduce risk of CHD events in women

There were no studies identified for this topic.

Summary and Recommendations

Obesity as a Risk Factor for CHD in Women

Findings of five cohort studies[59,105-112] suggest that obesity increases risk of CHD events in women, but the measure of obesity (weight, body mass index, skinfold thickness, or waist-hip ratio) that best predicts CHD risk women is not clear. A systematic review of this topic is feasible and could be clinically useful.

Weight Reduction to Reduce Risk of CHD Events in Women

No evidence was identified to address this topic. A systematic review is not feasible due to lack of data.

3.08a Inactivity as a risk factor for CHD in women

No systematic reviews of this topic were identified.

Prospective Cohort Studies

We reviewed data from three cohort studies. Among healthy women in the Nurses' Health Study[117-119] there was a 15 to 50 percent reduction in the risk of CHD events with physical activity. However, there appeared to be a threshold above which increasing levels of activity were not associated with increased benefit. Compared to healthy women with low fitness levels, healthy women with high fitness levels were at significantly less risk for a fatal event, but not for CVD death.[120] Among healthy women in the Framingham Heart Study,[121] increased physical activity was associated with an approximate 30 percent reduction in the risk of mortality, but not with a lower risk for CVD or CVD death.

G.1. Blair SN, Kohl HW, 3rd, Paffenbarger RS, Jr., Clark DG, Cooper KH, Gibbons LW. Physical fitness and all-cause mortality. A prospective study of healthy men and women. JAMA 1989;262(17):2395-401.[120]

G.2. Sherman SE, D'Agostino RB, Cobb JL, Kannel WB. Physical activity and mortality in women in the Framingham Heart Study. Am Heart J 1994;128(5):879-84.[121]

G.3. Manson JE, Hu FB, Rich-Edwards JW, Colditz GA, Stampfer MJ, Willett WC, et al. A prospective study of walking as compared with vigorous exercise in the prevention of coronary heart disease in women. N Engl J Med 1999;341(9):650-8.[117]

G.4. Lee IM, Rexrode KM, Cook NR, Manson JE, Buring JE. Physical activity and coronary heart disease in women: is "no pain, no gain" passe? JAMA 2001;285(11):1447-54.[118]

G.5. Rockhill B, Willett WC, Manson JE, Leitzmann MF, Stampfer MJ, Hunter DJ, et al. Physical activity and mortality: a prospective study among women. Am J Public Health 2001;91(4):578-83.[119]

3.08b Exercise to reduce risk of CHD events in women

There were no systematic reviews identified for this topic that provide separate data on women. We know of three systematic reviews of randomized trials that assessed the effect of exercise as part of a cardiac rehabilitation program following an acute ischemic event on risk for subsequent CHD events.[122-124] However, the randomized trials included in these analyses were small and included few women.

Summary and Recommendations

Inactivity as a Risk Factor for CHD in Women

It is not clear that inactivity is a risk factor for CHD events in women. Three cohort studies suggest that risk for all-cause mortality is increased with inactivity, but the evidence regarding the association of inactivity and risk for CHD and CVD events is mixed.[117-119] The limited number of studies that provide data on women and variations in measurement of activity level limit the feasibility of a systemic review of this topic.

Exercise to Reduce Risk of CHD Events in Women

There is insufficient evidence in women to address this question.

3.09 Age as a Risk Factor for CHD events in women

Systematic Reviews

F.1. Pocock SJ, McCormack V, Gueyffier F, Boutitie F, Fagard RH, Boissel JP. A score for predicting risk of death from cardiovascular disease in adults with raised blood pressure, based on individual patient data from randomised controlled trials. BMJ 2001;323(7304):75-81.[125]

This is a systematic review of data from eight randomized controlled trials that studied the effect of treatment for hypertension on CVD risk and are included in the Individual Data Analysis of Antihypertensive intervention trials (INDANA) database. Pooled data from the trials were used in an prospective cohort design to determine the effect of various risk factors on CVD events and to develop a score for predicting risk of death from CVD. Baseline measures of 16 potential CVD risk factors (age, sex, height, body mass index, smoking, systolic and diastolic blood pressure, heart rate, total cholesterol, creatinine, uric acid, previous MI, stroke or diabetes, left ventricular hypertrophy on ECG and blood pressure treatment) were included in a multivariate Cox proportional hazards model. Regression coefficients from this model were used to develop a risk score for the probability of cardiovascular death within a five year interval. All participants had elevated blood pressure at entry in the trials. The primary outcomes were fatal CVD and fatal CHD events. Associations between age and fatal events are presented below:

		Men (N=27,987)		Women (N=20,802)		
Outcome	RR*	95% CI	p-value	RR*	95% CI	p-value
CVD death						
nonsmokers†	1.43	NA	<.0001	1.58	NA	<.0001
smokers†	1.33	NA	<.0001	1.46	NA	<.0001
CHD death	1.35	NA	<.0001	1.58	NA	<.0001

* per 5 year increase in age

† interaction between age and smoking status required stratified estimates for the relative risk associated with age

The risk for CVD and CHD death increased 50 to 60 percent with each 5-year increase in age among women. The effect of age is similar, but slightly weaker in men, with a 30 to 40 percent increase in risk of CVD or CHD death with each 5-year increase in age.

This study was rated fair quality because inclusion was restricted to selected clinical trials among hypertensive persons.

Prospective Cohort Studies Not Included in the Systematic Review

These two articles present risk estimates for CHD events associated with increasing age among white men and women in the Framingham Heart Study. The article by D'Agostino et al.[126] also presents associations between age and risk of CHD events stratified by race from seven other cohort studies. Data from each of the cohort studies was used to construct a multivariate Cox proportional hazards model that included age, race, sex, blood pressure, cholesterol, smoking, and diabetes as risk factors and CHD death or nonfatal MI as the outcome. Models were gender and race-specific. Multivariate relative risks for a one-year increase in age from these studies are presented below:

	Men		Women	
Race and Study*	RR†	95% CI	RR†	95% CI
White				
FHS	1.05	1.04-1.07	1.19	.97-1.45
ARIC	1.05	1.02-1.07	1.67	.73-3.38
PHS	1.01	1.00-1.02	NA	NA
CHS	1.07	0.99-1.16	2.83	.02-530.8
Black				
ARIC	1.05	1.01-1.10	.88	.33-2.33
Japanese-American				
HHP	1.06	1.04-1.08	NA	NA
Hispanic				
PR	1.03	1.00-1.05	NA	NA
Native American				
SHS	1.05	1.02-1.09	1.47	.71-3.05

*FHS = Framingham Heart Study; ARIC = Atherosclerosis Risk in Communities; PHS = Physicians' Health Study; CHS = Cardiovascular Health Study; HHP = Honolulu Heart Program; PR = Puerto Rico Heart Health Program, and SHS = Strong Heart Study.
† relative risk for CHD death and nonfatal MI for each one year increase in age

For each one-year increase in age, men of all races have about a 5 percent increase in risk of CHD events. There appears to be a greater increase in CHD risk with increasing age among women than in men, but the associations are difficult to interpret in women because the number of outcomes was small and none of the risk estimates are statistically significant. The small number of women studied also makes it difficult to determine if risk associated with increasing age differs with race.

G.2. Lerner DJ, Kannel WB. Patterns of coronary heart disease morbidity and mortality in the sexes: a 26-year follow-up of the Framingham population. Am Heart J 1986;111(2):383-90.[3]
G.3. 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(2):180-7.[126]

Summary and Recommendations

Among men, cohort studies consistently show a 5 percent increase in risk of CHD events per year of age among white, black, Japanese-American, Hispanic and Native American men.[3,126] Among women, increasing age seems to be a stronger risk factor for CHD events than among men, but the evidence is inconclusive due to the small number of women included in the studies.

A systematic review of this topic could provide important information regarding the effect of aging on CHD risk and on differences in this association between men and women. Such a review would be challenging because increasing age is also associated with higher prevalence and severity of other risk factors for CHD. In addition, as indicated by the results of Pocock et al.,[125] the effects of age and gender may interact with other risk factors, such as smoking.

3.10 Age at menopause and risk for CHD

There were no systematic reviews identified for this topic.

Prospective Cohort Studies

We reviewed data from three prospective cohort studies. The Nurses' Health Study[127] and the Diagnostisch Onderzoek Mammacarcinoom (Diagnostic Investigation of Mammary Cancer)[128] found a 2 to 3 percent increased risk of CHD events with each one year decrease in age at menopause. Age at natural menopause was not a significant predictor of CHD deaths among women in the National Health and Examination Survey (NHANES).[129] Inadequate adjustment for cigarette smoking may confound the association of age at menopause and CHD risk, as smokers have an increased risk for CHD events and earlier age at menopause.[127]

G.1. Hu FB, Grodstein F, Hennekens CH, Colditz GA, Johnson M, Manson JE, et al. Age at natural menopause and risk of cardiovascular disease. Arch Intern Med 1999;159(10):1061-6.[127]
G.2. van der Schouw YT, van der Graaf Y, Steyerberg EW, Eijkemans JC, Banga JD. Age at menopause as a risk factor for cardiovascular mortality. Lancet 1996;347(9003):714-8.[128]
G.3. Cooper GS, Sandler DP. Age at natural menopause and mortality. Ann Epidemiol 1998;8(4):229-35.[129]

Summary and Recommendations

Evidence that earlier age at menopause is associated with increased risk for CHD events is weak because the number of studies identified was small and their results are not consistent.[127-129] Several large community-based studies may provide sufficient data to perform a systematic review.

3.11 Ethnicity as a risk factor for CHD in women

There were no systematic reviews identified for this topic.

Prospective Cohort Studies

We reviewed data from three cohorts, comparing risk for CHD outcomes between African-American and white women. Among participants in the Charleston Heart Study[130] the risk of coronary heart disease death and mortality did not differ significantly by race. However, case fatality rates after myocardial infarction were 1.5 to 3-times higher among African-American women compared to white women in the Atherosclerosis Risk in Communities study[131] and in the National Hospital Discharge Survey.[132]

F.1. Roig E, Castaner A, Simmons B, Patel R, Ford E, Cooper R. In-hospital mortality rates from acute myocardial infarction by race in U.S. hospitals: findings from the National Hospital Discharge Survey. Circulation 1987;76(2):280-8.[132]
G.2. Keil JE, Sutherland SE, Knapp RG, Lackland DT, Gazes PC, Tyroler HA. Mortality rates and risk factors for coronary disease in black as compared with white men and women. N Engl J Med 1993;329(2):73-8.[130]
F.3. White AD, Rosamond WD, Chambless LE, Thomas N, Conwill D, Cooper LS, et al. Sex and race differences in short-term prognosis after acute coronary heart disease events: the Atherosclerosis Risk In Communities (ARIC) study. Am Heart J 1999;138(3 Pt 1):540-8.[131]

Summary and Recommendations

The three cohort studies that we reviewed provide conflicting evidence regarding the association between race/ethnicity and coronary heart disease risk in women.[130-132] Several large community-based studies may provide sufficient data to perform a systematic review, but such a review would be challenging because relative risk estimates comparing CHD risk by ethnicity must be adjusted for other cardiovascular risk factors.

3.12 Socioeconomic status and risk for CHD

There were no systematic reviews identified for this topic.

Prospective Cohort Studies

We reviewed three cohort studies. After adjustment for age and other coronary heart disease risk factors, income,[133] socioeconomic deprivation score,[134] and postcode of residence[135] correlated with risk for CHD events, such that women with lower socioeconomic status (SES) measures were at an approximate 2-fold increased risk for CHD events compared to women with higher SES. However, among women in the Charleston Heart Study, level of education was not a significant predictor of coronary

heart disease deaths for white or African-American women after adjustment for other CHD risk factors.[130]

G.1. Keil JE, Sutherland SE, Knapp RG, Lackland DT, Gazes PC, Tyroler HA. Mortality rates and risk factors for coronary disease in black as compared with white men and women. N Engl J Med 1993;329(2):73-8.[130]
G.2. Salomaa V, Miettinen H, Niemela M, Ketonen M, Mahonen M, Immonen-Raiha P, et al. Relation of socioeconomic position to the case fatality, prognosis and treatment of myocardial infarction events; the FINMONICA MI Register Study. J Epidemiol Community Health 2001;55(7):475-82.[133]
G.3. Capewell S, MacIntyre K, Stewart S, Chalmers JW, Boyd J, Finlayson A, et al. Age, sex, and social trends in out-of-hospital cardiac deaths in Scotland 1986-95: a retrospective cohort study. Lancet 2001;358(9289):1213-7.[134]
G.4. Morrison C, Woodward M, Leslie W, Tunstall-Pedoe H. Effect of socioeconomic group on incidence of, management of, and survival after myocardial infarction and coronary death: analysis of community coronary event register. BMJ 1997;314(7080):541-6.[135]

Summary and Recommendations

Three cohort studies suggest that socioeconomic status may be associated with an increased CHD risk, but the evidence is weak due to the small number of studies identified and differences in the definition of socioeconomic status.[133-135] Several large community-based studies may provide sufficient data to perform a systematic review, but such a review would be challenging because relative risk estimates comparing CHD risk by ethnicity should be adjusted for other cardiovascular risk factors and definitions of socioeconomic status vary.

QUESTION 4

4. Are accurate tests (defined in #1), effective treatments (defined in #2), or risk factor modifications (defined in #3) underutilized in women (or among women of various race/ethnic populations) compared to men?

We searched the medical literature to identify studies that compared the use of tests, treatments and risk factor reduction for CHD in men and women. We have described results only for those subtopics for which studies were identified.

1.0 Non-invasive testing for CHD

Exercise Tolerance Testing

Cross-sectional Studies

Among patients hospitalized with ischemic chest pain, women were approximately 20-40 percent less likely than men to undergo exercise stress testing, even after adjustment for other risk factors.[136, 137] Men with positive exercise stress test results were 1.5 to 2-fold more likely to undergo invasive or non-invasive follow-up testing,[14, 136, 137] despite the fact that risk of a subsequent MI or cardiac death was 5-fold higher in women than in men.[14] Between 1995 and 1996, primary care providers in a major managed-care network were 2-fold more likely to refer men than women with ischemic symptoms for exercise stress testing ($p<.0001$).[138] Among the oldest patients in this population (age > 70 years), rates of referral for exercise testing were similar in men and women.

F.1. Shaw LJ, Miller DD, Romeis JC, Kargl D, Younis LT, Chaitman BR. Gender differences in the noninvasive evaluation and management of patients with suspected coronary artery disease. Ann Intern Med 1994;120(7):559-66.[14]
G.2. Johnson PA, Goldman L, Orav J, Zhou L, Garcia T, et al. Gender differences in the management of acute chest pain. Support for the "Yentl Syndrome." J Gen Intern Med 1996;11:209-17.[136]
G.3. Roger VL, Farkouh ME, Weston SA, Reeder GS, Jacobsen SJ, et al. Sex differences in evaluation and outcome of unstable angina. JAMA 2000;283:646-52.[137]
F.4. Battleman DS, Callhan M. Gender differences in utilization of exercise treadmill testing: a claims-based analysis. J Healthcare Quality 2001;23:38-41.[138]

2.0 Treatments for CHD

Aspirin

Cross-sectional Studies

Compared to women, men in six large cross-sectional studies were more likely than women to receive aspirin during hospitalization for an acute MI[12, 139-142] or as secondary prophylaxis for a CVD event.[143] Rates of aspirin treatment among men compared to women were 38 percent higher at hospital admission,[12] 10 to 20 perccnt higher during hospitalization,[139, 141, 142] 6 percent higher on discharge,[140] and 40 percent higher after a CVD event.[143]

The Atherosclerotic Risk in Communities (ARIC) prospective cohort study reported similar rates of aspirin use between black women and black men (10 percent), but higher prevalence of use among white men than among white women (31 percent vs. 28 percent;p<.001). Overall, the prevalence of aspirin use was almost 3-fold greater among whites compared to blacks.[144] Between 1986 and 1990 the use of antiplatelet agents in women increased 4-fold in one study,[139] but remained unchanged in another.[144]

G.1. Steingart RM, Packer M, Hamm P, Coglianese ME, Gersh B, et al. Sex differences in the management of coronary artery disease. N Engl J Med 1991;325:226-30.[12]

G.2. Pagley PR, Yarzebski J, Goldberg R, Chen Z, Chiriboga D, et al. Gender differences in the treatment of patients with acute myocardial infarction. Arch Intern Med 1993;153:625-9.[139]

F.3. Clarke KW, Gray D, Keating NA, Hampton JR. Do women with acute myocardial infarction receive the same treatment as men? BMJ 1994;309:563-6.[140]

F.4. Tsuyuki RT, Teo KK, Ikuta RM, Bay KS, Greenwood PV, Montague TJ. Mortality risk and patterns of practice in 2,070 patients with acute myocardial infarction, 1987-92. Chest 1994;105:1687-92.[141]

G.5. Shahar E, Folsom AR, Romm FJ, Bisgard KM, Metcalf PA, et al. Patterns of aspirin use in middle-aged adults: the Atherosclerosis Risk in Communities (ARIC) Study. Am Heart J 1996;131:915-22.[144]

G.6. Chandra NC, Ziegelstein RC, Rogers WJ, Tiefenbrunn AJ, Gore JM, et al. Observations of the treatment of women in the United States with myocardial infarction. Arch Intern Med 1998;158:981-8.[142]

G.7. Rojas-Fernandez CH, Kephart GC, Sketris IS, Kass K. Underuse of acetylsalicylic acid in individuals with myocardial infarction, ischemic heart disease or stroke: data from the 1995 population-based Nova Scotia Health Survey. Can J Cardiol 1999;15(3):291-6.[143]

Beta-Blockers

Cross-sectional Studies

After adjustment for age, women were 10 to 30 percent less likely than men with symptoms of an acute MI to receive beta-blockers during hospitalization[141, 142] and approximately 45 percent less likely to be discharged on beta-blockers.[140]

Several studies found no gender difference in beta-blocker use prior to or during hospitalization for an acute MI.[12, 139] Between 1986 and 1990, the use of beta-blockers increased by 15 percent in hospitalized women (48.4 percent) and by 17 percent in hospitalized men (60.0 percent).[139]

G.1. Steingart RM, Packer M, Hamm P, Coglianese ME, Gersh B, et al. Sex differences in the management of coronary artery disease. N Engl J Med 1991;325:226-30.[12]
G.2. Pagley PR, Yarzebski J, Goldberg R, Chen Z, Chiriboga D, et al. Gender differences in the treatment of patients with acute myocardial infarction. Arch Intern Med 1993;153:625-9.[139]
F.3. Clarke KW, Gray D, Keating NA, Hampton JR. Do women with acute myocardial infarction receive the same treatment as men? BMJ 1994;309:563-6.[140]
F.4. Tsuyuki RT, Teo KK, Ikuta RM, Bay KS, Greenwood PV, Montague TJ. Mortality risk and patterns of practice in 2,070 patients with acute myocardial infarction, 1987-92. Chest 1994;105:1687-92.[141]
G.5. Chandra NC, Ziegelstein RC, Rogers WJ, Tiefenbrunn AJ, Gore JM, et al. Observations of the treatment of women in the United States with myocardial infarction. Arch Intern Med 1998;158:981-8.[142]

Thrombolysis

Cross-sectional Studies

Six large cohort studies found that men were 1.5 to 2-fold more likely than women to receive thrombolytic therapy during hospitalization for symptoms of acute MI.[140-142, 145-147] However, among patients who had been admitted to a coronary care unit, men and women were equally likely to receive thrombolytic treatment.[140] In the SAVE trial, the odds of receiving thrombolysis were 56 percent higher for men than women; however, after adjustment for other variables related to indication for thrombolysis, gender was not an independent predictor of thrombolytic therapy.[148] Between 1986 and 1990, the use of thrombolytics in women increased 6-fold.[139, 142]

In contrast, two studies did not find a significant gender difference in thrombolytic therapy during hospitalization for acute MI.[139, 149]

F.1. Maynard C, Althouse R, Cerqueira M, Olsufka M, Kennedy JW. Underutilization of thrombolytic therapy in eligible women with acute myocardial infarction. Am J Cardiol 1991;68:529-30.[145]
G.2. Pfeffer Ma, Moye LA, Braunwald E, Basta L, Brown EJ, et al. Selection bias in the use of thrombolytic therapy in acute myocardial infarction. JAMA 1991;266:528-32.[148]
G.3. Maynard C, Litwin PE, Martin JS, Weaver WD. Gender differences in the treatment and outcome of acute myocardial infarction. Arch Intern Med 1992;152:972-6.[146]
G.4. Pagley PR, Yarzebski J, Goldberg R, Chen Z, Chiriboga D, et al. Gender differences in the treatment of patients with acute myocardial infarction. Arch Intern Med 1993;153:625-9.[139]
F.5. Clarke KW, Gray D, Keating NA, Hampton JR. Do women with acute myocardial infarction receive the same treatment as men? BMJ 1994;309:563-6.[140]
F.6. Tsuyuki RT, Teo KK, Ikuta RM, Bay KS, Greenwood PV, Montague TJ. Mortality risk and patterns of practice in 2,070 patients with acute myocardial infarction, 1987-92. Chest 1994;105:1687-92.[141]
G.7. Kudenchuk PJ, Maynard C, Martin JS, Wirkus M, Weaver WD. Comparison of presentation, treatment, and outcome of acute myocardial infarction in men versus women (The Myocardial Infarction Triage and Intervention Registry). Am J Cardiol 1996;78:9-14.[149]
G.8. Yarzebski J, Col N, Pagley P, Savageau J, Gore J, Goldberg R. Gender differences and factors associated with the receipt of thrombolytic therapy in patients with acute myocardial infarction: a community-wide perspective. Am Heart J 1996;131(1):43-50.[147]
G.9. Chandra NC, Ziegelstein RC, Rogers WJ, Tiefenbrunn AJ, Gore JM, et al. Observations of the treatment of women in the United States with myocardial infarction. Arch Intern Med 1998;158:981-8.[142]

Percutaneous Transluminal Coronary Angioplasty (PTCA) and Coronary Artery Bypass Graft Surgery (CABG)

Cross-sectional Studies

We reviewed 21 cross-sectional studies comparing gender differences in revascularization procedures (PTCA and CABG). Most studies included patients who were admitted to the hospital for evaluation of acute coronary symptoms. Because women appear to be less likely than men to undergo cardiac catheterization, we categorized studies that evaluated all patients admitted for acute coronary syndromes and those that provided data on procedures subsequent to cardiac catheterization.

Procedures among all patients evaluated for acute coronary syndromes

Two European studies found significant gender differences in revascularization procedure rates among patients with known CHD, including a 50 to 60 percent higher rate for men compared to women in the United Kingdom[150] and a 36 percent higher rate for men in Austria.[151] In 1995, the lowest PTCA rates in Austria were among women over the age of 64 years.[151] These finding were similar to data from the United States, where CHD-adjusted rates of revascularization in men were 30 to 45 percent higher than in women.[13] In the same study, revascularization rates remained higher in men than in women hospitalized for an acute MI, suggesting that potential biases in admitting practices could not explain the gender differences.[13]

In adjusted models, men discharged from California hospitals in 1989 were 35 percent more likely to have undergone PTCA and 2-fold more likely to have undergone CABG than women.[152] In Massachusetts, men were 2.5-fold more likely than women to undergo PTCA following acute MI, but equally likely to undergo CABG.[153] Among patients

referred for non-invasive testing, men were twice as likely as women to undergo a subsequent revascularization procedure.[14] Data from the National Registry of Myocardial Infarction indicate that, among patients who did not receive thrombolytic therapy, 19 percent of men underwent PTCA compared with 13.8 percent of women, and 12.6 percent of men underwent CABG compared with 8.0 percent of women.[142] However, after thrombolytic therapy, 28.3 percent of women vs. 30.6 percent of men underwent PTCA and 11.0 percent of women vs. 13.5 percent of men underwent CABG.[142]

Race and gender rates of revascularization indicate that black and white women are as likely as white men to undergo PTCA, but white women are 35 percent less likely and black women 63 percent less likely to undergo CABG than white men, even after adjustment for multiple risk factors.[154] Medicare data suggest that white men have the highest rates of CABG (40.4 per 10,000 persons) and black women the lowest (6.4 per 10,000 persons).[155]

Procedures among patients who have had cardiac angiography

Among participants in the population-based Corpus Christi Heart Project,[156] age-adjusted rates of PTCA and CABG were 1.5-times higher for men than women. However, after acute MI and coronary angiography, there was no evidence of differential revascularization rates between genders. After adjustment for CHD risk factors, there were only slight differences in rates of PTCA between Mexican-Americans and non-Hispanic Whites.[156]

In similar analyses among persons who had coronary angiography, women were as likely as men to undergo PTCA but 40 percent less likely to undergo CABG.[157, 158] Gender differences in intervention rates were most significant among younger participants. Findings from several cohort studies indicate that after coronary angiography, women

were more likely to undergo PTCA[159-161] while men more likely to undergo CABG.[160, 161] After adjustment for CHD risk factors, gender was not a significant predictor of revascularization procedure in one,[161] but not all[159, 160] studies. In GUSTO-I, the rates of coronary angiography were similar in men and women (52 percent vs. 57 percent), but women were significantly more likely than men to undergo PTCA (35 percent vs. 32 percent; $p < .001$) and less likely to undergo CABG (7 percent vs. 9 percent; $p < .001$).[160] Four studies found that men were 1.5 to 2-fold more likely than women to undergo revascularization (PTCA or CABG) subsequent to acute coronary symptoms; however, once a diagnostic procedure had been performed, gender was a non-significant predictor of revascularization.[12, 146, 159, 162]

Three studies found no significant gender differences in the referral rates for PTCA or CABG after coronary angiography.[60, 149, 163] However, men were more likely to undergo revascularization procedures during the early phases of infarction,[149] or when the risk of cardiac death was low.[163] In one study, women were half as likely to undergo early intervention for MI (thrombolysis, catheterization, PTCA, CABG).[149]

G.1. Giles TD, Fisher MB, Rush JE. Lisinopril and captopril in the treatment of heart failure in older patients. Comparison of a long- and short-acting angiotensin-converting enzyme inhibitor. Am J Med 1988;85(3B):44-7.[154]
G.2. Ayanian JZ, Epstein AM. Differences in the use of procedures between women and men hospitalized for coronary heart disease. N Engl J Med 1991;325:221-5.[13]
G.3. Steingart RM, Packer M, Hamm P, Coglianese ME, Gersh B, et al. Sex differences in the management of coronary artery disease. N Engl J Med 1991;325:226-30.[12]
F.4. Bickell NA, Pieper KS, Lee KL, Mark DB, Glower DD, et al. Referral patterns for coronary artery disease treatment: gender bias or good clinical judgment? Ann Int Med 1992;116:791-7.[163]
F.5. Goldberg KC, Hartz AJ, Jacobsen SJ, Krakauer H, Rimm AA. Racial and community factors influencing coronary artery bypass graft surgery rates for all 1986 Medicare patients. JAMA 1992;267(11):1473-7.[155]
G.6. Krumholz HM, Douglas PS, Lauer MS, Pasternak RC. Selection of patients for coronary angiography and coronary revascularization early after myocardial infarction: is there evidence for a gender bias? Ann Intern Med 1992;116(10):785-90.[157]
G.7. Maynard C, Litwin PE, Martin JS, Weaver WD. Gender differences in the treatment and outcome of acute myocardial infarction. Results from the Myocardial Infarction Triage and Intervention Registry. Arch Intern Med 1992;152(5):972-6.[146]
G.8. Chiriboga DE, Yarzebski J, Goldberg RJ, Chen Z, Gurwitz J, Gore JM, et al. A community-wide perspective of gender differences and temporal trends in the use of diagnostic and revascularization procedures for acute myocardial infarction. Am J Cardiol 1993;71(4):268-73.[153]
G.9. Petticrew M, McKee M, Jones J. Coronary artery surgery: are women discriminated against? BMJ 1993;306(6886):1164-6.[150]

G.10. Jaglal SB, Goel V, Naylor CD. Sex differences in the use of invasive coronary procedures in Ontario. Can J Cardiol 1994;10(2):239-44.[162]

F.11. Shaw LJ, Miller DD, Romeis JC, Kargl D, Younis LT, Chaitman BR. Gender differences in the noninvasive evaluation and management of patients with suspected coronary artery disease. Ann Intern Med 1994;120(7):559-66.[14]

F.12. Bergelson BA, Tommaso CL. Gender difference in clinical evaluation and triage in coronary artery disease. Chest 1995;108:1510-13.[158]

G.13. D'Hoore W, Sicotte C, Tilquin C. Sex bias in the management of coronary artery disease in Quebec. Am J Public Health 1994;84(6):1013-5.[159]

G.14. Davis KB, Chaitman B, Ryan T, Bittner V, Kennedy JW. Comparison of 15-year survival for men and women after initial medical or surgical treatment for coronary artery disease: a CASS registry study. Coronary Artery Surgery Study. J Am Coll Cardiol 1995;25(5):1000-9.[60]

G.15. Giacomini MK. Gender and ethnic differences in hospital-based procedure utilization in California. Arch Intern Med. 1996;156:1217-24.[152]

G.16. Kudenchuk PJ, Maynard C, Martin JS, Wirkus M, Weaver WD. Comparison of presentation, treatment, and outcome of acute myocardial infarction in men versus women (The Myocardial Infarction Triage and Intervention Registry). Am J Cardiol 1996;78:9-14.[149]

F.17. Weaver WD, White HD, Wilcox RG, Aylward PE, Morris D, Guerci A, et al. Comparisons of characteristics and outcomes among women and men with acute myocardial infarction treated with thrombolytic therapy. GUSTO-I investigators. JAMA 1996;275(10):777-82.[160]

G.18. Ramsey DJ, Goff DC, Wear ML, Labarthe DR, Nichaman MZ. Sex and ethnic differences in use of myocardial revascularization procedures in Mexican Americans and non-Hispanic whites: the Corpus Christi Heart Project. J Clin Epidemiol 1997;50(5):603-9.[156]

G.19. Chandra NC, Ziegelstein RC, Rogers WJ, Tiefenbrunn AJ, Gore JM, et al. Observations of the treatment of women in the United States with myocardial infarction. Arch Intern Med 1998;158:981-8.[142]

G.20. Strauss R, Pfeifer C, Muhlberger V, Ulmer H, Pfeiffer KP. Effects of morbidity, age, gender and region on percutaneous transluminal coronary angioplasty (PTCA) utilisation. Public Health 1999;113(2):79-87.[151]

G.21. Miller TD, Roger VL, Hodge DO, Hopfenspirger MR, Bailey KR, et al. Gender differences and temporal trends in Clinical Characteristics, stress test results and use of invasive procedures in patients undergoing evaluation for coronary artery disease. J am Coll Cardiol 2001;38:690-7.[161]

Treatment of hypertension

Systematic Review

F.1. Klungel OH, deBoer A, Paes A, Seidell JC, Bakker A. Sex differences in the pharmacological treatment of hypertension: a review of population-based studies. J

Hypertension 1997;15:591-600.[164]

In this systematic review, data from 46 population-based studies published between 1966 and 1996 were analyzed to assess gender differences in the pharmacological treatment of hypertension. Data on 108,184 men and 59,575 women with hypertension are included. Crude differences in treatment practices were also evaluated by antihypertensive drug class and by country.

	Crude Prevalence Ratio	
Outcome	Female:Male	95% CI
Any pharmacological treatment	1.33	1.32 – 1.34
Diuretics	1.12	1.09 – 1.15
β-Blockers	.82	.79 - .85
ACE inhibitors	.67	.59 - .76
Calcium antagonists	.85	.77 - .95

Women with hypertension were approximately 30 percent more likely than men to receive treatment for hypertension. Women were more likely than men to be treated with a diuretic, while men were more likely to be treated with beta-blockers, ACE inhibitors and calcium antagonists. Among participants aged 20-29, women were 2-fold more likely than men to receive treatment for hypertension. By age 60-69 the prevalence of treatment was only 22 percent higher in women than in men. Gender differences in treatment practices declined between 1970 and 1991.

Lipid lowering

Cross-sectional Studies

Three international cross-sectional studies document that rates of medication usage and gender differences in use rates vary by country.[165-167]

F.1. Sketris IS, Kephart GC, Hicks VA, Hubbard EJ, Brown MG, et al. Prescribing patterns of antilipemic drugs and prevalence of hypercholesterolemia in the Nova Scotia population more than 65 years old. Ann Pharmacother 1995;29:576-81.[165]
F.2. Magrini N, Elinarson T, Vaccheri A, McManus P, Montanaro N, Bergman U. Use of lipid-lowering drugs from 1990 to 1994: an international comparison among Australia, Finland, Italy (Emilia Romagna Region), Norway and Sweden. Eur J Clin Pharmacol 1991;53:185-9.[166]
F.3. Majeed A, Moser K, Maxwell R. Age, sex and practice variations in the use of statins in general practice in England and Wales. J Publ Hlth Med 2000;22:275-9.[167]

Summary and Recommendations

Available studies suggest that men are more likely than women to undergo diagnostic testing[14,136-138] and treatment for CHD,[12-14,60,139-163,165-167] but that women are more likely

to be treated for hypertension.[164] Several theories have been proposed to explain these gender differences.

It is possible that women have less severe CHD symptoms or findings than men and more comorbidities that contraindicate tests and procedures. This theory is supported by the fact that gender differences appear to be minimized in studies with inadequate control for potential confounding. Coronary tests and procedures may not be underused in women, but overused in men. For example, lower rates of CABG among low risk women may indicate a more appropriate treatment referral pattern among women than men. A panel of nationally recognized experts assessed the appropriateness of coronary angiography, PTCA, and CABG based on hospital data from New York and found that the rate of inappropriate cardiovascular procedures was not significantly different by gender.[168]

Women may be more reluctant than men to undergo invasive coronary procedures. Among patients scheduled for exercise stress testing, Saha et al. found that women were more willing than men to undergo coronary angiography and equally willing to undergo PTCA or CABG.[169]

A systematic review of the literature is feasible and could provide clinically important information for treatment practice guidelines.

QUESTION 5

5. What is the prognostic value of biochemical markers for acute myocardial infarction or unstable angina in women? (3 subtopics labeled 5.01-5.02)

Specifically, does the prognostic value of the following markers differ in women and men? What is the incremental prognostic benefit of new cardiac markers in addition to history, physical exam, and other laboratory data including electrocardiography?

5.01 troponin
5.02 creatinine kinase myocardial bands (CKMB) including isoforms
5.03 myoglobin

5.01 Troponins

There were no systematic reviews identified for this topic.

5.02 Creatine kinase MB

There were no systematic reviews identified for this topic.

5.03 Myoglobin

There were no systematic reviews identified for this topic.

Chapter 4: Conclusions

Summary and Recommendations by Key Question

Table 3 presents a summary of the findings of the evidence review for each key question. We have classified the evidence as none, weak, fair or good, defined as follows:

Classification	Evidence
None	no publications that address the key question in women
Weak	some evidence, but no systematic review *or* definitive evidence from randomized trials
Fair	at least one systematic review, but the review is only fair quality or outdated *or* evidence from randomized trials, but the trials are small or have inconsistent findings
Good	at least one recent, good quality systematic review *or* several major randomized trials with consistent findings

As noted in Chapter 2, Methodology, Hierarchy of Evidence and Completeness of Searches, we are confident that we have identified all systematic reviews and major randomized trials, but some large cohort or cross-sectional studies may not have been identified. Importantly, we were only able to include the results of studies if the results were stratified by gender. Thus, many completed studies may have the potential to provide evidence on women if the study investigators are willing and able to produce stratified results.

A new systematic review was considered feasible when we identified at least 5 or more studies using similar methods that could likely be included in a systematic review. In some cases, even though a systematic review is feasible, it was not recommended if a recent, methodologically sound systematic review has already been completed or a definitive randomized trial has been completed or is under way.

Findings by Level of Evidence and Key Question

Assuming that the strength of a risk factor is a different question from the effect of modifying the same risk factor, and that the effects of a treatment in primary prevention are different from the effect in secondary prevention, we reviewed the medical literature related to 42 questions pertaining to CHD in women. We found no data in women to address 13 of the questions, weak data to address 15, fair data for eight and good data to address six questions (Table 4).

Summary of Major Findings

There was fair data suggesting that the accuracy of exercise EKG and exercise thallium testing (using either conventional or SPECT imaging) for CHD in women is poor and that exercise echocardiography might be more accurate.

While evidence for many treatments was lacking, we found fair or good data to suggest that beta-blockers, aspirin and angiotensin converting enzyme inhibitors reduce risk for CHD events in women with coronary disease. Good evidence suggests that nitrates do not reduce risk for CHD events in women with known heart disease. There was fair evidence to suggest that IIb/IIIa drugs given to women undergoing percutaneous revascularization result in a reduced risk of CHD events and need for repeat revascularization. Fair evidence also suggests that IIb/IIIa drugs given to women suffering acute coronary syndromes result in increased mortality. This was the only treatment for which there appeared to be an interaction by gender: men treated with IIb/IIIa drugs during acute coronary syndromes appear to benefit.

We found only weak evidence linking most of the risk factors of interest and CHD risk in women. For the most part, this is because all of the studies addressing the strength of risk factors are observational, and very few good quality systematic reviews have been completed. However, there was fair evidence to suggest that hyperlipidemia and hyperhomocysteinemia are risk factors for CHD in women and good evidence that diabetes is a risk factor. Risk factors seem to be equally strong in men and women with the possible exceptions of age, diabetes, and specific lipoproteins. Increasing age seems to be a stronger risk factor for CHD events in women than men, but the evidence is inconclusive due to the small number of women included in the studies. Diabetes may be a stronger risk factor for CHD in women than in men and patterns of risk associated with lipoprotein subfractions appear to differ in men and women.

There was fair or good evidence to suggest that smoking cessation after MI and treatment of hypertension and of hyperlipidemia lower the risk for CHD events in women. In contrast, we found no evidence for the effectiveness of other interventions to modify risk factors in women.

Available studies suggest that men are more likely than women to undergo diagnostic testing and treatment for CHD, but that women are more likely to be treated for hypertension. These observed differences may be due to inadequate control for differences in severity of disease and comorbidities in men and women or result from overtreatment in men.

We found no evidence to address the prognostic value of troponins, creatine kinase or myoglobin in women with ischemia.

In general, no evidence addressed differences in the accuracy of diagnostic tests, strength of risk factors, effects of treatment or prognostic value of markers for ischemia in women of different races or ethnicity. The only evidence regarding differences by ethnicity suggests that African American women may benefit more from treatment of hypertension than white women.

Chapter 5: Future Research

Based on our reviews of published studies that include data on women, we believe that a systematic review of the literature is probably not feasible for 19 of the 42 key questions (Table 3). However, systematic reviews of some of these questions might be feasible if unpublished gender-specific findings can be obtained. Systematic reviews of the remaining 23 topics are likely feasible. For some questions, however, we did not recommended a systematic review because the question appears to have been adequately addressed by completed clinical trials or a definitive clinical trial is currently in progress (Table 3).

We believe that a systematic review is feasible and should be recommended for the subtopics listed below (Table 3).

Exercise tolerance testing
Exercise echocardiogram
Aspirin - secondary prevention
Beta-blockers - secondary prevention
Hypertension as a risk factor
Diabetes as a risk factor
Hyperlipidemia as a risk factor
Hyperlipidemia treatment
Homocysteine as a risk factor
Smoking as a risk factor
Smoking cessation
Obesity as a risk factor
Age as a risk factor
Differences in utilization between men and women

The major limitation in performing these systematic reviews will be the availability of data on women and minority populations. Women typically comprise only 20 to 30 percent and minorities a substantially lower proportion of participants in randomized trials. For questions where several trials have been completed, data on women and minorities could be summarized in a systematic review. However, risk estimates for women and minorities are infrequently published. Thus, investigators attempting to systematically review the medical literature must attempt to contact investigators and obtain unpublished risk estimates. For a variety of reasons, these subgroup analyses are often not obtainable. Randomized trials of the benefit of beta-blockers in CHF provide an excellent example of this problem. At least 20 randomized trials of the effect of beta-blockers on mortality in persons with CHF have been published. Most of these have included women, but only 4 that we were able to identify included analyses among women and these data were generally limited to the primary outcome. Thus, even though the National Institutes of Health and other funding agencies appear to have succeeded in assuring that women and minorities are included in randomized trials, data from such participation is not generally available. We recommend that, in addition to demanding

participation of women and minorities in research, the National Institutes of Health, Federal Drug Administration and other funding sources should insist that primary and secondary outcome data by subgroup be published or archived.

Similarly, most systematic reviews of the literature do not provide subgroup estimates for women or minorities. This is due primarily to the difficulty of obtaining unpublished subgroup estimates, as noted above. However, as demonstrated by several excellent systematic reviews included in this report, it is possible with additional effort to obtain subgroup estimates for women and minorities. We recommend that funding agencies that support systematic reviews require inclusion of subgroup estimates in women and minorities whenever possible.

Table 5: Findings by Level of Evidence and Recommendation for Systematic Review

		Systematic Review Feasible		
Level of Evidence	Number of Key Questions	no	yes	maybe
None	13	13	0	0
Weak	15	5	6	4
Fair	8	0	8	0
Good	6	1	5	0

References

1. Grady D, Rubin SM, Petitti DB, et al. Hormone therapy to prevent disease and prolong life in postmenopausal women. Ann Intern Med 1992;117(12):1016-37.
2. Wenger NK, Speroff L, Packard B. Cardiovascular health and disease in women. N Engl J Med 1993;329(4):247-56.
3. Lerner DJ, Kannel WB. Patterns of coronary heart disease morbidity and mortality in the sexes: a 26-year follow-up of the Framingham population. Am Heart J 1986;111(2):383-90.
4. Healy B. The Yentl syndrome. N Engl J Med 1991;325(4):274-6.
5. Chaitman BR, Bourassa MG, Davis K, et al. Angiographic prevalence of high-risk coronary artery disease in patient subsets (CASS). Circulation 1981;64(2):360-7.
6. Greenland P, Reicher-Reiss H, Goldbourt U, et al. In-hospital and 1-year mortality in 1,524 women after myocardial infarction. Comparison with 4,315 men. Circulation 1991;83(2):484-91.
7. Kelsey SF, James M, Holubkov AL, et al. Results of percutaneous transluminal coronary angioplasty in women. 1985-1986 National Heart, Lung, and Blood Institute's Coronary Angioplasty Registry. Circulation 1993;87(3):720-7.
8. O'Connor GT, Morton JR, Diehl MJ, et al. Differences between men and women in hospital mortality associated with coronary artery bypass graft surgery. The Northern New England Cardiovascular Disease Study Group. Circulation 1993;88(5 Pt 1):2104-10.
9. Kannel WB, Sorlie P, McNamara PM. Prognosis after initial myocardial infarction: the Framingham study. Am J Cardiol 1979;44(1):53-9.
10. Puletti M, Sunseri L, Curione M, et al. Acute myocardial infarction: sex-related differences in prognosis. Am Heart J 1984;108(1):63-6.
11. Tofler GH, Stone PH, Muller JE, et al. Effects of gender and race on prognosis after myocardial infarction: adverse prognosis for women, particularly black women. J Am Coll Cardiol 1987;9(3):473-82.
12. Steingart RM, Packer M, Hamm P, et al. Sex differences in the management of coronary artery disease. Survival and Ventricular Enlargement Investigators. N Engl J Med 1991;325(4):226-30.
13. Ayanian JZ, Epstein AM. Differences in the use of procedures between women and men hospitalized for coronary heart disease. N Engl J Med 1991;325(4):221-5.
14. Shaw LJ, Miller DD, Romeis JC, et al. Gender differences in the noninvasive evaluation and management of patients with suspected coronary artery disease. Ann Intern Med 1994;120(7):559-66.
15. Grady D, Herrington D, Vittner V, et al. Cardiovascular disease outcomes during 6.8 years of hormone therapy. Heart and Estrogen/progestin Replacement Study Follow-up (HERS II). JAMA 2002;288:49-57.
16. Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women. Principal results from the Women's Health Initiative randomized controlled trial. JAMA 2002;288:321-33.
17. EndNote. In. 4.0 ed. Berkeley, CA: ISI ResearchSoft; 1988.
18. Microsoft Access. In. 9.0.4402 SR-1 ed. Redmond, WA: MIcrosoft Corporation; 1992.
19. Kwok Y, Kim C, Grady D, et al. Meta-analysis of exercise testing to detect coronary artery disease in women. Am J Cardiol 1999;83(5):660-6.
20. Gianrossi R, Detrano R, Mulvihill D, et al. Exercise-induced ST depression in the diagnosis of coronary artery disease. A meta-analysis. Circulation 1989;80(1):87-98.
21. Detrano R, Janosi A, Lyons KP, et al. Factors affecting sensitivity and specificity of a diagnostic test: the exercise thallium scintigram. Am J Med 1988;84(4):699-710.
22. Fleischmann KE, Hunink MG, Kuntz KM, et al. Exercise echocardiography or exercise SPECT imaging? A meta-analysis of diagnostic test performance. JAMA 1998;280(10):913-20.
23. 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.
24. Miller TD, Roger VL, Milavetz JJ, 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.
25. Detrano R, Hsiai T, Wang S, et al. Prognostic value of coronary calcification and angiographic stenoses in patients undergoing coronary angiography. J Am Coll Cardiol 1996;27(2):285-90.

26. Budoff MJ, Shokooh S, Shavelle RM, et al. Electron beam tomography and angiography: sex differences. Am Heart J 2002;143(5):877-82.
27. Collaborative overview of randomised trials of antiplatelet therapy--I: Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. Antiplatelet Trialists' Collaboration. BMJ 1994;308(6921):81-106.
28. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Lancet 1988;2(8607):349-60.
29. de Gaetano G. Low-dose aspirin and vitamin E in people at cardiovascular risk: a randomised trial in general practice. Collaborative Group of the Primary Prevention Project. Lancet 2001; 357(9250):89-95.
30. Hansson L, Zanchetti A, Carruthers SG, et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. Lancet 1998;351(9118):1755-62.
31. Kjeldsen SE, Kolloch RE, Leonetti G, et al. Influence of gender and age on preventing cardiovascular disease by antihypertensive treatment and acetylsalicylic acid. The HOT study. Hypertension Optimal Treatment. J Hypertens 2000;18(5):629-42.
32. Manson JE, Stampfer MJ, Colditz GA, et al. A prospective study of aspirin use and primary prevention of cardiovascular disease in women. JAMA 1991;266(4):521-7.
33. Leizorovicz A, Lechat P, Cucherat M, et al. Bisoprolol for the treatment of chronic heart failure: a meta-analysis on individual data of two placebo-controlled studies--CIBIS and CIBIS II. Cardiac Insufficiency Bisoprolol Study. Am Heart J 2002;143(2):301-7.
34. Ghali JK, Pina IL, Gottlieb SS, et al. Metoprolol CR/XL in female patients with heart failure: analysis of the experience in Metoprolol Extended-Release Randomized Intervention Trial in Heart Failure (MERIT-HF). Circulation 2002;105(13):1585-91.
35. The Beta-Blocker Pooling Project (BBPP): subgroup findings from randomized trials in post infarction patients. The Beta-Blocker Pooling Project Research Group. Eur Heart J 1988;9(1):8-16.
36. Olsson G, Wikstrand J, Warnold I, et al. Metoprolol-induced reduction in postinfarction mortality: pooled results from five double-blind randomized trials. Eur Heart J 1992;13(1):28-32.
37. Garg R, Yusuf S. Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. Collaborative Group on ACE Inhibitor Trials. JAMA 1995;273(18):1450-6.
38. Flather MD, Yusuf S, Kober L, et al. Long-term ACE-inhibitor therapy in patients with heart failure or left-ventricular dysfunction: a systematic overview of data from individual patients. ACE-Inhibitor Myocardial Infarction Collaborative Group. Lancet 2000;355(9215):1575-81.
39. Yusuf S, Sleight P, Pogue J, et al. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. N Engl J Med 2000;342(3):145-53.
40. Dagenais GR, Yusuf S, Bourassa MG, et al. Effects of ramipril on coronary events in high-risk persons: results of the Heart Outcomes Prevention Evaluation Study. Circulation 2001;104(5):522-6.
41. Lonn E, Roccaforte R, Yi Q, et al. Effect of long-term therapy with ramipril in high-risk women. J Am Coll Cardiol 2002;40(4):693.
42. Indications for ACE inhibitors in the early treatment of acute myocardial infarction: systematic overview of individual data from 100,000 patients in randomized trials. ACE Inhibitor Myocardial Infarction Collaborative Group. Circulation 1998;97(22):2202-12.
43. GISSI-3: effects of lisinopril and transdermal glyceryl trinitrate singly and together on 6-week mortality and ventricular function after acute myocardial infarction. Gruppo Italiano per lo Studio della Sopravvivenza nell'infarto Miocardico. Lancet 1994;343(8906):1115-22.
44. ISIS-4: a randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. Lancet 1995;345(8951):669-85.
45. Six-month effects of early treatment with lisinopril and transdermal glyceryl trinitrate singly and together withdrawn six weeks after acute myocardial infarction: the GISSI-3 trial. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico. J Am Coll Cardiol 1996;27(2):337-44.
46. Cho L, Topol EJ, Balog C, et al. Clinical benefit of glycoprotein IIb/IIIa blockade with Abciximab is independent of gender: pooled analysis from EPIC, EPILOG and EPISTENT trials. Evaluation of 7E3 for the Prevention of Ischemic Complications. Evaluation in Percutaneous Transluminal Coronary Angioplasty

to Improve Long-Term Outcome with Abciximab GP IIb/IIIa blockade. Evaluation of Platelet IIb/IIIa Inhibitor for Stent. J Am Coll Cardiol 2000;36(2):381-6.
47. Boersma E, Harrington RA, Moliterno DJ, et al. Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: a meta-analysis of all major randomised clinical trials. Lancet 2002;359(9302):189-98.
48. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Lancet 1994;343(8893):311-22.
49. Stone GW, Grines CL, Browne KF, et al. Comparison of in-hospital outcome in men versus women treated by either thrombolytic therapy or primary coronary angioplasty for acute myocardial infarction. Am J Cardiol 1995;75(15):987-92.
50. Yusuf S, Zhao F, Mehta SR, et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. N Engl J Med 2001;345(7):494-502.
51. Mehta SR, Yusuf S, Peters RJ, et al. Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study. Lancet 2001;358(9281):527-33.
52. Coronary angioplasty versus medical therapy for angina: the second Randomised Intervention Treatment of Angina (RITA-2) trial. RITA-2 trial participants. Lancet 1997;350(9076):461-8.
53. First-year results of CABRI (Coronary Angioplasty versus Bypass Revascularisation Investigation). CABRI Trial Participants. Lancet 1995;346(8984):1179-84.
54. Holmes DR, Jr., Holubkov R, Vlietstra RE, et al. Comparison of complications during percutaneous transluminal coronary angioplasty from 1977 to 1981 and from 1985 to 1986: the National Heart, Lung, and Blood Institute Percutaneous Transluminal Coronary Angioplasty Registry. J Am Coll Cardiol 1988;12(5):1149-55.
55. Weintraub WS, Wenger NK, Kosinski AS, et al. Percutaneous transluminal coronary angioplasty in women compared with men. J Am Coll Cardiol 1994;24(1):81-90.
56. Mehilli J, Kastrati A, Dirschinger J, et al. Differences in prognostic factors and outcomes between women and men undergoing coronary artery stenting. JAMA 2000;284(14):1799-805.
57. Bell MR, Holmes DR, Jr., Berger PB, et al. The changing in-hospital mortality of women undergoing percutaneous transluminal coronary angioplasty. JAMA 1993;269(16):2091-5.
58. Ellis SG, Roubin GS, King SB, 3rd, et al. In-hospital cardiac mortality after acute closure after coronary angioplasty: analysis of risk factors from 8,207 procedures. J Am Coll Cardiol 1988;11(2):211-6.
59. Bell MR, Grill DE, Garratt KN, et al. Long-term outcome of women compared with men after successful coronary angioplasty. Circulation 1995;91(12):2876-81.
60. Davis KB, Chaitman B, Ryan T, et al. Comparison of 15-year survival for men and women after initial medical or surgical treatment for coronary artery disease: a CASS registry study. Coronary Artery Surgery Study. J Am Coll Cardiol 1995;25(5):1000-9.
61. Jacobs AK, Kelsey SF, Brooks MM, et al. Better outcome for women compared with men undergoing coronary revascularization: a report from the bypass angioplasty revascularization investigation (BARI). Circulation 1998;98(13):1279-85.
62. Fiebach NH, Hebert PR, Stampfer MJ, et al. A prospective study of high blood pressure and cardiovascular disease in women. Am J Epidemiol 1989;130(4):646-54.
63. Kannel WB. Blood pressure as a cardiovascular risk factor: prevention and treatment. JAMA 1996;275(20):1571-6.
64. Nielsen WB, Vestbo J, Jensen GB. Isolated systolic hypertension as a major risk factor for stroke and myocardial infarction and an unexploited source of cardiovascular prevention: a prospective population-based study. J Hum Hypertens 1995;9(3):175-80.
65. Perlman JA, Wolf PH, Ray R, et al. Cardiovascular risk factors, premature heart disease, and all-cause mortality in a cohort of northern California women. Am J Obstet Gynecol 1988;158(6 Pt 2):1568-74.
66. Gueyffier F, Boutitie F, Boissel JP, et al. Effect of antihypertensive drug treatment on cardiovascular outcomes in women and men. A meta-analysis of individual patient data from randomized, controlled trials. The INDANA Investigators. Ann Intern Med 1997;126(10):761-7.
67. Quan A, Kerlikowske K, Gueyffier F, et al. Efficacy of treating hypertension in women. J Gen Intern Med 1999;14(12):718-29.
68. Quan A, Kerlikowske K, Gueyffier F, et al. Pharmacotherapy for hypertension in women of different races. Cochrane Database Syst Rev 2000(3):CD002146.

69. Wang JG, Staessen JA, Gong L, et al. Chinese trial on isolated systolic hypertension in the elderly. Systolic Hypertension in China (Syst-China) Collaborative Group. Arch Intern Med 2000;160(2):211-20.
70. Orchard TJ. The impact of gender and general risk factors on the occurrence of atherosclerotic vascular disease in non-insulin-dependent diabetes mellitus. Ann Med 1996;28(4):323-33.
71. Lee WL, Cheung AM, Cape D, et al. Impact of diabetes on coronary artery disease in women and men: a meta-analysis of prospective studies. Diabetes Care 2000;23(7):962-8.
72. Abbott RD, Donahue RP, Kannel WB, et al. The impact of diabetes on survival following myocardial infarction in men vs women. The Framingham Study. JAMA 1988;260(23):3456-60.
73. Brand FN, Abbott RD, Kannel WB. Diabetes, intermittent claudication, and risk of cardiovascular events. The Framingham Study. Diabetes 1989;38(4):504-9.
74. Kannel WB, D'Agostino RB, Wilson PW, et al. Diabetes, fibrinogen, and risk of cardiovascular disease: the Framingham experience. Am Heart J 1990;120(3):672-6.
75. Manson JE, Colditz GA, Stampfer MJ, et al. A prospective study of maturity-onset diabetes mellitus and risk of coronary heart disease and stroke in women. Arch Intern Med 1991;151(6):1141-7.
76. Hu FB, Stampfer MJ, Solomon CG, et al. The impact of diabetes mellitus on mortality from all causes and coronary heart disease in women: 20 years of follow-up. Arch Intern Med 2001;161(14):1717-23.
77. Donahue RP, Goldberg RJ, Chen Z, et al. The influence of sex and diabetes mellitus on survival following acute myocardial infarction: a community-wide perspective. J Clin Epidemiol 1993;46(3):245-52.
78. Malmberg K, Yusuf S, Gerstein HC, et al. Impact of diabetes on long-term prognosis in patients with unstable angina and non-Q-wave myocardial infarction: results of the OASIS (Organization to Assess Strategies for Ischemic Syndromes) Registry. Circulation 2000;102(9):1014-9.
79. Manolio TA, Pearson TA, Wenger NK, et al. Cholesterol and heart disease in older persons and women. Review of an NHLBI workshop. Ann Epidemiol 1992;2(1-2):161-76.
80. Jacobs D, Blackburn H, Higgins M, et al. Report of the Conference on Low Blood Cholesterol: Mortality Associations. Circulation 1992;86(3):1046-60.
81. Hokanson JE, Austin MA. Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population-based prospective studies. J Cardiovasc Risk 1996;3(2):213-9.
82. Austin MA, Hokanson JE, Edwards KL. Hypertriglyceridemia as a cardiovascular risk factor. Am J Cardiol 1998;81(4A):7B-12B.
83. Craig WY, Neveux LM, Palomaki GE, et al. Lipoprotein(a) as a risk factor for ischemic heart disease: metaanalysis of prospective studies. Clin Chem 1998;44(11):2301-6.
84. Walsh JM, Grady D. Treatment of hyperlipidemia in women. JAMA 1995;274(14):1152-8.
85. Byington RP, Jukema JW, Salonen JT, et al. Reduction in cardiovascular events during pravastatin therapy. Pooled analysis of clinical events of the Pravastatin Atherosclerosis Intervention Program. Circulation 1995;92(9):2419-25.
86. Buchwald H, Campos CT, Boen JR, et al. Gender-based mortality follow-up from the Program on the Surgical Control of the Hyperlipidemias (POSCH) and meta-analysis of lipid intervention trials. Women in POSCH and other lipid trials. Ann Surg 1996;224(4):486-98; discussion 498-500.
87. LaRosa JC, He J, Vupputuri S. Effect of statins on risk of coronary disease: a meta-analysis of randomized controlled trials. JAMA 1999;282(24):2340-6.
88. Miettinen TA, Pyorala K, Olsson AG, et al. Cholesterol-lowering therapy in women and elderly patients with myocardial infarction or angina pectoris: findings from the Scandinavian Simvastatin Survival Study (4S). Circulation 1997;96(12):4211-8.
89. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet 2002;360(9326):7-22.
90. Boushey CJ, Beresford SA, Omenn GS, et al. A quantitative assessment of plasma homocysteine as a risk factor for vascular disease. Probable benefits of increasing folic acid intakes. JAMA 1995;274(13):1049-57.
91. Lowering blood homocysteine with folic acid based supplements: meta-analysis of randomised trials. Homocysteine Lowering Trialists' Collaboration. BMJ 1998;316(7135):894-8.
92. Ridker PM, Buring JE, Shih J, et al. Prospective study of C-reactive protein and the risk of future cardiovascular events among apparently healthy women. Circulation 1998;98(8):731-3.
93. Ridker PM, Hennekens CH, Buring JE, et al. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. N Engl J Med 2000;342(12):836-43.

94. Willett WC, Green A, Stampfer MJ, et al. Relative and absolute excess risks of coronary heart disease among women who smoke cigarettes. N Engl J Med 1987;317(21):1303-9.
95. Kawachi I, Colditz GA, Stampfer MJ, et al. Smoking cessation and time course of decreased risks of coronary heart disease in middle-aged women. Arch Intern Med 1994;154(2):169-75.
96. Paganini-Hill A, Hsu G. Smoking and mortality among residents of a California retirement community. Am J Public Health 1994;84(6):992-5.
97. Njolstad I, Arnesen E, Lund-Larsen PG. Smoking, serum lipids, blood pressure, and sex differences in myocardial infarction. A 12-year follow-up of the Finnmark Study. Circulation 1996;93(3):450-6.
98. Prescott E, Hippe M, Schnohr P, et al. Smoking and risk of myocardial infarction in women and men: longitudinal population study. BMJ 1998;316(7137):1043-7.
99. Kannel WB, D'Agostino RB, Belanger AJ. Fibrinogen, cigarette smoking, and risk of cardiovascular disease: insights from the Framingham Study. Am Heart J 1987;113(4):1006-10.
100. Freund KM, Belanger AJ, D'Agostino RB, et al. The health risks of smoking. The Framingham Study: 34 years of follow-up. Ann Epidemiol 1993;3(4):417-24.
101. LaCroix AZ, Lang J, Scherr P, et al. Smoking and mortality among older men and women in three communities. N Engl J Med 1991;324(23):1619-25.
102. Wilson K, Gibson N, Willan A, et al. Effect of smoking cessation on mortality after myocardial infarction: meta-analysis of cohort studies. Arch Intern Med 2000;160(7):939-44.
103. Omenn GS, Anderson KW, Kronmal RA, et al. The temporal pattern of reduction of mortality risk after smoking cessation. Am J Prev Med 1990;6(5):251-7.
104. Kawachi I, Colditz GA, Stampfer MJ, et al. Smoking cessation in relation to total mortality rates in women. A prospective cohort study. Ann Intern Med 1993;119(10):992-1000.
105. Harris T, Cook EF, Garrison R, et al. Body mass index and mortality among nonsmoking older persons. The Framingham Heart Study. JAMA 1988;259(10):1520-4.
106. Kannel WB, Cupples LA, Ramaswami R, et al. Regional obesity and risk of cardiovascular disease; the Framingham Study. J Clin Epidemiol 1991;44(2):183-90.
107. Manson JE, Colditz GA, Stampfer MJ, et al. A prospective study of obesity and risk of coronary heart disease in women. N Engl J Med 1990;322(13):882-9.
108. Manson JE, Willett WC, Stampfer MJ, et al. Body weight and mortality among women. N Engl J Med 1995;333(11):677-85.
109. Willett WC, Manson JE, Stampfer MJ, et al. Weight, weight change, and coronary heart disease in women. Risk within the 'normal' weight range. JAMA 1995;273(6):461-5.
110. Rexrode KM, Carey VJ, Hennekens CH, et al. Abdominal adiposity and coronary heart disease in women. JAMA 1998;280(21):1843-8.
111. Field AE, Coakley EH, Must A, et al. Impact of overweight on the risk of developing common chronic diseases during a 10-year period. Arch Intern Med 2001;161(13):1581-6.
112. Folsom AR, Burke GL, Byers CL, et al. Implications of obesity for cardiovascular disease in blacks: the CARDIA and ARIC studies. Am J Clin Nutr 1991;53(6 Suppl):1604S-1611S.
113. Folsom AR, French SA, Zheng W, et al. Weight variability and mortality: the Iowa Women's Health Study. Int J Obes Relat Metab Disord 1996;20(8):704-9.
114. French SA, Folsom AR, Jeffery RW, et al. Weight variability and incident disease in older women: the Iowa Women's Health Study. Int J Obes Relat Metab Disord 1997;21(3):217-23.
115. Folsom AR, Kushi LH, Anderson KE, et al. Associations of general and abdominal obesity with multiple health outcomes in older women: the Iowa Women's Health Study. Arch Intern Med 2000;160(14):2117-28.
116. Folsom AR, Stevens J, Schreiner PJ, et al. Body mass index, waist/hip ratio, and coronary heart disease incidence in African Americans and whites. Atherosclerosis Risk in Communities Study Investigators. Am J Epidemiol 1998;148(12):1187-94.
117. Manson JE, Hu FB, Rich-Edwards JW, et al. A prospective study of walking as compared with vigorous exercise in the prevention of coronary heart disease in women. N Engl J Med 1999;341(9):650-8.
118. Lee IM, Rexrode KM, Cook NR, et al. Physical activity and coronary heart disease in women: is "no pain, no gain" passe? JAMA 2001;285(11):1447-54.
119. Rockhill B, Willett WC, Manson JE, et al. Physical activity and mortality: a prospective study among women. Am J Public Health 2001;91(4):578-83.
120. Blair SN, Kohl HW, 3rd, Paffenbarger RS, Jr., et al. Physical fitness and all-cause mortality. A prospective study of healthy men and women. JAMA 1989;262(17):2395-401.

121. Sherman SE, D'Agostino RB, Cobb JL, et al. Physical activity and mortality in women in the Framingham Heart Study. Am Heart J 1994;128(5):879-84.
122. Oldridge NB, Guyatt GH, Fischer ME, et al. Cardiac rehabilitation after myocardial infarction. Combined experience of randomized clinical trials. JAMA 1988;260(7):945-50.
123. O'Connor GT, Buring JE, Yusuf S, et al. An overview of randomized trials of rehabilitation with exercise after myocardial infarction. Circulation 1989;80(2):234-44.
124. Jolliffe JA, Rees K, Taylor RS, et al. Exercise-based rehabilitation for coronary heart disease. Cochrane Database Syst Rev 2000;4.
125. Pocock SJ, McCormack V, Gueyffier F, et al. A score for predicting risk of death from cardiovascular disease in adults with raised blood pressure, based on individual patient data from randomised controlled trials. BMJ 2001;323(7304):75-81.
126. D'Agostino RB, Sr., Grundy S, Sullivan LM, et al. Validation of the Framingham coronary heart disease prediction scores: results of a multiple ethnic groups investigation. JAMA 2001;286(2):180-7.
127. Hu FB, Grodstein F, Hennekens CH, et al. Age at natural menopause and risk of cardiovascular disease. Arch Intern Med 1999;159(10):1061-6.
128. van der Schouw YT, van der Graaf Y, Steyerberg EW, et al. Age at menopause as a risk factor for cardiovascular mortality. Lancet 1996;347(9003):714-8.
129. Cooper GS, Sandler DP. Age at natural menopause and mortality. Ann Epidemiol 1998;8(4):229-35.
130. Keil JE, Sutherland SE, Knapp RG, et al. Mortality rates and risk factors for coronary disease in black as compared with white men and women. N Engl J Med 1993;329(2):73-8.
131. White AD, Rosamond WD, Chambless LE, et al. Sex and race differences in short-term prognosis after acute coronary heart disease events: the Atherosclerosis Risk In Communities (ARIC) study. Am Heart J 1999;138(3 Pt 1):540-8.
132. Roig E, Castaner A, Simmons B, et al. In-hospital mortality rates from acute myocardial infarction by race in U.S. hospitals: findings from the National Hospital Discharge Survey. Circulation 1987;76(2):280-8.
133. Salomaa V, Miettinen H, Niemela M, et al. Relation of socioeconomic position to the case fatality, prognosis and treatment of myocardial infarction events; the FINMONICA MI Register Study. J Epidemiol Community Health 2001;55(7):475-82.
134. Capewell S, MacIntyre K, Stewart S, et al. Age, sex, and social trends in out-of-hospital cardiac deaths in Scotland 1986-95: a retrospective cohort study. Lancet 2001;358(9289):1213-7.
135. Morrison C, Woodward M, Leslie W, et al. Effect of socioeconomic group on incidence of, management of, and survival after myocardial infarction and coronary death: analysis of community coronary event register. BMJ 1997;314(7080):541-6.
136. Johnson PA, Goldman L, Orav EJ, et al. Gender differences in the management of acute chest pain. Support for the "Yentl syndrome". J Gen Intern Med 1996;11(4):209-17.
137. Roger VL, Farkouh ME, Weston SA, et al. Sex differences in evaluation and outcome of unstable angina. JAMA 2000;283(5):646-52.
138. Battleman DS, Callahan M. Gender differences in utilization of exercise treadmill testing: a claims-based analysis. J Healthc Qual 2001;23(3):38-41.
139. Pagley PR, Yarzebski J, Goldberg R, et al. Gender differences in the treatment of patients with acute myocardial infarction. A multihospital, community-based perspective. Arch Intern Med 1993;153(5):625-9.
140. Clarke KW, Gray D, Keating NA, et al. Do women with acute myocardial infarction receive the same treatment as men? Bmj 1994;309(6954):563-6.
141. Tsuyuki RT, Teo KK, Ikuta RM, et al. Mortality risk and patterns of practice in 2,070 patients with acute myocardial infarction, 1987-92. Relative importance of age, sex, and medical therapy. Chest 1994;105(6):1687-92.
142. Chandra NC, Ziegelstein RC, Rogers WJ, et al. Observations of the treatment of women in the United States with myocardial infarction: a report from the National Registry of Myocardial Infarction-I. Arch Intern Med 1998;158(9):981-8.
143. Rojas-Fernandez CH, Kephart GC, Sketris IS, et al. Underuse of acetylsalicylic acid in individuals with myocardial infarction, ischemic heart disease or stroke: data from the 1995 population-based Nova Scotia Health Survey. Can J Cardiol 1999;15(3):291-6.
144. Shahar E, Folsom AR, Romm FJ, et al. Patterns of aspirin use in middle-aged adults: the Atherosclerosis Risk in Communities (ARIC) Study. Am Heart J 1996;131(5):915-22.

145. Maynard C, Althouse R, Cerqueira M, et al. Underutilization of thrombolytic therapy in eligible women with acute myocardial infarction. Am J Cardiol 1991;68(5):529-30.
146. Maynard C, Litwin PE, Martin JS, et al. Gender differences in the treatment and outcome of acute myocardial infarction. Results from the Myocardial Infarction Triage and Intervention Registry. Arch Intern Med 1992;152(5):972-6.
147. Yarzebski J, Col N, Pagley P, et al. Gender differences and factors associated with the receipt of thrombolytic therapy in patients with acute myocardial infarction: a community-wide perspective. Am Heart J 1996;131(1):43-50.
148. Pfeffer MA, Moye LA, Braunwald E, et al. Selection bias in the use of thrombolytic therapy in acute myocardial infarction. The SAVE Investigators. JAMA 1991;266(4):528-32.
149. Kudenchuk PJ, Maynard C, Martin JS, et al. Comparison of presentation, treatment, and outcome of acute myocardial infarction in men versus women (the Myocardial Infarction Triage and Intervention Registry). Am J Cardiol 1996;78(1):9-14.
150. Petticrew M, McKee M, Jones J. Coronary artery surgery: are women discriminated against? Bmj 1993;306(6886):1164-6.
151. Strauss R, Pfeifer C, Muhlberger V, et al. Effects of morbidity, age, gender and region on percutaneous transluminal coronary angioplasty (PTCA) utilisation. Public Health 1999;113(2):79-87.
152. Giacomini MK. Gender and ethnic differences in hospital-based procedure utilization in California. Arch Intern Med 1996;156(11):1217-24.
153. Chiriboga DE, Yarzebski J, Goldberg RJ, et al. A community-wide perspective of gender differences and temporal trends in the use of diagnostic and revascularization procedures for acute myocardial infarction. Am J Cardiol 1993;71(4):268-73.
154. Giles TD, Fisher MB, Rush JE. Lisinopril and captopril in the treatment of heart failure in older patients. Comparison of a long- and short-acting angiotensin-converting enzyme inhibitor. Am J Med 1988;85(3B):44-7.
155. Goldberg KC, Hartz AJ, Jacobsen SJ, et al. Racial and community factors influencing coronary artery bypass graft surgery rates for all 1986 Medicare patients. JAMA 1992;267(11):1473-7.
156. Ramsey DJ, Goff DC, Wear ML, et al. Sex and ethnic differences in use of myocardial revascularization procedures in Mexican Americans and non-Hispanic whites: the Corpus Christi Heart Project. J Clin Epidemiol 1997;50(5):603-9.
157. Krumholz HM, Douglas PS, Lauer MS, et al. Selection of patients for coronary angiography and coronary revascularization early after myocardial infarction: is there evidence for a gender bias? Ann Intern Med 1992;116(10):785-90.
158. Bergelson BA, Tommaso CL. Gender differences in clinical evaluation and triage in coronary artery disease. Chest 1995;108(6):1510-3.
159. D'Hoore W, Sicotte C, Tilquin C. Sex bias in the management of coronary artery disease in Quebec. Am J Public Health 1994;84(6):1013-5.
160. Weaver WD, White HD, Wilcox RG, et al. Comparisons of characteristics and outcomes among women and men with acute myocardial infarction treated with thrombolytic therapy. GUSTO-I investigators. JAMA 1996;275(10):777-82.
161. Miller TD, Roger VL, Hodge DO, et al. Gender differences and temporal trends in clinical characteristics, stress test results and use of invasive procedures in patients undergoing evaluation for coronary artery disease. J Am Coll Cardiol 2001;38(3):690-7.
162. Jaglal SB, Goel V, Naylor CD. Sex differences in the use of invasive coronary procedures in Ontario. Can J Cardiol 1994;10(2):239-44.
163. Bickell NA, Pieper KS, Lee KL, et al. Referral patterns for coronary artery disease treatment: gender bias or good clinical judgment? Ann Intern Med 1992;116(10):791-7.
164. Klungel OH, de Boer A, Paes AH, et al. Sex differences in the pharmacological treatment of hypertension: a review of population-based studies. J Hypertens 1997;15(6):591-600.
165. Sketris IS, Kephart GC, Hicks VA, et al. Prescribing patterns of antilipemic drugs and prevalence of hypercholesterolemia in the Nova Scotia population more than 65 years old. Ann Pharmacother 1995;29(6):576-81.
166. Magrini N, Einarson T, Vaccheri A, et al. Use of lipid-lowering drugs from 1990 to 1994: an international comparison among Australia, Finland, Italy (Emilia Romagna Region), Norway and Sweden. Eur J Clin Pharmacol 1997;53(3-4):185-9.

167. Majeed A, Moser K, Maxwell R. Age, sex and practice variations in the use of statins in general practice in England and Wales. J Public Health Med 2000;22(3):275-9.
168. Bernstein SJ, Hilborne LH, Leape LL, et al. The appropriateness of use of cardiovascular procedures in women and men. Arch Intern Med 1994;154(23):2759-65.
169. Saha S, Stettin GD, Redberg RF. Gender and willingness to undergo invasive cardiac procedures. J Gen Intern Med 1999;14(2):122-5.

Evidence Table 1: Articles containing evidence on key question arranged by key question, type of research design, and level of quality

1.01 Exercise tolerance testing

Systematic Review

[a]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):913-2.

[a]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.

Cross Sectional

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;4:329-35.

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

1.02 Exercise echocardiogram

Systematic Review

[a]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.

[a]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.

1.03 Coronary artery calcification score

Cross-sectional

[a]Budoff MJ, Shokooh S, Shavelle RM, Kim HT, French WJ. Electron beam tomography and angiography: sex differences. Am Heart J 2002;143(5):877-82.

[a]Detrano R, Hsiai T, Wang S, Puentes G, Fallavollita J, Shields P, et al. Prognostic value of coronary calcification and angiographic stenoses in patients undergoing coronary angiography. J Am Coll Cardiol 1996;27(2):285-90.

[a]indicates "good quality" article

Evidence Table 1: Articles containing evidence on key question arranged by key question, type of research design, and level of quality (continued)

2.01 Aspirin

Systematic Review

[a]Collaborative overview of randomised trials of antiplatelet therapy--I: Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. Antiplatelet Trialists' Collaboration. BMJ 1994;308(6921):81-106.

Clinical Trial

[a]Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Lancet 1988;2(8607):349-60.

[a]de Gaetano G. Low-dose aspirin and vitamin E in people at cardiovascular risk: a randomised trial in general practice. Collaborative Group of the Primary Prevention Project. Lancet 2001;357(9250):89-95.

[a]Hansson L, Zanchetti A, Carruthers SG, Dahlof B, Elmfeldt D, Julius S, et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. Lancet 1998;351(9118):1755-62.

[a]Kjeldsen SE, Kolloch RE, Leonetti G, Mallion JM, Zanchetti A, Elmfeldt D, et al. Influence of gender and age on preventing cardiovascular disease by antihypertensive treatment and acetylsalicylic acid. The HOT study. Hypertension Optimal Treatment. J Hypertens 2000;18(5):629-42.

Prospective Cohort

[a]Manson JE, Stampfer MJ, Colditz GA, Willett WC, Rosner B, Speizer FE, et al. A prospective study of aspirin use and primary prevention of cardiovascular disease in women. JAMA 1991;266(4):521-7.

2.02 Beta-blockers

Systematic Review

The Beta-Blocker Pooling Project (BBPP): subgroup findings from randomized trials in post infarction patients. The Beta-Blocker Pooling Project Research Group. Eur Heart J 1988;9(1):8-16.

Leizorovicz A, Lechat P, Cucherat M, Bugnard F. Bisoprolol for the treatment of chronic heart failure: a meta-analysis on individual data of two placebo-controlled studies--CIBIS and CIBIS II. Cardiac Insufficiency Bisoprolol Study. Am Heart J 2002;143(2):301-7.

Olsson G, Wikstrand J, Warnold I, Manger Cats V, McBoyle D, Herlitz J, et al. Metoprolol-induced reduction in postinfarction mortality: pooled results from five double-blind randomized trials. Eur Heart J 1992;13(1):28-32.

[a]indicates "good quality" article

Evidence Table 1: Articles containing evidence on key question arranged by key question, type of research design, and level of quality (continued)

Clinical Trial

Ghali JK, Pina IL, Gottlieb SS, Deedwania PC, Wikstrand JC. Metoprolol CR/XL in female patients with heart failure: analysis of the experience in Metoprolol Extended-Release Randomized Intervention Trial in Heart Failure (MERIT-HF). Circulation 2002;105(13):1585-91.

2.03 Angiotensin converting enzyme (ACE) inhibitors

Systematic Review

[a]Indications for ACE inhibitors in the early treatment of acute myocardial infarction: systematic overview of individual data from 100,000 patients in randomized trials. ACE Inhibitor Myocardial Infarction Collaborative Group. Circulation 1998;97(22):2202-12.

[a]Flather MD, Yusuf S, Kober L, Pfeffer M, Hall A, Murray G, et al. Long-term ACE-inhibitor therapy in patients with heart failure or left-ventricular dysfunction: a systematic overview of data from individual patients. ACE-Inhibitor Myocardial Infarction Collaborative Group. Lancet 2000;355(9215):1575-81.

[a]Garg R, Yusuf S. Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. Collaborative Group on ACE Inhibitor Trials. JAMA 1995;273(18):1450-6.

Clinical Trial

GISSI-3: effects of lisinopril and transdermal glyceryl trinitrate singly and together on 6-week mortality and ventricular function after acute myocardial infarction. Gruppo Italiano per lo Studio della Sopravvivenza nell'infarto Miocardico. Lancet 1994;343(8906):1115-22.

[a]Dagenais GR, Yusuf S, Bourassa MG, Yi Q, Bosch J, Lonn EM, et al. Effects of ramipril on coronary events in high-risk persons: results of the Heart Outcomes Prevention Evaluation Study. Circulation 2001;104(5):522-6.

[a]Lonn E, Roccafort R, Yi Q, Dagenais G, Sleight P, et al. Effect of long-term therapy with ramipril in high-risk women. J Am Coll Cardiol 2002;40:6930702.

[a]Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. N Engl J Med 2000;342(3):145-53.

2.05 Nitrates

Clinical Trial

GISSI-3: effects of lisinopril and transdermal glyceryl trinitrate singly and together on 6-week mortality and ventricular function after acute myocardial infarction. Gruppo Italiano per lo Studio della Sopravvivenza nell'infarto Miocardico. Lancet 1994;343(8906):1115-22.

[a]indicates "good quality" article

[a]ISIS-4: a randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. Lancet 1995;345(8951):669-85.

Six-month effects of early treatment with lisinopril and transdermal glyceryl trinitrate singly and together withdrawn six weeks after acute myocardial infarction: the GISSI-3 trial. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico. J Am Coll Cardiol 1996;27(2):337-44.

2.07 Glycoprotein IIb/IIIa Drugs

Systematic Review

[a]Boersma E, Harrington RA, Moliterno DJ, White H, Theroux P, Van de Werf F, et al. Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: a meta-analysis of all major randomised clinical trials. Lancet 2002;359(9302):189-98.

Cho L, Topol EJ, Balog C, Foody JM, Booth JE, Cabot C, et al. Clinical benefit of glycoprotein IIb/IIIa blockade with Abciximab is independent of gender: pooled analysis from EPIC, EPILOG and EPISTENT trials. Evaluation of 7E3 for the Prevention of Ischemic Complications. Evaluation in Percutaneous Transluminal Coronary Angioplasty to Improve Long-Term Outcome with Abciximab GP IIb/IIIa blockade. Evaluation of Platelet IIb/IIIa Inhibitor for Stent. J Am Coll Cardiol 2000;36(2):381-6.

2.08 Thrombolysis

Systematic Review

[a]Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Lancet 1994;343(8893):311-22.

Clinical Trial

Stone GW, Grines CL, Browne KF, Marco J, Rothbaum D, O'Keefe J, et al. Comparison of in-hospital outcome in men versus women treated by either thrombolytic therapy or primary coronary angioplasty for acute myocardial infarction. Am J Cardiol 1995;75(15):987-92.

2.10 Clopidogrel

Clinical Trial

[a]Mehta SR, Yusuf S, Peters RJ, et al. Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study. Lancet 2001;358(9281):527-33.

[a]Yusuf S, Zhao F, Mehta SR, et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. N Engl J Med 2001;345(7):494-502

[a]indicates "good quality" article

Evidence Table 1: Articles containing evidence on key question arranged by key question, type of research design, and level of quality (continued)

2.11 Percutaneous transluminal coronary angioplasty (PTCA) and stenting

Clinical Trial

Stone GW, Grines CL, Browne KF, Marco J, Rothbaum D, O'Keefe J, et al. Comparison of in-hospital outcome in men versus women treated by either thrombolytic therapy or primary coronary angioplasty for acute myocardial infarction. Am J Cardiol 1995;75(15):987-92.

[a]First-year results of CABRI (Coronary Angioplasty versus Bypass Revascularisation Investigation). CABRI Trial Participants. Lancet 1995;346(8984):1179-84.

Coronary angioplasty versus medical therapy for angina: the second Randomised Intervention Treatment of Angina (RITA-2) trial. RITA-2 trial participants. Lancet 1997;350(9076):461-8.

Prospective Cohort

Bell MR, Grill DE, Garratt KN, Berger PB, Gersh BJ, Holmes DR, Jr. Long-term outcome of women compared with men after successful coronary angioplasty. Circulation 1995;91(12):2876-81.

Bell MR, Holmes DR, Jr., Berger PB, Garratt KN, Bailey KR, Gersh BJ. The changing in-hospital mortality of women undergoing percutaneous transluminal coronary angioplasty. JAMA 1993;269(16):2091-5.

[a]Ellis SG, Roubin GS, King SB, 3rd, Douglas JS, Jr., Shaw RE, Stertzer SH, et al. In-hospital cardiac mortality after acute closure after coronary angioplasty: analysis of risk factors from 8,207 procedures. J Am Coll Cardiol 1988;11(2):211-6.

[a]Holmes DR, Jr., Holubkov R, Vlietstra RE, Kelsey SF, Reeder GS, Dorros G, et al. Comparison of complications during percutaneous transluminal coronary angioplasty from 1977 to 1981 and from 1985 to 1986: the National Heart, Lung, and Blood Institute Percutaneous Transluminal Coronary Angioplasty Registry. J Am Coll Cardiol 1988;12(5):1149-55.

[a]Kelsey SF, James M, Holubkov AL, Holubkov R, Cowley MJ, Detre KM. Results of percutaneous transluminal coronary angioplasty in women. 1985-1986 National Heart, Lung, and Blood Institute's Coronary Angioplasty Registry. Circulation 1993;87(3):720-7.

[a]Mehilli J, Kastrati A, Dirschinger J, Bollwein H, Neumann FJ, Schomig A. Differences in prognostic factors and outcomes between women and men undergoing coronary artery stenting. JAMA 2000;284(14):1799-805.

Shaw LJ, Miller DD, Romeis JC, Kargl D, Younis LT, Chaitman BR. Gender differences in the noninvasive evaluation and management of patients with suspected coronary artery disease. Ann Intern Med 1994;120(7):559-66.

[a]Weintraub WS, Wenger NK, Kosinski AS, Douglas JS, Jr., Liberman HA, Morris DC, et al. Percutaneous transluminal coronary angioplasty in women compared with men. J Am

Coll Cardiol 1994;24(1):81-90.

2.12 Coronary artery bypass surgery (CABG)

Clinical Trial

[a]First-year results of CABRI (Coronary Angioplasty versus Bypass Revascularisation Investigation). CABRI Trial Participants. Lancet 1995;346(8984):1179-84.

[a]Jacobs AK, Kelsey SF, Brooks MM, Faxon DP, Chaitman BR, Bittner V, et al. Better outcome for women compared with men undergoing coronary revascularization: a report from the bypass angioplasty revascularization investigation (BARI). Circulation 1998;98(13):1279-85.

Prospective Cohort

[a]Davis KB, Chaitman B, Ryan T, Bittner V, Kennedy JW. Comparison of 15-year survival for men and women after initial medical or surgical treatment for coronary artery disease: a CASS registry study. Coronary Artery Surgery Study. J Am Coll Cardiol 1995;25(5):1000-9.

3.01a Hypertension as a risk factor for CHD in women

Propsective Cohort

[a]Fiebach NH, Hebert PR, Stampfer MJ, Colditz GA, Willett WC, Rosner B, et al. A prospective study of high blood pressure and cardiovascular disease in women. Am J Epidemiol 1989;130(4):646-54.

[a]Kannel WB. Blood pressure as a cardiovascular risk factor: prevention and treatment. JAMA 1996;275(20):1571-6.

Nielsen WB, Vestbo J, Jensen GB. Isolated systolic hypertension as a major risk factor for stroke and myocardial infarction and an unexploited source of cardiovascular prevention: a prospective population-based study. J Hum Hypertens 1995;9:175-80.

Perlman JA, Wolf PH, Ray R, Lieberknecht G. Cardiovascular risk factors, premature heart disease, and all-cause mortality in a cohort of Northern California women. Am J Obstet Gynecol. 1988;158:1568-74.

3.01b Treatment of hypertension to reduce risk of CHD events in women

Systematic Review

Gueyffier F, Boutitie F, Boissel JP, Pocock S, Coope J, Cutler J, et al. Effect of antihypertensive drug treatment on cardiovascular outcomes in women and men. A meta-analysis of individual patient data from randomized, controlled trials. The INDANA Investigators. Ann Intern Med 1997;126(10):761-7.

[a]Quan A, Kerlikowske K, Gueyffier F, Boissel JP. Efficacy of treating hypertension in women. J Gen Intern Med 1999;14(12):718-29.

[a]Quan A, Kerlikowske K, Gueyffier F, Boissel JP. Pharmacotherapy for hypertension in women of different races. Cochrane Database Syst Rev 2000(3):CD002146.

Clinical Trial

Wang J, Staessen JA, Gong L, Liu L. Chinese trial on isolated systolic hypertension in the elderly. The Systolic Hypertension in China (Syst-China) Collaborative Group. Arch Intern Med 2000;160:211-220.

3.02a Diabetes as a risk factor for CHD in women

Systematic Review

[a]Lee WL, Cheung AM, Cape D, Zinman B. Impact of diabetes on coronary artery disease in women and men: a meta-analysis of prospective studies. Diabetes Care 2000;23(7):962-8.

Orchard TJ. The impact of gender and general risk factors on the occurrence of atherosclerotic vascular disease in non-insulin-dependent diabetes mellitus. Ann Med 1996;28(4):323-33.

Prospective Cohort

[a]Abbott RD, Donahue RP, Kannel WB, Wilson PW. The impact of diabetes on survival following myocardial infarction in men vs women. The Framingham Study. JAMA 1988;260(23):3456-60.

[a]Brand FN, Abbott RD, Kannel WB. Diabetes, intermittent claudication, and risk of cardiovascular events. The Framingham Study. Diabetes 1989;38(4):504-9.

[a]Donahue RP, Goldberg RJ, Chen Z, Gore JM, Alpert JS. The influence of sex and diabetes mellitus on survival following acute myocardial infarction: a community-wide perspective. J Clin Epidemiol 1993;46(3):245-52.

[a]Hu FB, Stampfer MJ, Solomon CG, Liu S, Willett WC, Speizer FE, et al. The impact of diabetes mellitus on mortality from all causes and coronary heart disease in women: 20 years of follow-up. Arch Intern Med *Kannel WB, D'Agostino RB, Wilson PW,

[a]Kannel WB, D'Agostino RB, Wilson PW, Belanger AJ, Gagnon DR. Diabetes, fibrinogen, and risk of cardiovascular disease: the Framingham experience. Am Heart J 1990;120(3):672-6.

[a]Malmberg K, Yusuf S, Gerstein HC, Brown J, Zhao F, Hunt D, et al. Impact of diabetes on long-term prognosis in patients with unstable angina and non-Q-wave myocardial infarction: results of the OASIS (Organization to Assess Strategies for Ischemic Syndromes) Registry. Circulation 2000;102(9):1014-9.

[a]Manson JE, Colditz GA, Stampfer MJ, Willett WC, Krolewski AS, Rosner B, et al. A prospective study of maturity-onset diabetes mellitus and risk of coronary heart disease and stroke in women. Arch Intern Med 1991;151(6):1141-7.

Evidence Table 1: Articles containing evidence on key question arranged by key question, type of research design, and level of quality (continued)

3.03a Hyperlipidemia as a risk factor for CHD in women

Systematic Review

[a]Austin MA, Hokanson JE, Edwards KL. Hypertriglyceridemia as a cardiovascular risk factor. Am J Cardiol 1998;81(4A):7B-12B.

Craig WY, Neveux LM, Palomaki GE, Cleveland MM, Haddow JE. Lipoprotein(a) as a risk factor for ischemic heart disease:metaanalysis of prospective studies. Clin Chem 1998;44(11):2301-6.

[a]Hokanson JE, Austin MA. Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population-based prospective studies. J Cardiovasc Risk 1996;3(2):213-9.

Jacobs D, Blackburn H, Higgins M, Reed D, Iso H, McMillan G, et al. Report of the Conference on Low Blood Cholesterol: Mortality Associations. Circulation 1992;86(3):1046-60.

Manolio TA, Pearson TA, Wenger NK, Barrett-Connor E, Payne GH, Harlan WR. Cholesterol and heart disease in older persons and women. Review of an NHLBI workshop. Ann Epidemiol 1992;2(1-2):161-76.

3.03b Treatment of hyperlipidemia to reduce risk of CHD events in women

Systematic Review

Byington RP, Jukema JW, Salonen JT, Pitt B, Bruschke AV, Hoen H, et al. Reduction in cardiovascular events during pravastatin therapy. Pooled analysis of clinical events of the Pravastatin Atherosclerosis Intervention Program. Circulation 1995;92(9):2419-25.

Buchwald H, Campos CT, Boen JR, Nguyen P, Williams SE, Lau J, et al. Gender-based mortality follow-up from the Program on the Surgical Control of the Hyperlipidemias (POSCH) and meta-analysis of lipid intervention trials. Women in POSCH and other lipid trials. Ann Surg 1996;224(4):486-98; discussion 498-500.

[a]LaRosa JC, He J, Vupputuri S. Effect of statins on risk of coronary disease: a meta-analysis of randomized controlled trials. JAMA 1999;282(24):2340-6.

Walsh JM, Grady D. Treatment of hyperlipidemia in women. JAMA 1995;274(14):1152-8.

Clinical Trial

[a]MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,538 high-risk individuals: a randomized placebo controlled trial. Heart Protection Study Collaborative Group. Lancet 2002; 360:7-22.

[a]Miettinen TA, Pyorala K, Olsson AG, Musliner TA, Cook TJ, Faergeman O, et al. Cholesterol-lowering therapy in women and elderly patients with myocardial infarction or angina pectoris: findings from the Scandinavian Simvastatin Survival Study (4S). Circulation 1997;96(12):4211-8.

[a]indicates "good quality" article

Evidence Table 1: Articles containing evidence on key question arranged by key question, type of research design, and level of quality (continued)

3.04a Elevated homocysteine as a risk factor for CHD in women

Systematic Review

Boushey CJ, Beresford SA, Omenn GS, Motulsky AG. A quantitative assessment of plasma homocysteine as a risk factor for vascular disease. Probable benefits of increasing folic acid intakes. JAMA 1995;274(13):1049-57.

3.05a C-reactive protein as a risk factor for CHD events in women

Prospective Cohort

[a]Ridker PM, Buring JE, Shih J, Matias M, Hennekens CH. Prospective study of C-reactive protein and the risk of future cardiovascular events among apparently healthy women. Circulation 1998;98(8):731-3.

[a]Ridker PM, Hennekens CH, Buring JE, Rifai N. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. N Engl J Med 2000;342(12):836-43.

3.06a Smoking as a risk factor for CHD in women

Prospective Cohort

[a]Freund KM, Belanger AJ, D'Agostino RB, Kannel WB. The health risks of smoking. The Framingham Study: 34 years of follow-up. Ann Epidemiol 1993;3(4):417-24.

[a]Kannel WB, D'Agostini RB, Belanger AJ. Fibrinogen, Cigarette smoking, and risk of cardiovascular disease: insights from the Framingham Study." Am Heart J 1987;113:1006-1010.

[a]Kawachi I, Colditz GA, Stampfer MJ, Willett WC, Manson JE, Rosner B, et al. Smoking cessation and time course of decreased risks of coronary heart disease in middle-aged women. Arch Intern Med 1994;154(2):169-75.

[a]LaCroix AZ, Lang J, Scherr P, Wallace RB, Cornoni-Huntley J, Berkman L, et al. Smoking and mortality among older men and women in three communities. N Engl J Med 1991;324(23):1619-25.

[a]Njolstad I, Arnesen E, Lund-Larsen PG. Smoking, serum lipids, blood pressure, and sex differences in myocardial infarction. A 12-year follow-up of the Finnmark Study. Circulation 1996;93(3):450-6.

[a]Paganini-Hill A, Hsu G. Smoking and mortality among residents of a California retirement community. Am J Public Health 1994;84(6):992-5.

[a]Prescott E, Hippe M, Schnohr P, Hein HO, Vestbo J. Smoking and risk of myocardial infarction in women and men: longitudinal population study. BMJ 1998;316(7137):1043-7.

[a]Willett WC, Green A, Stampfer MJ, Speizer FE, Colditz GA, Rosner B, et al. Relative and absolute excess risks of coronary heart disease among women who smoke cigarettes. N Engl J Med 1987;317(21):1303-9.

3.06b Smoking cessation to reduce risk of CHD in women

Prospective Cohort

[a]Kawachi I, Colditz GA, Stampfer MJ, Willett WC, Manson JE, Rosner B, et al. Smoking cessation in relation to total mortality rates in women. A prospective cohort study. Ann Intern Med 1993;119(10):992-1000.

[a]Kawachi I, Colditz GA, Stampfer MJ, Willett WC, Manson JE, Rosner B, et al. Smoking cessation and time course of decreased risks of coronary heart disease in middle-aged women. Arch Intern Med 1994;154(2):169-75.

[a]LaCroix AZ, Lang J, Scherr P, Wallace RB, Cornoni-Huntley J, Berkman L, et al. Smoking and mortality among older men and women in three communities. N Engl J Med 1991;324(23):1619-25.

[a]Njolstad I, Arnesen E, Lund-Larsen PG. Smoking, serum lipids, blood pressure, and sex differences in myocardial infarction. A 12-year follow-up of the Finnmark Study. Circulation 1996;93(3):450-6.

[a]Omenn GS, Anderson KW, Kronmal RA, Vlietstra RE. The temporal pattern of reduction of mortality risk after smoking cessation. Am J Prev Med 1990;6(5):251-7.

[a]Paganini-Hill A, Hsu G. Smoking and mortality among residents of a California retirement community. Am J Public Health 1994;84(6):992-5.

[a]Prescott E, Hippe M, Schnohr P, Hein HO, Vestbo J. Smoking and risk of myocardial infarction in women and men: longitudinal population study. BMJ 1998;316(7137):1043-7.

[a]Willett WC, Green A, Stampfer MJ, Speizer FE, Colditz GA, Rosner B, et al. Relative and absolute excess risks of coronary heart disease among women who smoke cigarettes. N Engl J Med 1987;317(21):1303-9.

Systematic Review

[a]Wilson K, Gibson N, Willan A, Cook D. Effect of smoking cessation on mortality after myocardial infarction: meta-analysis of cohort studies. Arch Intern Med 2000;160(7):939-44.

3.07a Obesity as a risk factor for CHD in women

Prospective Cohort

[a]Field AE, Coakley EH, Must A, Spadano JL, Laird N, Dietz WH, et al. Impact of overweight on the risk of developing common chronic diseases during a 10-year period. Arch Intern Med 2001;161(13):1581-6.

[a]Folsom AR, Stevens J, Schreiner PJ, McGovern PG. Body mass index, waist/hip ratio, and coronary heart disease incidence in African Americans and whites. Atherosclerosis

Risk in Communities Study Investigators. Am J Epidemiol 1998;148(12):1187-94.

[a]Folsom AR, Burke GL, Byers CL, Hutchinson RG, Heiss G, Flack JM, et al. Implications of obesity for cardiovascular disease in blacks: the CARDIA and ARIC studies. Am J Clin Nutr 1991;53(6 Suppl):1604S-1611S.

[a]Folsom AR, French SA, Zheng W, Baxter JE, Jeffery RW. Weight variability and mortality: the Iowa Women's Health Study. Int J Obes Relat Metab Disord 1996;20(8):704-9.

[a]Folsom AR, Kushi LH, Anderson KE, Mink PJ, Olson JE, Hong CP, et al. Associations of general and abdominal obesity with multiple health outcomes in older women: the Iowa Women's Health Study. Arch Intern Med 2000;160(14):2117-28.

[a]French SA, Folsom AR, Jeffery RW, Zheng W, Mink PJ, Baxter JE. Weight variability and incident disease in older women: the Iowa Women's Health Study. Int J Obes Relat Metab Disord 1997;21(3):217-23.

[a]Harris T, Cook EF, Garrison R, Higgins M, Kannel W, Goldman L. Body mass index and mortality among nonsmoking older persons. The Framingham Heart Study. JAMA 1988;259(10):1520-4.

[a]Kannel WB, Cupples LA, Ramaswami R, Stokes J, 3rd, Kreger BE, Higgins M. Regional obesity and risk of cardiovascular disease; the Framingham Study. J Clin Epidemiol 1991;44(2):183-90.

[a]Manson JE, Willett WC, Stampfer MJ, Colditz GA, Hunter DJ, Hankinson SE, et al. Body weight and mortality among women. N Engl J Med 1995;333(11):677-85.

[a]Manson JE, Colditz GA, Stampfer MJ, Willett WC, Rosner B, Monson RR, et al. A prospective study of obesity and risk of coronary heart disease in women. N Engl J Med 1990;322(13):882-9.

[a]Rexrode KM, Carey VJ, Hennekens CH, Walters EE, Colditz GA, Stampfer MJ, et al. Abdominal adiposity and coronary heart disease in women. JAMA 1998;280(21):1843-8.

[a]Willett WC, Manson JE, Stampfer MJ, Colditz GA, Rosner B, Speizer FE, et al. Weight, weight change, and coronary heart disease in women. Risk within the 'normal' weight range. JAMA 1995;273(6):461-5.

3.08a Inactivity as a risk factor for CHD in women

Prospective Cohort

[a]Blair SN, Kohl HW, 3rd, Paffenbarger RS, Jr., Clark DG, Cooper KH, Gibbons LW. Physical fitness and all-cause mortality. A prospective study of healthy men and women. JAMA 1989;262(17):2395-401.

[a]Lee IM, Rexrode KM, Cook NR, Manson JE, Buring JE. Physical activity and coronary heart disease in women: is "no pain, no gain" passe? JAMA 2001;285(11):1447-54.

[a]Manson JE, Hu FB, Rich-Edwards JW, Colditz GA, Stampfer MJ, Willett WC, et al. A prospective study of walking as compared with vigorous exercise in the prevention of coronary heart disease in women. N Engl J Med 1999;341(9):650-8.

[a]Rockhill B, Willett WC, Manson JE, Leitzmann MF, Stampfer MJ, Hunter DJ, et al. Physical activity and mortality: a prospective study among women. Am J Public Health 2001;91(4):578-83.

[a]Sherman SE, D'Agostino RB, Cobb JL, Kannel WB. Physical activity and mortality in women in the Framingham Heart Study. Am Heart J 1994;128(5):879-84.

3.09 Age as a risk for CHD events in women

Systematic Review

Pocock SJ, McCormack V, Gueyffier F, Boutitie F, Fagard RH, Boissel JP. A score for predicting risk of death from cardiovascular disease in adults with raised blood pressure, based on individual patient data from randomised controlled trials. BMJ 2001;323(7304):75-81.

Prospective Cohort

[a]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(2):180-7.

[a]Lerner DJ, Kannel WB. Patterns of coronary heart disease morbidity and mortality in the sexes: a 26-year follow-up of the Framingham population. Am Heart J 1986;111(2):383-90..

3.10 Age at menopause and risk for CHD

Prospective Cohort

[a]Cooper GS, Sandler DP. Age at natural menopause and mortality. Ann Epidemiol 1998;8(4):229-35.

[a]Hu FB, Grodstein F, Hennekens CH, Colditz GA, Johnson M, Manson JE, et al. Age at natural menopause and risk of cardiovascular disease. Arch Intern Med 1999;159(10):1061-6.

[a]van der Schouw YT, van der Graaf Y, Steyerberg EW, Eijkemans JC, Banga JD. Age at menopause as a risk factor for cardiovascular mortality. Lancet 1996;347(9003):714-8.

3.11 Ethnicity

Prospective Cohort

[a]Keil JE, Sutherland SE, Knapp RG, Lackland DT, Gazes PC, Tyroler HA. Mortality rates and risk factors for coronary disease in black as compared with white men and women. N

Engl J Med 1993;329(2):73-8.

Roig E, Castaner A, Simmons B, Patel R, Ford E, Cooper R. In-hospital mortality rates from acute myocardial infarction by race in U.S. hospitals: findings from the National Hospital Discharge Survey. Circulation 1987;76(2):280-8.

White AD, Rosamond WD, Chambless LE, Thomas N, Conwill D, Cooper LS, et al. Sex and race differences in short-term prognosis after acute coronary heart disease events: the Atherosclerosis Risk In Communities (ARIC) study. Am Heart J 1999;138(3 Pt 1):540-8.

3.12 Socioeconomic status and risk for CHD

Prospective Cohort

[a]Capewell S, MacIntyre K, Stewart S, Chalmers JW, Boyd J, Finlayson A, et al. Age, sex, and social trends in out-of-hospital cardiac deaths in Scotland 1986-95: a retrospective cohort study. Lancet 2001;358(9289):1213-7.

[a]Keil JE, Sutherland SE, Knapp RG, Lackland DT, Gazes PC, Tyroler HA. Mortality rates and risk factors for coronary disease in black as compared with white men and women. N Engl J Med 1993;329(2):73-8.

[a]Morrison, M. Woodward, W. Leslie and H. Tunstall-Pedoe (1997) “Effect of socioeconomic group on incidence 3 of, management of, and survival after myocardial infarction and coronary death: analysis of community coronary event register” BMJ 314 541-6.

[a]Salomaa V, Miettinen H, Niemela M, Ketonen M, Mahonen M, Immonen-Raiha P, et al. Relation of socioeconomic position to the case fatality, prognosis and treatment of myocardial infarction events; the FINMONICA MI Register Study. J Epidemiol Community Health 2001;55(7):475-82.

4.0 Differences in utilization between women and men

Systematic Review

Klungel OH, deBoer A, Paes A, Seidell JC, Bakker A. Sex differences in the pharmacological treatment of hypertension: a review of population-based studies. J Hypertension 1997;15:591-600.

Cross-sectional

[a]Ayanian JZ, Epstein AM. Differences in the use of procedures between women and men hospitalized for coronary heart disease. N Engl J Med 1991;325:221-5.

Battleman DS, Callhan M. Gender differences in utilization of exercise treadmill testing: a claims-based analysis. J Healthcare Quality 2001;23:38-41.

Bergelson BA, Tommaso CL. Gender difference in clinical evaluation and triage in coronary artery disease. Chest 1995;108:1510-13.

Evidence Table 1: Articles containing evidence on key question arranged by key question, type of research design, and level of quality (continued)

Bickell NA, Pieper KS, Lee KL, Mark DB, Glower DD, et al. Referral patterns for coronary artery disease treatment: gender bias or good clinical judgment? Ann Int Med 1992;116:791-797.

[a]Chandra NC, Ziegelstein RC, Rogers WJ, Tiefenbrunn AJ, Gore JM, et al. Observations of the treatment of women in the United States with myocardial infarction. Arch Intern Med 1998;158:981-988.

[a]Chiriboga DE, Yarzebski J, Goldberg RJ, Chen Z, Gurwitz J, Gore JM, et al. A community-wide perspective of gender differences and temporal trends in the use of diagnostic and revascularization procedures for acute myocardial infarction. Am J Cardiol 1993;71(4):268-73.

Clarke KW, Gray D, Keating NA, Hampton JR. Do women with acute myocardial infarction receive the same treatment as men? BMJ 1994;309:563-566.

[a]D'Hoore W, Sicotte C, Tilquin C. Sex bias in the management of coronary artery disease in Quebec. Am J Public Health 1994;84(6):1013-5Bergelson BA, Tommaso CL. Gender difference in clinical evaluation and triage in coronary artery disease. Chest 1995;108:1510-13.

[a]Davis KB, Chaitman B, Ryan T, Bittner V, Kennedy JW. Comparison of 15-year survival for men and women after initial medical or surgical treatment for coronary artery disease: a CASS registry study. Coronary Artery Surgery Study. J Am Coll Cardiol 1995;25(5):1000-9.

[a]Giacomini MK. Gender and ethnic differences in hospital-based procedure utilization in California. Arch Intern Med. 1996;156:1217-1224.

[a]Giles TD, Fisher MB, Rush JE. Lisinopril and captopril in the treatment of heart failure in older patients. Comparison of a long- and short-acting angiotensin-converting enzyme inhibitor. Am J Med 1988;85(3B):44-7.

Goldberg KC, Hartz AJ, Jacobsen SJ, Krakauer H, Rimm AA. Racial and community factors influencing coronary artery bypass graft surgery rates for all 1986 Medicare patients. JAMA 1992;267(11):1473-7.

[a]Jaglal SB, Goel V, Naylor CD. Sex differences in the use of invasive coronary procedures in Ontario. Can J Cardiol 1994;10(2):239-44.

[a]Johnson PA, Goldman L, Orav J, Zhou L, Garcia T, et al. Gender differences in the management of acute chest pain. Support for the "Yentl Syndrome." J Gen Intern Med 1996;11:209-217.

[a]Krumholz HM, Douglas PS, Lauer MS, Pasternak RC. Selection of patients for coronary angiography and coronary revascularization early after myocardial infarction: is there evidence for a gender bias? Ann Intern Med 1992;116(10):785-90.

[a]indicates "good quality" article

Evidence Table 1: Articles containing evidence on key question arranged by key question, type of research design, and level of quality (continued)

[a]Kudenchuk PJ, Maynard C, Martin JS, Wirkus M, Weaver WD. Comparison of presentation, treatment, and outcome of acute myocardial infarction in men versus women (The Myocardial Infarction Triage and Intervention Registry). Am J Cardiol 1996;78:9-14.

Mageed A, Moser K, Maxwell R. Age, sex and practice variations in the use of statins in general practice in England and Wales. J Publ Hlth Med 2000;22:275-279.

Magrini N, Elinarson T, Vaccheri A, McManus P, Montanaro N, Bergman U. Use of lipid-lowering drugs from 1990 to 1994: an international comparison among Australia, Finland, Italy (Emilia Romagna Region), Norway and Sweden. Eur J Clin Pharmacol 1991;53:185-189.

Maynard C, Althouse R, Cerqueira M, Olsufka M, Kennedy JW. Underutilization of thrombolytic therapy in eligible women with acute myocardial infarction. Am J Cardiol 1991;68:529-530.

[a]Maynard C, Litwin PE, Martin JS, Weaver WD. Gender differences in the treatment and outcome of acute myocardial infarction. Arch Intern Med 1992;152:972-976.

[a]Miller TD, Roger VL, Hodge DO, Hopfenspirger MR, Bailey KR, et al. Gender differences and temporal trends in Clinical Characteristics, stress test results and use of invasive procedures in patients undergoing evaluation for coronary artery disease. J am Coll Cardiol 2001;38:690-7.

[a]Pagley PR, Yarzebski J, Goldberg R, Chen Z, Chiriboga D, et al. Gender differences in the treatment of patients with acute myocardial infarction. Arch Intern Med 1993;153:625-629.

[a]Petticrew M, McKee M, Jones J. Coronary artery surgery: are women discriminated against? BMJ 1993;306(6886):1164-6.

[a]Pfeffer Ma, Moye LA, Braunwald E, Basta L, Brown EJ, et al. Selection bias in the use of thrombolytic therapy in acute myocardial infarction. JAMA 1991;266:528-532.

[a]Ramsey DJ, Goff DC, Wear ML, Labarthe DR, Nichaman MZ. Sex and ethnic differences in use of myocardial revascularization procedures in Mexican Americans and non-Hispanic whites: the Corpus Christi Heart Project. J Clin Epidemiol 1997;50(5):603-9.

[a]Roger VL, Farkouh ME, Weston SA, Reeder GS, Jacobsen SJ, et al. Sex differences in evaluation and outcome of unstable angina. JAMA 2000;283:646-652.

[a]Rojas-Fernandez CH, Kephart GC, Sketris IS, Kass K. Underuse of acetylsalicylic acid in individuals with myocardial infarction, ischemic heart disease or stroke: data from the 1995 population-based Nova Scotia Health Survey. Can J Cardiol 1999;15(3):291-6.

[a]Shahar E, Folsom AR, Romm FJ, Bisgard KM, Metcalf PA, et al. Patterns of aspirin use in middle-aged adults: the Atherosclerosis Risk in Communities (ARIC) Study. Am Heart J 1996;131:915-22.

[a]indicates "good quality" article

Evidence Table 1: Articles containing evidence on key question arranged by key question, type of research design, and level of quality (continued)

Shaw LJ, Miller DD, Romeis JC, Kargl D, Younis LT, Chaitman BR. Gender differences in the noninvasive evaluation and management of patients with suspected coronary artery disease. Ann Intern Med 1994;120(7):559-66.

Sketris IS, Kephart GC, Hicks VA, Hubbard EJ, Brown MG, et al. Prescribing patterns of antilipemic drugs and prevalence of hypercholesterolemia in the Nova Scotia population more than 65 years old. Ann Pharmacother 1995;29:576-81.

[a]Steingart RM, Packer M, Hamm P, Coglianese ME, Gersh B, et al. Sex differences in the management of coronary artery disease. N Engl J Med 1991;325:226-230.

[a]Strauss R, Pfeifer C, Muhlberger V, Ulmer H, Pfeiffer KP. Effects of morbidity, age, gender and region on percutaneous transluminal coronary angioplasty (PTCA) utilisation. Public Health 1999;113(2):79-87.

Tsuyuki RT, Teo KK, Ikuta RM, Bay KS, Greenwood PV, Montague TJ. Mortality risk and patterns of practice in 2,070 patients with acute myocardial infarction, 1987-92. Chest 1994;105:1687-92.

Weaver WD, White HD, Wilcox RG, Aylward PE, Morris D, Guerci A, et al. Comparisons of characteristics and outcomes among women and men with acute myocardial infarction treated with thrombolytic therapy. GUSTO-I investigators. JAMA 1996;275(10):777-82.

[a]Yarzebski J, Col N, Pagley P, Savageau J, Gore J, Goldberg R. Gender differences and factors associated with the receipt of thrombolytic therapy in patients with acute myocardial infarction: a community-wide perspective. Am Heart J 1996;131(1):43-50.

[a]indicates "good quality" article

Bibliography

1. The Beta-Blocker Pooling Project (BBPP): subgroup findings from randomized trials in post infarction patients. The Beta-Blocker Pooling Project Research Group. Eur Heart J 1988;9(1):8-16.
2. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Lancet 1988;2(8607):349-60.
3. Persistence of reduction in blood pressure and mortality of participants in the Hypertension Detection and Follow-up Program. Hypertension Detection and Follow-up Program Cooperative Group. Jama 1988;259(14):2113-22.
4. 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.
5. Morning peak in the incidence of myocardial infarction: experience in the ISIS-2 trial. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Eur Heart J 1992;13(5):594-8.
6. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet 1994;344(8934):1383-9.
7. GISSI-3: effects of lisinopril and transdermal glyceryl trinitrate singly and together on 6-week mortality and ventricular function after acute myocardial infarction. Gruppo Italiano per lo Studio della Sopravvivenza nell'infarto Miocardico. Lancet 1994;343(8906):1115-22.
8. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Lancet 1994;343(8893):311-22.
9. Collaborative overview of randomised trials of antiplatelet therapy--III: Reduction in venous thrombosis and pulmonary embolism by antiplatelet prophylaxis among surgical and medical patients. Antiplatelet Trialists' Collaboration. Bmj 1994;308(6923):235-46.
10. Collaborative overview of randomised trials of antiplatelet therapy--I: Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. Antiplatelet Trialists' Collaboration. BMJ 1994;308(6921):81-106.
11. ISIS-4: a randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. Lancet 1995;345(8951):669-85.
12. First-year results of CABRI (Coronary Angioplasty versus Bypass Revascularisation Investigation). CABRI Trial Participants. Lancet 1995;346(8984):1179-84.
13. Six-month effects of early treatment with lisinopril and transdermal glyceryl trinitrate singly and together withdrawn six weeks after acute myocardial infarction: the GISSI-3 trial. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico. J Am Coll Cardiol 1996;27(2):337-44.
14. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). CAPRIE Steering Committee. Lancet 1996;348(9038):1329-39.
15. 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.
16. Coronary angioplasty versus medical therapy for angina: the second Randomised Intervention Treatment of Angina (RITA-2) trial. RITA-2 trial participants. Lancet 1997;350(9076):461-8.
17. Protocol for prospective collaborative overviews of major randomized trials of blood-pressure-lowering treatments. World Health Organization-International Society of Hypertension Blood Pressure Lowering Treatment Trialists' Collaboration. J Hypertens 1998;16(2):127-37.
18. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. N Engl J Med 1998;339(19):1349-57.
19. Indications for ACE inhibitors in the early treatment of acute myocardial infarction: systematic overview of individual data from 100,000 patients in randomized trials. ACE Inhibitor Myocardial Infarction Collaborative Group. Circulation 1998;97(22):2202-12.

20. Lowering blood homocysteine with folic acid based supplements: meta-analysis of randomised trials. Homocysteine Lowering Trialists' Collaboration. BMJ 1998;316(7135):894-8.
21. Collaborative overview ('meta-analysis') of prospective observational studies of the associations of usual blood pressure and usual cholesterol levels with common causes of death: protocol for the second cycle of the Prospective Studies Collaboration. J Cardiovasc Risk 1999;6(5):315-20.
22. Prediction of risk for patients with unstable angina. Evid Rep Technol Assess (Summ) 2000(31):1-3.
23. Direct thrombin inhibitors in acute coronary syndromes and during percutaneous coronary intervention: design of a meta-analysis based on individual patient data. Direct Thrombin Inhibitor Trialists' Collaborative Group. Am Heart J 2001;141(1):E2.
24. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet 2002;360(9326):7-22.
25. Abbott RD, Donahue RP, Kannel WB, et al. The impact of diabetes on survival following myocardial infarction in men vs women. The Framingham Study. JAMA 1988;260(23):3456-60.
26. Abbott RD, Wilson PW, Kannel WB, et al. High density lipoprotein cholesterol, total cholesterol screening, and myocardial infarction. The Framingham Study. Arteriosclerosis 1988;8(3):207-11.
27. Ades PA, Savage PD, Poehlman ET, et al. Lipid lowering in the cardiac rehabilitation setting. J Cardiopulm Rehabil 1999;19(4):255-60.
28. Afonso LC, Edelson GW, Sowers JR. Metabolic abnormalities in hypertension. Curr Opin Nephrol Hypertens 1997;6(3):219-23.
29. Airaksinen KE. Autonomic mechanisms and sudden death after abrupt coronary occlusion. Ann Med 1999;31(4):240-5.
30. Al Suwaidi J, Berger PB, Holmes DR, Jr. Coronary artery stents. Jama 2000;284(14):1828-36.
31. Albert MA, Danielson E, Rifai N, et al. Effect of statin therapy on C-reactive protein levels: the pravastatin inflammation/CRP evaluation (PRINCE): a randomized trial and cohort study. Jama 2001;286(1):64-70.
32. Alderman MH, Ooi WL, Madhavan S, et al. Treatment-induced blood pressure reduction and the risk of myocardial infarction. Jama 1989;262(7):920-4.
33. Alexander KP, Shaw LJ, Shaw LK, et al. Value of exercise treadmill testing in women. J Am Coll Cardiol 1998;32(6):1657-64.
34. Allison JJ, Kiefe CI, Centor RM, et al. Racial differences in the medical treatment of elderly Medicare patients with acute myocardial infarction. J Gen Intern Med 1996;11(12):736-43.
35. Amanullah AM, Kiat H, Friedman JD, et al. Adenosine technetium-99m sestamibi myocardial perfusion SPECT in women: diagnostic efficacy in detection of coronary artery disease. J Am Coll Cardiol 1996;27(4):803-9.
36. Anand SS, Yusuf S. Oral anticoagulant therapy in patients with coronary artery disease: a meta-analysis. Jama 1999;282(21):2058-67.
37. Anderson KM, Castelli WP, Levy D. Cholesterol and mortality. 30 years of follow-up from the Framingham study. Jama 1987;257(16):2176-80.
38. Ansell BJ, Watson KE, Fogelman AM. An evidence-based assessment of the NCEP Adult Treatment Panel II guidelines. National Cholesterol Education Program. Jama 1999;282(21):2051-7.
39. Antman EM, Cohen M, Radley D, et al. Assessment of the treatment effect of enoxaparin for unstable angina/non-Q-wave myocardial infarction. TIMI 11B-ESSENCE meta-analysis. Circulation 1999;100(15):1602-8.
40. Aronow WS. Management of older persons after myocardial infarction. J Am Geriatr Soc 1998;46(11):1459-68.
41. Arruda-Olson AM, Juracan EM, Mahoney DW, et al. Prognostic value of exercise echocardiography in 5,798 patients: is there a gender difference? J Am Coll Cardiol 2002;39(4):625-31.
42. Ascherio A, Willett WC. Health effects of trans fatty acids. Am J Clin Nutr 1997;66(4 Suppl):1006S-1010S.
43. Atrens DM. The questionable wisdom of a low-fat diet and cholesterol reduction. Soc Sci Med 1994;39(3):433-47.
44. Austin MA. Plasma triglyceride as a risk factor for cardiovascular disease. Can J Cardiol 1998;14(Suppl B):14B-17B.
45. Austin MA. Epidemiology of hypertriglyceridemia and cardiovascular disease. Am J Cardiol 1999;83(9B):13F-16F.

46. Austin MA, Hokanson JE, Edwards KL. Hypertriglyceridemia as a cardiovascular risk factor. Am J Cardiol 1998;81(4A):7B-12B.
47. Avezum A, Tsuyuki RT, Pogue J, et al. Beta-blocker therapy for congestive heart failure: a systemic overview and critical appraisal of the published trials. Can J Cardiol 1998;14(8):1045-53.
48. Ayanian JZ, Epstein AM. Differences in the use of procedures between women and men hospitalized for coronary heart disease. N Engl J Med 1991;325(4):221-5.
49. Azar RR, Waters DD, McKay RG, et al. Short- and medium-term outcome differences in women and men after primary percutaneous transluminal mechanical revascularization for acute myocardial infarction. Am J Cardiol 2000;85(6):675-9.
50. Baevsky RM, Petrov VM, Cornelissen G, et al. Meta-analyzed heart rate variability, exposure to geomagnetic storms, and the risk of ischemic heart disease. Scr Med (Brno) 1997;70(4-5):201-6.
51. Balk EM, Ioannidis JP, Salem D, et al. Accuracy of biomarkers to diagnose acute cardiac ischemia in the emergency department: a meta-analysis. Ann Emerg Med 2001;37(5):478-94.
52. Bandyopadhyay S, Bayer AJ, O'Mahony MS. Age and gender bias in statin trials. Qjm 2001;94(3):127-32.
53. Barbour MM, Hume AL, Lapane KL, et al. Predictors of future antihypertensive use in patients with mildly elevated blood pressure. Pharmacotherapy 1995;15(3):272-8.
54. Barnes V, Schneider R, Alexander C, et al. Stress, stress reduction, and hypertension in African Americans: an updated review. J Natl Med Assoc 1997;89(7):464-76.
55. Barratt A, Irwig L. Is cholesterol testing/treatment really beneficial? Med J Aust 1993;159(10):644-7.
56. Barrett-Connor EL. Obesity, atherosclerosis, and coronary artery disease. Ann Intern Med 1985;103(6 (Pt 2)):1010-9.
57. Basinski A, Naylor CD. Aspirin and fibrinolysis in acute myocardial infarction: meta-analytic evidence for synergy. J Clin Epidemiol 1991;44(10):1085-96.
58. Batchelor WB, Anstrom KJ, Muhlbaier LH, et al. Contemporary outcome trends in the elderly undergoing percutaneous coronary interventions: results in 7,472 octogenarians. National Cardiovascular Network Collaboration. J Am Coll Cardiol 2000;36(3):723-30.
59. Bates DW, Miller E, Bernstein SJ, et al. Coronary angiography and angioplasty after acute myocardial infarction. Ann Intern Med 1997;126(7):539-50.
60. Battleman DS, Callahan M. Gender differences in utilization of exercise treadmill testing: a claims-based analysis. J Healthc Qual 2001;23(3):38-41.
61. Bax JJ, Wijns W, Cornel JH, et al. Accuracy of currently available techniques for prediction of functional recovery after revascularization in patients with left ventricular dysfunction due to chronic coronary artery disease: comparison of pooled data. J Am Coll Cardiol 1997;30(6):1451-60.
62. Beck CA, Lauzon C, Eisenberg MJ, et al. Discharge prescriptions following admission for acute myocardial infarction at tertiary care and community hospitals in Quebec. Can J Cardiol 2001;17(1):33-40.
63. Becker RC. Late thrombolytic therapy: mechanism of benefit and potential risk among patients treated beyond 6 hours. Coron Artery Dis 1993;4(3):293-304.
64. Becker RC, Terrin M, Ross R, et al. Comparison of clinical outcomes for women and men after acute myocardial infarction. The Thrombolysis in Myocardial Infarction Investigators. Ann Intern Med 1994;120(8):638-45.
65. Beckett N, Nunes M, Bulpitt C. Is it advantageous to lower cholesterol in the elderly hypertensive? Cardiovasc Drugs Ther 2000;14(4):397-405.
66. Beckwith C, Munger MA. Effect of angiotensin-converting enzyme inhibitors on ventricular remodeling and survival following myocardial infarction. Ann Pharmacother 1993;27(6):755-66.
67. Bell DM. Analysis of number needed to treat and cost of platelet glycoprotein IIb/IIIa inhibitors in percutaneous coronary interventions and acute coronary syndromes. Pharmacotherapy 1999;19(9):1086-93.
68. Bell MR, Grill DE, Garratt KN, et al. Long-term outcome of women compared with men after successful coronary angioplasty. Circulation 1995;91(12):2876-81.
69. Bell MR, Holmes DR, Jr., Berger PB, et al. The changing in-hospital mortality of women undergoing percutaneous transluminal coronary angioplasty. JAMA 1993;269(16):2091-5.
70. Bergelson BA, Tommaso CL. Gender differences in clinical evaluation and triage in coronary artery disease. Chest 1995;108(6):1510-3.
71. Bergelson BA, Tommaso CL. Gender differences in percutaneous interventional therapy of coronary artery disease. Cathet Cardiovasc Diagn 1996;37(1):1-4.

72. Bergfeldt L. HLA-B27-associated cardiac disease. Ann Intern Med 1997;127(8 Pt 1):621-9.
73. Bergman U, Anderssen M, Vaccheri A, et al. Marked differences in lipid-lowering drug use in Bologna, Italy and Funen, Denmark. Eur Heart J 1999;20(15):1135.
74. Berlin JA, Colditz GA. A meta-analysis of physical activity in the prevention of coronary heart disease. Am J Epidemiol 1990;132(4):612-28.
75. Bernstein SJ, Hilborne LH, Leape LL, et al. The appropriateness of use of cardiovascular procedures in women and men. Arch Intern Med 1994;154(23):2759-65.
76. Bhatt DL, Topol EJ. Current role of platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes. Jama 2000;284(12):1549-58.
77. Bhopal R. What is the risk of coronary heart disease in South Asians? A review of UK research. J Public Health Med 2000;22(3):375-85.
78. Bickell NA, Pieper KS, Lee KL, et al. Referral patterns for coronary artery disease treatment: gender bias or good clinical judgment? Ann Intern Med 1992;116(10):791-7.
79. Bijsterveld NR, Hettiarachchi R, Peters R, et al. Low-molecular weight heparins in venous and arterial thrombotic disease. Thromb Haemost 1999;82(Suppl 1):139-47.
80. Bizjak ED, Mauro VF. Thrombolytic therapy: a review of its use in acute myocardial infarction. Ann Pharmacother 1998;32(7-8):769-84.
81. Bjorntorp P. Evolution of the understanding of the role of exercise in obesity and its complications. Int J Obes Relat Metab Disord 1995;19(Suppl 4):S1-4.
82. Blair SN, Brodney S. Effects of physical inactivity and obesity on morbidity and mortality: current evidence and research issues. Med Sci Sports Exerc 1999;31(11 Suppl):S646-62.
83. Blair SN, Kohl HW, 3rd, Paffenbarger RS, Jr., et al. Physical fitness and all-cause mortality. A prospective study of healthy men and women. Jama 1989;262(17):2395-401.
84. Blankenhorn DH, Hodis HN. Atherosclerosis--reversal with therapy. West J Med 1993;159(2):172-9.
85. Blazing MA, O'Connor CM. Evidence supporting secondary prevention strategies. Curr Opin Cardiol 1999;14(4):303-9.
86. Blustein J, Weitzman BC. Access to hospitals with high-technology cardiac services: how is race important? Am J Public Health 1995;85(3):345-51.
87. Boden WE, Vray M, Eschwege E, et al. Heart rate-lowering and -regulating effects of once-daily sustained-release diltiazem. Clin Cardiol 2001;24(1):73-9.
88. Boersma E, Akkerhuis KM, Theroux P, et al. Platelet glycoprotein IIb/IIIa receptor inhibition in non-ST-elevation acute coronary syndromes: early benefit during medical treatment only, with additional protection during percutaneous coronary intervention. Circulation 1999;100(20):2045-8.
89. Boersma E, Harrington RA, Moliterno DJ, et al. Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: a meta-analysis of all major randomised clinical trials. Lancet 2002;359(9302):189-98.
90. Boersma E, Maas AC, Deckers JW, et al. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. Lancet 1996;348(9030):771-5.
91. Boissel JP, Peyrieux JC, Destors JM. Is it possible to reduce the risk of cardiovascular events in subjects suffering from intermittent claudication of the lower limbs? Thromb Haemost 1989;62(2):681-5.
92. Bonet S, Agusti A, Arnau JM, et al. Beta-adrenergic blocking agents in heart failure: benefits of vasodilating and non-vasodilating agents according to patients' characteristics: a meta-analysis of clinical trials. Arch Intern Med 2000;160(5):621-7.
93. Borgia MC, Medici F. Perspectives in the treatment of dyslipidemias in the prevention of coronary heart disease. Angiology 1998;49(5):339-48.
94. Borzak S, Ridker PM. Discordance between meta-analyses and large-scale randomized, controlled trials. Examples from the management of acute myocardial infarction. Ann Intern Med 1995;123(11):873-7.
95. Bostom AG, Silbershatz H, Rosenberg IH, et al. Nonfasting plasma total homocysteine levels and all-cause and cardiovascular disease mortality in elderly Framingham men and women. Arch Intern Med 1999;159(10):1077-80.
96. Boushey CJ, Beresford SA, Omenn GS, et al. A quantitative assessment of plasma homocysteine as a risk factor for vascular disease. Probable benefits of increasing folic acid intakes. JAMA 1995;274(13):1049-57.

97. Bradley KA, Badrinath S, Bush K, et al. Medical risks for women who drink alcohol. J Gen Intern Med 1998;13(9):627-39.
98. Brand FN, Abbott RD, Kannel WB. Diabetes, intermittent claudication, and risk of cardiovascular events. The Framingham Study. Diabetes 1989;38(4):504-9.
99. Brand FN, Kiely DK, Kannel WB, et al. Family patterns of coronary heart disease mortality: the Framingham Longevity Study. J Clin Epidemiol 1992;45(2):169-74.
100. Braunwald E, Maseri A, Armstrong PW, et al. Rationale and clinical evidence for the use of GP IIb/IIIa inhibitors in acute coronary syndromes. Eur Heart J 1998;19(Suppl D):D22-30.
101. Brezinka V, Kittel F. Psychosocial factors of coronary heart disease in women: a review. Soc Sci Med 1996;42(10):1351-65.
102. Brophy JM, Joseph L, Rouleau JL. Beta-blockers in congestive heart failure. A Bayesian meta-analysis. Ann Intern Med 2001;134(7):550-60.
103. Brown BG, Zhao XQ, Chait A, et al. Lipid altering or antioxidant vitamins for patients with coronary disease and very low HDL cholesterol? The HDL-Atherosclerosis Treatment Study Design. Can J Cardiol 1998;14(Suppl A):6A-13A.
104. Brown DL, Fann CS, Chang CJ. Effect of glycoprotein IIb/IIIa inhibitors on the individual components of composite endpoints used in clinical trials of unstable angina and non-Q-wave myocardial infarction. Cardiovasc Drugs Ther 2000;14(3):253-8.
105. Brown DL, Fann CS, Chang CJ. Meta-analysis of effectiveness and safety of abciximab versus eptifibatide or tirofiban in percutaneous coronary intervention. Am J Cardiol 2001;87(5):537-41.
106. Bucher HC, Griffith LE, Guyatt GH. Systematic review on the risk and benefit of different cholesterol-lowering interventions. Arterioscler Thromb Vasc Biol 1999;19(2):187-95.
107. Buchwald H, Campos CT, Boen JR, et al. Gender-based mortality follow-up from the Program on the Surgical Control of the Hyperlipidemias (POSCH) and meta-analysis of lipid intervention trials. Women in POSCH and other lipid trials. Ann Surg 1996;224(4):486-98; discussion 498-500.
108. Budoff MJ, Diamond GA, Raggi P, et al. Continuous probabilistic prediction of angiographically significant coronary artery disease using electron beam tomography. Circulation 2002;105(15):1791-6.
109. Budoff MJ, Shokooh S, Shavelle RM, et al. Electron beam tomography and angiography: sex differences. Am Heart J 2002;143(5):877-82.
110. Burke AP, Farb A, Malcom GT, et al. Effect of risk factors on the mechanism of acute thrombosis and sudden coronary death in women. Circulation 1998;97(21):2110-6.
111. Bush TL, Fried LP, Barrett-Connor E. Cholesterol, lipoproteins, and coronary heart disease in women. Clin Chem 1988;34(8B):B60-70.
112. Byington RP, Jukema JW, Salonen JT, et al. Reduction in cardiovascular events during pravastatin therapy. Pooled analysis of clinical events of the Pravastatin Atherosclerosis Intervention Program. Circulation 1995;92(9):2419-25.
113. Califf RM, Harrell FE, Jr., Lee KL, et al. The evolution of medical and surgical therapy for coronary artery disease. A 15-year perspective. Jama 1989;261(14):2077-86.
114. Cantor WJ, Peterson ED, Popma JJ, et al. Provisional stenting strategies: systematic overview and implications for clinical decision-making. J Am Coll Cardiol 2000;36(4):1142-51.
115. Capewell S, MacIntyre K, Stewart S, et al. Age, sex, and social trends in out-of-hospital cardiac deaths in Scotland 1986-95: a retrospective cohort study. Lancet 2001;358(9289):1213-7.
116. Capewell S, Morrison CE, McMurray JJ. Contribution of modern cardiovascular treatment and risk factor changes to the decline in coronary heart disease mortality in Scotland between 1975 and 1994. Heart 1999;81(4):380-6.
117. Carlisle DM, Leake BD, Shapiro MF. Racial and ethnic differences in the use of invasive cardiac procedures among cardiac patients in Los Angeles County, 1986 through 1988. Am J Public Health 1995;85(3):352-6.
118. Carlisle DM, Leake BD, Shapiro MF. Racial and ethnic disparities in the use of cardiovascular procedures: associations with type of health insurance. Am J Public Health 1997;87(2):263-7.
119. Carter BL, Kriesel HT, Steinkraus L, et al. Antihypertensive drug-prescribing patterns of internists and family physicians. J Fam Pract 1989;29(3):257-61.
120. Castelli WP. Cholesterol and lipids in the risk of coronary artery disease--the Framingham Heart Study. Can J Cardiol 1988;4(Suppl A):5A-10A.
121. Castelli WP. Diet, smoking, and alcohol: influence on coronary heart disease risk. Am J Kidney Dis 1990;16(4 Suppl 1):41-6.

122. Castelli WP, Anderson K, Wilson PW, et al. Lipids and risk of coronary heart disease. The Framingham Study. Ann Epidemiol 1992;2(1-2):23-8.
123. Castelli WP, Garrison RJ, Wilson PW, et al. Incidence of coronary heart disease and lipoprotein cholesterol levels. The Framingham Study. Jama 1986;256(20):2835-8.
124. Castelli WP, Wilson PW, Levy D, et al. Cardiovascular risk factors in the elderly. Am J Cardiol 1989;63(16):12H-19H.
125. Castillo PA, Palmer CS, Halpern MT, et al. Cost-effectiveness of thrombolytic therapy for acute myocardial infarction. Ann Pharmacother 1997;31(5):596-603.
126. Celis H, Fagard R, Staessen J, et al. The older hypertensive. Assessment and treatment. Neth J Med 1993;43(Suppl 1):S66-77.
127. Cerqueira MD. Diagnostic testing strategies for coronary artery disease: special issues related to gender. Am J Cardiol 1995;75(11):52D-60D.
128. Chaitman BR, Bourassa MG, Davis K, et al. Angiographic prevalence of high-risk coronary artery disease in patient subsets (CASS). Circulation 1981;64(2):360-7.
129. Chandra NC, Ziegelstein RC, Rogers WJ, et al. Observations of the treatment of women in the United States with myocardial infarction: a report from the National Registry of Myocardial Infarction-I. Arch Intern Med 1998;158(9):981-8.
130. Chew DP, Bhatt DL, Sapp S, et al. Increased Mortality With Oral Platelet Glycoprotein IIb/IIIa Antagonists : A Meta-Analysis of Phase III Multicenter Randomized Trials. Circulation 2001;103(2):201-206.
131. Chiamvimonvat V, Sternberg L. Coronary artery disease in women. Can Fam Physician 1998;44:2709-17.
132. Chiriboga DE, Yarzebski J, Goldberg RJ, et al. A community-wide perspective of gender differences and temporal trends in the use of diagnostic and revascularization procedures for acute myocardial infarction. Am J Cardiol 1993;71(4):268-73.
133. Cho L, Bhatt DL, Wolski K, et al. Effect of smoking status and abciximab use on outcome after percutaneous coronary revascularization: Pooled analysis from EPIC, EPILOG, and EPISTENT. Am Heart J 2001;141(4):599-602.
134. Cho L, Topol EJ, Balog C, et al. Clinical benefit of glycoprotein IIb/IIIa blockade with Abciximab is independent of gender: pooled analysis from EPIC, EPILOG and EPISTENT trials. Evaluation of 7E3 for the Prevention of Ischemic Complications. Evaluation in Percutaneous Transluminal Coronary Angioplasty to Improve Long-Term Outcome with Abciximab GP IIb/IIIa blockade. Evaluation of Platelet IIb/IIIa Inhibitor for Stent. J Am Coll Cardiol 2000;36(2):381-6.
135. Christenson RH, Duh SH. Evidence based approach to practice guides and decision thresholds for cardiac markers. Scand J Clin Lab Invest Suppl 1999;230:90-102.
136. Clarke KW, Gray D, Keating NA, et al. Do women with acute myocardial infarction receive the same treatment as men? Bmj 1994;309(6954):563-6.
137. Clarkson TB, Kaplan JR, Adams MR, et al. Psychosocial influences on the pathogenesis of atherosclerosis among nonhuman primates. Circulation 1987;76(1 Pt 2):I29-40.
138. Cleland JG, Bristow MR, Erdmann E, et al. Beta-blocking agents in heart failure. Should they be used and how? Eur Heart J 1996;17(11):1629-39.
139. Cleophas TJ, Hornstra N, van Hoogstraten B, et al. Homocysteine, a risk factor for coronary artery disease or not? A meta-analysis. Am J Cardiol 2000;86(9):1005-9, A8.
140. Clyne CA. Antithrombotic therapy in the primary and secondary prevention of coronary-related death and infarction: focus on gender differences. Cardiology 1990;77(Suppl 2):99-109.
141. Cohen M. The role of low-molecular-weight heparins in arterial diseases: optimizing antithrombotic therapy. Thromb Res 2000;100(2):V131-9.
142. Colditz GA, Halvorsen KT, Goldhaber SZ. Randomized clinical trials of transdermal nitroglycerin systems for the treatment of angina: a meta-analysis. Am Heart J 1988;116(1 Pt 1):174-80.
143. Colditz GA, Willett WC, Stampfer MJ, et al. Menopause and the risk of coronary heart disease in women. N Engl J Med 1987;316(18):1105-10.
144. Collins R, MacMahon S, Flather M, et al. Clinical effects of anticoagulant therapy in suspected acute myocardial infarction: systematic overview of randomised trials. Bmj 1996;313(7058):652-9.
145. Collins R, Peto R, Parish S, et al. ISIS-3 and GISSI-2: no survival advantage with tissue plasminogen activator over streptokinase, but a significant excess of strokes with tissue plasminogen activator in both trials. Am J Cardiol 1993;71(12):1127-30.

146. Conlan MG, Folsom AR, Finch A, et al. Correlation of plasma protein C levels with cardiovascular risk factors in middle-aged adults: the Atherosclerosis Risk in Communities (ARIC) Study. Thromb Haemost 1993;70(5):762-7.
147. Conti CR. Large vessel coronary vasospasm: diagnosis, natural history and treatment. Am J Cardiol 1985;55(3):41B-49B.
148. Conti CR. Clinical decision making using cumulative meta-analysis. Clin Cardiol 1993;16(3):167-8.
149. Cooke HM, Lynch A. Biorhythms and chronotherapy in cardiovascular disease. Am J Hosp Pharm 1994;51(20):2569-80.
150. Cooper GS, Sandler DP. Age at natural menopause and mortality. Ann Epidemiol 1998;8(4):229-35.
151. Cooper R. The role of genetic and environmental factors in cardiovascular disease in African Americans. Am J Med Sci 1999;317(3):208-13.
152. Cooper RS, Ghali JK. Coronary heart disease: black-white differences. Cardiovasc Clin 1991;21(3):205-25.
153. Corrao G, Rubbiati L, Bagnardi V, et al. Alcohol and coronary heart disease: a meta-analysis. Addiction 2000;95(10):1505-23.
154. Corti MC, Guralnik JM, Bilato C. Coronary heart disease risk factors in older persons. Aging (Milano) 1996;8(2):75-89.
155. Coutinho M, Gerstein HC, Wang Y, et al. The relationship between glucose and incident cardiovascular events. A metaregression analysis of published data from 20 studies of 95,783 individuals followed for 12.4 years. Diabetes Care 1999;22(2):233-40.
156. Craig WY, Neveux LM, Palomaki GE, et al. Lipoprotein(a) as a risk factor for ischemic heart disease: metaanalysis of prospective studies. Clin Chem 1998;44(11):2301-6.
157. Croft JB, Keenan NL, Sheridan DP, et al. Waist-to-hip ratio in a biracial population: measurement, implications, and cautions for using guidelines to define high risk for cardiovascular disease. J Am Diet Assoc 1995;95(1):60-4.
158. Cucherat M, Bonnefoy E, Tremeau G. Primary angioplasty versus intravenous thrombolysis for acute myocardial infarction. Cochrane Database Syst Rev 2000(2):CD001560.
159. Cui Y, Blumenthal RS, Flaws JA, et al. Non-high-density lipoprotein cholesterol level as a predictor of cardiovascular disease mortality. Arch Intern Med 2001;161(11):1413-9.
160. Cullen P. Evidence that triglycerides are an independent coronary heart disease risk factor. Am J Cardiol 2000;86(9):943-9.
161. Cutlip DE, Baim DS, Ho KK, et al. Stent thrombosis in the modern era: a pooled analysis of multicenter coronary stent clinical trials. Circulation 2001;103(15):1967-71.
162. D'Agostino RB, Cobb JL, Wolf PA, et al. Aspirin use and cardiovascular disease in women. Jama 1992;267(3):364-5.
163. D'Agostino RB, Sr., Grundy S, Sullivan LM, et al. Validation of the Framingham coronary heart disease prediction scores: results of a multiple ethnic groups investigation. Jama 2001;286(2):180-7.
164. D'Agostino RB, Kannel WB, Belanger AJ, et al. Trends in CHD and risk factors at age 55-64 in the Framingham Study. Int J Epidemiol 1989;18(3 Suppl 1):S67-72.
165. D'Agostino RB, Kannel WB, Stepanians MN, et al. Efficacy and tolerability of lovastatin in hypercholesterolemic women. Clin Ther 1992;14(3):390-5.
166. 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(2 Pt 1):272-81.
167. D'Hoore W, Sicotte C, Tilquin C. Sex bias in the management of coronary artery disease in Quebec. Am J Public Health 1994;84(6):1013-5.
168. Dagenais GR, Yusuf S, Bourassa MG, et al. Effects of ramipril on coronary events in high-risk persons: results of the Heart Outcomes Prevention Evaluation Study. Circulation 2001;104(5):522-6.
169. Dahlof B, Devereux RB, Kjeldsen SE, et al. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. Lancet 2002;359(9311):995-1003.
170. Danesh J, Collins R, Appleby P, et al. Association of fibrinogen, C-reactive protein, albumin, or leukocyte count with coronary heart disease: meta-analyses of prospective studies. Jama 1998;279(18):1477-82.

171. Danesh J, Collins R, Peto R. Lipoprotein(a) and coronary heart disease. Meta-analysis of prospective studies. Circulation 2000;102(10):1082-5.
172. Dargie HJ, Ford I, Fox KM. Total Ischaemic Burden European Trial (TIBET). Effects of ischaemia and treatment with atenolol, nifedipine SR and their combination on outcome in patients with chronic stable angina. The TIBET Study Group. Eur Heart J 1996;17(1):104-12.
173. Dattilo AM, Kris-Etherton PM. Effects of weight reduction on blood lipids and lipoproteins: a meta-analysis. Am J Clin Nutr 1992;56(2):320-8.
174. Davie AP. ACE inhibitors after myocardial infarction. Clinical and economic considerations. Pharmacoeconomics 2000;17(3):237-43.
175. Davis KB, Chaitman B, Ryan T, et al. Comparison of 15-year survival for men and women after initial medical or surgical treatment for coronary artery disease: a CASS registry study. Coronary Artery Surgery Study. J Am Coll Cardiol 1995;25(5):1000-9.
176. 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.
177. de Feyter PJ, Keane D, Deckers JW, et al. Medium- and long-term outcome after coronary balloon angioplasty. Prog Cardiovasc Dis 1994;36(5):385-96.
178. de Gaetano G. Low-dose aspirin and vitamin E in people at cardiovascular risk: a randomised trial in general practice. Collaborative Group of the Primary Prevention Project. Lancet 2001;357(9250):89-95.
179. de Jaegere PP, Eefting FD, Popma JJ, et al. Clinical trials on intracoronary stenting. Semin Interv Cardiol 1996;1(4):233-45.
180. Degeare VS, Dangas G, Stone GW, et al. Interventional procedures in acute myocardial infarction. Am Heart J 2001;141(1):15-24.
181. DeGeare VS, Stone GW, Grines L, et al. Angiographic and clinical characteristics associated with increased in-hospital mortality in elderly patients with acute myocardial infarction undergoing percutaneous intervention (a pooled analysis of the primary angioplasty in myocardial infarction trials). Am J Cardiol 2000;86(1):30-4.
182. Denollet J. Type D personality. A potential risk factor refined. J Psychosom Res 2000;49(4):255-66.
183. Denvir MA, Martin W, Tweddel AC, et al. A comparison of adenosine and exercise stress 201T1 scintigraphy. Nucl Med Commun 1994;15(6):410-6.
184. 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.
185. 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.
186. Detrano R, Gianrossi R, Mulvihill D, 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.
187. Detrano R, Hsiai T, Wang S, et al. Prognostic value of coronary calcification and angiographic stenoses in patients undergoing coronary angiography. J Am Coll Cardiol 1996;27(2):285-90.
188. Detrano R, Janosi A, Lyons KP, et al. Factors affecting sensitivity and specificity of a diagnostic test: the exercise thallium scintigram. Am J Med 1988;84(4):699-710.
189. Detrano R, Lyons KP, Marcondes G, et al. Methodologic problems in exercise testing research. Are we solving them? Arch Intern Med 1988;148(6):1289-95.
190. Detre KM, Rosen AD, Bost JE, et al. Contemporary practice of coronary revascularization in U.S. hospitals and hospitals participating in the bypass angioplasty revascularization investigation (BARI). J Am Coll Cardiol 1996;28(3):609-15.
191. Di Salvo TT, Paul SD, Lloyd-Jones D, et al. Care of acute myocardial infarction by noninvasive and invasive cardiologists: procedure use, cost and outcome. J Am Coll Cardiol 1996;27(2):262-9.
192. Diaz LA, Brunken RC, Blackstone EH, et al. Independent contribution of myocardial perfusion defects to exercise capacity and heart rate recovery for prediction of all-cause mortality in patients with known or suspected coronary heart disease. J Am Coll Cardiol 2001;37(6):1558-64.
193. DiBianco R. Bepridil treatment of chronic stable angina: a review of comparative studies versus placebo, nifedipine, and diltiazem. Am J Cardiol 1992;69(11):56D-62D.
194. Dickes MS, Stammers AH, Pierce ML, et al. Outcome analysis of coronary artery bypass grafting: minimally invasive versus standard techniques. Perfusion 1999;14(6):461-72.

195. Dimmitt SB. Recent insights into dietary fats and cardiovascular disease. Clin Exp Pharmacol Physiol 1995;22(3):204-8.
196. Dippel DW. The results of CAPRIE, IST and CAST. Clopidogrel vs. Aspirin in Patients at Risk of Ischaemic Events. International Stroke Trial. Chinese Acute Stroke Trial. Thromb Res 1998;92(1 Suppl 1):S13-6.
197. Doherty TM, Detrano RC, Mautner SL, et al. Coronary calcium: the good, the bad, and the uncertain. Am Heart J 1999;137(5):806-14.
198. Doliszny KM, Luepker RV, Burke GL, et al. Estimated contribution of coronary artery bypass graft surgery to the decline in coronary heart disease mortality: the Minnesota Heart Survey. J Am Coll Cardiol 1994;24(1):95-103.
199. Dollery C. Diuretic agents and beta-blockers in the treatment of hypertension. Hypertension 1989;13(5 Suppl):I62-5.
200. Domanski MJ, Exner DV, Borkowf CB, et al. Effect of angiotensin converting enzyme inhibition on sudden cardiac death in patients following acute myocardial infarction. A meta-analysis of randomized clinical trials. J Am Coll Cardiol 1999;33(3):598-604.
201. Donahue RP, Goldberg RJ, Chen Z, et al. The influence of sex and diabetes mellitus on survival following acute myocardial infarction: a community-wide perspective. J Clin Epidemiol 1993;46(3):245-52.
202. Doran JP, Howie AJ, Townend JN, et al. Detection of myocardial infarction by immunohistological staining for C9 on formalin fixed, paraffin wax embedded sections. J Clin Pathol 1996;49(1):34-7.
203. Doughty RN, Rodgers A, Sharpe N, et al. Effects of beta-blocker therapy on mortality in patients with heart failure. A systematic overview of randomized controlled trials. Eur Heart J 1997;18(4):560-5.
204. Downs JR, Clearfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. Air Force/Texas Coronary Atherosclerosis Prevention Study. Jama 1998;279(20):1615-22.
205. Du W, Ash AS, Berlowitz DR, et al. Variations in the management of acute myocardial infarction. Importance of clinical measures of disease severity. J Gen Intern Med 1996;11(6):334-41.
206. Duprez D. Is vascular disease in the female different from men? Int Angiol 1993;12(4):331-4.
207. Dzavik V, Carere RG, Teo KK, et al. An open design, multicentre, randomized trial of percutaneous transluminal coronary angioplasty versus stenting, with a heparin-coated stent, of totally occluded coronary arteries: rationale, trial design and baseline patient characteristics. Total Occlusion Study of Canada (TOSCA) Investigators. Can J Cardiol 1998;14(6):825-32.
208. Eaton CB. Relation of physical activity and cardiovascular fitness to coronary heart disease, Part I: A meta-analysis of the independent relation of physical activity and coronary heart disease. J Am Board Fam Pract 1992;5(1):31-42.
209. Ebell MH, White LL, Weismantel D. A systematic review of troponin T and I values as a prognostic tool for patients with chest pain. J Fam Pract 2000;49(8):746-53.
210. Ebrahim S, Smith GD. Systematic review of randomised controlled trials of multiple risk factor interventions for preventing coronary heart disease. Bmj 1997;314(7095):1666-74.
211. Eckman MH, Wong JB, Salem DN, et al. Direct angioplasty for acute myocardial infarction. A review of outcomes in clinical subsets. Ann Intern Med 1992;117(8):667-76.
212. Eikelboom JW, Anand SS, Malmberg K, et al. Unfractionated heparin and low-molecular-weight heparin in acute coronary syndrome without ST elevation: a meta-analysis. Lancet 2000;355(9219):1936-42.
213. Einbinder LC, Schulman KA. The effect of race on the referral process for invasive cardiac procedures. Med Care Res Rev 2000;57(Suppl 1):162-80.
214. Elliott WJ. Circadian variation in blood pressure: implications for the elderly patient. Am J Hypertens 1999;12(2 Pt 2):43S-49S.
215. Ellis SG, Da Silva ER, Spaulding CM, et al. Review of immediate angioplasty after fibrinolytic therapy for acute myocardial infarction: insights from the RESCUE I, RESCUE II, and other contemporary clinical experiences. Am Heart J 2000;139(6):1046-53.
216. Ellis SG, Roubin GS, King SB, 3rd, et al. In-hospital cardiac mortality after acute closure after coronary angioplasty: analysis of risk factors from 8,207 procedures. J Am Coll Cardiol 1988;11(2):211-6.
217. Emery EM, Schmid TL, Kahn HS, et al. A review of the association between abdominal fat distribution, health outcome measures, and modifiable risk factors. Am J Health Promot 1993;7(5):342-53.

218. Engman ML. An update on EBCT (Ultrafast CT) scans for coronary artery disease. J Insur Med 1998;30(3):175-9.
219. Eysmann SB, Douglas PS. Reperfusion and revascularization strategies for coronary artery disease in women. Jama 1992;268(14):1903-7.
220. Fager G, Wiklund O. Cholesterol reduction and clinical benefit. Are there limits to our expectations? Arterioscler Thromb Vasc Biol 1997;17(12):3527-33.
221. Feit F, Mueller HS, Braunwald E, et al. Thrombolysis in Myocardial Infarction (TIMI) phase II trial: outcome comparison of a "conservative strategy" in community versus tertiary hospitals. The TIMI Research Group. J Am Coll Cardiol 1990;16(7):1529-34.
222. Ferguson TB, Jr., Muhlbaier LH, Salai DL, et al. Coronary bypass grafting after failed elective and failed emergent percutaneous angioplasty. Relative risks of emergent surgical intervention. J Thorac Cardiovasc Surg 1988;95(5):761-72.
223. Fernandes CJ, Jr., Akamine N, Knobel E. Cardiac troponin: a new serum marker of myocardial injury in sepsis. Intensive Care Med 1999;25(10):1165-8.
224. Fiebach NH, Hebert PR, Stampfer MJ, et al. A prospective study of high blood pressure and cardiovascular disease in women. Am J Epidemiol 1989;130(4):646-54.
225. Field AE, Coakley EH, Must A, et al. Impact of overweight on the risk of developing common chronic diseases during a 10-year period. Arch Intern Med 2001;161(13):1581-6.
226. Findlay IN. Coronary bypass surgery in women. Curr Opin Cardiol 1994;9(6):650-7.
227. Fioretti F, Tavani A, Gallus S, et al. Menopause and risk of non-fatal acute myocardial infarction: an Italian case-control study and a review of the literature. Hum Reprod 2000;15(3):599-603.
228. Fiorino AS. Electron-beam computed tomography, coronary artery calcium, and evaluation of patients with coronary artery disease. Ann Intern Med 1998;128(10):839-47.
229. Flather MD, Yusuf S, Kober L, et al. Long-term ACE-inhibitor therapy in patients with heart failure or left-ventricular dysfunction: a systematic overview of data from individual patients. ACE-Inhibitor Myocardial Infarction Collaborative Group. Lancet 2000;355(9215):1575-81.
230. Fleischmann KE, Hunink MG, Kuntz KM, et al. Exercise echocardiography or exercise SPECT imaging? A meta-analysis of diagnostic test performance. Jama 1998;280(10):913-20.
231. Flores-Runk P, Raasch RH. Ticlopidine and antiplatelet therapy. Ann Pharmacother 1993;27(9):1090-8.
232. Fodor JG, Boulet AP, Savard D, et al. The role of diltiazem in treating hypertension and coronary artery disease: new approaches to preventing first events. Can J Cardiol 1997;13(5):495-503.
233. Folsom AR. Epidemiology of fibrinogen. Eur Heart J 1995;16(Suppl A):21-3; discussion 23-4.
234. Folsom AR, Arnett DK, Hutchinson RG, et al. Physical activity and incidence of coronary heart disease in middle-aged women and men. Med Sci Sports Exerc 1997;29(7):901-9.
235. Folsom AR, Burke GL, Byers CL, et al. Implications of obesity for cardiovascular disease in blacks: the CARDIA and ARIC studies. Am J Clin Nutr 1991;53(6 Suppl):1604S-1611S.
236. Folsom AR, French SA, Zheng W, et al. Weight variability and mortality: the Iowa Women's Health Study. Int J Obes Relat Metab Disord 1996;20(8):704-9.
237. Folsom AR, Kushi LH, Anderson KE, et al. Associations of general and abdominal obesity with multiple health outcomes in older women: the Iowa Women's Health Study. Arch Intern Med 2000;160(14):2117-28.
238. Folsom AR, Nieto FJ, McGovern PG, et al. Prospective study of coronary heart disease incidence in relation to fasting total homocysteine, related genetic polymorphisms, and B vitamins: the Atherosclerosis Risk in Communities (ARIC) study. Circulation 1998;98(3):204-10.
239. Folsom AR, Stevens J, Schreiner PJ, et al. Body mass index, waist/hip ratio, and coronary heart disease incidence in African Americans and whites. Atherosclerosis Risk in Communities Study Investigators. Am J Epidemiol 1998;148(12):1187-94.
240. Folsom AR, Szklo M, Stevens J, et al. A prospective study of coronary heart disease in relation to fasting insulin, glucose, and diabetes. The Atherosclerosis Risk in Communities (ARIC) Study. Diabetes Care 1997;20(6):935-42.
241. Ford ES, Cooper RS. Racial/ethnic differences in health care utilization of cardiovascular procedures: a review of the evidence. Health Serv Res 1995;30(1 Pt 2):237-52.
242. Fox KA. Comparative analysis of long-term mortality after thrombolytic therapy. Am J Cardiol 1991;68(16):38E-44E.

243. Freemantle N, Cleland J, Young P, et al. beta Blockade after myocardial infarction: systematic review and meta regression analysis. Bmj 1999;318(7200):1730-7.
244. French JK, Webster MW, Neutze JM, et al. Evidence-based assessment of the benefit of revascularisation in coronary disease: beyond the randomised trials. Aust N Z J Med 1996;26(4):490-4.
245. French SA, Folsom AR, Jeffery RW, et al. Weight variability and incident disease in older women: the Iowa Women's Health Study. Int J Obes Relat Metab Disord 1997;21(3):217-23.
246. Freund KM, Belanger AJ, D'Agostino RB, et al. The health risks of smoking. The Framingham Study: 34 years of follow-up. Ann Epidemiol 1993;3(4):417-24.
247. Froom J, Froom P, Benjamin M, et al. Measurement and management of hyperlipidemia for the primary prevention of coronary heart disease. J Am Board Fam Pract 1998;11(1):12-22.
248. Fu Y, Chang WC, Mark D, et al. Canadian-American differences in the management of acute coronary syndromes in the GUSTO IIb trial: one-year follow-up of patients without ST-segment elevation. Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) II Investigators. Circulation 2000;102(12):1375-81.
249. Fuentes R, Ilmaniemi N, Laurikainen E, et al. Hypertension in developing economies: a review of population-based studies carried out from 1980 to 1998. J Hypertens 2000;18(5):521-9.
250. Fuller JH, Stevens LK, Wang SL. International variations in cardiovascular mortality associated with diabetes mellitus: the WHO Multinational Study of Vascular Disease in Diabetes. Ann Med 1996;28(4):319-22.
251. Furberg CD. Lipid-lowering trials: results and limitations. Am Heart J 1994;128(6 Pt 2):1304-8.
252. Furberg CD, Pitt B. Are all angiotensin-converting enzyme inhibitors interchangeable? J Am Coll Cardiol 2001;37(5):1456-60.
253. Furberg CD, Psaty BM. Corrections to the nifedipine meta-analysis. Circulation 1996;93(7):1475-6.
254. Furberg CD, Psaty BM, Meyer JV. Nifedipine. Dose-related increase in mortality in patients with coronary heart disease. Circulation 1995;92(5):1326-31.
255. Garber AM, Browner WS, Hulley SB. Cholesterol screening in asymptomatic adults, revisited. Part 2. Ann Intern Med 1996;124(5):518-31.
256. 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.
257. Garg R, Yusuf S. Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. Collaborative Group on ACE Inhibitor Trials. Jama 1995;273(18):1450-6.
258. Garrison RJ, Gold RS, Wilson PW, et al. Educational attainment and coronary heart disease risk: the Framingham Offspring Study. Prev Med 1993;22(1):54-64.
259. 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.
260. Gaziano JM, Skerrett PJ, Buring JE. Aspirin in the treatment and prevention of cardiovascular disease. Haemostasis 2000;30(Suppl 3):1-13.
261. Genest J, Jr., Jenner JL, McNamara JR, et al. Prevalence of lipoprotein (a) [Lp(a)] excess in coronary artery disease. Am J Cardiol 1991;67(13):1039-145.
262. Ghali JK, Pina IL, Gottlieb SS, et al. Metoprolol CR/XL in female patients with heart failure: analysis of the experience in Metoprolol Extended-Release Randomized Intervention Trial in Heart Failure (MERIT-HF). Circulation 2002;105(13):1585-91.
263. Giacomini MK. Gender and ethnic differences in hospital-based procedure utilization in California. Arch Intern Med 1996;156(11):1217-24.
264. Gianrossi R, Detrano R, Mulvihill D, et al. Exercise-induced ST depression in the diagnosis of coronary artery disease. A meta-analysis. Circulation 1989;80(1):87-98.
265. Gibbons RJ, Balady GJ, Beasley JW, et al. ACC/AHA guidelines for exercise testing: executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Exercise Testing). Circulation 1997;96(1):345-54.
266. Gibbons RJ, Balady GJ, Beasley JW, 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.
267. Gibson CM, Moynihan JL, Al-Mousa EN, et al. Glycoprotein IIb/IIIa receptor inhibition in interventional cardiology. J Thromb Thrombolysis 1999;7(3):287-302.

268. Gibson RS, Boden WE. Calcium channel antagonists: friend or foe in postinfarction patients? Am J Hypertens 1996;9(12 Pt 2):172S-176S.
269. Giles TD, Fisher MB, Rush JE. Lisinopril and captopril in the treatment of heart failure in older patients. Comparison of a long- and short-acting angiotensin-converting enzyme inhibitor. Am J Med 1988;85(3B):44-7.
270. Gill D, Mayou R, Dawes M, et al. Presentation, management and course of angina and suspected angina in primary care. J Psychosom Res 1999;46(4):349-58.
271. Giugliano RP, Llevadot J, Wilcox RG, et al. Geographic variation in patient and hospital characteristics, management, and clinical outcomes in ST-elevation myocardial infarction treated with fibrinolysis. Results from InTIME-II. Eur Heart J 2001;22(18):1702-15.
272. Giugliano RP, McCabe CH, Antman EM, et al. Lower-dose heparin with fibrinolysis is associated with lower rates of intracranial hemorrhage. Am Heart J 2001;141(5):742-50.
273. Glasser SP, Frishman W, White WB, et al. Circadian heart rate response to chronotherapy versus conventional therapy in patients with hypertension and myocardial ischemia. Clin Cardiol 2000;23(7):524-9.
274. Godsland IF, Wynn V, Crook D, et al. Sex, plasma lipoproteins, and atherosclerosis: prevailing assumptions and outstanding questions. Am Heart J 1987;114(6):1467-503.
275. Goldberg KC, Hartz AJ, Jacobsen SJ, et al. Racial and community factors influencing coronary artery bypass graft surgery rates for all 1986 Medicare patients. Jama 1992;267(11):1473-7.
276. Goldberg L, Elliot DL. The effect of physical activity on lipid and lipoprotein levels. Med Clin North Am 1985;69(1):41-55.
277. Goldman L, Coxson P, Hunink MG, et al. The relative influence of secondary versus primary prevention using the National Cholesterol Education Program Adult Treatment Panel II guidelines. J Am Coll Cardiol 1999;34(3):768-76.
278. Goldman L, Weinstein MC, Williams LW. Relative impact of targeted versus populationwide cholesterol interventions on the incidence of coronary heart disease. Projections of the Coronary Heart Disease Policy Model. Circulation 1989;80(2):254-60.
279. Gonzalez MA, Rodriguez Artalejo F, Calero JR. Relationship between socioeconomic status and ischaemic heart disease in cohort and case-control studies: 1960-1993. Int J Epidemiol 1998;27(3):350-8.
280. Gotto AM, Jr. Heart disease in the assessment and treatment of hypercholesterolemia: coronary artery disease and other atherosclerotic disease, family history, and left ventricular hypertrophy. Am J Med 1994;96(6A):9S-18S.
281. Gotto AM, Jr., Grundy SM. Lowering LDL cholesterol: questions from recent meta-analyses and subset analyses of clinical trial DataIssues from the Interdisciplinary Council on Reducing the Risk for Coronary Heart Disease, ninth Council meeting. Circulation 1999;99(8):E1-7.
282. Gould AL, Cariski AT. Meta-analysis by the Program on the Surgical Control of the Hyperlipidemias (POSCH) investigators. Ann Surg 1998;227(2):314-6.
283. Gould AL, Rossouw JE, Santanello NC, et al. Cholesterol reduction yields clinical benefit. A new look at old data. Circulation 1995;91(8):2274-82.
284. Gould AL, Rossouw JE, Santanello NC, et al. Cholesterol reduction yields clinical benefit: impact of statin trials. Circulation 1998;97(10):946-52.
285. Grady D, Herrington D, Vittner V, et al. Cardiovascular disease outcomes during 6.8 years of hormone therapy. Heart and Estrogen/progestin Replacement Study Follow-up (HERS II). JAMA 2002;288:49-57.
286. Grady D, Rubin SM, Petitti DB, et al. Hormone therapy to prevent disease and prolong life in postmenopausal women. Ann Intern Med 1992;117(12):1016-37.
287. Granger CB, Hirsch J, Califf RM, et al. Activated partial thromboplastin time and outcome after thrombolytic therapy for acute myocardial infarction: results from the GUSTO-I trial. Circulation 1996;93(5):870-8.
288. Greendale GA, Lee NP, Arriola ER. The menopause. Lancet 1999;353(9152):571-80.
289. Greenland P, Reicher-Reiss H, Goldbourt U, et al. In-hospital and 1-year mortality in 1,524 women after myocardial infarction. Comparison with 4,315 men. Circulation 1991;83(2):484-91.
290. Gregoire JP, Moisan J, Guibert R, et al. Tolerability of antihypertensive drugs in a community-based setting. Clin Ther 2001;23(5):715-26.
291. Gronbaek M. Wine and mortality. Evidence for causal inference? Dan Med Bull 2000;47(4):271-82.

292. Grumbach K, Anderson GM, Luft HS, et al. Regionalization of cardiac surgery in the United States and Canada. Geographic access, choice, and outcomes. Jama 1995;274(16):1282-8.
293. Guerci AD, Spadaro LA, Goodman KJ, 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.
294. Gueyffier F, Boissel JP, Boutitie F, et al. Effect of antihypertensive treatment in patients having already suffered from stroke. Gathering the evidence. The INDANA (INdividual Data ANalysis of Antihypertensive intervention trials) Project Collaborators. Stroke 1997;28(12):2557-62.
295. Gueyffier F, Boissel JP, Pocock S, et al. Identification of risk factors in hypertensive patients: contribution of randomized controlled trials through an individual patient database. Circulation 1999;100(18):e88-94.
296. Gueyffier F, Boutitie F, Boissel JP, et al. Effect of antihypertensive drug treatment on cardiovascular outcomes in women and men. A meta-analysis of individual patient data from randomized, controlled trials. The INDANA Investigators. Ann Intern Med 1997;126(10):761-7.
297. Gueyffier F, Froment A, Gouton M. New meta-analysis of treatment trials of hypertension: improving the estimate of therapeutic benefit. J Hum Hypertens 1996;10(1):1-8.
298. Gunnell D, Harvey I, Smith L. The invasive management of angina: issues for consumers and commissioners. J Epidemiol Community Health 1995;49(4):335-43.
299. Gurwitz JH, Col NF, Avorn J. The exclusion of the elderly and women from clinical trials in acute myocardial infarction. Jama 1992;268(11):1417-22.
300. Guyton JR. Effect of niacin on atherosclerotic cardiovascular disease. Am J Cardiol 1998;82(12A):18U-23U; discussion 39U-41U.
301. Haberbosch W, Jantos C. Chlamydia pneumoniae infection is not an independent risk factor for arterial disease. Herz 2000;25(2):79-83.
302. Hachamovitch R, Berman DS, Kiat H, et al. Effective risk stratification using exercise myocardial perfusion SPECT in women: gender-related differences in prognostic nuclear testing. J Am Coll Cardiol 1996;28(1):34-44.
303. Hachamovitch R, Berman DS, Kiat H, et al. Value of stress myocardial perfusion single photon emission computed tomography in patients with normal resting electrocardiograms: an evaluation of incremental prognostic value and cost-effectiveness. Circulation 2002;105(7):823-9.
304. Haffner SM. Impaired glucose tolerance, insulin resistance and cardiovascular disease. Diabet Med 1997;14(Suppl 3):S12-8.
305. Hagberg JM, Park JJ, Brown MD. The role of exercise training in the treatment of hypertension: an update. Sports Med 2000;30(3):193-206.
306. Hamilton CA, Link KM, Salido TB, et al. Is imaging at intermediate doses necessary during dobutamine stress magnetic resonance imaging? J Cardiovasc Magn Reson 2001;3(4):297-302.
307. Hankey GJ, Sudlow CL, Dunbabin DW. Thienopyridines or aspirin to prevent stroke and other serious vascular events in patients at high risk of vascular disease? A systematic review of the evidence from randomized trials. Stroke 2000;31(7):1779-84.
308. Hankey GJ, Sudlow CL, Dunbabin DW. Thienopyridine derivatives (ticlopidine, clopidogrel) versus aspirin for preventing stroke and other serious vascular events in high vascular risk patients. Cochrane Database Syst Rev 2000(2):CD001246.
309. Hannan EL, Kilburn H, Jr., O'Donnell JF, et al. Interracial access to selected cardiac procedures for patients hospitalized with coronary artery disease in New York State. Med Care 1991;29(5):430-41.
310. Hannan EL, Kumar D. Geographic variation in the utilization and choice of procedures for treating coronary artery disease in New York State. Ischaemic Heart Disease Patient Outcomes Research Team (PORT). J Health Serv Res Policy 1997;2(3):137-43.
311. Hansen EF, Andersen LT, Von Eyben FE. Cigarette smoking and age at first acute myocardial infarction, and influence of gender and extent of smoking. Am J Cardiol 1993;71(16):1439-42.
312. Hansen JF. Treatment with verapamil during and after an acute myocardial infarction: a review based on the Danish Verapamil Infarction Trials I and II. The Danish Study Group on Verapamil in Myocardial Infarction. J Cardiovasc Pharmacol 1991;18(Suppl 6):S20-5.
313. Hansen JF. Review of postinfarct treatment with verapamil: combined experience of early and late intervention studies with verapamil in patients with acute myocardial infarction. Danish Study Group on Verapamil in Myocardial Infarction. Cardiovasc Drugs Ther 1994;8(Suppl 3):543-7.

314. Hansson L, Zanchetti A, Carruthers SG, et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. Lancet 1998;351(9118):1755-62.
315. Harker LA, Boissel JP, Pilgrim AJ, et al. Comparative safety and tolerability of clopidogrel and aspirin: results from CAPRIE. CAPRIE Steering Committee and Investigators. Clopidogrel versus aspirin in patients at risk of ischaemic events. Drug Saf 1999;21(4):325-35.
316. Harnick DJ, Cohen JL, Schechter CB, et al. Effects of practice setting on quality of lipid-lowering management in patients with coronary artery disease. Am J Cardiol 1998;81(12):1416-20.
317. Harris T, Cook EF, Garrison R, et al. Body mass index and mortality among nonsmoking older persons. The Framingham Heart Study. Jama 1988;259(10):1520-4.
318. Hart RG, Halperin JL, McBride R, et al. Aspirin for the primary prevention of stroke and other major vascular events: meta-analysis and hypotheses. Arch Neurol 2000;57(3):326-32.
319. Hasdai D, Holmes DR, Jr., Topol EJ, et al. Frequency and clinical outcome of cardiogenic shock during acute myocardial infarction among patients receiving reteplase or alteplase. Results from GUSTO-III. Global Use of Strategies to Open Occluded Coronary Arteries. Eur Heart J 1999;20(2):128-35.
320. Haymart MR, Dickfeld T, Nass C, et al. Percutaneous coronary intervention vs. medical therapy: what are the implications for women? J Womens Health Gend Based Med 2002;11(4):347-55.
321. He J, Whelton PK. Elevated systolic blood pressure as a risk factor for cardiovascular and renal disease. J Hypertens Suppl 1999;17(2):S7-13.
322. Healy B. The Yentl syndrome. N Engl J Med 1991;325(4):274-6.
323. Hebert PR, Gaziano JM, Chan KS, et al. Cholesterol lowering with statin drugs, risk of stroke, and total mortality. An overview of randomized trials. Jama 1997;278(4):313-21.
324. Hebert PR, Hennekens CH. An overview of the 4 randomized trials of aspirin therapy in the primary prevention of vascular disease. Arch Intern Med 2000;160(20):3123-7.
325. Heiat A, Vaccarino V, Krumholz HM. An evidence-based assessment of federal guidelines for overweight and obesity as they apply to elderly persons. Arch Intern Med 2001;161(9):1194-203.
326. Heidenreich PA, Alloggiamento T, Melsop K, et al. The prognostic value of troponin in patients with non-ST elevation acute coronary syndromes: a meta-analysis. J Am Coll Cardiol 2001;38(2):478-85.
327. Heidenreich PA, Lee TT, Massie BM. Effect of beta-blockade on mortality in patients with heart failure: a meta-analysis of randomized clinical trials. J Am Coll Cardiol 1997;30(1):27-34.
328. Heidenreich PA, McClellan M. Trends in treatment and outcomes for acute myocardial infarction: 1975-1995. Am J Med 2001;110(3):165-74.
329. Heidenreich PA, McDonald KM, Hastie T, et al. Meta-analysis of trials comparing beta-blockers, calcium antagonists, and nitrates for stable angina. Jama 1999;281(20):1927-36.
330. Held PH, Teo KK, Yusuf S. Effects of tissue-type plasminogen activator and anisoylated plasminogen streptokinase activator complex on mortality in acute myocardial infarction. Circulation 1990;82(5):1668-74.
331. Held PH, Yusuf S, Furberg CD. Calcium channel blockers in acute myocardial infarction and unstable angina: an overview. Bmj 1989;299(6709):1187-92.
332. Hennekens CH. Thrombolytic therapy: pre- and post-GISSI-2, ISIS-3, and GUSTO-1. Clin Cardiol 1994;17(1 Suppl 1):I15-7.
333. Hennekens CH, Albert CM, Godfried SL, et al. Adjunctive drug therapy of acute myocardial infarction--evidence from clinical trials. N Engl J Med 1996;335(22):1660-7.
334. Hermanson B, Omenn GS, Kronmal RA, et al. Beneficial six-year outcome of smoking cessation in older men and women with coronary artery disease. Results from the CASS registry. N Engl J Med 1988;319(21):1365-9.
335. Herold PM, Kinsella JE. Fish oil consumption and decreased risk of cardiovascular disease: a comparison of findings from animal and human feeding trials. Am J Clin Nutr 1986;43(4):566-98.
336. Hill K. The demography of menopause. Maturitas 1996;23(2):113-27.
337. Hillegass WB, Newman AR, Raco DL. Glycoprotein IIb/IIIa receptor therapy in percutaneous coronary intervention and non-ST-segment elevation acute coronary syndromes. Estimating the economic implications. Pharmacoeconomics 2001;19(1):41-55.
338. Hlatky MA, Pryor DB, Harrell FE, Jr., et al. Factors affecting sensitivity and specificity of exercise electrocardiography. Multivariable analysis. Am J Med 1984;77(1):64-71.

339. Hochman JS, McCabe CH, Stone PH, et al. Outcome and profile of women and men presenting with acute coronary syndromes: a report from TIMI IIIB. TIMI Investigators. Thrombolysis in Myocardial Infarction. J Am Coll Cardiol 1997;30(1):141-8.
340. Hochman JS, Tamis JE, Thompson TD, et al. Sex, clinical presentation, and outcome in patients with acute coronary syndromes. Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes IIb Investigators. N Engl J Med 1999;341(4):226-32.
341. Hoes AW, Grobbee DE, Lubsen J. Does drug treatment improve survival? Reconciling the trials in mild-to-moderate hypertension. J Hypertens 1995;13(7):805-11.
342. Hoher M, Wohrle J, Grebe OC, et al. A randomized trial of elective stenting after balloon recanalization of chronic total occlusions. J Am Coll Cardiol 1999;34(3):722-9.
343. Hokanson JE, Austin MA. Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population-based prospective studies. J Cardiovasc Risk 1996;3(2):213-9.
344. Holme I. Relation of coronary heart disease incidence and total mortality to plasma cholesterol reduction in randomised trials: use of meta-analysis. Br Heart J 1993;69(1 Suppl):S42-7.
345. Holme I. Effects of lipid-lowering therapy on total and coronary mortality. Curr Opin Lipidol 1995;6(6):374-8.
346. Holme I. Cholesterol reduction and its impact on coronary artery disease and total mortality. Am J Cardiol 1995;76(9):10C-17C.
347. Holme I. Relationship between total mortality and cholesterol reduction as found by meta-regression analysis of randomized cholesterol-lowering trials. Control Clin Trials 1996;17(1):13-22.
348. Holme I, Ekelund LG, Hjermann I, et al. Quality-adjusted meta-analysis of the hypertension/coronary dilemma. Am J Hypertens 1994;7(8):703-12.
349. Holmes DR, Jr., Holubkov R, Vlietstra RE, et al. Comparison of complications during percutaneous transluminal coronary angioplasty from 1977 to 1981 and from 1985 to 1986: the National Heart, Lung, and Blood Institute Percutaneous Transluminal Coronary Angioplasty Registry. J Am Coll Cardiol 1988;12(5):1149-55.
350. Honan MB, Harrell FE, Jr., Reimer KA, et al. Cardiac rupture, mortality and the timing of thrombolytic therapy: a meta-analysis. J Am Coll Cardiol 1990;16(2):359-67.
351. Horton HL, Marinchak RA, Rials SJ, et al. Gender differences in device therapy for malignant ventricular arrhythmias. Arch Intern Med 1995;155(21):2342-5.
352. Houghton T, Freemantle N, Cleland JG. Are beta-blockers effective in patients who develop heart failure soon after myocardial infarction? A meta-regression analysis of randomised trials. Eur J Heart Fail 2000;2(3):333-40.
353. Howard G, Manolio TA, Burke GL, et al. Does the association of risk factors and atherosclerosis change with age? An analysis of the combined ARIC and CHS cohorts. The Atherosclerosis Risk in Communities (ARIC) and Cardiovascular Health Study (CHS) investigators. Stroke 1997;28(9):1693-701.
354. Howes LG, Simons LA. Efficacy of drug intervention for lipids in the prevention of coronary artery disease. Aust N Z J Med 1994;24(1):107-12.
355. Hu FB, Grodstein F, Hennekens CH, et al. Age at natural menopause and risk of cardiovascular disease. Arch Intern Med 1999;159(10):1061-6.
356. Hu FB, Stampfer MJ, Solomon CG, et al. The impact of diabetes mellitus on mortality from all causes and coronary heart disease in women: 20 years of follow-up. Arch Intern Med 2001;161(14):1717-23.
357. Hubert HB, Feinleib M, McNamara PM, et al. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation 1983;67(5):968-77.
358. Huckell VF, Bernstein V, Cairns JA, et al. Angiotensin-converting enzyme inhibition in myocardial infarction--Part 1: Clinical data. Can J Cardiol 1997;13(2):161-9.
359. Hughes GC, Abdel-aleem S, Biswas SS, et al. Transmyocardial laser revascularization: experimental and clinical results. Can J Cardiol 1999;15(7):797-806.
360. Hughes GC, Annex BH, Yin B, et al. Transmyocardial laser revascularization limits in vivo adenoviral-mediated gene transfer in porcine myocardium. Cardiovasc Res 1999;44(1):81-90.
361. Hume AL, Barbour MM, Willey CJ, et al. Changing trends in antihypertensive therapy in two New England communities during the 1980s. Pharmacotherapy 1993;13(3):244-51.

362. Hunink MG, Kuntz KM, Fleischmann KE, et al. Noninvasive imaging for the diagnosis of coronary artery disease: focusing the development of new diagnostic technology. Ann Intern Med 1999;131(9):673-80.
363. Hussain KM, Kogan A, Estrada AQ, et al. Referral pattern and outcome in men and women undergoing coronary artery bypass surgery--a critical review. Angiology 1998;49(4):243-50.
364. Hutchinson LA, Pasternack PF, Baumann FG, et al. Is there detrimental gender bias in preoperative cardiac management of patients undergoing vascular surgery? Circulation 1994;90(5 Pt 2):II220-3.
365. Hutchinson RG, Watson RL, Davis CE, et al. Racial differences in risk factors for atherosclerosis. The ARIC Study. Atherosclerosis Risk in Communities. Angiology 1997;48(4):279-90.
366. Insua JT, Sacks HS, Lau TS, et al. Drug treatment of hypertension in the elderly: a meta-analysis. Ann Intern Med 1994;121(5):355-62.
367. Ioannidis JP, Salem D, Chew PW, et al. Accuracy of imaging technologies in the diagnosis of acute cardiac ischemia in the emergency department: a meta-analysis. Ann Emerg Med 2001;37(5):471-7.
368. 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.
369. Izzat MB, West RR, Bryan AJ, et al. Coronary artery bypass surgery: current practice in the United Kingdom. Br Heart J 1994;71(4):382-5.
370. Jackson RE, Anderson W, Peacock WFt, et al. Effect of a patient's sex on the timing of thrombolytic therapy. Ann Emerg Med 1996;27(1):8-15.
371. Jacobs AK, Kelsey SF, Brooks MM, et al. Better outcome for women compared with men undergoing coronary revascularization: a report from the bypass angioplasty revascularization investigation (BARI). Circulation 1998;98(13):1279-85.
372. Jacobs AK, Kelsey SF, Yeh W, et al. Documentation of decline in morbidity in women undergoing coronary angioplasty (a report from the 1993-94 NHLBI Percutaneous Transluminal Coronary Angioplasty Registry). National Heart, Lung, and Blood Institute. Am J Cardiol 1997;80(8):979-84.
373. Jacobs D, Blackburn H, Higgins M, et al. Report of the Conference on Low Blood Cholesterol: Mortality Associations. Circulation 1992;86(3):1046-60.
374. Jacobson TA. "The lower the better" in hypercholesterolemia therapy: a reliable clinical guideline? Ann Intern Med 2000;133(7):549-54.
375. Jaglal SB, Goel V, Naylor CD. Sex differences in the use of invasive coronary procedures in Ontario. Can J Cardiol 1994;10(2):239-44.
376. Janzon M, Levin LA, Swahn E. Cost-effectiveness of an invasive strategy in unstable coronary artery disease; results from the FRISC II invasive trial. The Fast Revascularisation during InStability in Coronary artery disease. Eur Heart J 2002;23(1):31-40.
377. Jarrett RJ. The cardiovascular risk associated with impaired glucose tolerance. Diabet Med 1996;13(3 Suppl 2):S15-9.
378. Jenkins PL, Weinehall L, Erb TA, et al. The Norsjo-Cooperstown healthy heart project: a case study combining data from different studies without the use of meta-analysis. Scand J Public Health 2001;Suppl(56):40-5.
379. Johnson PA, Goldman L, Orav EJ, et al. Gender differences in the management of acute chest pain. Support for the "Yentl syndrome". J Gen Intern Med 1996;11(4):209-17.
380. Johnson PA, Lee TH, Cook EF, et al. Effect of race on the presentation and management of patients with acute chest pain. Ann Intern Med 1993;118(8):593-601.
381. Jolliffe JA, Rees K, Taylor RS, et al. Exercise-based rehabilitation for coronary heart disease. Cochrane Database Syst Rev 2000;4.
382. Jones RH, Hannan EL, Hammermeister KE, et al. Identification of preoperative variables needed for risk adjustment of short-term mortality after coronary artery bypass graft surgery. The Working Group Panel on the Cooperative CABG Database Project. J Am Coll Cardiol 1996;28(6):1478-87.
383. Jones RH, Kesler K, Phillips HR, 3rd, et al. Long-term survival benefits of coronary artery bypass grafting and percutaneous transluminal angioplasty in patients with coronary artery disease. J Thorac Cardiovasc Surg 1996;111(5):1013-25.
384. Kannel WB. Blood pressure as a cardiovascular risk factor: prevention and treatment. Jama 1996;275(20):1571-6.

385. Kannel WB, Cupples LA, Ramaswami R, et al. Regional obesity and risk of cardiovascular disease; the Framingham Study. J Clin Epidemiol 1991;44(2):183-90.
386. Kannel WB, D'Agostino RB, Belanger AJ. Fibrinogen, cigarette smoking, and risk of cardiovascular disease: insights from the Framingham Study. Am Heart J 1987;113(4):1006-10.
387. Kannel WB, D'Agostino RB, Belanger AJ. Risk reduction after quitting smoking. Quality of Life and Cardiovascular Care 1989:84-85.
388. Kannel WB, D'Agostino RB, Wilson PW, et al. Diabetes, fibrinogen, and risk of cardiovascular disease: the Framingham experience. Am Heart J 1990;120(3):672-6.
389. Kannel WB, Schatzkin A. Sudden death: lessons from subsets in population studies. J Am Coll Cardiol 1985;5(6 Suppl):141B-149B.
390. Kannel WB, Sorlie P, McNamara PM. Prognosis after initial myocardial infarction: the Framingham study. Am J Cardiol 1979;44(1):53-9.
391. Kannel WB, Wilson PW. Efficacy of lipid profiles in prediction of coronary disease. Am Heart J 1992;124(3):768-74.
392. Katan MB. High-oil compared with low-fat, high-carbohydrate diets in the prevention of ischemic heart disease. Am J Clin Nutr 1997;66(4 Suppl):974S-979S.
393. Kawachi I, Colditz GA, Speizer FE, et al. A prospective study of passive smoking and coronary heart disease. Circulation 1997;95(10):2374-9.
394. Kawachi I, Colditz GA, Stampfer MJ, et al. Smoking cessation in relation to total mortality rates in women. A prospective cohort study. Ann Intern Med 1993;119(10):992-1000.
395. Kawachi I, Colditz GA, Stampfer MJ, et al. Smoking cessation and decreased risks of total mortality, stroke, and coronary heart disease incidence among women: a prospective cohort study. In: Burns DM, Garfinkel L, Samet JM, editors. Changes in cigarette-related disease risks and thier implications for prevention and control. Bethesda: National Cancer Institute; 1997. p. 531-65.
396. Kawachi I, Colditz GA, Stampfer MJ, et al. Smoking cessation and time course of decreased risks of coronary heart disease in middle-aged women. Arch Intern Med 1994;154(2):169-75.
397. Keelan PC, Bielak LF, Ashai K, et al. Long-term prognostic value of coronary calcification detected by electron-beam computed tomography in patients undergoing coronary angiography. Circulation 2001;104(4):412-7.
398. Keenan CR, Chou TM. Revascularization in coronary artery disease. A review of randomized trial data. West J Med 1998;168(4):280-5.
399. Keil JE, Sutherland SE, Knapp RG, et al. Mortality rates and risk factors for coronary disease in black as compared with white men and women. N Engl J Med 1993;329(2):73-8.
400. Keil U. Coronary artery disease: the role of lipids, hypertension and smoking. Basic Res Cardiol 2000;95(Suppl 1):I52-8.
401. Kellett J, Clarke J. Comparison of "accelerated" tissue plasminogen activator with streptokinase for treatment of suspected myocardial infarction. Med Decis Making 1995;15(4):297-310.
402. Kelly R. Selections from current literature: treatment of hypertension. Fam Pract 1992;9(1):104-8.
403. Kelsey SF, James M, Holubkov AL, et al. Results of percutaneous transluminal coronary angioplasty in women. 1985-1986 National Heart, Lung, and Blood Institute's Coronary Angioplasty Registry. Circulation 1993;87(3):720-7.
404. Kennedy J, Shavelle R, Wang S, et al. Coronary calcium and standard risk factors in symptomatic patients referred for coronary angiography. Am Heart J 1998;135(4):696-702.
405. Ketola E, Sipila R, Makela M. Effectiveness of individual lifestyle interventions in reducing cardiovascular disease and risk factors. Ann Med 2000;32(4):239-51.
406. Khan SS, Nessim S, Gray R, et al. Increased mortality of women in coronary artery bypass surgery: evidence for referral bias. Ann Intern Med 1990;112(8):561-7.
407. Kilaru PK, Kelly RF, Calvin JE, et al. Utilization of coronary angiography and revascularization after acute myocardial infarction in men and women risk stratified by the American College of Cardiology/American Heart Association guidelines. J Am Coll Cardiol 2000;35(4):974-9.
408. Kim RJ, Hillenbrand HB, Judd RM. Evaluation of myocardial viability by MRI. Herz 2000;25(4):417-30.
409. Kimmelstiel C, Goldberg RJ. Congestive heart failure in women: focus on heart failure due to coronary artery disease and diabetes. Cardiology 1990;77(Suppl 2):71-9.
410. King SB, 3rd. The impact of performing a clinical trial on patient outcomes: lessons from the Emory Angioplasty vs. Surgery Trial. Trans Am Clin Climatol Assoc 1995;107:68-77; discussion 77-8.

411. Kinn JW, O'Neill WW, Benzuly KH, et al. Primary angioplasty reduces risk of myocardial rupture compared to thrombolysis for acute myocardial infarction. Cathet Cardiovasc Diagn 1997;42(2):151-7.
412. Kinney MR, Burfitt SN, Stullenbarger E, et al. Quality of life in cardiac patient research: a meta-analysis. Nurs Res 1996;45(3):173-80.
413. Kjeldsen SE, Kolloch RE, Leonetti G, et al. Influence of gender and age on preventing cardiovascular disease by antihypertensive treatment and acetylsalicylic acid. The HOT study. Hypertension Optimal Treatment. J Hypertens 2000;18(5):629-42.
414. Kjeldsen SE, Warnold I, Hansson L. Influence of gender on prevention of myocardial infarction by antihypertensives and acetylsalicylic acid: the HOT study. J Gend Specif Med 2000;3(8):35-8.
415. Kloner RA, Vetrovec GW, Materson BJ, et al. Safety of long-acting dihydropyridine calcium channel blockers in hypertensive patients. Am J Cardiol 1998;81(2):163-9.
416. Klungel OH, de Boer A, Paes AH, et al. Sex differences in the pharmacological treatment of hypertension: a review of population-based studies. J Hypertens 1997;15(6):591-600.
417. Klungel OH, de Boer A, Paes AH, et al. Sex differences in antihypertensive drug use: determinants of the choice of medication for hypertension. J Hypertens 1998;16(10):1545-53.
418. Klungel OH, Paes AH, de Boer A, et al. Sex differences in the medication choice for hypertension in general practice. A study with written case simulations. Pharm World Sci 2000;22(4):140-6.
419. Knapp RG, Sutherland SE, Keil JE, et al. A comparison of the effects of cholesterol on CHD mortality in black and white women: twenty-eight years of follow-up in the Charleston Heart Study. J Clin Epidemiol 1992;45(10):1119-29.
420. 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(6):393-403.
421. Ko W, Gold JP, Lazzaro R, et al. Survival analysis of octogenarian patients with coronary artery disease managed by elective coronary artery bypass surgery versus conventional medical treatment. Circulation 1992;86(5 Suppl):II191-7.
422. Koenig W. Fibrinogen and coronary risk. Curr Cardiol Rep 1999;1(2):112-8.
423. Kong DF, Califf RM, Miller DP, et al. Clinical outcomes of therapeutic agents that block the platelet glycoprotein IIb/IIIa integrin in ischemic heart disease. Circulation 1998;98(25):2829-35.
424. Kong DF, Topol EJ, Bittl JA, et al. Clinical outcomes of bivalirudin for ischemic heart disease. Circulation 1999;100(20):2049-53.
425. 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.
426. Krumholz HM, Douglas PS, Lauer MS, et al. Selection of patients for coronary angiography and coronary revascularization early after myocardial infarction: is there evidence for a gender bias? Ann Intern Med 1992;116(10):785-90.
427. Kudenchuk PJ, Maynard C, Martin JS, et al. Comparison of presentation, treatment, and outcome of acute myocardial infarction in men versus women (the Myocardial Infarction Triage and Intervention Registry). Am J Cardiol 1996;78(1):9-14.
428. Kuller LH, Simkin-Silverman LR, Wing RR, et al. Women's Healthy Lifestyle Project: A randomized clinical trial: results at 54 months. Circulation 2001;103(1):32-7.
429. Kuntz KM, Tsevat J, Weinstein MC, et al. Expert panel vs decision-analysis recommendations for postdischarge coronary angiography after myocardial infarction. Jama 1999;282(23):2246-51.
430. Kwok Y, Kim C, Grady D, et al. Meta-analysis of exercise testing to detect coronary artery disease in women. Am J Cardiol 1999;83(5):660-6.
431. La Vecchia C. Sex hormones and cardiovascular risk. Hum Reprod 1992;7(2):162-7.
432. LaCroix AZ, Lang J, Scherr P, et al. Smoking and mortality among older men and women in three communities. N Engl J Med 1991;324(23):1619-25.
433. LaRosa JC, He J, Vupputuri S. Effect of statins on risk of coronary disease: a meta-analysis of randomized controlled trials. Jama 1999;282(24):2340-6.
434. Larsen J, Vaccheri A, Andersen M, et al. Lack of adherence to lipid-lowering drug treatment. A comparison of utilization patterns in defined populations in Funen, Denmark and Bologna, Italy. Br J Clin Pharmacol 2000;49(5):463-71.
435. Latini R, Maggioni AP, Flather M, et al. ACE inhibitor use in patients with myocardial infarction. Summary of evidence from clinical trials. Circulation 1995;92(10):3132-7.
436. Latini R, Tognoni G, Maggioni AP, et al. Clinical effects of early angiotensin-converting enzyme inhibitor treatment for acute myocardial infarction are similar in the presence and absence of aspirin:

systematic overview of individual data from 96,712 randomized patients. Angiotensin-converting Enzyme Inhibitor Myocardial Infarction Collaborative Group. J Am Coll Cardiol 2000;35(7):1801-7.
437. Lau GS, Chan JC, Chu PL, et al. Use of antidiabetic and antihypertensive drugs in hospital and outpatient settings in Hong Kong. Ann Pharmacother 1996;30(3):232-7.
438. Lau J, Antman EM, Jimenez-Silva J, et al. Cumulative meta-analysis of therapeutic trials for myocardial infarction. N Engl J Med 1992;327(4):248-54.
439. Lau J, Ioannidis JP, Balk EM, 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.
440. Law MR, Wald NJ, Thompson SG. By how much and how quickly does reduction in serum cholesterol concentration lower risk of ischaemic heart disease? Bmj 1994;308(6925):367-72.
441. Lear JT, Lawrence IG, Burden AC, et al. A comparison of stress test referral rates and outcome between Asians and Europeans. J R Soc Med 1994;87(11):661-2.
442. Lear JT, Lawrence IG, Pohl JE, et al. Myocardial infarction and thrombolysis: a comparison of the Indian and European populations on a coronary care unit. J R Coll Physicians Lond 1994;28(2):143-7.
443. Lechat P, Packer M, Chalon S, et al. Clinical effects of beta-adrenergic blockade in chronic heart failure: a meta-analysis of double-blind, placebo-controlled, randomized trials. Circulation 1998;98(12):1184-91.
444. Lee IM, Rexrode KM, Cook NR, et al. Physical activity and coronary heart disease in women: is "no pain, no gain" passe? Jama 2001;285(11):1447-54.
445. Lee S, Spencer A. Beta-blockers to reduce mortality in patients with systolic dysfunction: a meta-analysis. J Fam Pract 2001;50(6):499-504.
446. Lee TH, Boucher CA. Clinical practice. Noninvasive tests in patients with stable coronary artery disease. N Engl J Med 2001;344(24):1840-5.
447. Lee WL, Cheung AM, Cape D, et al. Impact of diabetes on coronary artery disease in women and men: a meta-analysis of prospective studies. Diabetes Care 2000;23(7):962-8.
448. Leis HP, Jr. The relationship of diet to cancer, cardiovascular disease and longevity. Int Surg 1991;76(1):1-5.
449. Leizorovicz A, Lechat P, Cucherat M, et al. Bisoprolol for the treatment of chronic heart failure: a meta-analysis on individual data of two placebo-controlled studies--CIBIS and CIBIS II. Cardiac Insufficiency Bisoprolol Study. Am Heart J 2002;143(2):301-7.
450. Lerner DJ, Kannel WB. Patterns of coronary heart disease morbidity and mortality in the sexes: a 26-year follow-up of the Framingham population. Am Heart J 1986;111(2):383-90.
451. Lewington S, MacMahon S. Blood pressure, cholesterol, and common causes of death: a review. Prospective Studies Collaboration. Am J Hypertens 1999;12(10 Pt 2):96S-98S.
452. Lewis SJ, Sacks FM, Mitchell JS, et al. Effect of pravastatin on cardiovascular events in women after myocardial infarction: the cholesterol and recurrent events (CARE) trial. J Am Coll Cardiol 1998;32(1):140-6.
453. Lewsey JD, Murray GD, Leyland AH, et al. Comparing outcomes of percutaneous transluminal coronary angioplasty with coronary artery bypass grafting; can routine health service data complement and enhance randomized controlled trials? Eur Heart J 1999;20(23):1731-5.
454. Lieu TA, Gurley RJ, Lundstrom RJ, et al. Primary angioplasty and thrombolysis for acute myocardial infarction: an evidence summary. J Am Coll Cardiol 1996;27(3):737-50.
455. Lincoff AM, Califf RM, Anderson KM, et al. Evidence for prevention of death and myocardial infarction with platelet membrane glycoprotein IIb/IIIa receptor blockade by abciximab (c7E3 Fab) among patients with unstable angina undergoing percutaneous coronary revascularization. EPIC Investigators.Evaluation of 7E3 in Preventing Ischemic Complications. J Am Coll Cardiol 1997;30(1):149-56.
456. Lincoff AM, Califf RM, Ellis SG, et al. Thrombolytic therapy for women with myocardial infarction: is there a gender gap? Thrombolysis and Angioplasty in Myocardial Infarction Study Group. J Am Coll Cardiol 1993;22(7):1780-7.
457. Link N, Tanner M. Coronary artery disease: Part 1. Epidemiology and diagnosis. West J Med 2001;174(4):257-61.
458. Lip GY, Beevers DG. Alcohol, hypertension, coronary disease and stroke. Clin Exp Pharmacol Physiol 1995;22(3):189-94.

459. Lobo RA. Lipids, clotting factors, and diabetes: endogenous risk factors for cardiovascular disease. Am J Obstet Gynecol 1988;158(6 Pt 2):1584-91.
460. Loewen P, Sunderji R, Gin K. The efficacy and safety of combination warfarin and ASA therapy: a systematic review of the literature and update of guidelines. Can J Cardiol 1998;14(5):717-26.
461. Lonn E, Roccaforte R, Yi Q, et al. Effect of long-term therapy with ramipril in high-risk women. J Am Coll Cardiol 2002;40(4):693.
462. Lonn EM, Yusuf S. Evidence based cardiology: emerging approaches in preventing cardiovascular disease. Bmj 1999;318(7194):1337-41.
463. Lowel H, Lewis M, Hormann A, et al. Case finding, data quality aspects and comparability of myocardial infarction registers: results of a south German register study. J Clin Epidemiol 1991;44(3):249-60.
464. Lubsen J. The calcium channel antagonist debate: recent developments. Eur Heart J 1998;19(Suppl I):I3-7.
465. MacMahon S, Sharpe N. Long-term antiplatelet therapy for the prevention of vascular disease. Med J Aust 1991;154(7):477-80.
466. Maggioni AP, Sessa F, Latini R, et al. Treatment of acute myocardial infarction today. Am Heart J 1997;134(2 Pt 2):S9-14.
467. Magrini N, Einarson T, Vaccheri A, et al. Use of lipid-lowering drugs from 1990 to 1994: an international comparison among Australia, Finland, Italy (Emilia Romagna Region), Norway and Sweden. Eur J Clin Pharmacol 1997;53(3-4):185-9.
468. Mahaffey KW, Granger CB, Collins R, et al. Overview of randomized trials of intravenous heparin in patients with acute myocardial infarction treated with thrombolytic therapy. Am J Cardiol 1996;77(8):551-6.
469. Mahaffey KW, Granger CB, Toth CA, et al. Diabetic retinopathy should not be a contraindication to thrombolytic therapy for acute myocardial infarction: review of ocular hemorrhage incidence and location in the GUSTO-I trial. Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries. J Am Coll Cardiol 1997;30(7):1606-10.
470. Majeed A, Moser K, Maxwell R. Age, sex and practice variations in the use of statins in general practice in England and Wales. J Public Health Med 2000;22(3):275-9.
471. Majumdar SR, Gurwitz JH, Soumerai SB. Undertreatment of hyperlipidemia in the secondary prevention of coronary artery disease. J Gen Intern Med 1999;14(12):711-7.
472. Makela P, Valkonen T, Poikolainen K. Estimated numbers of deaths from coronary heart disease "caused" and "prevented" by alcohol: an example from Finland. J Stud Alcohol 1997;58(5):455-63.
473. Malenka DJ, O'Rourke D, Miller MA, et al. Cause of in-hospital death in 12,232 consecutive patients undergoing percutaneous transluminal coronary angioplasty. The Northern New England Cardiovascular Disease Study Group. Am Heart J 1999;137(4 Pt 1):632-8.
474. Malhotra S, Karan RS, Bhargava VK, et al. A meta-analysis of controlled clinical trials comparing low-molecular weight heparins with unfractionated heparin in unstable angina. Indian Heart J 2001;53(2):197-202.
475. Malmberg K, Yusuf S, Gerstein HC, et al. Impact of diabetes on long-term prognosis in patients with unstable angina and non-Q-wave myocardial infarction: results of the OASIS (Organization to Assess Strategies for Ischemic Syndromes) Registry. Circulation 2000;102(9):1014-9.
476. Manolio TA, Pearson TA, Wenger NK, et al. Cholesterol and heart disease in older persons and women. Review of an NHLBI workshop. Ann Epidemiol 1992;2(1-2):161-76.
477. Manson JE, Colditz GA, Stampfer MJ, et al. A prospective study of maturity-onset diabetes mellitus and risk of coronary heart disease and stroke in women. Arch Intern Med 1991;151(6):1141-7.
478. Manson JE, Colditz GA, Stampfer MJ, et al. A prospective study of obesity and risk of coronary heart disease in women. N Engl J Med 1990;322(13):882-9.
479. Manson JE, Hu FB, Rich-Edwards JW, et al. A prospective study of walking as compared with vigorous exercise in the prevention of coronary heart disease in women. N Engl J Med 1999;341(9):650-8.
480. Manson JE, Stampfer MJ, Colditz GA, et al. A prospective study of aspirin use and primary prevention of cardiovascular disease in women. Jama 1991;266(4):521-7.
481. Manson JE, Tosteson H, Ridker PM, et al. The primary prevention of myocardial infarction. N Engl J Med 1992;326(21):1406-16.
482. Manson JE, Willett WC, Stampfer MJ, et al. Body weight and mortality among women. N Engl J Med 1995;333(11):677-85.

483. Marber M, MacRae C, Joy M. Delay to invasive investigation and revascularisation for coronary heart disease in south west Thames region: a two tier system? Bmj 1991;302(6786):1189-91.
484. Marchioli R, Marfisi RM, Carinci F, et al. Meta-analysis, clinical trials, and transferability of research results into practice. The case of cholesterol-lowering interventions in the secondary prevention of coronary heart disease. Arch Intern Med 1996;156(11):1158-72.
485. Marine JE, Freedberg KA, Davidoff R. Cost-effectiveness of stress-echocardiography. Cardiol Clin 1999;17(3):583-95, x.
486. Mark DB, Hlatky MA, Califf RM, et al. Cost effectiveness of thrombolytic therapy with tissue plasminogen activator as compared with streptokinase for acute myocardial infarction. N Engl J Med 1995;332(21):1418-24.
487. Mark DB, Nelson CL, Califf RM, et al. Continuing evolution of therapy for coronary artery disease. Initial results from the era of coronary angioplasty. Circulation 1994;89(5):2015-25.
488. Mark DB, Shaw L, Harrell FE, Jr., et al. Prognostic value of a treadmill exercise score in outpatients with suspected coronary artery disease. N Engl J Med 1991;325(12):849-53.
489. Maron DJ. Percutaneous coronary intervention versus medical therapy for coronary heart disease. Curr Atheroscler Rep 2000;2(4):290-6.
490. Martikainen J, Klaukka T, Reunanen A, et al. Recent trends in the consumption of lipid-lowering drugs in Finland. J Clin Epidemiol 1996;49(12):1453-57.
491. Marwick TH, Shaw LJ, Lauer MS, et al. The noninvasive prediction of cardiac mortality in men and women with known or suspected coronary artery disease. Economics of Noninvasive Diagnosis (END) Study Group. Am J Med 1999;106(2):172-8.
492. Marz W, Wieland H. HMG-CoA reductase inhibition: anti-inflammatory effects beyond lipid lowering? Herz 2000;25(2):117-25.
493. Mathis AS. Newer antithrombotic strategies in the initial management of non-ST-segment elevation acute coronary syndromes. Ann Pharmacother 2000;34(2):208-27.
494. Matsui K, Polanczyk CA, Gaspoz JM, et al. Management of patients with acute myocardial infarction at five academic medical centers: clinical characteristics, resource utilization, and outcome. J Investig Med 1999;47(3):134-40.
495. Matsuo T, Kobayashi H, Kario K, et al. Fibrin D-dimer in thrombogenic disorders. Semin Thromb Hemost 2000;26(1):101-7.
496. Maynard C, Althouse R, Cerqueira M, et al. Underutilization of thrombolytic therapy in eligible women with acute myocardial infarction. Am J Cardiol 1991;68(5):529-30.
497. Maynard C, Litwin PE, Martin JS, et al. Gender differences in the treatment and outcome of acute myocardial infarction. Results from the Myocardial Infarction Triage and Intervention Registry. Arch Intern Med 1992;152(5):972-6.
498. McGlynn EA, Naylor CD, Anderson GM, et al. Comparison of the appropriateness of coronary angiography and coronary artery bypass graft surgery between Canada and New York State. Jama 1994;272(12):934-40.
499. McGregor M, Brophy JM. Use of abciximab (c7E3 Fab, ReoPro) as an adjunct to balloon angioplasty. Can J Cardiol 1999;15(2):201-7.
500. McLeod AL, Northridge DB, Uren NG. Ultrasound guided stenting. Heart 2001;85(6):605-6.
501. McNamara DJ. Dietary cholesterol and atherosclerosis. Biochim Biophys Acta 2000;1529(1-3):310-20.
502. Mehilli J, Kastrati A, Dirschinger J, et al. Differences in prognostic factors and outcomes between women and men undergoing coronary artery stenting. Jama 2000;284(14):1799-805.
503. Mehta RH, Bates ER. Coronary stent implantation in acute myocardial infarction. Am Heart J 1999;137(4 Pt 1):603-11.
504. Mehta RH, Bossone E, Eagle KA. Current concepts in secondary prevention after acute myocardial infarction. Herz 2000;25(1):47-60.
505. Mehta SR, Eikelboom JW, Natarajan MK, et al. Impact of right ventricular involvement on mortality and morbidity in patients with inferior myocardial infarction. J Am Coll Cardiol 2001;37(1):37-43.
506. Mehta SR, Yusuf S. The Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) trial programme; rationale, design and baseline characteristics including a meta-analysis of the effects of thienopyridines in vascular disease. Eur Heart J 2000;21(24):2033-41.

507. Mehta SR, Yusuf S, Peters RJ, et al. Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study. Lancet 2001;358(9281):527-33.
508. Meilahn EN. Hemostatic factors and risk of cardiovascular disease in women. An overview. Arch Pathol Lab Med 1992;116(12):1313-7.
509. Meleady R, Graham I. Plasma homocysteine as a cardiovascular risk factor: causal, consequential, or of no consequence? Nutr Rev 1999;57(10):299-305.
510. Mendelson G, Aronow WS. Underutilization of measurement of serum low-density lipoprotein cholesterol levels and of lipid-lowering therapy in older patients with manifest atherosclerotic disease. J Am Geriatr Soc 1998;46(9):1128-31.
511. Merlo J, Ranstam J, Rastam L, et al. Age standardisation of drug utilisation: comparisons of different methods using cardiovascular drug data from Sweden and Spain. Eur J Clin Pharmacol 1994;46(5):393-8.
512. Messeri P, Workman S, Saunders C, et al. The application of meta-analysis in assessing racial differences in the effects of antihypertensive medication. J Natl Med Assoc 1997;89(7):477-85.
513. Messerli FH. Case-control study, meta-analysis, and bouillabaisse: putting the calcium antagonist scare into context. Ann Intern Med 1995;123(11):888-9.
514. Michels KB, Rosner BA, Manson JE, et al. Prospective study of calcium channel blocker use, cardiovascular disease, and total mortality among hypertensive women: the Nurses' Health Study. Circulation 1998;97(16):1540-8.
515. Michels KB, Yusuf S. Does PTCA in acute myocardial infarction affect mortality and reinfarction rates? A quantitative overview (meta-analysis) of the randomized clinical trials. Circulation 1995;91(2):476-85.
516. Midgette AS, O'Connor GT, Baron JA, et al. Effect of intravenous streptokinase on early mortality in patients with suspected acute myocardial infarction. A meta-analysis by anatomic location of infarction. Ann Intern Med 1990;113(12):961-8.
517. Midgette AS, Wong JB, Beshansky JR, et al. Cost-effectiveness of streptokinase for acute myocardial infarction: A combined meta-analysis and decision analysis of the effects of infarct location and of likelihood of infarction. Med Decis Making 1994;14(2):108-17.
518. Mieres JH, Udelson JE. Meta-analysis of exercise testing to detect coronary artery disease in women. Am J Cardiol 1999;84(12):1454-6.
519. Miettinen TA, Pyorala K, Olsson AG, et al. Cholesterol-lowering therapy in women and elderly patients with myocardial infarction or angina pectoris: findings from the Scandinavian Simvastatin Survival Study (4S). Circulation 1997;96(12):4211-8.
520. Millard PS, Sturrock WA. Heparin and thrombolysis in acute MI. J Fam Pract 1996;43(1):20-1.
521. Miller M, Byington R, Hunninghake D, et al. Sex bias and underutilization of lipid-lowering therapy in patients with coronary artery disease at academic medical centers in the United States and Canada. Prospective Randomized Evaluation of the Vascular Effects of Norvasc Trial (PREVENT) Investigators. Arch Intern Med 2000;160(3):343-7.
522. Miller TD, Roger VL, Hodge DO, et al. Gender differences and temporal trends in clinical characteristics, stress test results and use of invasive procedures in patients undergoing evaluation for coronary artery disease. J Am Coll Cardiol 2001;38(3):690-7.
523. Miller TD, Roger VL, Milavetz JJ, 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.
524. Milne R. HMG CO-A reductase inhibitor treatment in the prevention of coronary heart disease. Southampton: Wessex Institute for Health Research and Development; 1997. Report No.: DEC Report No. 72.
525. Moen EK, Asher CR, Miller DP, et al. Long-term follow-up of gender-specific outcomes after thrombolytic therapy for acute myocardial infarction from the GUSTO-I trial. Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries. J Womens Health 1997;6(3):285-93.
526. Montagne O, Vedel I, Durand-Zaleski I. Assessment of the impact of fibrates and diet on survival and their cost-effectiveness: evidence from randomized, controlled trials in coronary heart disease and health economic evaluations. Clin Ther 1999;21(11):2027-35.

527. Montague T, Tsuyuki R, Burton J, et al. Prevention and regression of coronary atherosclerosis. Is it safe and efficacious therapy? Chest 1994;105(3):718-26.
528. Moore RD, Pearson TA. Moderate alcohol consumption and coronary artery disease. A review. Medicine (Baltimore) 1986;65(4):242-67.
529. Morris JL, Cowan JC. Nitrates in myocardial infarction: a current perspective. Can J Cardiol 1995;11(Suppl B):5B-10B.
530. Morrison C, Woodward M, Leslie W, et al. Effect of socioeconomic group on incidence of, management of, and survival after myocardial infarction and coronary death: analysis of community coronary event register. Bmj 1997;314(7080):541-6.
531. Morrison LJ, Verbeek PR, McDonald AC, et al. Mortality and prehospital thrombolysis for acute myocardial infarction: A meta-analysis. Jama 2000;283(20):2686-92.
532. Moulds RF. Measurement of cost-effectiveness of drug therapy: a review of the treatment of hypertension. Med J Aust 1990;153(Suppl):S4-6.
533. Muldoon MF, Manuck SB, Mendelsohn AB, et al. Cholesterol reduction and non-illness mortality: meta-analysis of randomised clinical trials. Bmj 2001;322(7277):11-5.
534. Nallamothu BK, Saint S, Bielak LF, et al. Electron-beam computed tomography in the diagnosis of coronary artery disease: a meta-analysis. Arch Intern Med 2001;161(6):833-8.
535. Naylor CD, Ugnat AM, Weinkauf D, et al. Coronary artery bypass grafting in Canada: What is its rate of use? Which rate is right? Cmaj 1992;146(6):851-9.
536. Neal B, MacMahon S. An overview of 37 randomised trials of blood pressure lowering agents among 270,000 individuals. World Health Organization-International Society of Hypertension Blood Pressure Lowering Treatment Trialists' Collaboration. Clin Exp Hypertens 1999;21(5-6):517-29.
537. Neal B, MacMahon S, Chapman N. Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: results of prospectively designed overviews of randomised trials. Blood Pressure Lowering Treatment Trialists' Collaboration. Lancet 2000;356(9246):1955-64.
538. Nelson KM, Yeager BF. What is the role of angiotensin-converting enzyme inhibitors in congestive heart failure and after myocardial infarction? Ann Pharmacother 1996;30(9):986-93.
539. Nemergut C, Cheng JW. Use of direct thrombin inhibitors in acute coronary syndrome. Clin Ther 2000;22(8):937-48; discussion 898.
540. Newby K. Clinical outcomes according to time to treatment. Clin Cardiol 1997;20(11 Suppl 3):III11-5.
541. Nielsen WB, Vestbo J, Jensen GB. Isolated systolic hypertension as a major risk factor for stroke and myocardial infarction and an unexploited source of cardiovascular prevention: a prospective population-based study. J Hum Hypertens 1995;9(3):175-80.
542. Nilsson R. A qualitative and quantitative risk assessment of snuff dipping. Regul Toxicol Pharmacol 1998;28(1):1-16.
543. Njolstad I, Arnesen E, Lund-Larsen PG. Smoking, serum lipids, blood pressure, and sex differences in myocardial infarction. A 12-year follow-up of the Finnmark Study. Circulation 1996;93(3):450-6.
544. O'Connor GT, Buring JE, Yusuf S, et al. An overview of randomized trials of rehabilitation with exercise after myocardial infarction. Circulation 1989;80(2):234-44.
545. O'Connor GT, Morton JR, Diehl MJ, et al. Differences between men and women in hospital mortality associated with coronary artery bypass graft surgery. The Northern New England Cardiovascular Disease Study Group. Circulation 1993;88(5 Pt 1):2104-10.
546. O'Malley PG, Taylor AJ, Jackson JL, et al. Prognostic value of coronary electron-beam computed tomography for coronary heart disease events in asymptomatic populations. Am J Cardiol 2000;85(8):945-8.
547. O'Rourke RA, Brundage BH, Froelicher VF, et al. American College of Cardiology/American Heart Association Expert Consensus Document on electron-beam computed tomography for the diagnosis and prognosis of coronary artery disease. J Am Coll Cardiol 2000;36(1):326-40.
548. O'Shea EB. A study of the use of aspirin by general practitioners in suspected myocardial infarction. Ir Med J 2001;94(2):48-50, 52.
549. Okin PM, Kligfield P. Gender-specific criteria and performance of the exercise electrocardiogram. Circulation 1995;92(5):1209-16.

550. Olatidoye AG, Wu AH, Feng YJ, et al. Prognostic role of troponin T versus troponin I in unstable angina pectoris for cardiac events with meta-analysis comparing published studies. Am J Cardiol 1998;81(12):1405-10.
551. Oldridge NB, Guyatt GH, Fischer ME, et al. Cardiac rehabilitation after myocardial infarction. Combined experience of randomized clinical trials. Jama 1988;260(7):945-50.
552. Oler A, Whooley MA, Oler J, et al. 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.
553. Oliver MF. Cholesterol and coronary disease--outstanding questions. Cardiovasc Drugs Ther 1992;6(2):131-6.
554. Olsson G, Wikstrand J, Warnold I, et al. Metoprolol-induced reduction in postinfarction mortality: pooled results from five double-blind randomized trials. Eur Heart J 1992;13(1):28-32.
555. Omenn GS, Anderson KW, Kronmal RA, et al. The temporal pattern of reduction of mortality risk after smoking cessation. Am J Prev Med 1990;6(5):251-7.
556. Onder G, Gambassi G, Landi F, et al. Trends in antihypertensive drugs in the elderly: the decline of thiazides. J Hum Hypertens 2001;15(5):291-7.
557. Opie LH, Yusuf S, Kubler W. Current status of safety and efficacy of calcium channel blockers in cardiovascular diseases: a critical analysis based on 100 studies. Prog Cardiovasc Dis 2000;43(2):171-96.
558. Orchard TJ. The impact of gender and general risk factors on the occurrence of atherosclerotic vascular disease in non-insulin-dependent diabetes mellitus. Ann Med 1996;28(4):323-33.
559. Orlandini A, Tuero E, Paolasso E, et al. Usefulness of pharmacologic stress echocardiography in a chest pain center. Am J Cardiol 2000;86(11):1247-50, A6.
560. Ottani F, Galvani M, Nicolini FA, et al. Elevated cardiac troponin levels predict the risk of adverse outcome in patients with acute coronary syndromes. Am Heart J 2000;140(6):917-27.
561. Packer M, Bristow MR, Cohn JN, et al. The effect of carvedilol on morbidity and mortality in patients with chronic heart failure. U.S. Carvedilol Heart Failure Study Group. N Engl J Med 1996;334(21):1349-55.
562. Packer M, Coats AJ, Fowler MB, et al. Effect of carvedilol on survival in severe chronic heart failure. N Engl J Med 2001;344(22):1651-8.
563. Paganini-Hill A, Hsu G. Smoking and mortality among residents of a California retirement community. Am J Public Health 1994;84(6):992-5.
564. Pagley PR, Yarzebski J, Goldberg R, et al. Gender differences in the treatment of patients with acute myocardial infarction. A multihospital, community-based perspective. Arch Intern Med 1993;153(5):625-9.
565. Pahor M, Psaty BM, Alderman MH, et al. Health outcomes associated with calcium antagonists compared with other first-line antihypertensive therapies: a meta-analysis of randomised controlled trials. Lancet 2000;356(9246):1949-54.
566. Pahor M, Psaty BM, Alderman MH, et al. Therapeutic benefits of ACE inhibitors and other antihypertensive drugs in patients with type 2 diabetes. Diabetes Care 2000;23(7):888-92.
567. Pancholy SB, Fattah AA, Kamal AM, et al. Independent and incremental prognostic value of exercise thallium single-photon emission computed tomographic imaging in women. J Nucl Cardiol 1995;2(2 Pt 1):110-6.
568. Pearce KA, Furberg CD, Rushing J. Does antihypertensive treatment of the elderly prevent cardiovascular events or prolong life? A meta-analysis of hypertension treatment trials. Arch Fam Med 1995;4(11):943-9; discussion 950.
569. Pearson ML, Kahn KL, Harrison ER, et al. Differences in quality of care for hospitalized elderly men and women. Jama 1992;268(14):1883-9.
570. Pepine CJ, Faich G, Makuch R. Verapamil use in patients with cardiovascular disease: an overview of randomized trials. Clin Cardiol 1998;21(9):633-41.
571. Perlman JA, Wolf PH, Ray R, et al. Cardiovascular risk factors, premature heart disease, and all-cause mortality in a cohort of northern California women. Am J Obstet Gynecol 1988;158(6 Pt 2):1568-74.
572. Perreault S, Hamilton VH, Lavoie F, et al. A head-to-head comparison of the cost effectiveness of HMG-CoA reductase inhibitors and fibrates in different types of primary hyperlipidemia. Cardiovasc Drugs Ther 1997;10(6):787-94.
573. Peterson ED, Lansky AJ, Anstrom KJ, et al. Evolving trends in interventional device use and outcomes: results from the National Cardiovascular Network Database. Am Heart J 2000;139(2 Pt 1):198-207.

574. Peto R, Collins R, Gray R. Large-scale randomized evidence: large, simple trials and overviews of trials. Ann N Y Acad Sci 1993;703:314-40.
575. Petticrew M, McKee M, Jones J. Coronary artery surgery: are women discriminated against? Bmj 1993;306(6886):1164-6.
576. Pfeffer MA, Moye LA, Braunwald E, et al. Selection bias in the use of thrombolytic therapy in acute myocardial infarction. The SAVE Investigators. Jama 1991;266(4):528-32.
577. Pfisterer M, Cox JL, Granger CB, et al. Atenolol use and clinical outcomes after thrombolysis for acute myocardial infarction: the GUSTO-I experience. Global Utilization of Streptokinase and TPA (alteplase) for Occluded Coronary Arteries. J Am Coll Cardiol 1998;32(3):634-40.
578. Philbin EF, McCullough PA, DiSalvo TG, et al. Underuse of invasive procedures among Medicaid patients with acute myocardial infarction. Am J Public Health 2001;91(7):1082-8.
579. Pi-Sunyer FX. Comorbidities of overweight and obesity: current evidence and research issues. Med Sci Sports Exerc 1999;31(11 Suppl):S602-8.
580. Picano E, Bedetti G, Varga A, et al. The comparable diagnostic accuracies of dobutamine-stress and dipyridamole-stress echocardiographies: a meta-analysis. Coron Artery Dis 2000;11(2):151-9.
581. Pignone M, Phillips C, Mulrow C. Use of lipid lowering drugs for primary prevention of coronary heart disease: meta-analysis of randomised trials. Bmj 2000;321(7267):983-6.
582. Pilote L, Califf RM, Sapp S, et al. Regional variation across the United States in the management of acute myocardial infarction. GUSTO-1 Investigators. Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries. N Engl J Med 1995;333(9):565-72.
583. Pilote L, Granger C, Armstrong PW, et al. Differences in the treatment of myocardial infarction between the United States and Canada. A survey of physicians in the GUSTO trial. Med Care 1995;33(6):598-610.
584. Pocock SJ, Henderson RA, Rickards AF, et al. Meta-analysis of randomised trials comparing coronary angioplasty with bypass surgery. Lancet 1995;346(8984):1184-9.
585. Pocock SJ, McCormack V, Gueyffier F, et al. A score for predicting risk of death from cardiovascular disease in adults with raised blood pressure, based on individual patient data from randomised controlled trials. BMJ 2001;323(7304):75-81.
586. Podrid PJ. Proarrhythmia, a serious complication of antiarrhythmic drugs. Curr Cardiol Rep 1999;1(4):289-96.
587. Popma JJ, Chuang YC, Satler LF, et al. Primary coronary angioplasty in patients with acute myocardial infarction. Tex Heart Inst J 1994;21(2):148-57.
588. Popma JJ, Topol EJ. Adjuncts to thrombolysis for myocardial reperfusion. Ann Intern Med 1991;115(1):34-44.
589. Porsova-Dutoit I, Sulcova J, Starka L. Do DHEA/DHEAS play a protective role in coronary heart disease? Physiol Res 2000;49(Suppl 1):S43-56.
590. Port S, Demer L, Jennrich R, et al. Systolic blood pressure and mortality. Lancet 2000;355(9199):175-80.
591. Potts JL, Thomas J. Traditional coronary risk factors in African Americans. Am J Med Sci 1999;317(3):189-92.
592. Prescott E, Hippe M, Schnohr P, et al. Smoking and risk of myocardial infarction in women and men: longitudinal population study. BMJ 1998;316(7137):1043-7.
593. Pretre R, Turina MI. Analysis of trials of surgery vs angioplasty in myocardial revascularization. Semin Interv Cardiol 1999;4(4):235-43.
594. Primatesta P, Poulter NR. Lipid concentrations and the use of lipid lowering drugs: evidence from a national cross sectional survey. Bmj 2000;321(7272):1322-5.
595. Prosser LA, Stinnett AA, Goldman PA, et al. Cost-effectiveness of cholesterol-lowering therapies according to selected patient characteristics. Ann Intern Med 2000;132(10):769-79.
596. Psaty BM, Smith NL, Siscovick DS, et al. Health outcomes associated with antihypertensive therapies used as first-line agents. A systematic review and meta-analysis. Jama 1997;277(9):739-45.
597. Puletti M, Sunseri L, Curione M, et al. Acute myocardial infarction: sex-related differences in prognosis. Am Heart J 1984;108(1):63-6.
598. Quan A, Kerlikowske K, Gueyffier F, et al. Efficacy of treating hypertension in women. J Gen Intern Med 1999;14(12):718-29.
599. Quan A, Kerlikowske K, Gueyffier F, et al. Pharmacotherapy for hypertension in women of different races. Cochrane Database Syst Rev 2000(3):CD002146.

600. Quinn MJ, Plow EF, Topol EJ. Platelet glycoprotein IIb/IIIa inhibitors: recognition of a two-edged sword? Circulation 2002;106(3):379-85.
601. Raggi P. Coronary calcium on electron beam tomography imaging as a surrogate marker of coronary artery disease. Am J Cardiol 2001;87(4A):27A-34A.
602. Raine RA, Crayford TJ, Chan KL, et al. Gender differences in the treatment of patients with acute myocardial ischemia and infarction in England. Int J Technol Assess Health Care 1999;15(1):136-46.
603. Ramsey DJ, Goff DC, Wear ML, et al. Sex and ethnic differences in use of myocardial revascularization procedures in Mexican Americans and non-Hispanic whites: the Corpus Christi Heart Project. J Clin Epidemiol 1997;50(5):603-9.
604. Rao AV. Coronary heart disease risk factors in women: focus on gender differences. J La State Med Soc 1998;150(2):67-72.
605. Redberg RF, Rifai N, Gee L, et al. Lack of association of C-reactive protein and coronary calcium by electron beam computed tomography in postmenopausal women: implications for coronary artery disease screening. J Am Coll Cardiol 2000;36(1):39-43.
606. Rembold CM. Number-needed-to-treat analysis of the prevention of myocardial infarction and death by antidyslipidemic therapy. J Fam Pract 1996;42(6):577-86.
607. Rexrode KM, Carey VJ, Hennekens CH, et al. Abdominal adiposity and coronary heart disease in women. Jama 1998;280(21):1843-8.
608. Ridker PM. High-sensitivity C-reactive protein: potential adjunct for global risk assessment in the primary prevention of cardiovascular disease. Circulation 2001;103(13):1813-8.
609. Ridker PM, Buring JE, Shih J, et al. Prospective study of C-reactive protein and the risk of future cardiovascular events among apparently healthy women. Circulation 1998;98(8):731-3.
610. Ridker PM, Glynn RJ, Hennekens CH. C-reactive protein adds to the predictive value of total and HDL cholesterol in determining risk of first myocardial infarction. Circulation 1998;97(20):2007-11.
611. Ridker PM, Haughie P. Prospective studies of C-reactive protein as a risk factor for cardiovascular disease. J Investig Med 1998;46(8):391-5.
612. Ridker PM, Hennekens CH, Buring JE, et al. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. N Engl J Med 2000;342(12):836-43.
613. Ridker PM, Manson JE, Gaziano JM, et al. Low-dose aspirin therapy for chronic stable angina. A randomized, placebo-controlled clinical trial. Ann Intern Med 1991;114(10):835-9.
614. Ridker PM, O'Donnell C, Marder VJ, et al. Large-scale trials of thrombolytic therapy for acute myocardial infarction: GISSI-2, ISIS-3, and GUSTO-1. Ann Intern Med 1993;119(6):530-2.
615. Ridker PM, Rifai N, Pfeffer MA, et al. Long-term effects of pravastatin on plasma concentration of C-reactive protein. The Cholesterol and Recurrent Events (CARE) Investigators. Circulation 1999;100(3):230-5.
616. Rifai N, Ridker PM. High-sensitivity C-reactive protein: a novel and promising marker of coronary heart disease. Clin Chem 2001;47(3):403-11.
617. Rifkind BM. High-density lipoprotein cholesterol and coronary artery disease: survey of the evidence. Am J Cardiol 1990;66(6):3A-6A.
618. Rihal CS, Yusuf S. Chronic coronary artery disease: drugs, angioplasty, or surgery? Bmj 1996;312(7026):265-6.
619. Rill V, Brown DL. Practice of coronary angioplasty in California in 1995 : comparison to 1989 and impact of coronary stenting. Circulation 1999;99(21):e12.
620. Rivetti LA, Gandra SM. An intraluminal shunt for off-pump coronary artery bypass grafting. Report of 501 consecutive cases and review of the technique. Heart Surg Forum 1998;1(1):30-6.
621. Rochon PA, Clark JP, Binns MA, et al. Reporting of gender-related information in clinical trials of drug therapy for myocardial infarction. Cmaj 1998;159(4):321-7.
622. Rockhill B, Willett WC, Manson JE, et al. Physical activity and mortality: a prospective study among women. Am J Public Health 2001;91(4):578-83.
623. Roger VL, Farkouh ME, Weston SA, et al. Sex differences in evaluation and outcome of unstable angina. Jama 2000;283(5):646-52.
624. Roger VL, Pellikka PA, Bell MR, et al. Sex and test verification bias. Impact on the diagnostic value of exercise echocardiography. Circulation 1997;95(2):405-10.
625. Roig E, Castaner A, Simmons B, et al. In-hospital mortality rates from acute myocardial infarction by race in U.S. hospitals: findings from the National Hospital Discharge Survey. Circulation 1987;76(2):280-8.

626. Rojas-Fernandez CH, Kephart GC, Sketris IS, et al. Underuse of acetylsalicylic acid in individuals with myocardial infarction, ischemic heart disease or stroke: data from the 1995 population-based Nova Scotia Health Survey. Can J Cardiol 1999;15(3):291-6.
627. Rosamond WD, Shahar E, McGovern PG, et al. Trends in coronary thrombolytic therapy for acute myocardial infarction (the Minnesota Heart Survey Registry, 1990 to 1993). Am J Cardiol 1996;78(3):271-7.
628. Rosano GM, Panina G. Oestrogens and the heart. Therapie 1999;54(3):381-5.
629. Rosenberg L, Hennekens CH, Rosner B, et al. Early menopause and the risk of myocardial infarction. Am J Obstet Gynecol 1981;139(1):47-51.
630. Roux S, Christeller S, Ludin E. Effects of aspirin on coronary reocclusion and recurrent ischemia after thrombolysis: a meta-analysis. J Am Coll Cardiol 1992;19(3):671-7.
631. Rubins HB. Cholesterol in patients with coronary heart disease: how low should we go? J Gen Intern Med 1995;10(8):464-71.
632. Ruilope LM, Suarez C. How should we treat hypertensive women with cardiac and renal impairment? Am J Hypertens 1997;10(10 Pt 2):242S-246S.
633. Rumberger JA, Brundage BH, Rader DJ, et al. Electron beam computed tomographic coronary calcium scanning: a review and guidelines for use in asymptomatic persons. Mayo Clin Proc 1999;74(3):243-52.
634. Ryan TJ, Ryan TJ, Jr., Jacobs AK. Primary PTCA versus thrombolytic therapy: an evidence-based summary. Am Heart J 1999;138(2 Pt 2):S96-104.
635. Sacks FM. Lipid-lowering therapy in acute coronary syndromes. Jama 2001;285(13):1758-60.
636. Sacks FM, Pfeffer MA, Moye LA, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators. N Engl J Med 1996;335(14):1001-9.
637. Sacks HS, Chalmers TC, Berk AA, et al. Should mild hypertension be treated? An attempted meta-analysis of the clinical trials. Mt Sinai J Med 1985;52(4):265-70.
638. Sadowski ZP, Alexander JH, Skrabucha B, et al. Multicenter randomized trial and a systematic overview of lidocaine in acute myocardial infarction. Am Heart J 1999;137(5):792-8.
639. Safstrom K, Lindahl B, Swahn E. Risk stratification in unstable coronary artery disease--exercise test and troponin T from a gender perspective. FRISC-Study Group. Fragmin during InStability in Coronary artery disease. J Am Coll Cardiol 2000;35(7):1791-800.
640. Saha S, Stettin GD, Redberg RF. Gender and willingness to undergo invasive cardiac procedures. J Gen Intern Med 1999;14(2):122-5.
641. Salomaa V, Miettinen H, Niemela M, et al. Relation of socioeconomic position to the case fatality, prognosis and treatment of myocardial infarction events; the FINMONICA MI Register Study. J Epidemiol Community Health 2001;55(7):475-82.
642. Sane DC, Stump DC, Topol EJ, et al. Racial differences in responses to thrombolytic therapy with recombinant tissue-type plasminogen activator. Increased fibrin(ogen)olysis in blacks. The Thrombolysis and Angioplasty in Myocardial Infarction Study Group. Circulation 1991;83(1):170-5.
643. Sanmuganathan PS, Ghahramani P, Jackson PR, et al. Aspirin for primary prevention of coronary heart disease: safety and absolute benefit related to coronary risk derived from meta-analysis of randomised trials. Heart 2001;85(3):265-71.
644. Santana-Boado C, Candell-Riera J, Castell-Conesa J, et al. Diagnostic accuracy of technetium-99m-MIBI myocardial SPECT in women and men. J Nucl Med 1998;39(5):751-5.
645. Santiago P, Vacek JL, Rosamond TL. Dobutamine stress echocardiography: clinical utility and predictive value at various infusion rates. Am Heart J 1994;128(4):804-8.
646. Savoie I, Wright J, Bassett K. Lipid lowering therapy. Vancouver: BC Office of Health Technology Assessment, Centre for Health Services and Policy Research, University of British Columbia, Finnish Office for Health Care Technolog Assessment (FinOHTA); 1998. Report No.: 1896256112.
647. Schildkraut JM, Myers RH, Cupples LA, et al. Coronary risk associated with age and sex of parental heart disease in the Framingham Study. Am J Cardiol 1989;64(10):555-9.
648. Schneider EC, Leape LL, Weissman JS, et al. Racial differences in cardiac revascularization rates: does "overuse" explain higher rates among white patients? Ann Intern Med 2001;135(5):328-37.
649. Scott IA, Harden H, Coory M. What are appropriate rates of invasive procedures following acute myocardial infarction? A systematic review. Med J Aust 2001;174(3):130-6.

650. Selker HP, Zalenski RJ, Antman EM, 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.
651. Senior R, Soman P, Khattar RS, et al. Prognostic value of dobutamine stress echocardiography in patients undergoing diagnostic coronary arteriography. Am J Cardiol 1997;79(12):1610-4.
652. Serruys PW, Unger F, Sousa JE, et al. Comparison of coronary-artery bypass surgery and stenting for the treatment of multivessel disease. N Engl J Med 2001;344(15):1117-24.
653. Seymour RA, Steele JG. Is there a link between periodontal disease and coronary heart disease? Br Dent J 1998;184(1):33-8.
654. Shahar E, Folsom AR, Romm FJ, et al. Patterns of aspirin use in middle-aged adults: the Atherosclerosis Risk in Communities (ARIC) Study. Am Heart J 1996;131(5):915-22.
655. Shapira I, Fisman EZ, Drory Y, et al. Acute myocardial infarction in patients who have had coronary artery bypass surgery. South Med J 1997;90(11):1129-32.
656. Sharrett AR, Patsch W, Sorlie PD, et al. Associations of lipoprotein cholesterols, apolipoproteins A-I and B, and triglycerides with carotid atherosclerosis and coronary heart disease. The Atherosclerosis Risk in Communities (ARIC) Study. Arterioscler Thromb 1994;14(7):1098-104.
657. Shavelle DM, Budoff MJ, LaMont DH, et al. Exercise testing and electron beam computed tomography in the evaluation of coronary artery disease. J Am Coll Cardiol 2000;36(1):32-8.
658. Shaw LJ, Eagle KA, Gersh BJ, et al. Meta-analysis of intravenous dipyridamole-thallium-201 imaging (1985 to 1994) and dobutamine echocardiography (1991 to 1994) for risk stratification before vascular surgery. J Am Coll Cardiol 1996;27(4):787-98.
659. 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.
660. Shaw LJ, Miller DD, Romeis JC, et al. Gender differences in the noninvasive evaluation and management of patients with suspected coronary artery disease. Ann Intern Med 1994;120(7):559-66.
661. Shea S, Cook EF, Kannel WB, et al. Treatment of hypertension and its effect on cardiovascular risk factors: data from the Framingham Heart Study. Circulation 1985;71(1):22-30.
662. Shepherd J. New evidence, new guidelines. Atherosclerosis 1998;140(2):197-8.
663. Sherman SE, D'Agostino RB, Cobb JL, et al. Physical activity and mortality in women in the Framingham Heart Study. Am Heart J 1994;128(5):879-84.
664. Shibata MC, Flather MD, Wang D. Systematic review of the impact of beta blockers on mortality and hospital admissions in heart failure. Eur J Heart Fail 2001;3(3):351-7.
665. Shinton RA, Beevers DG. A meta-analysis of mortality and coronary prevention in hypertensive patients treated with beta-receptor blockers. J Hum Hypertens 1990;4(Suppl 2):31-4.
666. Silberberg JS, Henry DA. The benefits of reducing cholesterol levels: the need to distinguish primary from secondary prevention. 2. Implications for heart disease prevention in Australia. Med J Aust 1991;155(10):670-4.
667. Silberberg JS, Henry DA. The benefits of reducing cholesterol levels: the need to distinguish primary from secondary prevention. 1. A meta-analysis of cholesterol-lowering trials. Med J Aust 1991;155(10):665-6, 669-70.
668. Sim I, Gupta M, McDonald K, et al. A meta-analysis of randomized trials comparing coronary artery bypass grafting with percutaneous transluminal coronary angioplasty in multivessel coronary artery disease. Am J Cardiol 1995;76(14):1025-9.
669. Simes RJ. Low cholesterol and risk of non-coronary mortality. Aust N Z J Med 1994;24(1):113-9.
670. Simons-Morton DG, Calfas KJ, Oldenburg B, et al. Effects of interventions in health care settings on physical activity or cardiorespiratory fitness. Am J Prev Med 1998;15(4):413-30.
671. Sketris IS, Kephart GC, Hicks VA, et al. Prescribing patterns of antilipemic drugs and prevalence of hypercholesterolemia in the Nova Scotia population more than 65 years old. Ann Pharmacother 1995;29(6):576-81.
672. Smith BJ. Thrombolysis in acute myocardial infarction: analysis of studies comparing accelerated t-PA and streptokinase. J Accid Emerg Med 1999;16(6):407-11.
673. Smith GD, Song F, Sheldon TA. Cholesterol lowering and mortality: the importance of considering initial level of risk. Bmj 1993;306(6889):1367-73.
674. Solomon AJ, Gersh BJ. Management of chronic stable angina: medical therapy, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft surgery. Lessons from the randomized trials. Ann Intern Med 1998;128(3):216-23.

675. Soma MR, Baetta R, Crosignani P. The menopause and lipid metabolism: strategies for cardiovascular disease prevention. Curr Opin Lipidol 1997;8(4):229-35.
676. Soriano JB, Hoes AW, Meems L, et al. Increased survival with beta-blockers: importance of ancillary properties. Prog Cardiovasc Dis 1997;39(5):445-56.
677. Sorlie PD, Sharrett AR, Patsch W, et al. The relationship between lipids/lipoproteins and atherosclerosis in African Americans and whites: the Atherosclerosis Risk in Communities Study. Ann Epidemiol 1999;9(3):149-58.
678. Sowers KM, Sowers JR. Obesity, hypertension, and vas cular disease. Curr Hypertens Rep 1999;1(2):140-4.
679. Spinler SA, Cziraky MJ. Lipoprotein(A): physiologic function, association with atherosclerosis, and effects of lipid-lowering drug therapy. Ann Pharmacother 1994;28(3):343-51.
680. Spinler SA, Nawarskas JJ. Low-molecular-weight heparins for acute coronary syndromes. Ann Pharmacother 1998;32(1):103-10.
681. Spurgeon A, Harrington JM, Cooper CL. Health and safety problems associated with long working hours: a review of the current position. Occup Environ Med 1997;54(6):367-75.
682. Staessen JA, Fagard R, Thijs L, et al. Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. The Systolic Hypertension in Europe (Syst-Eur) Trial Investigators. Lancet 1997;350(9080):757-64.
683. Staessen JA, Gasowski J, Wang JG, et al. Risks of untreated and treated isolated systolic hypertension in the elderly: meta-analysis of outcome trials. Lancet 2000;355(9207):865-72.
684. Staessen JA, Ginocchio G, Wang JG, et al. Genetic variability in the renin-angiotensin system: prevalence of alleles and genotypes. J Cardiovasc Risk 1997;4(5-6):401-22.
685. Staessen JA, Kuznetsova T, Wang JG, et al. M235T angiotensinogen gene polymorphism and cardiovascular renal risk. J Hypertens 1999;17(1):9-17.
686. Staessen JA, Wang JG, Ginocchio G, et al. The deletion/insertion polymorphism of the angiotensin converting enzyme gene and cardiovascular-renal risk. J Hypertens 1997;15(12 Pt 2):1579-92.
687. Stampfer MJ, Colditz GA. Estrogen replacement therapy and coronary heart disease: a quantitative assessment of the epidemiologic evidence. Prev Med 1991;20(1):47-63.
688. Stampfer MJ, Colditz GA, Willett WC. Menopause and heart disease. A review. Ann N Y Acad Sci 1990;592:193-203; discussion 257-62.
689. Stason W, Schmid CH, Caubet JF, et al. Searching for signals: mortality and cardiovascular events in published randomized control trials of nifedipine in ischemic heart disease and hypertension. J Hypertens Suppl 1996;14(2):S5-7.
690. Stason WB, Schmid CH, Niedzwiecki D, et al. Safety of nifedipine in angina pectoris: a meta-analysis. Hypertension 1999;33(1):24-31.
691. Stason WB, Schmid CH, Niedzwiecki D, et al. Safety of nifedipine in patients with hypertension: a meta-analysis. Hypertension 1997;30(1 Pt 1):7-14.
692. Stefanick ML, Mackey S, Sheehan M, et al. Effects of diet and exercise in men and postmenopausal women with low levels of HDL cholesterol and high levels of LDL cholesterol. N Engl J Med 1998;339(1):12-20.
693. Steingart RM, Packer M, Hamm P, et al. Sex differences in the management of coronary artery disease. Survival and Ventricular Enlargement Investigators. N Engl J Med 1991;325(4):226-30.
694. Stephens MB. Is electron-beam computed tomography (EBCT) a reliable tool for predicting coronary outcomes in an asymptomatic population? J Fam Pract 2000;49(8):688.
695. Sterling TD, Rosenbaum WL, Weinkam JJ. Risk attribution and tobacco-related deaths. Am J Epidemiol 1993;138(2):128-39.
696. Stern MP, Haffner SM. Body fat dis tribution and hyperinsulinemia as risk factors for diabetes and cardiovascular disease. Arteriosclerosis 1986;6(2):123-30.
697. Stokes J, 3rd, Kannel WB, Wolf PA, et al. Blood pressure as a risk factor for cardiovascular disease. The Framingham Study--30 years of follow-up. Hypertension 1989;13(5 Suppl):I13-8.
698. Stone GW, Grines CL, Browne KF, et al. Comparison of in-hospital outcome in men versus women treated by either thrombolytic therapy or primary coronary angioplasty for acute myocardial infarction. Am J Cardiol 1995;75(15):987-92.
699. Stone PH, Thompson B, Anderson HV, et al. Influence of race, sex, and age on management of unstable angina and non-Q-wave myocardial infarction: The TIMI III registry. Jama 1996;275(14):1104-12.

700. Strandberg TE, Pitkanen A, Larjo P, et al. Attitude changes of general practitioners towards lowering LDL cholesterol. J Cardiovasc Risk 1998;5(1):43-6.
701. Strauss R, Pfeifer C, Muhlberger V, et al. Effects of morbidity, age, gender and region on percutaneous transluminal coronary angioplasty (PTCA) utilisation. Public Health 1999;113(2):79-87.
702. Stringer KA. The evolving role of platelet glycoprotein IIb/IIIa inhibitors in the management of acute coronary syndromes. Ann Pharmacother 1999;33(6):712-22.
703. Sudano JJ, Jr., Baker DW. Antihypertensive medication use in Hispanic adults: a comparison with black adults and white adults. Med Care 2001;39(6):575-87.
704. Sullivan AK, Holdright DR, Wright CA, et al. Chest pain in women: clinical, investigative, and prognostic features. Bmj 1994;308(6933):883-6.
705. Superko HR, Krauss RM. Coronary artery disease regression. Convincing evidence for the benefit of aggressive lipoprotein management. Circulation 1994;90(2):1056-69.
706. Swahn E. The care of patients with ischaemic heart disease from a gender perspective. Eur Heart J 1998;19(12):1758-65.
707. Sytkowski PA, Kannel WB, D'Agostino RB. Changes in risk factors and the decline in mortality from cardiovascular disease. The Framingham Heart Study. N Engl J Med 1990;322(23):1635-41.
708. Taggart DP. Angioplasty versus bypass surgery. Lancet 1996;347(8996):271-2; discussion 272-3.
709. Taillefer R, DePuey EG, Udelson JE, et al. Comparative diagnostic accuracy of Tl-201 and Tc-99m sestamibi SPECT imaging (perfusion and ECG-gated SPECT) in detecting coronary artery disease in women. J Am Coll Cardiol 1997;29(1):69-77.
710. Tavel ME. Specificity of electrocardiographic stress test in women versus men. Am J Cardiol 1992;70(4):545-7.
711. Tchernof A, Despres JP. Sex steroid hormones, sex hormone-binding globulin, and obesity in men and women. Horm Metab Res 2000;32(11-12):526-36.
712. Thadani U. Oral nitrates: more than symptomatic therapy in coronary artery disease? Cardiovasc Drugs Ther 1999;11(Suppl 1):213-8.
713. Thijs L, Fagard R, Lijnen P, et al. A meta-analysis of outcome trials in elderly hypertensives. J Hypertens 1992;10(10):1103-9.
714. Thompson D, Edelsberg J, Colditz GA, et al. Lifetime health and economic consequences of obesity. Arch Intern Med 1999;159(18):2177-83.
715. Tice JA, Ross E, Coxson PG, et al. Cost-effectiveness of vitamin therapy to lower plasma homocysteine levels for the prevention of coronary heart disease: effect of grain fortification and beyond. Jama 2001;286(8):936-43.
716. Tijssen JG. Low-dose and high-dose acetylsalicylic acid, with and without dipyridamole: a review of clinical trial results. Neurology 1998;51(3 Suppl 3):S15-6.
717. Tisdale JE. Antiplatelet therapy in coronary artery disease: review and update of efficacy studies. Am J Health Syst Pharm 1998;55(19 Suppl 1):S8-16.
718. Tobin JN, Wassertheil-Smoller S, Wexler JP, et al. Sex bias in considering coronary bypass surgery. Ann Intern Med 1987;107(1):19-25.
719. Tofler GH, Stone PH, Muller JE, et al. Effects of gender and race on prognosis after myocardial infarction: adverse prognosis for women, particularly black women. J Am Coll Cardiol 1987;9(3):473-82.
720. Toiber F, Murthy VS. Prescribing and usage patterns of two antihypertensive agents: a comparison of terazosin and enalapril. Hosp Formul 1991;26(10):811-3, 817-8.
721. Topol EJ. Coronary angioplasty for acute myocardial infarction. Ann Intern Med 1988;109(12):970-80.
722. Topol EJ. How should intravenous thrombolytic agents for acute myocardial infarction be selected? Cardiovasc Clin 1990;21(1):57-75; discussion 76-8.
723. Topol EJ. Treatment of acute myocardial infarction: in which patients should primary percutaneous transluminal coronary angioplasty be preferred to thrombolysis? Cardiologia 1996;41(9):843-7.
724. Topol EJ, Holmes DR, Rogers WJ. Coronary angiography after thrombolytic therapy for acute myocardial infarction. Ann Intern Med 1991;114(10):877-85.
725. Tsang TS, Barnes ME, Gersh BJ, et al. Risks of coronary heart disease in women: current understanding and evolving concepts. Mayo Clin Proc 2000;75(12):1289-303.

726. Tsuyuki RT, Teo KK, Ikuta RM, et al. Mortality risk and patterns of practice in 2,070 patients with acute myocardial infarction, 1987-92. Relative importance of age, sex, and medical therapy. Chest 1994;105(6):1687-92.
727. Tyroler HA. Serum lipoproteins as risk factors: recent epidemiologic studies in individuals with and without prevalent cardiovascular disease. Eur Heart J 1990;11(Suppl H):21-5.
728. Vaccarino V, Horwitz RI, Meehan TP, et al. Sex differences in mortality after myocardial infarction: evidence for a sex-age interaction. Arch Intern Med 1998;158(18):2054-62.
729. Vaccarino V, Krumholz HM, Berkman LF, et al. Sex differences in mortality after myocardial infarction. Is there evidence for an increased risk for women? Circulation 1995;91(6):1861-71.
730. Vaccarino V, Krumholz HM, Yarzebski J, et al. Sex differences in 2-year mortality after hospital discharge for myocardial infarction. Ann Intern Med 2001;134(3):173-81.
731. Vaccarino V, Parsons L, Every NR, et al. Impact of history of diabetes mellitus on hospital mortality in men and women with first acute myocardial infarction. The National Registry of Myocardial Infarction 2 Participants. Am J Cardiol 2000;85(12):1486-9; A7.
732. Vaitkus PT. Percutaneous transluminal coronary angioplasty versus thrombolysis in acute myocardial infarction: a meta-analysis. Clin Cardiol 1995;18(1):35-8.
733. van Campen LC, Visser FC, Visser CA. Ejection fraction improvement by beta-blocker treatment in patients with heart failure: an analysis of studies published in the literature. J Cardiovasc Pharmacol 1998;32(Suppl 1):S31-5.
734. Van de Werf F. Implications of the GUSTO trial for thrombolytic therapy. Drugs 1996;52(3):307-12.
735. Van de Werf F, Topol EJ, Lee KL, et al. Variations in patient management and outcomes for acute myocardial infarction in the United States and other countries. Results from the GUSTO trial. Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries. Jama 1995;273(20):1586-91.
736. van der Schouw YT, van der Graaf Y, Steyerberg EW, et al. Age at menopause as a risk factor for cardiovascular mortality. Lancet 1996;347(9003):714-8.
737. van der Weijden T, Knottnerus JA, Ament AJ, et al. Economic evaluation of cholesterol-related interventions in general practice. An appraisal of the evidence. J Epidemiol Community Health 1998;52(9):586-94.
738. Van Train KF, Maddahi J, Berman DS, et al. Quantitative analysis of tomographic stress thallium-201 myocardial scintigrams: a multicenter trial. J Nucl Med 1990;31(7):1168-79.
739. Vidt DG, Pohl MA. Aggressive blood pressure lowering is safe, but benefit is still hard to prove. Cleve Clin J Med 1999;66(2):105-11.
740. Vorchheimer DA, Badimon JJ, Fuster V. Platelet glycoprotein IIb/IIIa receptor antagonists in cardiovascular disease. Jama 1999;281(15):1407-14.
741. Wallenius S, Peura S, Klaukka T, et al. Who is using antihypertensive drugs? A prescription analysis from Finland. Scand J Prim Health Care 1996;14(1):54-61.
742. Walsh CR, Lloyd-Jones DM, Camargo CA, Jr., et al. Clinical trials of unfractionated heparin and low-molecular-weight heparin in addition to aspirin for the treatment of unstable angina pectoris: do the results apply to all patients? Am J Cardiol 2000;86(9):908-12.
743. Walsh JM, Grady D. Treatment of hyperlipidemia in women. Jama 1995;274(14):1152-8.
744. Wang JG, Staessen JA, Gong L, et al. Chinese trial on isolated systolic hypertension in the elderly. Systolic Hypertension in China (Syst-China) Collaborative Group. Arch Intern Med 2000;160(2):211-20.
745. Waters D. Calcium channel blockers: an evidence-based review. Can J Cardiol 1997;13(8):757-66.
746. Weaver WD, Simes RJ, Betriu A, et al. Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review. Jama 1997;278(23):2093-8.
747. Weaver WD, White HD, Wilcox RG, et al. Comparisons of characteristics and outcomes among women and men with acute myocardial infarction treated with thrombolytic therapy. GUSTO-I investigators. Jama 1996;275(10):777-82.
748. Weber MM. Surgical management of unstable angina and symptomatic coronary artery disease. J Cardiovasc Nurs 2000;15(1):27-42.
749. Weintraub WS, Wenger NK, Jones EL, et al. Changing clinical characteristics of coronary surgery patients. Differences between men and women. Circulation 1993;88(5 Pt 2):II79-86.

750. Weintraub WS, Wenger NK, Kosinski AS, et al. Percutaneous transluminal coronary angioplasty in women compared with men. J Am Coll Cardiol 1994;24(1):81-90.
751. Welty FK, Mittleman MA, Healy RW, et al. Similar results of percutaneous transluminal coronary angioplasty for women and men with postmyocardial infarction ischemia. J Am Coll Cardiol 1994;23(1):35-9.
752. Wenger NK, Speroff L, Packard B. Cardiovascular health and disease in women. N Engl J Med 1993;329(4):247-56.
753. Wexler L, Brundage B, Crouse J, et al. Coronary artery calcification: pathophysiology, epidemiology, imaging methods, and clinical implications. A statement for health professionals from the American Heart Association. Writing Group. Circulation 1996;94(5):1175-92.
754. White AD, Rosamond WD, Chambless LE, et al. Sex and race differences in short-term prognosis after acute coronary heart disease events: the Atherosclerosis Risk In Communities (ARIC) study. Am Heart J 1999;138(3 Pt 1):540-8.
755. White CW. Benefit of aggressive lipid-lowering therapy: insights from the post coronary artery bypass graft study and other trials. Am J Med 1998;105(1A):63S-68S.
756. White HD, Barbash GI, Califf RM, et al. Age and outcome with contemporary thrombolytic therapy. Results from the GUSTO-I trial. Global Utilization of Streptokinase and TPA for Occluded coronary arteries trial. Circulation 1996;94(8):1826-33.
757. Wikstrand J, Berglund G, Tuomilehto J. Beta-blockade in the primary prevention of coronary heart disease in hypertensive patients. Review of present evidence. Circulation 1991;84(6 Suppl):VI93-100.
758. Wilkinson P, Laji K, Ranjadayalan K, et al. Acute myocardial infarction in women: survival analysis in first six months. Bmj 1994;309(6954):566-9.
759. Willett WC, Green A, Stampfer MJ, et al. Relative and absolute excess risks of coronary heart disease among women who smoke cigarettes. N Engl J Med 1987;317(21):1303-9.
760. Willett WC, Manson JE, Stampfer MJ, et al. Weight, weight change, and coronary heart disease in women. Risk within the 'normal' weight range. Jama 1995;273(6):461-5.
761. Williams JE, Massing M, Rosamond WD, et al. Racial disparities in CHD mortality from 1968-1992 in the state economic areas surrounding the ARIC study communities. Atherosclerosis Risk in Communities. Ann Epidemiol 1999;9(8):472-80.
762. Williams PT. Physical fitness and activity as separate heart disease risk factors: a meta-analysis. Med Sci Sports Exerc 2001;33(5):754-61.
763. 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.
764. Wilson K, Gibson N, Willan A, et al. Effect of smoking cessation on mortality after myocardial infarction: meta-analysis of cohort studies. Arch Intern Med 2000;160(7):939-44.
765. Wilson PW, Abbott RD, Castelli WP. High density lipoprotein cholesterol and mortality. The Framingham Heart Study. Arteriosclerosis 1988;8(6):737-41.
766. Wong JB, Sonnenberg FA, Salem DN, et al. Myocardial revascularization for chronic stable angina. Analysis of the role of percutaneous transluminal coronary angioplasty based on data available in 1989. Ann Intern Med 1990;113(11):852-71.
767. Wong ND, Wilson PW, Kannel WB. Serum cholesterol as a prognostic factor after myocardial infarction: the Framingham Study. Ann Intern Med 1991;115(9):687-93.
768. Woodfield SL, Lundergan CF, Reiner JS, et al. Gender and acute myocardial infarction: is there a different response to thrombolysis? J Am Coll Cardiol 1997;29(1):35-42.
769. Wooster MB, Luzier AB. Reteplase: a new thrombolytic for the treatment of acute myocardial infarction. Ann Pharmacother 1999;33(3):318-24.
770. Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women. Principal results from the Women's Health Initiative randomized controlled trial. JAMA 2002;288:321-33.
771. Wu AH, Lane PL. Metaanalysis in clinical chemistry: validation of cardiac troponin T as a marker for ischemic heart diseases. Clin Chem 1995;41(8 Pt 2):1228-33.
772. Yapp CK, Taylor LS, Ow CY, et al. Hypertension management: a comparison of urban versus rural general practitioners in Western Australia. Clin Exp Pharmacol Physiol 1995;22(6-7):447-9.
773. Yarzebski J, Col N, Pagley P, et al. Gender differences and factors associated with the receipt of thrombolytic therapy in patients with acute myocardial infarction: a community-wide perspective. Am Heart J 1996;131(1):43-50.

774. Yudkin JS, Chaturvedi N. Developing risk stratification charts for diabetic and nondiabetic subjects. Diabet Med 1999;16(3):219-27.
775. Yusuf S. Interventions that potentially limit myocardial infarct size: overview of clinical trials. Am J Cardiol 1987;60(2):11A-17A.
776. Yusuf S. Calcium antagonists in coronary artery disease and hypertension. Time for reevaluation? Circulation 1995;92(5):1079-82.
777. Yusuf S, Anand S, Avezum A, Jr., et al. Treatment for acute myocardial infarction. Overview of randomized clinical trials. Eur Heart J 1996;17(Suppl F):16-29.
778. Yusuf S, Collins R, Peto R, et al. Intravenous and intracoronary fibrinolytic therapy in acute myocardial infarction: overview of results on mortality, reinfarction and side-effects from 33 randomized controlled trials. Eur Heart J 1985;6(7):556-85.
779. Yusuf S, Pogue J. Primary angioplasty compared with thrombolytic therapy for acute myocardial infarction. Jama 1997;278(23):2110-1.
780. Yusuf S, Sleight P, Pogue J, et al. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. N Engl J Med 2000;342(3):145-53.
781. Yusuf S, Zhao F, Mehta SR, et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. N Engl J Med 2001;345(7):494-502.
782. Yusuf S, Zucker D, Peduzzi P, et al. Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. Lancet 1994;344(8922):563-70.
783. Zahn R, Schiele R, Schneider S, et al. Decreasing hospital mortality between 1994 and 1998 in patients with acute myocardial infarction treated with primary angioplasty but not in patients treated with intravenous thrombolysis. Results from the pooled data of the Maximal Individual Therapy in Acute Myocardial Infarction (MITRA) Registry and the Myocardial Infarction Registry (MIR). J Am Coll Cardiol 2000;36(7):2064-71.
784. Zarembski DG, Nolan PE, Jr., Slack MK, et al. Meta-analysis of the use of low-dose beta-adrenergic blocking therapy in idiopathic or ischemic dilated cardiomyopathy. Am J Cardiol 1996;77(14):1247-50.
785. Zusman RM, Chesebro JH, Comerota A, et al. Antiplatelet therapy in the prevention of ischemic vascular events: literature review and evidence-based guidelines for drug selection. Clin Cardiol 1999;22(9):559-73.

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.

Gibbons RJ, Balady GJ, Beasley JW, Bricker JT, Duvernoy WF, Froelicher VF, et al. ACC/AHA guidelines for exercise testing: executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Exercise Testing). Circulation 1997;96(1):345-54.

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.

Lee TH, Boucher CA. Clinical practice. Noninvasive tests in patients with stable coronary artery disease. N Engl J Med 2001;344(24):1840-5.

Mark DB, Shaw L, Harrell FE, Jr., Hlatky MA, Lee KL, Bengtson JR, et al. Prognostic value of a treadmill exercise score in outpatients with suspected coronary artery disease. N Engl J Med 1991;325(12):849-53.

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.

Okin PM, Kligfield P. Gender-specific criteria and performance of the exercise electrocardiogram. Circulation 1995;92(5):1209-16.

Safstrom K, Lindahl B, Swahn E. Risk stratification in unstable coronary artery disease--exercise test and troponin T from a gender perspective. FRISC-Study Group. Fragmin during InStability in Coronary artery disease. J Am Coll Cardiol 2000;35(7):1791-800.

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)

Arruda-Olson AM, Juracan EM, Mahoney DW, McCully RB, Roger VL, Pellikka PA. Prognostic value of exercise echocardiography in 5,798 patients: is there a gender difference? J Am Coll Cardiol 2002;39(4):625-31.

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.

Diaz LA, Brunken RC, Blackstone EH, Snader CE, Lauer MS. Independent contribution of myocardial perfusion defects to exercise capacity and heart rate recovery for prediction of all-cause mortality in patients with known or suspected coronary heart disease. J Am Coll Cardiol 2001;37(6):1558-64.

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.

Hachamovitch R, Berman DS, Kiat H, Bairey CN, Cohen I, Cabico A, et al. Effective risk stratification using exercise myocardial perfusion SPECT in women: gender-related differences in prognostic nuclear testing. J Am Coll Cardiol 1996;28(1):34-44.

Hachamovitch R, Berman DS, Kiat H, Cohen I, Friedman JD, Shaw LJ. Value of stress myocardial perfusion single photon emission computed tomography in patients with normal resting electrocardiograms: an evaluation of incremental prognostic value and cost-effectiveness. Circulation 2002;105(7):823-9.

Hunink MG, Kuntz KM, Fleischmann KE, Brady TJ. Noninvasive imaging for the diagnosis of coronary artery disease: focusing the development of new diagnostic technology. Ann Intern Med 1999;131(9):673-80.

Ioannidis JP, Salem D, Chew PW, Lau J. Accuracy of imaging technologies in the diagnosis of acute cardiac ischemia in the emergency department: a meta-analysis. Ann Emerg Med 2001;37(5):471-7.

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.

Marine JE, Freedberg KA, Davidoff R. Cost-effectiveness of stress-echocardiography. Cardiol Clin 1999;17(3):583-95, x.

Marwick TH, Shaw LJ, Lauer MS, Kesler K, Hachamovitch R, Heller GV, et al. The noninvasive prediction of cardiac mortality in men and women with known or suspected coronary artery disease. Economics of Noninvasive Diagnosis (END) Study Group. Am J Med 1999;106(2):172-8.

Mieres JH, Udelson JE. Meta-analysis of exercise testing to detect coronary artery disease in women. Am J Cardiol 1999;84(12):1454-6.

Pancholy SB, Fattah AA, Kamal AM, Ghods M, Heo J, Iskandrian AS. Independent and incremental prognostic value of exercise thallium single-photon emission computed tomographic imaging in women. J Nucl Cardiol 1995;2(2 Pt 1):110-6.

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

Picano E, Bedetti G, Varga A, Cseh E. The comparable diagnostic accuracies of dobutamine-stress and dipyridamole-stress echocardiographies: a meta-analysis. Coron Artery Dis 2000;11(2):151-9.

Santana-Boado C, Candell-Riera J, Castell-Conesa J, Aguade-Bruix S, Garcia-Burillo A, Canela T, et al. Diagnostic accuracy of technetium-99m-MIBI myocardial SPECT in women and men. J Nucl Med 1998;39(5):751-5.

Senior R, Soman P, Khattar RS, Lahiri A. Prognostic value of dobutamine stress echocardiography in patients undergoing diagnostic coronary arteriography. Am J Cardiol 1997;79(12):1610-4.

Shaw LJ, Eagle KA, Gersh BJ, Miller DD. Meta-analysis of intravenous dipyridamole-thallium-201 imaging (1985 to 1994) and dobutamine echocardiography (1991 to 1994) for risk stratification before vascular surgery. J Am Coll Cardiol 1996;27(4):787-98.

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.

Tavel ME. Specificity of electrocardiographic stress test in women versus men. Am J Cardiol 1992;70(4):545-7.

1.03 Coronary artery calcification score

Amanullah AM, Kiat H, Friedman JD, Berman DS. Adenosine technetium-99m sestamibi myocardial perfusion SPECT in women: diagnostic efficacy in detection of coronary artery disease. J Am Coll Cardiol 1996;27(4):803-9.

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.

Budoff MJ, Shokooh S, Shavelle RM, Kim HT, French WJ. Electron beam tomography and angiography: sex differences. Am Heart J 2002;143(5):877-82.

Detrano R, Hsiai T, Wang S, Puentes G, Fallavollita J, Shields P, et al. Prognostic value of coronary calcification and angiographic stenoses in patients undergoing coronary angiography. J Am Coll Cardiol 1996;27(2):285-90.

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.

Fiorino AS. Electron-beam computed tomography, coronary artery calcium, and evaluation of patients with coronary artery disease. Ann Intern Med 1998;128(10):839-47.

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)

Hunink MG, Kuntz KM, Fleischmann KE, Brady TJ. Noninvasive imaging for the diagnosis of coronary artery disease: focusing the development of new diagnostic technology. Ann Intern Med 1999;131(9):673-80.

Keelan PC, Bielak LF, Ashai K, Jamjoum LS, Denktas AE, Rumberger JA, et al. Long-term prognostic value of coronary calcification detected by electron-beam computed tomography in patients undergoing coronary angiography. Circulation 2001;104(4):412-7.

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.

Nallamothu BK, Saint S, Bielak LF, Sonnad SS, Peyser PA, Rubenfire M, et al. Electron-beam computed tomography in the diagnosis of coronary artery disease: a meta-analysis. Arch Intern Med 2001;161(6):833-8.

O'Malley PG, Taylor AJ, Jackson JL, Doherty TM, Detrano RC. Prognostic value of coronary electron-beam computed tomography for coronary heart disease events in asymptomatic populations. Am J Cardiol 2000;85(8):945-8.

O'Rourke RA, Brundage BH, Froelicher VF, Greenland P, Grundy SM, Hachamovitch R, et al. American College of Cardiology/American Heart Association Expert Consensus Document on electron-beam computed tomography for the diagnosis and prognosis of coronary artery disease. J Am Coll Cardiol 2000;36(1):326-40.

Raggi P. Coronary calcium on electron beam tomography imaging as a surrogate marker of coronary artery disease. Am J Cardiol 2001;87(4A):27A-34A.

Rumberger JA, Brundage BH, Rader DJ, Kondos G. Electron beam computed tomographic coronary calcium scanning: a review and guidelines for use in asymptomatic persons. Mayo Clin Proc 1999;74(3):243-52.

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.

Stephens MB. Is electron-beam computed tomography (EBCT) a reliable tool for predicting coronary outcomes in an asymptomatic population? J Fam Pract 2000;49(8):688.

Van Train KF, Maddahi J, Berman DS, Kiat H, Areeda J, Prigent F, et al. Quantitative analysis of tomographic stress thallium-201 myocardial scintigrams: a multicenter trial. J Nucl Med 1990;31(7):1168-79.

Wexler L, Brundage B, Crouse J, Detrano R, Fuster V, Maddahi J, et al. Coronary artery calcification: pathophysiology, epidemiology, imaging methods, and clinical implications. A statement for health professionals from the American Heart Association. Writing Group. Circulation 1996;94(5):1175-92.

2.01 Aspirin

Collaborative overview of randomised trials of antiplatelet therapy--III: Reduction in venous thrombosis and pulmonary embolism by antiplatelet prophylaxis among surgical and medical patients. Antiplatelet Trialists' Collaboration. BMJ 1994;308(6923):235-46.

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

Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Lancet 1994;343(8893):311-22.

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.

Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Lancet 1988;2(8607):349-60.

Anand SS, Yusuf S. Oral anticoagulant therapy in patients with coronary artery disease: a meta-analysis. JAMA 1999;282(21):2058-67.

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

Capewell S, Morrison CE, McMurray JJ. Contribution of modern cardiovascular treatment and risk factor changes to the decline in coronary heart disease mortality in Scotland between 1975 and 1994. Heart 1999;81(4):380-6.

Collins R, MacMahon S, Flather M, Baigent C, Remvig L, Mortensen S, et al. Clinical effects of anticoagulant therapy in suspected acute myocardial infarction: systematic overview of randomised trials. BMJ 1996;313(7058):652-9.

D'Agostino RB, Cobb JL, Wolf PA, Wilson PW. Aspirin use and cardiovascular disease in women. JAMA 1992;267(3):364-5.

de Gaetano G. Low-dose aspirin and vitamin E in people at cardiovascular risk: a randomised trial in general practice. Collaborative Group of the Primary Prevention Project. Lancet 2001;357(9250):89-95.

Dippel DW. The results of CAPRIE, IST and CAST. Clopidogrel vs. Aspirin in Patients at Risk of Ischaemic Events. International Stroke Trial. Chinese Acute Stroke Trial. Thromb Res 1998;92(1 Suppl 1):S13-6.

Hankey GJ, Sudlow CL, Dunbabin DW. Thienopyridine derivatives (ticlopidine, clopidogrel) versus aspirin for preventing stroke and other serious vascular events in high vascular risk patients. Cochrane Database Syst Rev 2000(2):CD001246.

Hansson L, Zanchetti A, Carruthers SG, Dahlof B, Elmfeldt D, Julius S, et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. Lancet 1998;351(9118):1755-62.

Hart RG, Halperin JL, McBride R, Benavente O, Man-Son-Hing M, Kronmal RA. Aspirin for the primary prevention of stroke and other major vascular events: meta-analysis and hypotheses. Arch Neurol 2000;57(3):326-32.

Hebert PR, Hennekens CH. An overview of the 4 randomized trials of aspirin therapy in the primary prevention of vascular disease. Arch Intern Med 2000;160(20):3123-7.

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

Heidenreich PA, McClellan M. Trends in treatment and outcomes for acute myocardial infarction: 1975-1995. Am J Med 2001;110(3):165-74.

Kjeldsen SE, Kolloch RE, Leonetti G, Mallion JM, Zanchetti A, Elmfeldt D, et al. Influence of gender and age on preventing cardiovascular disease by antihypertensive treatment and acetylsalicylic acid. The HOT study. Hypertension Optimal Treatment. J Hypertens 2000;18(5):629-42.

Latini R, Tognoni G, Maggioni AP, Baigent C, Braunwald E, Chen ZM, et al. Clinical effects of early angiotensin-converting enzyme inhibitor treatment for acute myocardial infarction are similar in the presence and absence of aspirin: systematic overview of individual data from 96,712 randomized patients. Angiotensin-converting Enzyme Inhibitor Myocardial Infarction Collaborative Group. J Am Coll Cardiol 2000;35(7):1801-7.

Loewen P, Sunderji R, Gin K. The efficacy and safety of combination warfarin and ASA therapy: a systematic review of the literature and update of guidelines. Can J Cardiol 1998;14(5):717-26.

MacMahon S, Sharpe N. Long-term antiplatelet therapy for the prevention of vascular disease. Med J Aust 1991;154(7):477-80.

Manson JE, Stampfer MJ, Colditz GA, Willett WC, Rosner B, Speizer FE, et al. A prospective study of aspirin use and primary prevention of cardiovascular disease in women. JAMA 1991;266(4):521-7.

Manson JE, Tosteson H, Ridker PM, Satterfield S, Hebert P, O'Connor GT, et al. The primary prevention of myocardial infarction. N Engl J Med 1992;326(21):1406-16.

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.

Peto R, Collins R, Gray R. Large-scale randomized evidence: large, simple trials and overviews of trials. Ann N Y Acad Sci 1993;703:314-40.

Popma JJ, Topol EJ. Adjuncts to thrombolysis for myocardial reperfusion. Ann Intern Med 1991;115(1):34-44.

Rembold CM. Number-needed-to-treat analysis of the prevention of myocardial infarction and death by antidyslipidemic therapy. J Fam Pract 1996;42(6):577-86.

Ridker PM, Manson JE, Gaziano JM, Buring JE, Hennekens CH. Low-dose aspirin therapy for chronic stable angina. A randomized, placebo-controlled clinical trial. Ann Intern Med 1991;114(10):835-9.

Sanmuganathan PS, Ghahramani P, Jackson PR, Wallis EJ, Ramsay LE. Aspirin for primary prevention of coronary heart disease: safety and absolute benefit related to coronary risk derived from meta-analysis of randomised trials. Heart 2001;85(3):265-71.

Tijssen JG. Low-dose and high-dose acetylsalicylic acid, with and without dipyridamole: a review of clinical trial results. Neurology 1998;51(3 Suppl 3):S15-6.

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

Zusman RM, Chesebro JH, Comerota A, Hartmann JR, Massin EK, Raps E, et al. Antiplatelet therapy in the prevention of ischemic vascular events: literature review and evidence-based guidelines for drug selection. Clin Cardiol 1999;22(9):559-73.

2.02 Beta-blockers

The Beta-Blocker Pooling Project (BBPP): subgroup findings from randomized trials in post infarction patients. The Beta-Blocker Pooling Project Research Group. Eur Heart J 1988;9(1):8-16.

Aronow WS. Management of older persons after myocardial infarction. J Am Geriatr Soc 1998;46(11):1459-68.

Avezum A, Tsuyuki RT, Pogue J, Yusuf S. Beta-blocker therapy for congestive heart failure: a systemic overview and critical appraisal of the published trials. Can J Cardiol 1998;14(8):1045-53.

Blazing MA, O'Connor CM. Evidence supporting secondary prevention strategies. Curr Opin Cardiol 1999;14(4):303-9.

Bonet S, Agusti A, Arnau JM, Vidal X, Diogene E, Galve E, et al. Beta-adrenergic blocking agents in heart failure: benefits of vasodilating and non-vasodilating agents according to patients' characteristics: a meta-analysis of clinical trials. Arch Intern Med 2000;160(5):621-7.

Brophy JM, Joseph L, Rouleau JL. Beta-blockers in congestive heart failure. A Bayesian meta-analysis. Ann Intern Med 2001;134(7):550-60.

Cleland JG, Bristow MR, Erdmann E, Remme WJ, Swedberg K, Waagstein F. Beta-blocking agents in heart failure. Should they be used and how? Eur Heart J 1996;17(11):1629-39.

Conti CR. Clinical decision making using cumulative meta-analysis. Clin Cardiol 1993;16(3):167-8.

Doughty RN, Rodgers A, Sharpe N, MacMahon S. Effects of beta-blocker therapy on mortality in patients with heart failure. A systematic overview of randomized controlled trials. Eur Heart J 1997;18(4):560-5.

Freemantle N, Cleland J, Young P, Mason J, Harrison J. beta Blockade after myocardial infarction: systematic review and meta regression analysis. BMJ 1999;318(7200):1730-7.

Ghali JK, Pina IL, Gottlieb SS, Deedwania PC, Wikstrand JC. Metoprolol CR/XL in female patients with heart failure: analysis of the experience in Metoprolol Extended-Release Randomized Intervention Trial in Heart Failure (MERIT-HF). Circulation 2002;105(13):1585-91.

Gueyffier F, Boutitie F, Boissel JP, Pocock S, Coope J, Cutler J, et al. Effect of antihypertensive drug treatment on cardiovascular outcomes in women and men. A meta-analysis of individual patient data from randomized, controlled trials. The INDANA Investigators. Ann Intern Med 1997;126(10):761-7.

Heidenreich PA, McClellan M. Trends in treatment and outcomes for acute myocardial infarction: 1975-1995. Am J Med 2001;110(3):165-74.

Heidenreich PA, McDonald KM, Hastie T, Fadel B, Hagan V, Lee BK, et al. Meta-analysis of trials comparing beta-blockers, calcium antagonists, and nitrates for stable angina. JAMA 1999;281(20):1927-36.

Heidenreich PA, Lee TT, Massie BM. Effect of beta-blockade on mortality in patients with heart failure: a meta-analysis of randomized clinical trials. J Am Coll Cardiol 1997;30(1):27-34.

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

Houghton T, Freemantle N, Cleland JG. Are beta-blockers effective in patients who develop heart failure soon after myocardial infarction? A meta-regression analysis of randomised trials. Eur J Heart Fail 2000;2(3):333-40.

Lechat P, Packer M, Chalon S, Cucherat M, Arab T, Boissel JP. Clinical effects of beta-adrenergic blockade in chronic heart failure: a meta-analysis of double-blind, placebo-controlled, randomized trials. Circulation 1998;98(12):1184-91.

Lee S, Spencer A. Beta-blockers to reduce mortality in patients with systolic dysfunction: a meta-analysis. J Fam Pract 2001;50(6):499-504.

Leizorovicz A, Lechat P, Cucherat M, Bugnard F. Bisoprolol for the treatment of chronic heart failure: a meta-analysis on individual data of two placebo-controlled studies--CIBIS and CIBIS II. Cardiac Insufficiency Bisoprolol Study. Am Heart J 2002;143(2):301-7.

Olsson G, Wikstrand J, Warnold I, Manger Cats V, McBoyle D, Herlitz J, et al. Metoprolol-induced reduction in postinfarction mortality: pooled results from five double-blind randomized trials. Eur Heart J 1992;13(1):28-32.

Packer M, Coats AJ, Fowler MB, Katus HA, Krum H, Mohacsi P, et al. Effect of carvedilol on survival in severe chronic heart failure. N Engl J Med 2001;344(22):1651-8.

Pahor M, Psaty BM, Alderman MH, Applegate WB, Williamson JD, Cavazzini C, et al. Health outcomes associated with calcium antagonists compared with other first-line antihypertensive therapies: a meta-analysis of randomised controlled trials. Lancet 2000;356(9246):1949-54.

Popma JJ, Topol EJ. Adjuncts to thrombolysis for myocardial reperfusion. Ann Intern Med 1991;115(1):34-44.

Psaty BM, Smith NL, Siscovick DS, Koepsell TD, Weiss NS, Heckbert SR, et al. Health outcomes associated with antihypertensive therapies used as first-line agents. A systematic review and meta-analysis. JAMA 1997;277(9):739-45.

Ruilope LM, Suarez C. How should we treat hypertensive women with cardiac and renal impairment? Am J Hypertens 1997;10(10 Pt 2):242S-246S.

Shibata MC, Flather MD, Wang D. Systematic review of the impact of beta blockers on mortality and hospital admissions in heart failure. Eur J Heart Fail 2001;3(3):351-7.

Shinton RA, Beevers DG. A meta-analysis of mortality and coronary prevention in hypertensive patients treated with beta-receptor blockers. J Hum Hypertens 1990;4(Suppl 2):31-4.

Soriano JB, Hoes AW, Meems L, Grobbee DE. Increased survival with beta-blockers: importance of ancillary properties. Prog Cardiovasc Dis 1997;39(5):445-56.

van Campen LC, Visser FC, Visser CA. Ejection fraction improvement by beta-blocker treatment in patients with heart failure: an analysis of studies published in the literature. J Cardiovasc Pharmacol 1998;32(Suppl 1):S31-5

Wikstrand J, Berglund G, Tuomilehto J. Beta-blockade in the primary prevention of coronary heart disease in hypertensive patients. Review of present evidence. Circulation 1991;84(6 Suppl):VI93-100.

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

Yusuf S, Anand S, Avezum A, Jr., Flather M, Coutinho M. Treatment for acute myocardial infarction. Overview of randomized clinical trials. Eur Heart J 1996;17(Suppl F):16-29.

Yusuf S. Interventions that potentially limit myocardial infarct size: overview of clinical trials. Am J Cardiol 1987;60(2):11A-17A.

Zarembski DG, Nolan PE, Jr., Slack MK, Lui CY. Meta-analysis of the use of low-dose beta-adrenergic blocking therapy in idiopathic or ischemic dilated cardiomyopathy. Am J Cardiol 1996;77(14):1247-50.

2.03 Angiotensin converting enzyme inhibitors

GISSI-3: effects of lisinopril and transdermal glyceryl trinitrate singly and together on 6-week mortality and ventricular function after acute myocardial infarction. Gruppo Italiano per lo Studio della Sopravvivenza nell'infarto Miocardico. Lancet 1994;343(8906):1115-22.

Indications for ACE inhibitors in the early treatment of acute myocardial infarction: systematic overview of individual data from 100,000 patients in randomized trials. ACE Inhibitor Myocardial Infarction Collaborative Group. Circulation 1998;97(22):2202-12

ISIS-4: a randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. Lancet 1995;345(8951):669-85.

Six-month effects of early treatment with lisinopril and transdermal glyceryl trinitrate singly and together withdrawn six weeks after acute myocardial infarction: the GISSI-3 trial. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico. J Am Coll Cardiol 1996;27(2):337-44.

Aronow WS. Management of older persons after myocardial infarction. J Am Geriatr Soc 1998;46(11):1459-68.

Beckwith C, Munger MA. Effect of angiotensin-converting enzyme inhibitors on ventricular remodeling and survival following myocardial infarction. Ann Pharmacother 1993;27(6):755-66.

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

Dagenais GR, Yusuf S, Bourassa MG, Yi Q, Bosch J, Lonn EM, et al. Effects of ramipril on coronary events in high-risk persons: results of the Heart Outcomes Prevention Evaluation Study. Circulation 2001;104(5):522-6.

Davie AP. ACE inhibitors after myocardial infarction. Clinical and economic considerations. Pharmacoeconomics 2000;17(3):237-43.

Domanski MJ, Exner DV, Borkowf CB, Geller NL, Rosenberg Y, Pfeffer MA. Effect of angiotensin converting enzyme inhibition on sudden cardiac death in patients following acute myocardial infarction. A meta-analysis of randomized clinical trials. J Am Coll Cardiol 1999;33(3):598-604.

Flather MD, Yusuf S, Kober L, Pfeffer M, Hall A, Murray G, et al. Long-term ACE-inhibitor therapy in patients with heart failure or left-ventricular dysfunction: a systematic overview of data from individual patients. ACE-Inhibitor Myocardial Infarction Collaborative Group. Lancet 2000;355(9215):1575-81.

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

Furberg CD, Pitt B. Are all angiotensin-converting enzyme inhibitors interchangeable? J Am Coll Cardiol 2001;37(5):1456-60.

Garg R, Yusuf S. Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. Collaborative Group on ACE Inhibitor Trials. JAMA 1995;273(18):1450-6.

Hennekens CH, Albert CM, Godfried SL, Gaziano JM, Buring JE. Adjunctive drug therapy of acute myocardial infarction--evidence from clinical trials. N Engl J Med 1996;335(22):1660-7.

Huckell VF, Bernstein V, Cairns JA, Crowell R, Dagenais GR, Higginson LA, et al. Angiotensin-converting enzyme inhibition in myocardial infarction--Part 1: Clinical data. Can J Cardiol 1997;13(2):161-9.

Latini R, Maggioni AP, Flather M, Sleight P, Tognoni G. ACE inhibitor use in patients with myocardial infarction. Summary of evidence from clinical trials. Circulation 1995;92(10):3132-7.

Latini R, Tognoni G, Maggioni AP, Baigent C, Braunwald E, Chen ZM, et al. Clinical effects of early angiotensin-converting enzyme inhibitor treatment for acute myocardial infarction are similar in the presence and absence of aspirin: systematic overview of individual data from 96,712 randomized patients. Angiotensin-converting Enzyme Inhibitor Myocardial Infarction Collaborative Group. J Am Coll Cardiol 2000;35(7):1801-7.

Lonn EM, Yusuf S. Evidence based cardiology: emerging approaches in preventing cardiovascular disease. BMJ 1999;318(7194):1337-41.

Lonn E, Roccafort R, Yi Q, Dagenais G, Sleight P, et al. Effect of long-term therapy with ramipril in high-risk women. J Am Coll Cardiol 2002;40:6930702.

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

Neal B, MacMahon S, Chapman N. Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: results of prospectively designed overviews of randomised trials. Blood Pressure Lowering Treatment Trialists' Collaboration. Lancet 2000;356(9246):1955-64.

Nelson KM, Yeager BF. What is the role of angiotensin-converting enzyme inhibitors in congestive heart failure and after myocardial infarction? Ann Pharmacother 1996;30(9):986-93.

Pahor M, Psaty BM, Alderman MH, Applegate WB, Williamson JD, Cavazzini C, et al. Health outcomes associated with calcium antagonists compared with other first-line antihypertensive therapies: a meta-analysis of randomised controlled trials. Lancet 2000;356(9246):1949-54.

Pahor M, Psaty BM, Alderman MH, Applegate WB, Williamson JD, Furberg CD. Therapeutic benefits of ACE inhibitors and other antihypertensive drugs in patients with type 2 diabetes. Diabetes Care 2000;23(7):888-92.

Popma JJ, Topol EJ. Adjuncts to thrombolysis for myocardial reperfusion. Ann Intern Med 1991;115(1):34-44.

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

Psaty BM, Smith NL, Siscovick DS, Koepsell TD, Weiss NS, Heckbert SR, et al. Health outcomes associated with antihypertensive therapies used as first-line agents. A systematic review and meta-analysis. JAMA 1997;277(9):739-45.

Rochon PA, Clark JP, Binns MA, Patel V, Gurwitz JH. Reporting of gender-related information in clinical trials of drug therapy for myocardial infarction. Cmaj 1998;159(4):321-7.

Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. N Engl J Med 2000;342(3):145-53.

2.04 Calcium channel blockers

Aronow WS. Management of older persons after myocardial infarction. J Am Geriatr Soc 1998;46(11):1459-68.

Dargie HJ, Ford I, Fox KM. Total Ischaemic Burden European Trial (TIBET). Effects of ischaemia and treatment with atenolol, nifedipine SR and their combination on outcome in patients with chronic stable angina. The TIBET Study Group. Eur Heart J 1996;17(1):104-12.

Fodor JG, Boulet AP, Savard D, Nadeau C, Rakusan K, Chockalingam A, et al. The role of diltiazem in treating hypertension and coronary artery disease: new approaches to preventing first events. Can J Cardiol 1997;13(5):495-503.

Furberg CD, Psaty BM, Meyer JV. Nifedipine. Dose-related increase in mortality in patients with coronary heart disease. Circulation 1995;92(5):1326-31.

Furberg CD, Psaty BM. Corrections to the nifedipine meta-analysis. Circulation 1996;93(7):1475-6.

Gibson RS, Boden WE. Calcium channel antagonists: friend or foe in postinfarction patients? Am J Hypertens 1996;9(12 Pt 2):172S-176S.

Hansen JF. Review of postinfarct treatment with verapamil: combined experience of early and late intervention studies with verapamil in patients with acute myocardial infarction. Danish Study Group on Verapamil in Myocardial Infarction. Cardiovasc Drugs Ther 1994;8(Suppl 3):543-7.

Hansen JF. Treatment with verapamil during and after an acute myocardial infarction: a review based on the Danish Verapamil Infarction Trials I and II. The Danish Study Group on Verapamil in Myocardial Infarction. J Cardiovasc Pharmacol 1991;18 Suppl 6:S20-5.

Heidenreich PA, McDonald KM, Hastie T, Fadel B, Hagan V, Lee BK, et al. Meta-analysis of trials comparing beta-blockers, calcium antagonists, and nitrates for stable angina. JAMA 1999;281(20):1927-36.

Held PH, Yusuf S, Furberg CD. Calcium channel blockers in acute myocardial infarction and unstable angina: an overview. BMJ 1989;299(6709):1187-92.

Hennekens CH, Albert CM, Godfried SL, Gaziano JM, Buring JE. Adjunctive drug therapy of acute myocardial infarction--evidence from clinical trials. N Engl J Med 1996;335(22):1660-7.

Lubsen J. The calcium channel antagonist debate: recent developments. Eur Heart J 1998;19(Suppl I):I3-7.

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

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

Messeri P, Workman S, Saunders C, Francis C. The application of meta-analysis in assessing racial differences in the effects of antihypertensive medication. J Natl Med Assoc 1997;89(7):477-85.

Messerli FH. Case-control study, meta-analysis, and bouillabaisse: putting the calcium antagonist scare into context. Ann Intern Med 1995;123(11):888-9.

Michels KB, Rosner BA, Manson JE, Stampfer MJ, Walker AM, Willett WC, et al. Prospective study of calcium channel blocker use, cardiovascular disease, and total mortality among hypertensive women: the Nurses' Health Study. Circulation 1998;97(16):1540-8.

Neal B, MacMahon S, Chapman N. Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: results of prospectively designed overviews of randomised trials. Blood Pressure Lowering Treatment Trialists' Collaboration. Lancet 2000;356(9246):1955-64.

Opie LH, Yusuf S, Kubler W. Current status of safety and efficacy of calcium channel blockers in cardiovascular diseases: a critical analysis based on 100 studies. Prog Cardiovasc Dis 2000;43(2):171-96.

Pahor M, Psaty BM, Alderman MH, Applegate WB, Williamson JD, Cavazzini C, et al. Health outcomes associated with calcium antagonists compared with other first-line antihypertensive therapies: a meta-analysis of randomised controlled trials. Lancet 2000;356(9246):1949-54.

Pepine CJ, Faich G, Makuch R. Verapamil use in patients with cardiovascular disease: an overview of randomized trials. Clin Cardiol 1998;21(9):633-41.

Popma JJ, Topol EJ. Adjuncts to thrombolysis for myocardial reperfusion. Ann Intern Med 1991;115(1):34-44.

Psaty BM, Smith NL, Siscovick DS, Koepsell TD, Weiss NS, Heckbert SR, et al. Health outcomes associated with antihypertensive therapies used as first-line agents. A systematic review and meta-analysis. JAMA 1997;277(9):739-45.

Staessen JA, Fagard R, Thijs L, Celis H, Arabidze GG, Birkenhager WH, et al. Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. The Systolic Hypertension in Europe (Syst-Eur) Trial Investigators. Lancet 1997;350(9080):757-64.

Stason W, Schmid CH, Caubet JF, Kupelnick B, Cory D, Whiting G, et al. Searching for signals: mortality and cardiovascular events in published randomized control trials of nifedipine in ischemic heart disease and hypertension. J Hypertens Suppl 1996;14(2):S5-7.

Stason WB, Schmid CH, Niedzwiecki D, Whiting GW, Caubet JF, Cory D, et al. Safety of nifedipine in angina pectoris: a meta-analysis. Hypertension 1999;33(1):24-31.

Stason WB, Schmid CH, Niedzwiecki D, Whiting GW, Caubet JF, Luo D, et al. Safety of nifedipine in patients with hypertension: a meta-analysis. Hypertension 1997;30(1 Pt 1):7-14.

Waters D. Calcium channel blockers: an evidence-based review. Can J Cardiol 1997;13(8):757-66.

Yusuf S. Calcium antagonists in coronary artery disease and hypertension. Time for reevaluation? Circulation 1995;92(5):1079-82.

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

2.05 Nitrates

GISSI-3: effects of lisinopril and transdermal glyceryl trinitrate singly and together on 6-week mortality and ventricular function after acute myocardial infarction. Gruppo Italiano per lo Studio della Sopravvivenza nell'infarto Miocardico. Lancet 1994;343(8906):1115-22.

ISIS-4: a randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesiumsulphate in 58,050 patients with suspected acute myocardial infarction. ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. Lancet 1995;345(8951):669-85.

Six-month effects of early treatment with lisinopril and transdermal glyceryl trinitrate singly and together withdrawn six weeks after acute myocardial infarction: the GISSI-3 trial. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico. J Am Coll Cardiol 1996;27(2):337-44.

Aronow WS. Management of older persons after myocardial infarction. J Am Geriatr Soc 1998;46(11):1459-68.

Borzak S, Ridker PM. Discordance between meta-analyses and large-scale randomized, controlled trials. Examples from the management of acute myocardial infarction. Ann Intern Med 1995;123(11):873-7.

Colditz GA, Halvorsen KT, Goldhaber SZ. Randomized clinical trials of transdermal nitroglycerin systems for the treatment of angina: a meta-analysis. Am Heart J 1988;116(1 Pt 1):174-80.

Heidenreich PA, McDonald KM, Hastie T, Fadel B, Hagan V, Lee BK, et al. Meta-analysis of trials comparing beta-blockers, calcium antagonists, and nitrates for stable angina. JAMA 1999;281(20):1927-36.

Hennekens CH, Albert CM, Godfried SL, Gaziano JM, Buring JE. Adjunctive drug therapy of acute myocardial infarction--evidence from clinical trials. N Engl J Med 1996;335(22):1660-7.

Morris JL, Cowan JC. Nitrates in myocardial infarction: a current perspective. Can J Cardiol 1995;11(Suppl B):5B-10B.

Popma JJ, Topol EJ. Adjuncts to thrombolysis for myocardial reperfusion. Ann Intern Med 1991;115(1):34-44.

Thadani U. Oral nitrates: more than symptomatic therapy in coronary artery disease? Cardiovasc Drugs Ther 1999;11(Suppl 1): 213-8.

2.06 Heparin

Direct thrombin inhibitors in acute coronary syndromes and during percutaneous coronary intervention: design of a meta-analysis based on individual patient data. Direct Thrombin Inhibitor Trialists' Collaborative Group. Am Heart J 2001;141(1):E2.

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.

Antman EM, Cohen M, Radley D, McCabe C, Rush J, Premmereur J, et al. Assessment of the treatment effect of enoxaparin for unstable angina/non-Q-wave myocardial infarction. TIMI 11B-ESSENCE meta-analysis. Circulation 1999;100(15):1602-8.

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

Bijsterveld NR, Hettiarachchi R, Peters R, Prins MH, Levi M, Buller HR. Low-molecular weight heparins in venous and arterial thrombotic disease. Thromb Haemost 1999;82(Suppl 1):139-47.

Collins R, MacMahon S, Flather M, Baigent C, Remvig L, Mortensen S, et al. Clinical effects of anticoagulant therapy in suspected acute myocardial infarction: systematic overview of randomised trials. BMJ 1996;313(7058):652-9.

Eikelboom JW, Anand SS, Malmberg K, Weitz JI, Ginsberg JS, Yusuf S. Unfractionated heparin and low-molecular-weight heparin in acute coronary syndrome without ST elevation: a meta-analysis. Lancet 2000;355(9219):1936-42.

Heidenreich PA, McClellan M. Trends in treatment and outcomes for acute myocardial infarction: 1975-1995. Am J Med 2001;110(3):165-74.

Kong DF, Topol EJ, Bittl JA, White HD, Theroux P, Hasselblad V, et al. Clinical outcomes of bivalirudin for ischemic heart disease. Circulation 1999;100(20):2049-53.

Mahaffey KW, Granger CB, Collins R, O'Connor CM, Ohman EM, Bleich SD, et al. Overview of randomized trials of intravenous heparin in patients with acute myocardial infarction treated with thrombolytic therapy. Am J Cardiol 1996;77(8):551-6.

Millard PS, Sturrock WA. Heparin and thrombolysis in acute MI. J Fam Pract 1996;43(1):20-1.

Nemergut C, Cheng JW. Use of direct thrombin inhibitors in acute coronary syndrome. Clin Ther 2000;22(8):937-48; discussion 898.

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.

Popma JJ, Topol EJ. Adjuncts to thrombolysis for myocardial reperfusion. Ann Intern Med 1991;115(1):34-44.

Roux S, Christeller S, Ludin E. Effects of aspirin on coronary reocclusion and recurrent ischemia after thrombolysis: a meta-analysis. J Am Coll Cardiol 1992;19(3):671-7.

Spinler SA, Nawarskas JJ. Low-molecular-weight heparins for acute coronary syndromes. Ann Pharmacother 1998;32(1):103-10.

2.07 Glycoprotein IIb/IIIa Drugs

Bell DM. Analysis of number needed to treat and cost of platelet glycoprotein IIb/IIIa inhibitors in percutaneous coronary interventions and acute coronary syndromes. Pharmacotherapy 1999;19(9):1086-93.

Bhatt DL, Topol EJ. Current role of platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes. JAMA 2000;284(12):1549-58.

Boersma E, Akkerhuis KM, Theroux P, Califf RM, Topol EJ, Simoons ML. Platelet glycoprotein IIb/IIIa receptor inhibition in non-ST-elevation acute coronary syndromes: early benefit during medical treatment only, with additional protection during percutaneous coronary intervention. Circulation 1999;100(20):2045-8.

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

Boersma E, Harrington RA, Moliterno DJ, White H, Theroux P, Van de Werf F, et al. Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: a meta-analysis of all major randomised clinical trials. Lancet 2002;359(9302):189-98.

Braunwald E, Maseri A, Armstrong PW, Califf RM, Gibler WB, Hamm CW, et al. Rationale and clinical evidence for the use of GP IIb/IIIa inhibitors in acute coronary syndromes. Eur Heart J 1998;19(Suppl D):D22-30.

Brown DL, Fann CS, Chang CJ. Effect of glycoprotein IIb/IIIa inhibitors on the individual components of composite endpoints used in clinical trials of unstable angina and non-Q-wave myocardial infarction. Cardiovasc Drugs Ther 2000;14(3):253-8.

Brown DL, Fann CS, Chang CJ. Meta-analysis of effectiveness and safety of abciximab versus eptifibatide or tirofiban in percutaneous coronary intervention. Am J Cardiol 2001;87(5):537-41.

Chew DP, Bhatt DL, Sapp S, Topol EJ. Increased Mortality With Oral Platelet Glycoprotein IIb/IIIa Antagonists : A Meta-Analysis of Phase III Multicenter Randomized Trials. Circulation 2001;103(2):201-206.

Cho L, Topol EJ, Balog C, Foody JM, Booth JE, Cabot C, et al. Clinical benefit of glycoprotein IIb/IIIa blockade with Abciximab is independent of gender: pooled analysis from EPIC, EPILOG and EPISTENT trials. Evaluation of 7E3 for the Prevention of Ischemic Complications. Evaluation in Percutaneous Transluminal Coronary Angioplasty to Improve Long-Term Outcome with Abciximab GP IIb/IIIa blockade. Evaluation of Platelet IIb/IIIa Inhibitor for Stent. J Am Coll Cardiol 2000;36(2):381-6.

Gibson CM, Moynihan JL, Al-Mousa EN, Campsey M, Gandhi R, Murphy S, et al. Glycoprotein IIb/IIIa receptor inhibition in interventional cardiology. J Thromb Thrombolysis 1999;7(3):287-302.

Hillegass WB, Newman AR, Raco DL. Glycoprotein IIb/IIIa receptor therapy in percutaneous coronary intervention and non-ST-segment elevation acute coronary syndromes. Estimating the economic implications. Pharmacoeconomics 2001;19(1):41-55.

Kong DF, Topol EJ, Bittl JA, White HD, Theroux P, Hasselblad V, et al. Clinical outcomes of bivalirudin for ischemic heart disease. Circulation 1999;100(20):2049-53.

Lincoff AM, Califf RM, Anderson KM, Weisman HF, Aguirre FV, Kleiman NS, et al. Evidence for prevention of death and myocardial infarction with platelet membrane glycoprotein IIb/IIIa receptor blockade by abciximab (c7E3 Fab) among patients with unstable angina undergoing percutaneous coronary revascularization. EPIC Investigators.Evaluation of 7E3 in Preventing Ischemic Complications. J Am Coll Cardiol 1997;30(1):149-56.

McGregor M, Brophy JM. Use of abciximab (c7E3 Fab, ReoPro) as an adjunct to balloon angioplasty. Can J Cardiol 1999;15(2):201-7.

Quinn MJ, Plow EF, Topol EJ. Platelet glycoprotein IIb/IIIa inhibitors: recognition of a two-edged sword? Circulation 2002;106(3):379-85.

Stringer KA. The evolving role of platelet glycoprotein IIb/IIIa inhibitors in the management of acute coronary syndromes. Ann Pharmacother 1999;33(6):712-22.

Vorchheimer DA, Badimon JJ, Fuster V. Platelet glycoprotein IIb/IIIa receptor antagonists in cardiovascular disease. JAMA 1999;281(15):1407-14.

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

2.08 Thrombolysis

Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Lancet 1994;343(8893):311-22.

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.

Randomized trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2.ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. J Am Coll Cardiol 1988;12(6 Suppl A):3A-13A.

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

Becker RC. Late thrombolytic therapy: mechanism of benefit and potential risk among patients treated beyond 6 hours. Coron Artery Dis 1993;4(3):293-304.

Becker RC, Terrin M, et al. Comparison of clinical outcomes for women and men after acute myocardial infarction. The Thrombolysis in Myocardial Infarction Investigators. Ann Intern Med 1994;120(8): 638-45.

Bizjak ED, Mauro VF. Thrombolytic therapy: a review of its use in acute myocardial infarction. Ann Pharmacother 1998;32(7-8):769-84.

Boersma E, Maas AC, Deckers JW, Simoons ML. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. Lancet 1996;348(9030):771-5.

Burke AP, Farb A, et al. Effect of risk factors on the mechanism of acute thrombosis and sudden coronary death in women. Circulation 1998;97(21): 2110-6.

Castillo PA, Palmer CS, Halpern MT, Hatziandreu EJ, Gersh BJ. Cost-effectiveness of thrombolytic therapy for acute myocardial infarction. Ann Pharmacother 1997;31(5):596-603.

Clyne CA. Antithrombotic therapy in the primary and secondary prevention of coronary-related death and infarction: focus on gender differences. Cardiology 1990;77(Suppl 2):99-109.

Collins R, Peto R, Parish S, Sleight P. ISIS-3 and GISSI-2: no survival advantage with tissue plasminogen activator over streptokinase, but a significant excess of strokes with tissue plasminogen activator in both trials. Am J Cardiol 1993;71(12):1127-30.

Cucherat M, Bonnefoy E, Tremeau G. Primary angioplasty versus intravenous thrombolysis for acute myocardial infarction. Cochrane Database Syst Rev 2000(2):CD001560.

Fox KA. Comparative analysis of long-term mortality after thrombolytic therapy. Am J Cardiol 1991;68(16):38E-44E.

Gurwitz JH, Col NF, Avorn J. The exclusion of the elderly and women from clinical trials in acute myocardial infarction. JAMA 1992;268(11):1417-22.

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

Held PH, Teo KK, Yusuf S. Effects of tissue-type plasminogen activator and anisoylated plasminogen streptokinase activator complex on mortality in acute myocardial infarction. Circulation 1990;82(5):1668-74.

Hennekens CH. Thrombolytic therapy: pre- and post-GISSI-2, ISIS-3, and GUSTO-1. Clin Cardiol 1994;17(1 Suppl 1):I15-7.

Hochman JS, McCabe CH, Stone PH, Becker RC, Cannon CP, DeFeo-Fraulini T, et al. Outcome and profile of women and men presenting with acute coronary syndromes: a report from TIMI IIIB. TIMI Investigators. Thrombolysis in Myocardial Infarction. J Am Coll Cardiol 1997;30(1):141-8.

Hochman JS, Tamis JE, Thompson TD, Weaver WD, White HD, Van de Werf F, et al. Sex, clinical presentation, and outcome in patients with acute coronary syndromes. Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes IIb Investigators. N Engl J Med 1999;341(4):226-32.

Honan MB, Harrell FE, Jr., Reimer KA, Califf RM, Mark DB, Pryor DB, et al. Cardiac rupture, mortality and the timing of thrombolytic therapy: a meta-analysis. J Am Coll Cardiol 1990;16(2):359-67.

Kellett J, Clarke J. Comparison of "accelerated" tissue plasminogen activator with streptokinase for treatment of suspected myocardial infarction. Med Decis Making 1995;15(4):297-310.

Kong DF, Topol EJ, Bittl JA, White HD, Theroux P, Hasselblad V, et al. Clinical outcomes of bivalirudin for ischemic heart disease. Circulation 1999;100(20):2049-53.

Lau J, Antman EM, Jimenez-Silva J, Kupelnick B, Mosteller F, Chalmers TC. Cumulative meta-analysis of therapeutic trials for myocardial infarction. N Engl J Med 1992;327(4):248-54.

Lincoff AM, Califf RM, Ellis SG, Sigmon KN, Lee KL, Leimberger JD, et al. Thrombolytic therapy for women with myocardial infarction: is there a gender gap? Thrombolysis and Angioplasty in Myocardial Infarction Study Group. J Am Coll Cardiol 1993;22(7):1780-7.

Manson JE, Tosteson H, Ridker PM, Satterfield S, Hebert P, O'Connor GT, et al. The primary prevention of myocardial infarction. N Engl J Med 1992;326(21):1406-16.

Mark DB, Hlatky MA, Califf RM, Naylor CD, Lee KL, Armstrong PW, et al. Cost effectiveness of thrombolytic therapy with tissue plasminogen activator as compared with streptokinase for acute myocardial infarction. N Engl J Med 1995;332(21):1418-24.

Midgette AS, O'Connor GT, Baron JA, Bell J. Effect of intravenous streptokinase on early mortality in patients with suspected acute myocardial infarction. A meta-analysis by anatomic location of infarction. Ann Intern Med 1990;113(12):961-8.

Midgette AS, Wong JB, Beshansky JR, Porath A, Fleming C, Pauker SG. Cost-effectiveness of streptokinase for acute myocardial infarction: A combined meta-analysis and decision analysis of the effects of infarct location and of likelihood of infarction. Med Decis Making 1994;14(2):108-17.

Moen EK, Asher CR, Miller DP, Weaver WD, White HD, Califf RM, et al. Long-term follow-up of gender-specific outcomes after thrombolytic therapy for acute myocardial infarction from the GUSTO-I trial. Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries. J Womens Health 1997;6(3):285-93.

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

Morrison LJ, Verbeek PR, McDonald AC, Sawadsky BV, Cook DJ. Mortality and prehospital thrombolysis for acute myocardial infarction: A meta-analysis. JAMA 2000;283(20):2686-92.

Nemergut C, Cheng JW. Use of direct thrombin inhibitors in acute coronary syndrome. Clin Ther 2000;22(8):937-48; discussion 898.

Newby K. Clinical outcomes according to time to treatment. Clin Cardiol 1997;20(11 Suppl 3):III11-5.

Pfeffer MA, Moye LA, Braunwald E, Basta L, Brown EJ, Jr., Cuddy TE, et al. Selection bias in the use of thrombolytic therapy in acute myocardial infarction. The SAVE Investigators. JAMA 1991;266(4):528-32.

Ridker PM, O'Donnell C, Marder VJ, Hennekens CH. Large-scale trials of thrombolytic therapy for acute myocardial infarction: GISSI-2, ISIS-3, and GUSTO-1. Ann Intern Med 1993;119(6):530-2.

Rosamond WD, Shahar E, McGovern PG, Sides TL, Luepker RV. Trends in coronary thrombolytic therapy for acute myocardial infarction (the Minnesota Heart Survey Registry, 1990 to 1993). Am J Cardiol 1996;78(3):271-7.

Smith BJ. Thrombolysis in acute myocardial infarction: analysis of studies comparing accelerated t-PA and streptokinase. J Accid Emerg Med 1999;16(6):407-11.

Stone GW, Grines CL, Browne KF, Marco J, Rothbaum D, O'Keefe J, et al. Comparison of in-hospital outcome in men versus women treated by either thrombolytic therapy or primary coronary angioplasty for acute myocardial infarction. Am J Cardiol 1995;75(15):987-92.

Topol EJ. How should intravenous thrombolytic agents for acute myocardial infarction be selected? Cardiovasc Clin 1990;21(1):57-75; discussion 76-8.

Topol EJ. Treatment of acute myocardial infarction: in which patients should primary percutaneous transluminal coronary angioplasty be preferred to thrombolysis? Cardiologia 1996;41(9):843-7.

Vaitkus PT. Percutaneous transluminal coronary angioplasty versus thrombolysis in acute myocardial infarction: a meta-analysis. Clin Cardiol 1995;18(1):35-8.

Van de Werf F. Implications of the GUSTO trial for thrombolytic therapy. Drugs 1996;52(3):307-12.

Weaver WD, Simes RJ, Betriu A, Grines CL, Zijlstra F, Garcia E, et al. Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review. JAMA 1997;278(23):2093-8.

Weaver WD, White HD, Wilcox RG, Aylward PE, Morris D, Guerci A, et al. Comparisons of characteristics and outcomes among women and men with acute myocardial infarction treated with thrombolytic therapy. GUSTO-I investigators. JAMA 1996;275(10):777-82.

Woodfield SL, Lundergan CF, Reiner JS, Thompson MA, Rohrbeck SC, Deychak Y, et al. Gender and acute myocardial infarction: is there a different response to thrombolysis? J Am Coll Cardiol 1997;29(1):35-42.

Wooster MB, Luzier AB. Reteplase: a new thrombolytic for the treatment of acute myocardial infarction. Ann Pharmacother 1999;33(3):318-24.

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

Yusuf S, Collins R, Peto R, Furberg C, Stampfer MJ, Goldhaber SZ, et al. Intravenous and intracoronary fibrinolytic therapy in acute myocardial infarction: overview of results on mortality, reinfarction and side-effects from 33 randomized controlled trials. Eur Heart J 1985;6(7):556-85.

2.09 Ticlopidine

Boissel JP, Peyrieux JC, Destors JM. Is it possible to reduce the risk of cardiovascular events in subjects suffering from intermittent claudication of the lower limbs? Thromb Haemost 1989;62(2):681-5.

Cutlip DE, Baim DS, Ho KK, Popma JJ, Lansky AJ, Cohen DJ, et al. Stent thrombosis in the modern era: a pooled analysis of multicenter coronary stent clinical trials. Circulation 2001;103(15):1967-71.

Flores-Runk P, Raasch RH. Ticlopidine and antiplatelet therapy. Ann Pharmacother 1993;27(9):1090-8.

Hankey GJ, Sudlow CL, Dunbabin DW. Thienopyridine derivatives (ticlopidine, clopidogrel) versus aspirin for preventing stroke and other serious vascular events in high vascular risk patients. Cochrane Database Syst Rev 2000(2):CD001246.

Hankey GJ, Sudlow CL, Dunbabin DW. Thienopyridines or aspirin to prevent stroke and other serious vascular events in patients at high risk of vascular disease? A systematic review of the evidence from randomized trials. Stroke 2000;31(7):1779-84.

Mathis AS. Newer antithrombotic strategies in the initial management of non-ST-segment elevation acute coronary syndromes. Ann Pharmacother 2000;34(2):208-27.

Mehta SR, Yusuf S. The Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) trial programme; rationale, design and baseline characteristics including a meta-analysis of the effects of thienopyridines in vascular disease. Eur Heart J 2000;21(24):2033-41.

Tisdale JE. Antiplatelet therapy in coronary artery disease: review and update of efficacy studies. Am J Health Syst Pharm 1998;55(19 Suppl 1):S8-16.

Zusman RM, Chesebro JH, Comerota A, Hartmann JR, Massin EK, Raps E, et al. Antiplatelet therapy in the prevention of ischemic vascular events: literature review and evidence-based guidelines for drug selection. Clin Cardiol 1999;22(9):559-73.

2.10 Clopidogrel

A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). CAPRIE Steering Committee. Lancet 1996;348(9038):1329-39.

Dippel DW. The results of CAPRIE, IST and CAST. Clopidogrel vs. Aspirin in Patients at Risk of Ischaemic Events. International Stroke Trial. Chinese Acute Stroke Trial. Thromb Res 1998;92(1 Suppl 1):S13-6.

Hankey GJ, Sudlow CL, Dunbabin DW. Thienopyridine derivatives (ticlopidine, clopidogrel) versus aspirin for preventing stroke and other serious vascular events in high vascular risk patients. Cochrane Database Syst Rev 2000(2):CD001246.

Hankey GJ, Sudlow CL, Dunbabin DW. Thienopyridines or aspirin to prevent stroke and other serious vascular events in patients at high risk of vascular disease? A systematic review of the evidence from randomized trials. Stroke 2000;31(7):1779-84.

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

Harker LA, Boissel JP, Pilgrim AJ, Gent M. Comparative safety and tolerability of clopidogrel and aspirin: results from CAPRIE. CAPRIE Steering Committee and Investigators. Clopidogrel versus aspirin in patients at risk of ischaemic events. Drug Saf 1999;21(4):325-35.

Mehta SR, Yusuf S, Peters RJ, Bertrand ME, Lewis BS, Natarajan MK, et al. Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study. Lancet 2001;358(9281):527-33.

Yusuf S, Zhao F, Mehta SR, Chrolavicius S, Tognoni G, Fox KK. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. N Engl J Med 2001;345(7):494-502.

Zusman RM, Chesebro JH, Comerota A, Hartmann JR, Massin EK, Raps E, et al. Antiplatelet therapy in the prevention of ischemic vascular events: literature review and evidence-based guidelines for drug selection. Clin Cardiol 1999;22(9):559-73.

2.11 Percutaneous transluminal coronary angioplasty (PTCA) and stenting

Coronary angioplasty versus medical therapy for angina: the second Randomised Intervention Treatment of Angina (RITA-2) trial. RITA-2 trial participants. Lancet 1997;350(9076):461-8.

First-year results of CABRI (Coronary Angioplasty versus Bypass Revascularisation Investigation). CABRI Trial Participants. Lancet 1995;346(8984):1179-84.

Al Suwaidi J, Berger PB, et al. Coronary artery stents. JAMA 2000;284(14): 1828-36.

Batchelor WB, Anstrom KJ, et al. Contemporary outcome trends in the elderly undergoing percutaneous coronary interventions: results in 7,472 octogenarians. National Cardiovascular Network Collaboration. J Am Coll Cardiol 2000;36(3): 723-30.

Bates DW, Miller E, et al. Coronary angiography and angioplasty after acute myocardial infarction. Ann Intern Med 1997;126(7): 539-50.

Bell MR, Grill DE, Garratt KN, Berger PB, Gersh BJ, Holmes DR, Jr. Long-term outcome of women compared with men after successful coronary angioplasty. Circulation 1995;91(12):2876-81.

Bell MR, Holmes DR, Jr., Berger PB, Garratt KN, Bailey KR, Gersh BJ. The changing in-hospital mortality of women undergoing percutaneous transluminal coronary angioplasty. JAMA 1993;269(16):2091-5.

Boersma E, Akkerhuis KM, Theroux P, Califf RM, Topol EJ, Simoons ML. Platelet glycoprotein IIb/IIIa receptor inhibition in non-ST-elevation acute coronary syndromes: early benefit during medical treatment only, with additional protection during percutaneous coronary intervention. Circulation 1999;100(20):2045-8.

Bucher HC, Hengstler P, et al. Percutaneous transluminal coronary angioplasty versus medical treatment for non-acute coronary heart disease: meta-analysis of randomised controlled trials. BMJ 2000;321(7253): 73-7.

Cantor WJ, Peterson ED, et al. Provisional stenting strategies: systematic overview and implications for clinical decision-making. J Am Coll Cardiol 2000;36(4): 1142-51.

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

Cho L, Bhatt DL, Wolski K, Lincoff M, Topol EJ, Moliterno DJ. Effect of smoking status and abciximab use on outcome after percutaneous coronary revascularization: Pooled analysis from EPIC, EPILOG, and EPISTENT. Am Heart J 2001;141(4):599-602.

Cho L, Topol EJ, Balog C, Foody JM, Booth JE, Cabot C, et al. Clinical benefit of glycoprotein IIb/IIIa blockade with Abciximab is independent of gender: pooled analysis from EPIC, EPILOG and EPISTENT trials. Evaluation of 7E3 for the Prevention of Ischemic Complications. Evaluation in Percutaneous Transluminal Coronary Angioplasty to Improve Long-Term Outcome with Abciximab GP IIb/IIIa blockade. Evaluation of Platelet IIb/IIIa Inhibitor for Stent. J Am Coll Cardiol 2000;36(2):381-6.

Cucherat M, Bonnefoy E, Tremeau G. Primary angioplasty versus intravenous thrombolysis for acute myocardial infarction. Cochrane Database Syst Rev 2000(2):CD001560.

Cutlip DE, Baim DS, Ho KK, Popma JJ, Lansky AJ, Cohen DJ, et al. Stent thrombosis in the modern era: a pooled analysis of multicenter coronary stent clinical trials. Circulation 2001;103(15):1967-71.

de Feyter PJ, Keane D, Deckers JW, de Jaegere P. Medium- and long-term outcome after coronary balloon angioplasty. Prog Cardiovasc Dis 1994;36(5):385-96.

de Jaegere PP, Eefting FD, Popma JJ, Serruys PW. Clinical trials on intracoronary stenting. Semin Interv Cardiol 1996;1(4):233-45.

Degeare VS, Dangas G, Stone GW, Grines CL. Interventional procedures in acute myocardial infarction. Am Heart J 2001;141(1):15-24.

DeGeare VS, Stone GW, Grines L, Brodie BR, Cox DA, Garcia E, et al. Angiographic and clinical characteristics associated with increased in-hospital mortality in elderly patients with acute myocardial infarction undergoing percutaneous intervention (a pooled analysis of the primary angioplasty in myocardial infarction trials). Am J Cardiol 2000;86(1):30-4.

Eckman MH, Wong JB, Salem DN, Pauker SG. Direct angioplasty for acute myocardial infarction. A review of outcomes in clinical subsets. Ann Intern Med 1992;117(8):667-76.

Ellis SG, Da Silva ER, Spaulding CM, Nobuyoshi M, Weiner B, Talley JD. Review of immediate angioplasty after fibrinolytic therapy for acute myocardial infarction: insights from the RESCUE I, RESCUE II, and other contemporary clinical experiences. Am Heart J 2000;139(6):1046-53.

Ellis SG, Roubin GS, King SB, 3rd, Douglas JS, Jr., Shaw RE, Stertzer SH, et al. In-hospital cardiac mortality after acute closure after coronary angioplasty: analysis of risk factors from 8,207 procedures. J Am Coll Cardiol 1988;11(2):211-6.

Eysmann SB, Douglas PS. Reperfusion and revascularization strategies for coronary artery disease in women. JAMA 1992;268(14):1903-7.

French JK, Webster MW, Neutze JM, White HD. Evidence-based assessment of the benefit of revascularisation in coronary disease: beyond the randomised trials. Aust N Z J Med 1996;26(4):490-4.

Gunnell D, Harvey I, Smith L. The invasive management of angina: issues for consumers and commissioners. J Epidemiol Community Health 1995;49(4):335-43.

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

Heidenreich PA, McClellan M. Trends in treatment and outcomes for acute myocardial infarction: 1975-1995. Am J Med 2001;110(3):165-74.

Hillegass WB, Newman AR, Raco DL. Glycoprotein IIb/IIIa receptor therapy in percutaneous coronary intervention and non-ST-segment elevation acute coronary syndromes. Estimating the economic implications. Pharmacoeconomics 2001;19(1):41-55.

Holmes DR, Jr., Holubkov R, Vlietstra RE, Kelsey SF, Reeder GS, Dorros G, et al. Comparison of complications during percutaneous transluminal coronary angioplasty from 1977 to 1981 and from 1985 to 1986: the National Heart, Lung, and Blood Institute Percutaneous Transluminal Coronary Angioplasty Registry. J Am Coll Cardiol 1988;12(5):1149-55.

Hughes GC, Annex BH, Yin B, Pippen AM, Lin P, Kypson AP, et al. Transmyocardial laser revascularization limits in vivo adenoviral-mediated gene transfer in porcine myocardium. Cardiovasc Res 1999;44(1):81-90.

Jacobs AK, Kelsey SF, Yeh W, Holmes DR, Jr., Block PC, Cowley MJ, et al. Documentation of decline in morbidity in women undergoing coronary angioplasty (a report from the 1993-94 NHLBI Percutaneous Transluminal Coronary Angioplasty Registry). National Heart, Lung, and Blood Institute. Am J Cardiol 1997;80(8):979-84.

Keenan CR, Chou TM. Revascularization in coronary artery disease. A review of randomized trial data. West J Med 1998;168(4):280-5.

Kelsey SF, James M, Holubkov AL, Holubkov R, Cowley MJ, Detre KM. Results of percutaneous transluminal coronary angioplasty in women. 1985-1986 National Heart, Lung, and Blood Institute's Coronary Angioplasty Registry. Circulation 1993;87(3):720-7.

Kilaru PK, Kelly RF, Calvin JE, Parrillo JE. Utilization of coronary angiography and revascularization after acute myocardial infarction in men and women risk stratified by the American College of Cardiology/American Heart Association guidelines. J Am Coll Cardiol 2000;35(4):974-9.

Lieu TA, Gurley RJ, Lundstrom RJ, Parmley WW. Primary angioplasty and thrombolysis for acute myocardial infarction: an evidence summary. J Am Coll Cardiol 1996;27(3):737-50.

Maggioni AP, Sessa F, Latini R, Tognoni G. Treatment of acute myocardial infarction today. Am Heart J 1997;134(2 Pt 2):S9-14.

Malenka DJ, O'Rourke D, Miller MA, Hearne MJ, Shubrooks S, Kellett MA, Jr., et al. Cause of in-hospital death in 12,232 consecutive patients undergoing percutaneous transluminal coronary angioplasty. The Northern New England Cardiovascular Disease Study Group. Am Heart J 1999;137(4 Pt 1):632-8.

Mark DB, Nelson CL, Califf RM, Harrell FE, Jr., Lee KL, Jones RH, et al. Continuing evolution of therapy for coronary artery disease. Initial results from the era of coronary angioplasty. Circulation 1994;89(5):2015-25.

McGregor M, Brophy JM. Use of abciximab (c7E3 Fab, ReoPro) as an adjunct to balloon angioplasty. Can J Cardiol 1999;15(2):201-7.

McLeod AL, Northridge DB, Uren NG. Ultrasound guided stenting. Heart 2001;85(6):605-6.

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

Mehilli J, Kastrati A, Dirschinger J, Bollwein H, Neumann FJ, Schomig A. Differences in prognostic factors and outcomes between women and men undergoing coronary artery stenting. JAMA 2000;284(14):1799-805.

Mehta RH, Bates ER. Coronary stent implantation in acute myocardial infarction. Am Heart J 1999;137(4 Pt 1):603-11.

Michels KB, Yusuf S. Does PTCA in acute myocardial infarction affect mortality and reinfarction rates? A quantitative overview (meta-analysis) of the randomized clinical trials. Circulation 1995;91(2):476-85.

Peterson ED, Lansky AJ, Anstrom KJ, Muhlbaier LH, Popma JJ, Satler LF, et al. Evolving trends in interventional device use and outcomes: results from the National Cardiovascular Network Database. Am Heart J 2000;139(2 Pt 1):198-207.

Pocock SJ, Henderson RA, Rickards AF, Hampton JR, King SB, 3rd, Hamm CW, et al. Meta-analysis of randomised trials comparing coronary angioplasty with bypass surgery. Lancet 1995;346(8984):1184-9.

Popma JJ, Chuang YC, Satler LF, Kleiber B, Leon MB. Primary coronary angioplasty in patients with acute myocardial infarction. Tex Heart Inst J 1994;21(2):148-57.

Rihal CS, Yusuf S. Chronic coronary artery disease: drugs, angioplasty, or surgery? BMJ 1996;312(7026):265-6.

Ryan TJ, Ryan TJ, Jr., Jacobs AK. Primary PTCA versus thrombolytic therapy: an evidence-based summary. Am Heart J 1999;138(2 Pt 2):S96-104.

Scott IA, Harden H, Coory M. What are appropriate rates of invasive procedures following acute myocardial infarction? A systematic review. Med J Aust 2001;174(3):130-6.

Serruys PW, Unger F, Sousa JE, Jatene A, Bonnier HJ, Schonberger JP, et al. Comparison of coronary-artery bypass surgery and stenting for the treatment of multivessel disease. N Engl J Med 2001;344(15):1117-24.

Shaw LJ, Miller DD, Romeis JC, Kargl D, Younis LT, Chaitman BR. Gender differences in the noninvasive evaluation and management of patients with suspected coronary artery disease. Ann Intern Med 1994;120(7):559-66.

Sim I, Gupta M, McDonald K, Bourassa MG, Hlatky MA. A meta-analysis of randomized trials comparing coronary artery bypass grafting with percutaneous transluminal coronary angioplasty in multivessel coronary artery disease. Am J Cardiol 1995;76(14):1025-9.

Solomon AJ, Gersh BJ. Management of chronic stable angina: medical therapy, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft surgery. Lessons from the randomized trials. Ann Intern Med 1998;128(3):216-23.

Stone GW, Grines CL, Browne KF, Marco J, Rothbaum D, O'Keefe J, et al. Comparison of in-hospital outcome in men versus women treated by either thrombolytic therapy or primary coronary angioplasty for acute myocardial infarction. Am J Cardiol 1995;75(15):987-92.

Taggart DP. Angioplasty versus bypass surgery. Lancet 1996;347(8996):271-2; discussion 272-3.

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

Topol EJ, Holmes DR, Rogers WJ. Coronary angiography after thrombolytic therapy for acute myocardial infarction. Ann Intern Med 1991;114(10):877-85.

Topol EJ. Coronary angioplasty for acute myocardial infarction. Ann Intern Med 1988;109(12):970-80.

Topol EJ. Treatment of acute myocardial infarction: in which patients should primary percutaneous transluminal coronary angioplasty be preferred to thrombolysis? Cardiologia 1996;41(9):843-7.

Vaitkus PT. Percutaneous transluminal coronary angioplasty versus thrombolysis in acute myocardial infarction: a meta-analysis. Clin Cardiol 1995;18(1):35-8.

Weaver WD, Simes RJ, Betriu A, Grines CL, Zijlstra F, Garcia E, et al. Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review. JAMA 1997;278(23):2093-8.

Weber MM. Surgical management of unstable angina and symptomatic coronary artery disease. J Cardiovasc Nurs 2000;15(1):27-42.

Weintraub WS, Wenger NK, Kosinski AS, Douglas JS, Jr., Liberman HA, Morris DC, et al. Percutaneous transluminal coronary angioplasty in women compared with men. J Am Coll Cardiol 1994;24(1):81-90.

Welty FK, Mittleman MA, Healy RW, Muller JE, Shubrooks SJ, Jr. Similar results of percutaneous transluminal coronary angioplasty for women and men with postmyocardial infarction ischemia. J Am Coll Cardiol 1994;23(1):35-9.

Wong JB, Sonnenberg FA, Salem DN, Pauker SG. Myocardial revascularization for chronic stable angina. Analysis of the role of percutaneous transluminal coronary angioplasty based on data available in 1989. Ann Intern Med 1990;113(11):852-71.

Yusuf S, Pogue J. Primary angioplasty compared with thrombolytic therapy for acute myocardial infarction. JAMA 1997;278(23):2110-1.

Zahn R, Schiele R, Schneider S, Gitt AK, Wienbergen H, Seidl K, et al. Decreasing hospital mortality between 1994 and 1998 in patients with acute myocardial infarction treated with primary angioplasty but not in patients treated with intravenous thrombolysis. Results from the pooled data of the Maximal Individual Therapy in Acute Myocardial Infarction (MITRA) Registry and the Myocardial Infarction Registry (MIR). J Am Coll Cardiol 2000;36(7):2064-71.

2.12 Coronary artery bypass graft surgery (CABG)

First-year results of CABRI (Coronary Angioplasty versus Bypass Revascularisation Investigation). CABRI Trial Participants. Lancet 1995;346(8984):1179-84.

Califf RM, Harrell FE, Jr., Lee KL, Rankin JS, Hlatky MA, Mark DB, et al. The evolution of medical and surgical therapy for coronary artery disease. A 15-year perspective. JAMA 1989;261(14):2077-86.

Davis KB, Chaitman B, Ryan T, Bittner V, Kennedy JW. Comparison of 15-year survival for men and women after initial medical or surgical treatment for coronary artery disease: a CASS registry study. Coronary Artery Surgery Study. J Am Coll Cardiol 1995;25(5):1000-9.

Gunnell D, Harvey I, Smith L. The invasive management of angina: issues for consumers and commissioners. J Epidemiol Community Health 1995;49(4):335-43.

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

Hughes GC, Annex BH, Yin B, Pippen AM, Lin P, Kypson AP, et al. Transmyocardial laser revascularization limits in vivo adenoviral-mediated gene transfer in porcine myocardium. Cardiovasc Res 1999;44(1):81-90.

Jacobs AK, Kelsey SF, Brooks MM, Faxon DP, Chaitman BR, Bittner V, et al. Better outcome for women compared with men undergoing coronary revascularization: a report from the bypass angioplasty revascularization investigation (BARI). Circulation 1998;98(13):1279-85.

Jones RH, Hannan EL, Hammermeister KE, Delong ER, O'Connor GT, Luepker RV, et al. Identification of preoperative variables needed for risk adjustment of short-term mortality after coronary artery bypass graft surgery. The Working Group Panel on the Cooperative CABG Database Project. J Am Coll Cardiol 1996;28(6):1478-87.

Jones RH, Kesler K, Phillips HR, 3rd, Mark DB, Smith PK, Nelson CL, et al. Long-term survival benefits of coronary artery bypass grafting and percutaneous transluminal angioplasty in patients with coronary artery disease. J Thorac Cardiovasc Surg 1996;111(5):1013-25.

Kilaru PK, Kelly RF, Calvin JE, Parrillo JE. Utilization of coronary angiography and revascularization after acute myocardial infarction in men and women risk stratified by the American College of Cardiology/American Heart Association guidelines. J Am Coll Cardiol 2000;35(4):974-9.

Lewsey JD, Murray GD, Leyland AH, Boddy FA. Comparing outcomes of percutaneous transluminal coronary angioplasty with coronary artery bypass grafting; can routine health service data complement and enhance randomized controlled trials? Eur Heart J 1999;20(23):1731-5.

Mark DB, Nelson CL, Califf RM, Harrell FE, Jr., Lee KL, Jones RH, et al. Continuing evolution of therapy for coronary artery disease. Initial results from the era of coronary angioplasty. Circulation 1994;89(5):2015-25.

O'Connor GT, Morton JR, Diehl MJ, Olmstead EM, Coffin LH, Levy DG, et al. Differences between men and women in hospital mortality associated with coronary artery bypass graft surgery. The Northern New England Cardiovascular Disease Study Group. Circulation 1993;88(5 Pt 1):2104-10.

Peterson ED, Lansky AJ, Anstrom KJ, Muhlbaier LH, Popma JJ, Satler LF, et al. Evolving trends in interventional device use and outcomes: results from the National Cardiovascular Network Database. Am Heart J 2000;139(2 Pt 1):198-207.

Pocock SJ, Henderson RA, Rickards AF, Hampton JR, King SB, 3rd, Hamm CW, et al. Meta-analysis of randomised trials comparing coronary angioplasty with bypass surgery. Lancet 1995;346(8984):1184-9.

Serruys PW, Unger F, Sousa JE, Jatene A, Bonnier HJ, Schonberger JP, et al. Comparison of coronary-artery bypass surgery and stenting for the treatment of multivessel disease. N Engl J Med 2001;344(15):1117-24.

Shapira I, Fisman EZ, Drory Y, Pines A. Acute myocardial infarction in patients who have had coronary artery bypass surgery. South Med J 1997;90(11):1129-32.

Sim I, Gupta M, McDonald K, Bourassa MG, Hlatky MA. A meta-analysis of randomized trials comparing coronary artery bypass grafting with percutaneous transluminal coronary angioplasty in multivessel coronary artery disease. Am J Cardiol 1995;76(14):1025-9.

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

Solomon AJ, Gersh BJ. Management of chronic stable angina: medical therapy, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft surgery. Lessons from the randomized trials. Ann Intern Med 1998;128(3):216-23.

Yusuf S, Zucker D, Peduzzi P, Fisher LD, Takaro T, Kennedy JW, et al. Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. Lancet 1994;344(8922):563-70.

3.01 Hypertension

Collaborative overview ('meta-analysis') of prospective observational studies of the associations of usual blood pressure and usual cholesterol levels with common causes of death: protocol for the second cycle of the Prospective Studies Collaboration. J Cardiovasc Risk 1999;6(5):315-20.

Persistence of reduction in blood pressure and mortality of participants in the Hypertension Detection and Follow-up Program. Hypertension Detection and Follow-up Program Cooperative Group. Jama 1988;259(14):2113-22.

Protocol for prospective collaborative overviews of major randomized trials of blood-pressure-lowering treatments. World Health Organization-International Society of Hypertension Blood Pressure Lowering Treatment Trialists' Collaboration. J Hypertens 1998;16(2):127-37.

Alderman MH, Ooi WL, Madhavan S, Cohen H. Treatment-induced blood pressure reduction and the risk of myocardial infarction. JAMA 1989;262(7):920-4.

Celis H, Fagard R, Staessen J, Thijs L, Amery A. The older hypertensive. Assessment and treatment. Neth J Med 1993;43(Suppl 1):S66-77.

Dahlof B, Devereux RB, Kjeldsen SE, Julius S, Beevers G, Faire U, et al. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. Lancet 2002;359(9311):995-1003.

Ebrahim S, Smith GD. Systematic review of randomised controlled trials of multiple risk factor interventions for preventing coronary heart disease. BMJ 1997;314(7095):1666-74.

Fiebach NH, Hebert PR, Stampfer MJ, Colditz GA, Willett WC, Rosner B, et al. A prospective study of high blood pressure and cardiovascular disease in women. Am J Epidemiol 1989;130(4):646-54.

Gueyffier F, Boissel JP, Pocock S, Boutitie F, Coope J, Cutler J, et al. Identification of risk factors in hypertensive patients: contribution of randomized controlled trials through an individual patient database. Circulation 1999;100(18):e88-94.

Gueyffier F, Boutitie F, Boissel JP, Pocock S, Coope J, Cutler J, et al. Effect of antihypertensive drug treatment on cardiovascular outcomes in women and men. A meta-analysis of individual patient data from randomized, controlled trials. The INDANA Investigators. Ann Intern Med 1997;126(10):761-7.

Gueyffier F, Froment A, Gouton M. New meta-analysis of treatment trials of hypertension: improving the estimate of therapeutic benefit. J Hum Hypertens 1996;10(1):1-8.

He J, Whelton PK. Elevated systolic blood pressure as a risk factor for cardiovascular and renal disease. J Hypertens Suppl 1999;17(2):S7-13.

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

Hoes AW, Grobbee DE, Lubsen J. Does drug treatment improve survival? Reconciling the trials in mild-to-moderate hypertension. J Hypertens 1995;13(7):805-11.

Holme I, Ekelund LG, Hjermann I, Leren P. Quality-adjusted meta-analysis of the hypertension/coronary dilemma. Am J Hypertens 1994;7(8):703-12.

Insua JT, Sacks HS, Lau TS, Lau J, Reitman D, Pagano D, et al. Drug treatment of hypertension in the elderly: a meta-analysis. Ann Intern Med 1994;121(5):355-62.

Kannel WB. Blood pressure as a cardiovascular risk factor: prevention and treatment. JAMA 1996;275(20):1571-6.

Keil U. Coronary artery disease: the role of lipids, hypertension and smoking. Basic Res Cardiol 2000;95(Suppl 1):I52-8.

Kloner RA, Vetrovec GW, Materson BJ, Levenstein M. Safety of long-acting dihydropyridine calcium channel blockers in hypertensive patients. Am J Cardiol 1998;81(2):163-9.

Lewington S, MacMahon S. Blood pressure, cholesterol, and common causes of death: a review. Prospective Studies Collaboration. Am J Hypertens 1999;12(10 Pt 2):96S-98S.

Moulds RF. Measurement of cost-effectiveness of drug therapy: a review of the treatment of hypertension. Med J Aust 1990;153(Suppl):S4-6.

Neal B, MacMahon S, Chapman N. Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: results of prospectively designed overviews of randomised trials. Blood Pressure Lowering Treatment Trialists' Collaboration. Lancet 2000;356(9246):1955-64.

Neal B, MacMahon S. An overview of 37 randomised trials of blood pressure lowering agents among 270,000 individuals. World Health Organization-International Society of Hypertension Blood Pressure Lowering Treatment Trialists' Collaboration. Clin Exp Hypertens 1999;21(5-6):517-29.

Nielsen WB, Vestbo J, Jensen GB. Isolated systolic hypertension as a major risk factor for stroke and myocardial infarction and an unexploited source of cardiovascular prevention: a prospective population-based study. J Hum Hypertens 1995;9:175-80.

Pahor M, Psaty BM, Alderman MH, Applegate WB, Williamson JD, Cavazzini C, et al. Health outcomes associated with calcium antagonists compared with other first-line antihypertensive therapies: a meta-analysis of randomised controlled trials. Lancet 2000;356(9246):1949-54.

Pearce KA, Furberg CD, Rushing J. Does antihypertensive treatment of the elderly prevent cardiovascular events or prolong life? A meta-analysis of hypertension treatment trials. Arch Fam Med 1995;4(11):943-9; discussion 950.

Perlman JA, Wolf PH, Ray R, Lieberknecht G. Cardiovascular risk factors, premature heart disease, and all-cause mortality in a cohort of Northern California women. Am J Obstet Gynecol. 1988;158:1568-74.

Port S, Demer L, Jennrich R, Walter D, Garfinkel A. Systolic blood pressure and mortality. Lancet 2000;355(9199):175-80.

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

Psaty BM, Smith NL, Siscovick DS, Koepsell TD, Weiss NS, Heckbert SR, et al. Health outcomes associated with antihypertensive therapies used as first-line agents. A systematic review and meta-analysis. JAMA 1997;277(9):739-45.

Quan A, Kerlikowske K, Gueyffier F, Boissel JP. Efficacy of treating hypertension in women. J Gen Intern Med 1999;14(12):718-29.

Quan A, Kerlikowske K, Gueyffier F, Boissel JP. Pharmacotherapy for hypertension in women of different races. Cochrane Database Syst Rev 2000(3):CD002146.

Sacks HS, Chalmers TC, Berk AA, Reitman D. Should mild hypertension be treated? An attempted meta-analysis of the clinical trials. Mt Sinai J Med 1985;52(4):265-70.

Shea S, Cook EF, Kannel WB, Goldman L. Treatment of hypertension and its effect on cardiovascular risk factors: data from the Framingham Heart Study. Circulation 1985;71(1):22-30.

Shinton RA, Beevers DG. A meta-analysis of mortality and coronary prevention in hypertensive patients treated with beta-receptor blockers. J Hum Hypertens 1990;4(Suppl 2):31-4.

Staessen JA, Gasowski J, Wang JG, Thijs L, Den Hond E, Boissel JP, et al. Risks of untreated and treated isolated systolic hypertension in the elderly: meta-analysis of outcome trials. Lancet 2000;355(9207):865-72.

Stokes J, 3rd, Kannel WB, Wolf PA, D'Agostino RB, Cupples LA. Blood pressure as a risk factor for cardiovascular disease. The Framingham Study--30 years of follow-up. Hypertension 1989;13(5 Suppl):I13-8.

Thijs L, Fagard R, Lijnen P, Staessen J, Van Hoof R, Amery A. A meta-analysis of outcome trials in elderly hypertensives. J Hypertens 1992;10(10):1103-9.

Wang J, Staessen JA, Gong L, Liu L. Chinese trial on isolated systolic hypertension in the elderly. The Systolic Hypertension in China (Syst-China) Collaborative Group. Arch Intern Med 2000;160:211-220.

3.02 Diabetes

Abbott RD, Donahue RP, Kannel WB, Wilson PW. The impact of diabetes on survival following myocardial infarction in men vs women. The Framingham Study. JAMA 1988;260(23):3456-60.

Brand FN, Abbott RD, Kannel WB. Diabetes, intermittent claudication, and risk of cardiovascular events. The Framingham Study. Diabetes 1989;38(4):504-9.

Coutinho M, Gerstein HC, et al. The relationship between glucose and incident cardiovascular events. A metaregression analysis of published data from 20 studies of 95,783 individuals followed for 12.4 years [see comments]. Diabetes Care 1999 Feb;22(2):233-40.

Donahue RP, Goldberg RJ, Chen Z, Gore JM, Alpert JS. The influence of sex and diabetes mellitus on survival following acute myocardial infarction: a community-wide perspective. J Clin Epidemiol 1993;46(3):245-52.

Folsom AR, Nieto FJ, McGovern PG, Tsai MY, Malinow MR, Eckfeldt JH, et al. Prospective study of coronary heart disease incidence in relation to fasting total homocysteine, related genetic polymorphisms, and B vitamins: the Atherosclerosis Risk in Communities (ARIC) study. Circulation 1998;98(3):204-10.

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

Hu FB, Stampfer MJ, Solomon CG, Liu S, Willett WC, Speizer FE, et al. The impact of diabetes mellitus on mortality from all causes and coronary heart disease in women: 20 years of follow-up. Arch Intern Med 2001;161(14):1717-23.

Kannel WB, D'Agostino RB, Wilson PW, Belanger AJ, Gagnon DR. Diabetes, fibrinogen, and risk of cardiovascular disease: the Framingham experience. Am Heart J 1990;120(3):672-6.

Lee WL, Cheung AM, Cape D, Zinman B. Impact of diabetes on coronary artery disease in women and men: a meta-analysis of prospective studies. Diabetes Care 2000;23(7):962-8.

Malmberg K, Yusuf S, Gerstein HC, Brown J, Zhao F, Hunt D, et al. Impact of diabetes on long-term prognosis in patients with unstable angina and non-Q-wave myocardial infarction: results of the OASIS (Organization to Assess Strategies for Ischemic Syndromes) Registry. Circulation 2000;102(9):1014-9.

Manson JE, Colditz GA, Stampfer MJ, Willett WC, Krolewski AS, Rosner B, et al. A prospective study of maturity-onset diabetes mellitus and risk of coronary heart disease and stroke in women. Arch Intern Med 1991;151(6):1141-7.

Orchard TJ. The impact of gender and general risk factors on the occurrence of atherosclerotic vascular disease in non-insulin-dependent diabetes mellitus. Ann Med 1996;28(4):323-33.

Vaccarino V, Parsons L, et al. Impact of history of diabetes mellitus on hospital mortality in men and women with first acute myocardial infarction. The National Registry of Myocardial Infraction 2 Participants. Am J Cardiol 2000;85(12): 1486-9; A

Yudkin JS, Chaturvedi N. Developing risk stratification charts for diabetic and nondiabetic subjects [see comments]. Diabetic Medicine 1999;16(3): 219-27.

3.03a Hyperlipidemia as a risk factor for CHD in women

Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. N Engl J Med 1998;339(19):1349-57.

Abbott RD, Wilson PW, Kannel WB, Castelli WP. High density lipoprotein cholesterol, total cholesterol screening, and myocardial infarction. The Framingham Study. Arteriosclerosis 1988;8(3):207-11.

Anderson KM, Castelli WP, Levy D. Cholesterol and mortality. 30 years of follow-up from the Framingham study. JAMA 1987;257(16):2176-80.

Austin MA, Hokanson JE, Edwards KL. Hypertriglyceridemia as a cardiovascular risk factor. Am J Cardiol 1998;81(4A):7B-12B.

Austin MA. Epidemiology of hypertriglyceridemia and cardiovascular disease. Am J Cardiol 1999;83(9B):13F-16F.

Austin MA. Plasma triglyceride as a risk factor for cardiovascular disease. Can J Cardiol 1998;14(Suppl B):14B-17B.

Barratt A, Irwig L. Is cholesterol testing/treatment really beneficial? Med J Aust 1993;159(10):644-7.

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

Bucher HC, Griffith LE, Guyatt GH. Systematic review on the risk and benefit of different cholesterol-lowering interventions. Arterioscler Thromb Vasc Biol 1999;19(2):187-95.

Buchwald H, Campos CT, Boen JR, Nguyen P, Williams SE, Lau J, et al. Gender-based mortality follow-up from the Program on the Surgical Control of the Hyperlipidemias (POSCH) and meta-analysis of lipid intervention trials. Women in POSCH and other lipid trials. Ann Surg 1996;224(4):486-98; discussion 498-500.

Castelli WP, Anderson K, Wilson PW, Levy D. Lipids and risk of coronary heart disease. The Framingham Study. Ann Epidemiol 1992;2(1-2):23-8.

Castelli WP, Garrison RJ, Wilson PW, Abbott RD, Kalousdian S, Kannel WB. Incidence of coronary heart disease and lipoprotein cholesterol levels. The Framingham Study. JAMA 1986;256(20):2835-8.

Castelli WP. Cholesterol and lipids in the risk of coronary artery disease--the Framingham Heart Study. Can J Cardiol 1988;4(Suppl A):5A-10A.

Craig WY, Neveux LM, Palomaki GE, Cleveland MM, Haddow JE. Lipoprotein(a) as a risk factor for ischemic heart disease: metaanalysis of prospective studies. Clin Chem 1998;44(11):2301-6.

Cui Y, Blumenthal RS, Flaws JA, Whiteman MK, Langenberg P, Bachorik PS, et al. Non-high-density lipoprotein cholesterol level as a predictor of cardiovascular disease mortality. Arch Intern Med 2001;161(11):1413-9.

Cullen P. Evidence that triglycerides are an independent coronary heart disease risk factor. Am J Cardiol 2000;86(9):943-9.

Danesh J, Collins R, Peto R. Lipoprotein(a) and coronary heart disease. Meta-analysis of prospective studies. Circulation 2000;102(10):1082-5.

Ebrahim S, Smith GD. Systematic review of randomised controlled trials of multiple risk factor interventions for preventing coronary heart disease. BMJ 1997;314(7095):1666-74.

Fager G, Wiklund O. Cholesterol reduction and clinical benefit. Are there limits to our expectations? Arterioscler Thromb Vasc Biol 1997;17(12):3527-33.

Garber AM, Browner WS, Hulley SB. Cholesterol screening in asymptomatic adults, revisited. Part 2. Ann Intern Med 1996;124(5):518-31.

Genest J, Jr., Jenner JL, McNamara JR, Ordovas JM, Silberman SR, Wilson PW, et al. Prevalence of lipoprotein (a) [Lp(a)] excess in coronary artery disease. Am J Cardiol 1991;67(13):1039-145.

Goldman L, Weinstein MC, Williams LW. Relative impact of targeted versus populationwide cholesterol interventions on the incidence of coronary heart disease. Projections of the Coronary Heart Disease Policy Model. Circulation 1989;80(2):254-60.

Gotto AM, Jr. Heart disease in the assessment and treatment of hypercholesterolemia: coronary artery disease and other atherosclerotic disease, family history, and left ventricular hypertrophy. Am J Med 1994;96(6A):9S-18S.

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

Gotto AM, Jr., Grundy SM. Lowering LDL cholesterol: questions from recent meta-analyses and subset analyses of clinical trial DataIssues from the Interdisciplinary Council on Reducing the Risk for Coronary Heart Disease, ninth Council meeting. Circulation 1999;99(8):E1-7.

Gould AL, Rossouw JE, Santanello NC, Heyse JF, Furberg CD. Cholesterol reduction yields clinical benefit. A new look at old data. Circulation 1995;91(8):2274-82.

Hokanson JE, Austin MA. Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population-based prospective studies. J Cardiovasc Risk 1996;3(2):213-9.

Holme I. Cholesterol reduction and its impact on coronary artery disease and total mortality. Am J Cardiol 1995;76(9):10C-17C.

Holme I. Relationship between total mortality and cholesterol reduction as found by meta-regression analysis of randomized cholesterol-lowering trials. Control Clin Trials 1996;17(1):13-22.

Howes LG, Simons LA. Efficacy of drug intervention for lipids in the prevention of coronary artery disease. Aust N Z J Med 1994;24(1):107-12.

Jacobs D, Blackburn H, Higgins M, Reed D, Iso H, McMillan G, et al. Report of the Conference on Low Blood Cholesterol: Mortality Associations. Circulation 1992;86(3):1046-60.

Kannel WB, Wilson PWF. Efficacy of lipid profiles in prediction of coronary disease. Am Heart J 1992;768-774.

Keil U. Coronary artery disease: the role of lipids, hypertension and smoking. Basic Res Cardiol 2000;95(Suppl 1):I52-8.

Knapp RG, Sutherland SE, Keil JE, Rust PF, Lackland DT. A comparison of the effects of cholesterol on CHD mortality in black and white women: twenty-eight years of follow-up in the Charleston Heart Study. J Clin Epidemiol 1992;45(10):1119-29.

LaRosa JC, He J, Vupputuri S. Effect of statins on risk of coronary disease: a meta-analysis of randomized controlled trials. JAMA 1999;282(24):2340-6.

Law MR, Wald NJ, Thompson SG. By how much and how quickly does reduction in serum cholesterol concentration lower risk of ischaemic heart disease? Bmj 1994;308(6925):367-72.

Lewington S, MacMahon S. Blood pressure, cholesterol, and common causes of death: a review. Prospective Studies Collaboration. Am J Hypertens 1999;12(10 Pt 2):96S-98S.

Lewis SJ, Sacks FM, Mitchell JS, East C, Glasser S, Kell S, et al. Effect of pravastatin on cardiovascular events in women after myocardial infarction: the cholesterol and recurrent events (CARE) trial. J Am Coll Cardiol 1998;32(1):140-6.

Manolio TA, Pearson TA, Wenger NK, Barrett-Connor E, Payne GH, Harlan WR. Cholesterol and heart disease in older persons and women. Review of an NHLBI workshop. Ann Epidemiol 1992;2(1-2):161-76.

Marchioli R, Marfisi RM, Carinci F, Tognoni G. Meta-analysis, clinical trials, and transferability of research results into practice. The case of cholesterol-lowering interventions in the secondary prevention of coronary heart disease. Arch Intern Med 1996;156(11):1158-72.

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

Miettinen TA, Pyorala K, Olsson AG, Musliner TA, Cook TJ, Faergeman O, et al. Cholesterol-lowering therapy in women and elderly patients with myocardial infarction or angina pectoris: findings from the Scandinavian Simvastatin Survival Study (4S). Circulation 1997;96(12):4211-8.

Montague T, Tsuyuki R, Burton J, Williams R, Dzavik V, Teo K. Prevention and regression of coronary atherosclerosis. Is it safe and efficacious therapy? Chest 1994;105(3):718-26.

Orchard TJ. The impact of gender and general risk factors on the occurrence of atherosclerotic vascular disease in non-insulin-dependent diabetes mellitus. Ann Med 1996;28(4):323-33.

Pignone M, Phillips C, Mulrow C. Use of lipid lowering drugs for primary prevention of coronary heart disease: meta-analysis of randomised trials. BMJ 2000;321(7267):983-6.

Primatesta P, Poulter NR. Lipid concentrations and the use of lipid lowering drugs: evidence from a national cross sectional survey. BMJ 2000;321(7272):1322-5.

Rembold CM. Number-needed-to-treat analysis of the prevention of myocardial infarction and death by antidyslipidemic therapy. J Fam Pract 1996;42(6):577-86.

Sacks FM, Pfeffer MA, Moye LA, Rouleau JL, Rutherford JD, Cole TG, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators. N Engl J Med 1996;335(14):1001-9.

Sacks FM. Lipid-lowering therapy in acute coronary syndromes. JAMA 2001;285(13):1758-60.

Sharrett AR, Patsch W, Sorlie PD, Heiss G, Bond MG, Davis CE. Associations of lipoprotein cholesterols, apolipoproteins A-I and B, and triglycerides with carotid atherosclerosis and coronary heart disease. The Atherosclerosis Risk in Communities (ARIC) Study. Arterioscler Thromb 1994;14(7):1098-104.

Shepherd J. New evidence, new guidelines. Atherosclerosis 1998;140(2):197-8.

Sorlie PD, Sharrett AR, Patsch W, Schreiner PJ, Davis CE, Heiss G, et al. The relationship between lipids/lipoproteins and atherosclerosis in African Americans and whites: the Atherosclerosis Risk in Communities Study. Ann Epidemiol 1999;9(3):149-58.

Tyroler HA. Serum lipoproteins as risk factors: recent epidemiologic studies in individuals with and without prevalent cardiovascular disease. Eur Heart J 1990;11(Suppl H):21-5.

van der Weijden T, Knottnerus JA, Ament AJ, Stoffers HE, Grol RP. Economic evaluation of cholesterol-related interventions in general practice. An appraisal of the evidence. J Epidemiol Community Health 1998;52(9):586-94.

Walsh JM, Grady D. Treatment of hyperlipidemia in women. JAMA 1995;274(14):1152-8.

White CW. Benefit of aggressive lipid-lowering therapy: insights from the post coronary artery bypass graft study and other trials. Am J Med 1998;105(1A):63S-68S.

Wilson PW, Abbott RD, Castelli WP. High density lipoprotein cholesterol and mortality. The Framingham Heart Study. Arteriosclerosis 1988;8(6):737-41.

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

Wong ND, Wilson PW, Kannel WB. Serum cholesterol as a prognostic factor after myocardial infarction: the Framingham Study. Ann Intern Med 1991;115(9):687-93.

3.03b Treatment of hyperlipidemia to reduce risk of CHD events in women

MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,538 high-risk individuals: a randomized placebo controlled trial. Heart Protection Study Collaborative Group. Lancet 2002; 360:7-22.

Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet 1994;344(8934):1383-9.

Ansell BJ, Watson KE, Fogelman AM. An evidence-based assessment of the NCEP Adult Treatment Panel II guidelines. National Cholesterol Education Program. JAMA 1999;282(21):2051-7.

Borgia MC, Medici F. Perspectives in the treatment of dyslipidemias in the prevention of coronary heart disease. Angiology 1998;49(5):339-48.

Bucher HC, Griffith LE, Guyatt GH. Systematic review on the risk and benefit of different cholesterol-lowering interventions. Arterioscler Thromb Vasc Biol 1999;19(2):187-95.

Buchwald H, Campos CT, Boen JR, Nguyen P, Williams SE, Lau J, et al. Gender-based mortality follow-up from the Program on the Surgical Control of the Hyperlipidemias (POSCH) and meta-analysis of lipid intervention trials. Women in POSCH and other lipid trials. Ann Surg 1996;224(4):486-98; discussion 498-500.

Byington RP, Jukema JW, Salonen JT, Pitt B, Bruschke AV, Hoen H, et al. Reduction in cardiovascular events during pravastatin therapy. Pooled analysis of clinical events of the Pravastatin Atherosclerosis Intervention Program. Circulation 1995;92(9):2419-25.

D'Agostino RB, Kannel WB, Stepanians MN, D'Agostino LC. Efficacy and tolerability of lovastatin in hypercholesterolemic women. Clin Ther 1992;14(3):390-5.

Downs JR, Clearfield M, Weis S, Whitney E, Shapiro DR, Beere PA, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. Air Force/Texas Coronary Atherosclerosis Prevention Study. JAMA 1998;279(20):1615-22.

Ebrahim S, Smith GD. Systematic review of randomised controlled trials of multiple risk factor interventions for preventing coronary heart disease. BMJ 1997;314(7095):1666-74.

Fager G, Wiklund O. Cholesterol reduction and clinical benefit. Are there limits to our expectations? Arterioscler Thromb Vasc Biol 1997;17(12):3527-33.

Froom J, Froom P, Benjamin M, Benjamin BJ. Measurement and management of hyperlipidemia for the primary prevention of coronary heart disease. J Am Board Fam Pract 1998;11(1):12-22.

Furberg CD. Lipid-lowering trials: results and limitations. Am Heart J 1994;128(6 Pt 2):1304-8.

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

Goldman L, Coxson P, Hunink MG, Goldman PA, Tosteson AN, Mittleman M, et al. The relative influence of secondary versus primary prevention using the National Cholesterol Education Program Adult Treatment Panel II guidelines. J Am Coll Cardiol 1999;34(3):768-76.

Gould AL, Cariski AT. Meta-analysis by the Program on the Surgical Control of the Hyperlipidemias (POSCH) investigators. Ann Surg 1998;227(2):314-6.

Gould AL, Rossouw JE, Santanello NC, Heyse JF, Furberg CD. Cholesterol reduction yields clinical benefit. A new look at old data. Circulation 1995;91(8):2274-82.

Guyton JR. Effect of niacin on atherosclerotic cardiovascular disease. Am J Cardiol 1998;82(12A):18U-23U; discussion 39U-41U.

Hebert PR, Gaziano JM, Chan KS, Hennekens CH. Cholesterol lowering with statin drugs, risk of stroke, and total mortality. An overview of randomized trials. JAMA 1997;278(4):313-21.

Holme I. Cholesterol reduction and its impact on coronary artery disease and total mortality. Am J Cardiol 1995;76(9):10C-17C.

Holme I. Effects of lipid-lowering therapy on total and coronary mortality. Curr Opin Lipidol 1995;6(6):374-8.

Holme I. Relation of coronary heart disease incidence and total mortality to plasma cholesterol reduction in randomised trials: use of meta-analysis. Br Heart J 1993;69(1 Suppl):S42-7.

Holme I. Relationship between total mortality and cholesterol reduction as found by meta-regression analysis of randomized cholesterol-lowering trials. Control Clin Trials 1996;17(1):13-22.

Howes LG, Simons LA. Efficacy of drug intervention for lipids in the prevention of coronary artery disease. Aust N Z J Med 1994;24(1):107-12.

Jacobson TA. "The lower the better" in hypercholesterolemia therapy: a reliable clinical guideline? Ann Intern Med 2000;133(7):549-54.

LaRosa JC, He J, Vupputuri S. Effect of statins on risk of coronary disease: a meta-analysis of randomized controlled trials. JAMA 1999;282(24):2340-6.

Marchioli R, Marfisi RM, Carinci F, Tognoni G. Meta-analysis, clinical trials, and transferability of research results into practice. The case of cholesterol-lowering interventions in the secondary prevention of coronary heart disease. Arch Intern Med 1996;156(11):1158-72.

Milne R. HMG CO-A reductase inhibitor treatment in the prevention of coronary heart disease. Southampton: Wessex Institute for Health Research and Development. Wessex Institute for Health Research and Development. DEC Report No. 72. 1997.

Montagne O, Vedel I, Durand-Zaleski I. Assessment of the impact of fibrates and diet on survival and their cost-effectiveness: evidence from randomized, controlled trials in coronary heart disease and health economic evaluations. Clin Ther 1999;21(11):2027-35.

Muldoon MF, Manuck SB, Mendelsohn AB, Kaplan JR, Belle SH. Cholesterol reduction and non-illness mortality: meta-analysis of randomised clinical trials. BMJ 2001;322(7277):11-5.

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

Pignone M, Phillips C, Mulrow C. Use of lipid lowering drugs for primary prevention of coronary heart disease: meta-analysis of randomised trials. BMJ 2000;321(7267):983-6.

Prosser LA, Stinnett AA, Goldman PA, Williams LW, Hunink MG, Goldman L, et al. Cost-effectiveness of cholesterol-lowering therapies according to selected patient characteristics. Ann Intern Med 2000;132(10):769-79.

Rembold CM. Number-needed-to-treat analysis of the prevention of myocardial infarction and death by antidyslipidemic therapy. J Fam Pract 1996;42(6):577-86.

Rubins HB. Cholesterol in patients with coronary heart disease: how low should we go? J Gen Intern Med 1995;10(8):464-71.

Savoie I, Wright J, Bassett K. Lipid lowering therapy Vancouver: B.C. Office of Health technology Assessment, Centre for Health Services and Policy Research, University of British Columbia. Finnish Office for Health Care Technology Assessment (FinOHTA). 1896256112. BCOHTA 98:4J. 1998

Shepherd J. New evidence, new guidelines. Atherosclerosis 1998;140(2):197-8.

Silberberg JS, Henry DA. The benefits of reducing cholesterol levels: the need to distinguish primary from secondary prevention. 1. A meta-analysis of cholesterol-lowering trials. Med J Aust 1991;155(10):665-6, 669-70.

Silberberg JS, Henry DA. The benefits of reducing cholesterol levels: the need to distinguish primary from secondary prevention. 2. Implications for heart disease prevention in Australia. Med J Aust 1991;155(10):670-4.

Smith GD, Song F, Sheldon TA. Cholesterol lowering and mortality: the importance of considering initial level of risk. BMJ 1993;306(6889):1367-73.

Solomon AJ, Gersh BJ. Management of chronic stable angina: medical therapy, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft surgery. Lessons from the randomized trials. Ann Intern Med 1998;128(3):216-23.

Spinler SA, Cziraky MJ. Lipoprotein(A): physiologic function, association with atherosclerosis, and effects of lipid-lowering drug therapy. Ann Pharmacother 1994;28(3):343-51.

Superko HR, Krauss RM. Coronary artery disease regression. Convincing evidence for the benefit of aggressive lipoprotein management. Circulation 1994;90(2):1056-69.

Walsh JM, Grady D. Treatment of hyperlipidemia in women. JAMA 1995;274(14):1152-8.

3.04 Elevated homocysteine

Lowering blood homocysteine with folic acid based supplements: meta-analysis of randomised trials.Homocysteine Lowering Trialists' Collaboration. BMJ 1998;316(7135):894-8.

Bostom AG, Silbershatz H, Rosenberg IH, Selhub J, D'Agostino RB, Wolf PA, et al. Nonfasting plasma total homocysteine levels and all-cause and cardiovascular disease mortality in elderly Framingham men and women. Arch Intern Med 1999;159(10):1077-80.

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

Boushey CJ, Beresford SA, Omenn GS, Motulsky AG. A quantitative assessment of plasma homocysteine as a risk factor for vascular disease. Probable benefits of increasing folic acid intakes. JAMA 1995;274(13):1049-57.

Cleophas TJ, Hornstra N, van Hoogstraten B, van der Meulen J. Homocysteine, a risk factor for coronary artery disease or not? A meta-analysis. Am J Cardiol 2000;86(9):1005-9, A8.

Folsom AR, Nieto FJ, McGovern PG, Tsai MY, Malinow MR, Eckfeldt JH, et al. Prospective study of coronary heart disease incidence in relation to fasting total homocysteine, related genetic polymorphisms, and B vitamins: the Atherosclerosis Risk in Communities (ARIC) study. Circulation 1998;98(3):204-10.

Tice JA, Ross E, Coxson PG, Rosenberg I, Weinstein MC, Hunink MG, et al. Cost-effectiveness of vitamin therapy to lower plasma homocysteine levels for the prevention of coronary heart disease: effect of grain fortification and beyond. JAMA 2001;286(8):936-43.

3.05 Elevated C-reactive protein

Albert MA, Danielson E, Rifai N, Ridker PM. Effect of statin therapy on C-reactive protein levels: the pravastatin inflammation/CRP evaluation (PRINCE): a randomized trial and cohort study. JAMA 2001;286(1):64-70.

Conlan MG, Folsom AR, Finch A, Davis CE, Sorlie P, Wu KK. Correlation of plasma protein C levels with cardiovascular risk factors in middle-aged adults: the Atherosclerosis Risk in Communities (ARIC) Study. Thromb Haemost 1993;70(5):762-7.

Danesh J, Collins R, Appleby P, Peto R. Association of fibrinogen, C-reactive protein, albumin, or leukocyte count with coronary heart disease: meta-analyses of prospective studies. JAMA 1998;279(18):1477-82.

Redberg RF, Rifai N, Gee L, Ridker PM. Lack of association of C-reactive protein and coronary calcium by electron beam computed tomography in postmenopausal women: implications for coronary artery disease screening. J Am Coll Cardiol 2000;36(1):39-43.

Ridker PM, Glynn RJ, Hennekens CH. C-reactive protein adds to the predictive value of total and HDL cholesterol in determining risk of first myocardial infarction. Circulation 1998;97(20):2007-11.

Ridker PM, Haughie P. Prospective studies of C-reactive protein as a risk factor for cardiovascular disease. J Investig Med 1998;46(8):391-5.

Ridker PM, Hennekens CH, Buring JE, Rifai N. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. N Engl J Med 2000;342(12):836-43.

Ridker PM, Rifai N, Pfeffer MA, Sacks F, Braunwald E. Long-term effects of pravastatin on plasma concentration of C-reactive protein. The Cholesterol and Recurrent Events (CARE) Investigators. Circulation 1999;100(3):230-5.

Ridker PM. High-sensitivity C-reactive protein: potential adjunct for global risk assessment in the primary prevention of cardiovascular disease. Circulation 2001;103(13):1813-8.

3.06 Smoking

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

Blazing MA, O'Connor CM. Evidence supporting secondary prevention strategies. Curr Opin Cardiol 1999;14(4):303-9.

Castelli WP. Diet, smoking, and alcohol: influence on coronary heart disease risk. Am J Kidney Dis 1990;16:41-46.

Freund KM, Belanger AJ, D'Agostino RB, Kannel WB. The health risks of smoking. The Framingham Study: 34 years of follow-up. Ann Epidemiol 1993;3(4):417-24.

Gensini GF, Comeglio M, et al. Classical risk factors and emerging elements in the risk profile for coronary artery disease. Eur Heart J 1999;19(Suppl A): A53-61.

Hansen EF, Andersen LT, et al. Cigarette smoking and age at first acute myocardial infarction, and influence of gender and extent of smoking. Am J Cardiol 1993;71(16): 1439-42.

Hermanson B, Omenn GS, et al. Beneficial six-year outcome of smoking cessation in older men and women with coronary artery disease. Results from the CASS registry. N Engl J Med 1988;319(21): 1365-9.

Kannel WB, D'Agostino RB, Belanger AJ. Fibrinogen, cigarette smoking, and risk of cardiovascular disease: insights from the Framingham Study. Am Heart J 1987;113(4):1006-10.

Kannel WB, D'Agostino RB. Risk reduction after quitting smoking. Quality of Life and Cardiovascular Care 1989:84-85.

Kawachi I, Colditz GA, Speizer F, Manson JE, Stampfer MJ, Willett WC, Hennekens CH. A prospective study of passive smoking and coronary heart disease. Circulation 1997;95:2374-2379.

Kawachi I, Colditz GA, Stampfer MJ, Willett WC, Manson JE, Rosner B, et al. Smoking cessation and decreased risks of total mortality, stroke, and coronary heart disease incidence among women: a prospective cohort study. In: Burns DM, Garfinkel L, Samet JM, editors. Changes in cigarette-related disease risks and thier implications for prevention and control. Bethesda: National Cancer Institute; 1997. p. 531-65.

Kawachi I, Colditz GA, Stampfer MJ, Willett WC, Manson JE, Rosner B, et al. Smoking cessation and time course of decreased risks of coronary heart disease in middle-aged women. Arch Intern Med 1994;154(2):169-75.

Kawachi I, Colditz GA, Stampfer MJ, Willett WC, Manson JE, Rosner B, et al. Smoking cessation in relation to total mortality rates in women. A prospective cohort study. Ann Intern Med 1993;119(10):992-1000.

Keil U. Coronary artery disease: the role of lipids, hypertension and smoking. Basic Res Cardiol 2000;95(Suppl 1):I52-8.

Ketola E, Sipila R, et al. Effectiveness of individual lifestyle interventions in reducing cardiovascular disease and risk factors. Ann Med 200;32(4): 239-51.

LaCroix AZ, Lang J, Scherr P, Wallace RB, Cornoni-Huntley J, Berkman L, et al. Smoking and mortality among older men and women in three communities. N Engl J Med 1991;324(23):1619-25.

Njolstad I, Arnesen E, Lund-Larsen PG. Smoking, serum lipids, blood pressure, and sex differences in myocardial infarction. A 12-year follow-up of the Finnmark Study. Circulation 1996;93(3):450-6.

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

Omenn GS, Anderson KW, Kronmal RA, Vlietstra RE. The temporal pattern of reduction of mortality risk after smoking cessation. Am J Prev Med 1990;6(5):251-7.

Paganini-Hill A, Hsu G. Smoking and mortality among residents of a California retirement community. Am J Public Health 1994;84(6):992-5.

Prescott E, Hippe M, Schnohr P, Hein HO, Vestbo J. Smoking and risk of myocardial infarction in women and men: longitudinal population study. BMJ 1998;316(7137):1043-7.

Rosenberg L, Palmer JR, et al. Decline in the risk of myocardial infarction among women who stop smoking. N Engl J Med 1990;322(4): 213-7.

Sterling TD, Rosenbaum WL, et al. Risk attribution and tobacco-related deaths [see comments]. American Journal of Epidemiology 1993;138(2): 128-39.

Willett WC, Green A, Stampfer MJ, Speizer FE, Colditz GA, Rosner B, et al. Relative and absolute excess risks of coronary heart disease among women who smoke cigarettes. N Engl J Med 1987;317(21):1303-9.

Wilson K, Gibson N, Willan A, Cook D. Effect of smoking cessation on mortality after myocardial infarction: meta-analysis of cohort studies. Arch Intern Med 2000;160(7):939-44.

3.07 Obesity

Barrett-Connor EL. Obesity, atherosclerosis, and coronary artery disease. Ann Intern Med 1985;103(6 (Pt 2)):1010-9.

Blair SN, Brodney S. Effects of physical inactivity and obesity on morbidity and mortality: current evidence and research issues. Med Sci Sports Exerc 1999;31(11 Suppl):S646-62.

Dattilo AM, Kris-Etherton PM. Effects of weight reduction on blood lipids and lipoproteins: a meta-analysis. Am J Clin Nutr 1992;56(2):320-8.

Field AE, Coakley EH, Must A, Spadano JL, Laird N, Dietz WH, et al. Impact of overweight on the risk of developing common chronic diseases during a 10-year period. Arch Intern Med 2001;161(13):1581-6.

Folsom AR, Burke GL, Byers CL, Hutchinson RG, Heiss G, Flack JM, et al. Implications of obesity for cardiovascular disease in blacks: the CARDIA and ARIC studies. Am J Clin Nutr 1991;53(6 Suppl):1604S-1611S.

Folsom AR, French SA, Zheng W, Baxter JE, Jeffery RW. Weight variability and mortality: the Iowa Women's Health Study. Int J Obes Relat Metab Disord 1996;20(8):704-9.

Folsom AR, Kushi LH, Anderson KE, Mink PJ, Olson JE, Hong CP, et al. Associations of general and abdominal obesity with multiple health outcomes in older women: the Iowa Women's Health Study. Arch Intern Med 2000;160(14):2117-28.

Folsom AR, Stevens J, Schreiner PJ, McGovern PG. Body mass index, waist/hip ratio, and coronary heart disease incidence in African Americans and whites. Atherosclerosis Risk in Communities Study Investigators. Am J Epidemiol 1998;148(12):1187-94.

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

French SA, Folsom AR, Jeffery RW, Zheng W, Mink PJ, Baxter JE. Weight variability and incident disease in older women: the Iowa Women's Health Study. Int J Obes Relat Metab Disord 1997;21(3):217-23.

Harris T, Cook EF, Garrison R, Higgins M, Kannel W, Goldman L. Body mass index and mortality among nonsmoking older persons. The Framingham Heart Study. JAMA 1988;259(10):1520-4.

Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation 1983;67(5):968-77.

Kannel WB, D'Agostino RB, Belanger AJ. Fibrinogen, cigarette smoking, and risk of cardiovascular disease: insights from the Framingham Study. Am Heart J 1987;113(4):1006-10.

Kannel WB, Cupples LA, Ramaswami R, Stokes J, 3rd, Kreger BE, Higgins M. Regional obesity and risk of cardiovascular disease; the Framingham Study. J Clin Epidemiol 1991;44(2):183-90.

Ketola E, Sipila R, et al. Effectiveness of individual lifestyle interventions in reducing cardiovascular disease and risk factors. Ann Med 2000;32(4): 239-51.

Kuller LH, Simkin-Silverman LR, Wing RR, Meilahn EN, Ives DG. Women's Healthy Lifestyle Project: A randomized clinical trial: results at 54 months. Circulation 2001;103(1):32-7.

Manson JE, Colditz GA, Stampfer MJ, Willett WC, Rosner B, Monson RR, et al. A prospective study of obesity and risk of coronary heart disease in women. N Engl J Med 1990;322(13):882-9.

Manson JE, Willett WC, Stampfer MJ, Colditz GA, Hunter DJ, Hankinson SE, et al. Body weight and mortality among women. N Engl J Med 1995;333(11):677-85.

Pi-Sunyer FX. Comorbidities of overweight and obesity: current evidence and research issues. Med Sci Sports Exerc 1999;31(11 Suppl):S602-8.

Rexrode KM, Carey VJ, Hennekens CH, Walters EE, Colditz GA, Stampfer MJ, et al. Abdominal adiposity and coronary heart disease in women. JAMA 1998;280(21):1843-8.

Thompson D, Edelsberg J, Colditz GA, Bird AP, Oster G. Lifetime health and economic consequences of obesity. Arch Intern Med 1999;159(18):2177-83.

Willett WC, Manson JE, Stampfer MJ, Colditz GA, Rosner B, Speizer FE, et al. Weight, weight change, and coronary heart disease in women. Risk within the 'normal' weight range. JAMA 1995;273(6):461-5.

3.08 Inactivity

Berlin JA, Colditz GA. A meta-analysis of physical activity in the prevention of coronary heart disease. Am J Epidemiol 1990;132(4):612-28.

Blair SN, Brodney S. Effects of physical inactivity and obesity on morbidity and mortality: current evidence and research issues. Med Sci Sports Exerc 1999;31(11 Suppl):S646-62.

Blair SN, Kohl HW, 3rd, Paffenbarger RS, Jr., Clark DG, Cooper KH, Gibbons LW. Physical fitness and all-cause mortality. A prospective study of healthy men and women. JAMA 1989;262(17):2395-401.

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

Eaton CB. Relation of physical activity and cardiovascular fitness to coronary heart disease, Part I: A meta-analysis of the independent relation of physical activity and coronary heart disease. J Am Board Fam Pract 1992;5(1):31-42.

Folsom AR, Arnett DK, Hutchinson RG, Liao F, Clegg LX, Cooper LS. Physical activity and incidence of coronary heart disease in middle-aged women and men. Med Sci Sports Exerc 1997;29(7):901-9.

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.

Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346(6):393-403.

Kuller LH, Simkin-Silverman LR, Wing RR, Meilahn EN, Ives DG. Women's Healthy Lifestyle Project: A randomized clinical trial: results at 54 months. Circulation 2001;103(1):32-7.

Lee IM, Rexrode KM, Cook NR, Manson JE, Buring JE. Physical activity and coronary heart disease in women: is "no pain, no gain" passe? JAMA 2001;285(11):1447-54.

Manson JE, Hu FB, Rich-Edwards JW, Colditz GA, Stampfer MJ, Willett WC, et al. A prospective study of walking as compared with vigorous exercise in the prevention of coronary heart disease in women. N Engl J Med 1999;341(9):650-8.

O'Connor GT, Buring JE, Yusuf S, Goldhaber SZ, Olmstead EM, Paffenbarger RS, Jr., et al. An overview of randomized trials of rehabilitation with exercise after myocardial infarction. Circulation 1989;80(2):234-44.

Oldridge NB, Guyatt GH, Fischer ME, Rimm AA. Cardiac rehabilitation after myocardial infarction. Combined experience of randomized clinical trials. Jama 1988;260(7):945-50.

Rockhill B, Willett WC, Manson JE, Leitzmann MF, Stampfer MJ, Hunter DJ, et al. Physical activity and mortality: a prospective study among women. Am J Public Health 2001;91(4):578-83.

Sherman SE, D'Agostino RB, Cobb JL, Kannel WB. Physical activity and mortality in women in the Framingham Heart Study. Am Heart J 1994;128(5):879-84.

Stefanick ML, Mackey S, Sheehan M, Ellsworth N, Haskell WL, Wood PD. Effects of diet and exercise in men and postmenopausal women with low levels of HDL cholesterol and high levels of LDL cholesterol. N Engl J Med 1998;339(1):12-20.

Williams PT. Physical fitness and activity as separate heart disease risk factors: a meta-analysis. Med Sci Sports Exerc 2001;33(5):754-61.

3.09 Age

Beckett N, Nunes M, Bulpitt C. Is it advantageous to lower cholesterol in the elderly hypertensive? Cardiovasc Drugs Ther 2000;14(4):397-405.

Brand FN, Kiely DK, Kannel WB, Myers RH. Family patterns of coronary heart disease mortality: the Framingham Longevity Study. J Clin Epidemiol 1992;45(2):169-74.

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

Castelli WP, Wilson PW, Levy D, Anderson K. Cardiovascular risk factors in the elderly. Am J Cardiol 1989;63(16):12H-19H.

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

D'Agostino RB, Kannel WB, Belanger AJ, Sytkowski PA. Trends in CHD and risk factors at age 55-64 in the Framingham Study. Int J Epidemiol 1989;18(3 Suppl 1):S67-72.

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(2):180-7.

Gurwitz JH, Col NF, Avorn J. The exclusion of the elderly and women from clinical trials in acute myocardial infarction. JAMA 1992;268(11):1417-22.

Howard G, Manolio TA, Burke GL, Wolfson SK, O'Leary DH. Does the association of risk factors and atherosclerosis change with age? An analysis of the combined ARIC and CHS cohorts. The Atherosclerosis Risk in Communities (ARIC) and Cardiovascular Health Study (CHS) investigators. Stroke 1997;28(9):1693-701.

Hussain KM, Kogan A, Estrada AQ, Kostandy G, Foschi A, Dadkhah S. Referral pattern and outcome in men and women undergoing coronary artery bypass surgery--a critical review. Angiology 1998;49(4):243-50.

La Vecchia C. Sex hormones and cardiovascular risk. Hum Reprod 1992;7(2):162-7.

Lerner DJ, Kannel WB. Patterns of coronary heart disease morbidity and mortality in the sexes: a 26-year follow-up of the Framingham population. Am Heart J 1986;111(2):383-90.

Pearson ML, Kahn KL, et al. Differences in quality of care for hospitalized elderly men and women. JAMA 1992;268(14): 1883-9.

Pocock SJ, McCormack V, Gueyffier F, Boutitie F, Fagard RH, Boissel JP. A score for predicting risk of death from cardiovascular disease in adults with raised blood pressure, based on individual patient data from randomised controlled trials. BMJ 2001;323(7304):75-81.

Schildkraut JM, Myers RH, Cupples LA, Kiely D, Kannel WB. Coronary risk associated with age and sex of parental heart disease in the Framingham Study. Am J Cardiol 1989;64:555-559.

Tsang TS, Barnes ME, et al. Risks of coronary heart disease in women: current understanding and evolving concepts. Mayo Clin Proc 2000;75(12): 1289-303.

3.10 Age at Menopause

Colditz GA, Willett WC, Stampfer MJ, Rosner B, Speizer FE, Hennekens CH. Menopause and the risk of coronary heart disease in women. N Engl J Med 1987;316(18):1105-10.

Cooper GS, Sandler DP. Age at natural menopause and mortality. Ann Epidemiol 1998;8(4):229-35.

Fioretti F, Tavani A, Gallus S, Franceschi S, La Vecchia C. Menopause and risk of non-fatal acute myocardial infarction: an Italian case-control study and a review of the literature. Hum Reprod 2000;15(3):599-603.

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

Greendale GA, Lee NP, Arriola ER. The menopause. Lancet 1999;353(9152):571-80.

Hu FB, Grodstein F, Hennekens CH, Colditz GA, Johnson M, Manson JE, et al. Age at natural menopause and risk of cardiovascular disease. Arch Intern Med 1999;159(10):1061-6.

La Vecchia C. Sex hormones and cardiovascular risk. Hum Reprod 1992;7(2):162-7.

Rosenberg L, Hennekens CH, Rosner B, Belanger C, Rothman KJ, Speizer FE. Early menopause and the risk of myocardial infarction. Am J Obstet Gynecol 1981;139(1):47-51.

Stampfer MJ, Colditz GA, Willett WC. Menopause and heart disease. A review. Ann N Y Acad Sci 1990;592:193-203; discussion 257-62.

Stampfer MJ, Colditz GA. Estrogen replacement therapy and coronary heart disease: a quantitative assessment of the epidemiologic evidence. Prev Med 1991;20(1):47-63.

van der Schouw YT, van der Graaf Y, Steyerberg EW, Eijkemans JC, Banga JD. Age at menopause as a risk factor for cardiovascular mortality. Lancet 1996;347(9003):714-8.

3.11 Ethnicity

Bhopal R. What is the risk of coronary heart disease in South Asians? A review of UK research. J Public Health Med 2000;22(3):375-85.

Cooper R. The role of genetic and environmental factors in cardiovascular disease in African Americans. Am J Med Sci 1999;317(3):208-13.

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(2):180-7.

Hutchinson RG, Watson RL, Davis CE, Barnes R, Brown S, Romm F, et al. Racial differences in risk factors for atherosclerosis. The ARIC Study. Atherosclerosis Risk in Communities. Angiology 1997;48(4):279-90.

Keil JE, Sutherland SE, Knapp RG, Lackland DT, Gazes PC, Tyroler HA. Mortality rates and risk factors for coronary disease in black as compared with white men and women. N Engl J Med 1993;329(2):73-8.

Potts JL, Thomas J. Traditional coronary risk factors in African Americans. Am J Med Sci 1999;317(3):189-92.

Roig E, Castaner A, Simmons B, Patel R, Ford E, Cooper R. In-hospital mortality rates from acute myocardial infarction by race in U.S. hospitals: findings from the National Hospital Discharge Survey. Circulation 1987;76(2):280-8.

Stone PH, Thompson B, Anderson HV, Kronenberg MW, Gibson RS, Rogers WJ, et al. Influence of race, sex, and age on management of unstable angina and non-Q-wave myocardial infarction: The TIMI III registry. JAMA 1996;275(14):1104-12.

Tofler GH, Stone PH, Muller JE, Willich SN, Davis VG, Poole WK, et al. Effects of gender and race on prognosis after myocardial infarction: adverse prognosis for women, particularly black women. J Am Coll Cardiol 1987;9(3):473-82.

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

White AD, Rosamond WD, Chambless LE, Thomas N, Conwill D, Cooper LS, et al. Sex and race differences in short-term prognosis after acute coronary heart disease events: the Atherosclerosis Risk In Communities (ARIC) study. Am Heart J 1999;138(3 Pt 1):540-8.

Williams JE, Massing M, Rosamond WD, Sorlie PD, Tyroler HA. Racial disparities in CHD mortality from 1968-1992 in the state economic areas surrounding the ARIC study communities. Atherosclerosis Risk in Communities. Ann Epidemiol 1999;9(8):472-80.

3.12 Socioeconomic status

Brezinka V, Kittel F. Psychosocial factors of coronary heart disease in women: a review. Soc Sci Med 1996;42(10):1351-65.

Capewell S, MacIntyre K, Stewart S, Chalmers JW, Boyd J, Finlayson A, et al. Age, sex, and social trends in out-of-hospital cardiac deaths in Scotland 1986-95: a retrospective cohort study. Lancet 2001;358(9289):1213-7.

Garrison RJ, Gold RS, Wilson PW, Kannel WB. Educational attainment and coronary heart disease risk: the Framingham Offspring Study. Prev Med 1993;22(1):54-64.

Gonzalez MA, Rodriguez Artalejo F, Calero JR. Relationship between socioeconomic status and ischaemic heart disease in cohort and case-control studies: 1960-1993. Int J Epidemiol 1998;27(3):350-8.

Keil JE, Sutherland SE, Knapp RG, Lackland DT, Gazes PC, Tyroler HA. Mortality rates and risk factors for coronary disease in black as compared with white men and women. N Engl J Med 1993;329(2):73-8.

Morrison C, Woodward M, Leslie W, Tunstall-Pedoe H. Effect of socioeconomic group on incidence of, management of, and survival after myocardial infarction and coronary death: analysis of community coronary event register. BMJ 1997;314(7080):541-6.

Salomaa V, Miettinen H, Niemela M, Ketonen M, Mahonen M, Immonen-Raiha P, et al. Relation of socioeconomic position to the case fatality, prognosis and treatment of myocardial infarction events; the FINMONICA MI Register Study. J Epidemiol Community Health 2001;55(7):475-82.

4.0 Difference in utilization between women and men

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.

Allison JJ, Kiefe CI, Centor RM, Box JB, Farmer RM. Racial differences in the medical treatment of elderly Medicare patients with acute myocardial infarction. J Gen Intern Med 1996;11(12):736-43.

Ayanian JZ, Epstein AM. Differences in the use of procedures between women and men hospitalized for coronary heart disease. N Engl J Med 1991;325(4):221-5.

Azar RR, Waters DD, McKay RG, Giri S, Hirst JA, Mitchell JF, et al. Short- and medium-term outcome differences in women and men after primary percutaneous transluminal mechanical revascularization for acute myocardial infarction. Am J Cardiol 2000;85(6):675-9.

Bandyopadhyay S, Bayer AJ, O'Mahony MS. Age and gender bias in statin trials. QJM 2001;94(3):127-32.

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

Barbour MM, Hume AL, Lapane KL, Derby CA, Carleton RA. Predictors of future antihypertensive use in patients with mildly elevated blood pressure. Pharmacotherapy 1995;15(3):272-8.

Battleman DS, Callahan M. Gender differences in utilization of exercise treadmill testing: a claims-based analysis. J Healthc Qual 2001;23(3):38-41.

Beck CA, Lauzon C, Eisenberg MJ, Huynh T, Dion D, Roux R, et al. Discharge prescriptions following admission for acute myocardial infarction at tertiary care and community hospitals in Quebec. Can J Cardiol 2001;17(1):33-40.

Bell MR, Holmes DR, Jr., Berger PB, Garratt KN, Bailey KR, Gersh BJ. The changing in-hospital mortality of women undergoing percutaneous transluminal coronary angioplasty. JAMA 1993;269(16):2091-5.

Bergelson BA, Tommaso CL. Gender differences in clinical evaluation and triage in coronary artery disease. Chest 1995;108(6):1510-3.

Bergelson BA, Tommaso CL. Gender differences in percutaneous interventional therapy of coronary artery disease. Cathet Cardiovasc Diagn 1996;37(1):1-4.

Bergman U, Anderssen M, Vaccheri A, Larsen J, Montanaro N. Marked differences in lipid-lowering drug use in Bologna, Italy and Funen, Denmark. Eur Heart J 1999;20(15):1135.

Bernstein SJ, Hilborne LH, Leape LL, Park RE, Brook RH. The appropriateness of use of cardiovascular procedures in women and men. Arch Intern Med 1994;154(23):2759-65.

Bickell NA, Pieper KS, Lee KL, Mark DB, Glower DD, Pryor DB, et al. Referral patterns for coronary artery disease treatment: gender bias or good clinical judgment? Ann Intern Med 1992;116(10):791-7.

Blustein J, Weitzman BC. Access to hospitals with high-technology cardiac services: how is race important? Am J Public Health 1995;85(3):345-51.

Bush TL, Fried LP, Barrett-Connor E. Cholesterol, lipoproteins, and coronary heart disease in women. Clin Chem 1988;34(8B):B60-70.

Byington RP, Jukema JW, Salonen JT, Pitt B, Bruschke AV, Hoen H, et al. Reduction in cardiovascular events during pravastatin therapy. Pooled analysis of clinical events of the Pravastatin Atherosclerosis Intervention Program. Circulation 1995;92(9):2419-25.

Carlisle DM, Leake BD, Shapiro MF. Racial and ethnic differences in the use of invasive cardiac procedures among cardiac patients in Los Angeles County, 1986 through 1988. Am J Public Health 1995;85(3):352-6.

Carlisle DM, Leake BD, Shapiro MF. Racial and ethnic disparities in the use of cardiovascular procedures: associations with type of health insurance. Am J Public Health 1997;87(2):263-7.

Carter BL, Kriesel HT, Steinkraus L, Knudson R. Antihypertensive drug-prescribing patterns of internists and family physicians. J Fam Pract 1989;29(3):257-61.

Cerqueira MD. Diagnostic testing strategies for coronary artery disease: special issues related to gender. Am J Cardiol 1995;75(11):52D-60D.

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

Chandra NC, Ziegelstein RC, Rogers WJ, Tiefenbrunn AJ, Gore JM, French WJ, et al. Observations of the treatment of women in the United States with myocardial infarction: a report from the National Registry of Myocardial Infarction-I. Arch Intern Med 1998;158(9):981-8.

Chiriboga DE, Yarzebski J, Goldberg RJ, Chen Z, Gurwitz J, Gore JM, et al. A community-wide perspective of gender differences and temporal trends in the use of diagnostic and revascularization procedures for acute myocardial infarction. Am J Cardiol 1993;71(4):268-73.

Cho L, Topol EJ, Balog C, Foody JM, Booth JE, Cabot C, et al. Clinical benefit of glycoprotein IIb/IIIa blockade with Abciximab is independent of gender: pooled analysis from EPIC, EPILOG and EPISTENT trials. Evaluation of 7E3 for the Prevention of Ischemic Complications. Evaluation in Percutaneous Transluminal Coronary Angioplasty to Improve Long-Term Outcome with Abciximab GP IIb/IIIa blockade. Evaluation of Platelet IIb/IIIa Inhibitor for Stent. J Am Coll Cardiol 2000;36(2):381-6.

Clarke KW, Gray D, Keating NA, Hampton JR. Do women with acute myocardial infarction receive the same treatment as men? BMJ 1994;309(6954):563-6.

Cohen M. The role of low-molecular-weight heparins in arterial diseases: optimizing antithrombotic therapy. Thromb Res 2000;100(2):V131-9.

Cooper RS, Ghali JK. Coronary heart disease: black-white differences. Cardiovasc Clin 1991;21(3):205-25.

Corti MC, Guralnik JM, Bilato C. Coronary heart disease risk factors in older persons. Aging (Milano) 1996;8(2):75-89.

Croft JB, Keenan NL, Sheridan DP, Wheeler FC, Speers MA. Waist-to-hip ratio in a biracial population: measurement, implications, and cautions for using guidelines to define high risk for cardiovascular disease. J Am Diet Assoc 1995;95(1):60-4.

D'Hoore W, Sicotte C, Tilquin C. Sex bias in the management of coronary artery disease in Quebec. Am J Public Health 1994;84(6):1013-5.

Davis KB, Chaitman B, Ryan T, Bittner V, Kennedy JW. Comparison of 15-year survival for men and women after initial medical or surgical treatment for coronary artery disease: a CASS registry study. Coronary Artery Surgery Study. J Am Coll Cardiol 1995;25(5):1000-9.

Denvir MA, Martin W, Tweddel AC, Hutton I. A comparison of adenosine and exercise stress 201T1 scintigraphy. Nucl Med Commun 1994;15(6):410-6.

Detre KM, Rosen AD, Bost JE, Cooper ME, Sutton-Tyrrell K, Holubkov R, et al. Contemporary practice of coronary revascularization in U.S. hospitals and hospitals participating in the bypass angioplasty revascularization investigation (BARI). J Am Coll Cardiol 1996;28(3):609-15.

Di Salvo TT, Paul SD, Lloyd-Jones D, Smith AJ, Villarreal-Levy G, Bamezai V, et al. Care of acute myocardial infarction by noninvasive and invasive cardiologists: procedure use, cost and outcome. J Am Coll Cardiol 1996;27(2):262-9.

Dickes MS, Stammers AH, Pierce ML, Alonso A, Fristoe L, Taft KJ, et al. Outcome analysis of coronary artery bypass grafting: minimally invasive versus standard techniques. Perfusion 1999;14(6):461-72.

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

Doliszny KM, Luepker RV, Burke GL, Pryor DB, Blackburn H. Estimated contribution of coronary artery bypass graft surgery to the decline in coronary heart disease mortality: the Minnesota Heart Survey. J Am Coll Cardiol 1994;24(1):95-103.

Du W, Ash AS, Berlowitz DR, Schwartz JS, Moskowitz MA. Variations in the management of acute myocardial infarction. Importance of clinical measures of disease severity. J Gen Intern Med 1996;11(6):334-41.

Duprez D. Is vascular disease in the female different from men? Int Angiol 1993;12(4):331-4.

Einbinder LC, Schulman KA. The effect of race on the referral process for invasive cardiac procedures. Med Care Res Rev 2000;57(Suppl 1):162-80.

Emery EM, Schmid TL, Kahn HS, Filozof PP. A review of the association between abdominal fat distribution, health outcome measures, and modifiable risk factors. Am J Health Promot 1993;7(5):342-53.

Eysmann SB, Douglas PS. Reperfusion and revascularization strategies for coronary artery disease in women. JAMA 1992;268(14):1903-7.

Feit F, Mueller HS, Braunwald E, Ross R, Hodges M, Herman MV, et al. Thrombolysis in Myocardial Infarction (TIMI) phase II trial: outcome comparison of a "conservative strategy" in community versus tertiary hospitals. The TIMI Research Group. J Am Coll Cardiol 1990;16(7):1529-34.

Ferguson TB, Jr., Muhlbaier LH, Salai DL, Wechsler AS. Coronary bypass grafting after failed elective and failed emergent percutaneous angioplasty. Relative risks of emergent surgical intervention. J Thorac Cardiovasc Surg 1988;95(5):761-72.

Fernandes CJ, Jr., Akamine N, Knobel E. Cardiac troponin: a new serum marker of myocardial injury in sepsis. Intensive Care Med 1999;25(10):1165-8.

Findlay IN. Coronary bypass surgery in women. Curr Opin Cardiol 1994;9(6):650-7.

Ford ES, Cooper RS. Racial/ethnic differences in health care utilization of cardiovascular procedures: a review of the evidence. Health Serv Res 1995;30(1 Pt 2):237-52.

Fu Y, Chang WC, Mark D, Califf RM, Mackenzie B, Granger CB, et al. Canadian-American differences in the management of acute coronary syndromes in the GUSTO IIb trial: one-year follow-up of patients without ST-segment elevation. Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) II Investigators. Circulation 2000;102(12):1375-81.

Fuller JH, Stevens LK, Wang SL. International variations in cardiovascular mortality associated with diabetes mellitus: the WHO Multinational Study of Vascular Disease in Diabetes. Ann Med 1996;28(4):319-22.

Gaziano JM, Skerrett PJ, Buring JE. Aspirin in the treatment and prevention of cardiovascular disease. Haemostasis 2000;30(Suppl 3):1-13.

Giacomini MK. Gender and ethnic differences in hospital-based procedure utilization in California. Arch Intern Med 1996;156(11):1217-24.

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

Giles TD, Fisher MB, Rush JE. Lisinopril and captopril in the treatment of heart failure in older patients. Comparison of a long- and short-acting angiotensin-converting enzyme inhibitor. Am J Med 1988;85(3B):44-7.

Giugliano RP, Llevadot J, Wilcox RG, Gurfinkel EP, McCabe CH, Charlesworth A, et al. Geographic variation in patient and hospital characteristics, management, and clinical outcomes in ST-elevation myocardial infarction treated with fibrinolysis. Results from InTIME-II. Eur Heart J 2001;22(18):1702-15.

Godsland IF, Wynn V, Crook D, Miller NE. Sex, plasma lipoproteins, and atherosclerosis: prevailing assumptions and outstanding questions. Am Heart J 1987;114(6):1467-503.

Goldberg KC, Hartz AJ, Jacobsen SJ, Krakauer H, Rimm AA. Racial and community factors influencing coronary artery bypass graft surgery rates for all 1986 Medicare patients. JAMA 1992;267(11):1473-7.

Granger CB, Hirsch J, Califf RM, Col J, White HD, Betriu A, et al. Activated partial thromboplastin time and outcome after thrombolytic therapy for acute myocardial infarction: results from the GUSTO-I trial. Circulation 1996;93(5):870-8.

Gregoire JP, Moisan J, Guibert R, Ciampi A, Milot A, Cote I, et al. Tolerability of antihypertensive drugs in a community-based setting. Clin Ther 2001;23(5):715-26.

Grumbach K, Anderson GM, Luft HS, Roos LL, Brook R. Regionalization of cardiac surgery in the United States and Canada. Geographic access, choice, and outcomes. JAMA 1995;274(16):1282-8.

Gueyffier F, Boutitie F, Boissel JP, Pocock S, Coope J, Cutler J, et al. Effect of antihypertensive drug treatment on cardiovascular outcomes in women and men. A meta-analysis of individual patient data from randomized, controlled trials. The INDANA Investigators. Ann Intern Med 1997;126(10):761-7.

Haffner SM. Impaired glucose tolerance, insulin resistance and cardiovascular disease. Diabet Med 1997;14(Suppl 3):S12-8.

Hannan EL, Kilburn H, Jr., O'Donnell JF, Lukacik G, Shields EP. Interracial access to selected cardiac procedures for patients hospitalized with coronary artery disease in New York State. Med Care 1991;29(5):430-41.

Hannan EL, Kumar D. Geographic variation in the utilization and choice of procedures for treating coronary artery disease in New York State. Ischaemic Heart Disease Patient Outcomes Research Team (PORT). J Health Serv Res Policy 1997;2(3):137-43.

Hasdai D, Holmes DR, Jr., Topol EJ, Berger PB, Criger DA, Hochman JS, et al. Frequency and clinical outcome of cardiogenic shock during acute myocardial infarction among patients receiving reteplase or alteplase. Results from GUSTO-III. Global Use of Strategies to Open Occluded Coronary Arteries. Eur Heart J 1999;20(2):128-35.

Haymart MR, Dickfeld T, Nass C, Blumenthal RS. Percutaneous coronary intervention vs. medical therapy: what are the implications for women? J Womens Health Gend Based Med 2002;11(4):347-55.

Heiat A, Vaccarino V, Krumholz HM. An evidence-based assessment of federal guidelines for overweight and obesity as they apply to elderly persons. Arch Intern Med 2001;161(9):1194-203.

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

Hochman JS, McCabe CH, Stone PH, Becker RC, Cannon CP, DeFeo-Fraulini T, et al. Outcome and profile of women and men presenting with acute coronary syndromes: a report from TIMI IIIB. TIMI Investigators. Thrombolysis in Myocardial Infarction. J Am Coll Cardiol 1997;30(1):141-8.

Hume AL, Barbour MM, Willey CJ, Assaf AR, Lapane KL, Carleton RA. Changing trends in antihypertensive therapy in two New England communities during the 1980s. Pharmacotherapy 1993;13(3):244-51.

Hussain KM, Kogan A, Estrada AQ, Kostandy G, Foschi A, Dadkhah S. Referral pattern and outcome in men and women undergoing coronary artery bypass surgery--a critical review. Angiology 1998;49(4):243-50.

Hutchinson LA, Pasternack PF, Baumann FG, Grossi EA, Riles TS, Lamparello PJ, et al. Is there detrimental gender bias in preoperative cardiac management of patients undergoing vascular surgery? Circulation 1994;90(5 Pt 2):II220-3.

Izzat MB, West RR, Bryan AJ, Angelini GD. Coronary artery bypass surgery: current practice in the United Kingdom. Br Heart J 1994;71(4):382-5.

Jackson RE, Anderson W, Peacock WFt, Vaught L, Carley RS, Wilson AG. Effect of a patient's sex on the timing of thrombolytic therapy. Ann Emerg Med 1996;27(1):8-15.

Jaglal SB, Goel V, Naylor CD. Sex differences in the use of invasive coronary procedures in Ontario. Can J Cardiol 1994;10(2):239-44.

Janzon M, Levin LA, Swahn E. Cost-effectiveness of an invasive strategy in unstable coronary artery disease; results from the FRISC II invasive trial. The Fast Revascularisation during InStability in Coronary artery disease. Eur Heart J 2002;23(1):31-40.

Jarrett RJ. The cardiovascular risk associated with impaired glucose tolerance. Diabet Med 1996;13(3 Suppl 2):S15-9.

Johnson PA, Lee TH, Cook EF, Rouan GW, Goldman L. Effect of race on the presentation and management of patients with acute chest pain. Ann Intern Med 1993;118(8):593-601.

Johnson PA, Goldman L, Orav EJ, Zhou L, Garcia T, Pearson SD, et al. Gender differences in the management of acute chest pain. Support for the "Yentl syndrome". J Gen Intern Med 1996;11(4):209-17.

Khan SS, Nessim S, Gray R, Czer LS, Chaux A, Matloff J. Increased mortality of women in coronary artery bypass surgery: evidence for referral bias. Ann Intern Med 1990;112(8):561-7.

Kilaru PK, Kelly RF, Calvin JE, Parrillo JE. Utilization of coronary angiography and revascularization after acute myocardial infarction in men and women risk stratified by the American College of Cardiology/American Heart Association guidelines. J Am Coll Cardiol 2000;35(4):974-9.

Kinn JW, O'Neill WW, Benzuly KH, Jones DE, Grines CL. Primary angioplasty reduces risk of myocardial rupture compared to thrombolysis for acute myocardial infarction. Cathet Cardiovasc Diagn 1997;42(2):151-7.

Kloner RA, Vetrovec GW, Materson BJ, Levenstein M. Safety of long-acting dihydropyridine calcium channel blockers in hypertensive patients. Am J Cardiol 1998;81(2):163-9.

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

Klungel OH, de Boer A, Paes AH, Seidell JC, Bakker A. Sex differences in the pharmacological treatment of hypertension: a review of population-based studies. J Hypertens 1997;15(6):591-600.

Klungel OH, de Boer A, Paes AH, Seidell JC, Bakker A. Sex differences in antihypertensive drug use: determinants of the choice of medication for hypertension. J Hypertens 1998;16(10):1545-53.

Klungel OH, Paes AH, de Boer A, Kuyvenhoven MM, Seidell JC, Bakker A. Sex differences in the medication choice for hypertension in general practice. A study with written case simulations. Pharm World Sci 2000;22(4):140-6.

Ko W, Gold JP, Lazzaro R, Zelano JA, Lang S, Isom OW, et al. Survival analysis of octogenarian patients with coronary artery disease managed by elective coronary artery bypass surgery versus conventional medical treatment. Circulation 1992;86(5 Suppl):II191-7.

Krumholz HM, Douglas PS, Lauer MS, Pasternak RC. Selection of patients for coronary angiography and coronary revascularization early after myocardial infarction: is there evidence for a gender bias? Ann Intern Med 1992;116(10):785-90.

Kudenchuk PJ, Maynard C, Martin JS, Wirkus M, Weaver WD. Comparison of presentation, treatment, and outcome of acute myocardial infarction in men versus women (the Myocardial Infarction Triage and Intervention Registry). Am J Cardiol 1996;78(1):9-14.

Larsen J, Vaccheri A, Andersen M, Montanaro N, Bergman U. Lack of adherence to lipid-lowering drug treatment. A comparison of utilization patterns in defined populations in Funen, Denmark and Bologna, Italy. Br J Clin Pharmacol 2000;49(5):463-71.

Lau GS, Chan JC, Chu PL, Tse DC, Critchely JA. Use of antidiabetic and antihypertensive drugs in hospital and outpatient settings in Hong Kong. Ann Pharmacother 1996;30(3):232-7.

Lear JT, Lawrence IG, Burden AC, Pohl JE. A comparison of stress test referral rates and outcome between Asians and Europeans. J R Soc Med 1994;87(11):661-2.

Lear JT, Lawrence IG, Pohl JE, Burden AC. Myocardial infarction and thrombolysis: a comparison of the Indian and European populations on a coronary care unit. J R Coll Physicians Lond 1994;28(2):143-7.

Lee WL, Cheung AM, Cape D, Zinman B. Impact of diabetes on coronary artery disease in women and men: a meta-analysis of prospective studies. Diabetes Care 2000;23(7):962-8.

Lewsey JD, Murray GD, Leyland AH, Boddy FA. Comparing outcomes of percutaneous transluminal coronary angioplasty with coronary artery bypass grafting; can routine health service data complement and enhance randomized controlled trials? Eur Heart J 1999;20(23):1731-5.

Lincoff AM, Califf RM, Ellis SG, Sigmon KN, Lee KL, Leimberger JD, et al. Thrombolytic therapy for women with myocardial infarction: is there a gender gap? Thrombolysis and Angioplasty in Myocardial Infarction Study Group. J Am Coll Cardiol 1993;22(7):1780-7.

Lobo RA. Lipids, clotting factors, and diabetes: endogenous risk factors for cardiovascular disease. Am J Obstet Gynecol 1988;158(6 Pt 2):1584-91.

Magrini N, Einarson T, Vaccheri A, McManus P, Montanaro N, Bergman U. Use of lipid-lowering drugs from 1990 to 1994: an international comparison among Australia, Finland, Italy (Emilia Romagna Region), Norway and Sweden. Eur J Clin Pharmacol 1997;53(3-4):185-9.

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

Majeed A, Moser K, Maxwell R. Age, sex and practice variations in the use of statins in general practice in England and Wales. J Public Health Med 2000;22(3):275-9.

Majumdar SR, Gurwitz JH, Soumerai SB. Undertreatment of hyperlipidemia in the secondary prevention of coronary artery disease. J Gen Intern Med 1999;14(12):711-7.

Malenka DJ, O'Rourke D, Miller MA, Hearne MJ, Shubrooks S, Kellett MA, Jr., et al. Cause of in-hospital death in 12,232 consecutive patients undergoing percutaneous transluminal coronary angioplasty. The Northern New England Cardiovascular Disease Study Group. Am Heart J 1999;137(4 Pt 1):632-8.

Manolio TA, Pearson TA, Wenger NK, Barrett-Connor E, Payne GH, Harlan WR. Cholesterol and heart disease in older persons and women. Review of an NHLBI workshop. Ann Epidemiol 1992;2(1-2):161-76.

Marber M, MacRae C, Joy M. Delay to invasive investigation and revascularisation for coronary heart disease in south west Thames region: a two tier system? BMJ 1991;302(6786):1189-91.

Maron DJ. Percutaneous coronary intervention versus medical therapy for coronary heart disease. Curr Atheroscler Rep 2000;2(4):290-6.

Martikainen J, Klaukka T, Reunanen A, Peura S, Wahlroos H. Recent trends in the consumption of lipid-lowering drugs in Finland. J Clin Epidemiol 1996;49(12):1453-57.

Matsui K, Polanczyk CA, Gaspoz JM, Theres H, Kleber FX, Sobashima A, et al. Management of patients with acute myocardial infarction at five academic medical centers: clinical characteristics, resource utilization, and outcome. J Investig Med 1999;47(3):134-40.

Maynard C, Litwin PE, Martin JS, Weaver WD. Gender differences in the treatment and outcome of acute myocardial infarction. Results from the Myocardial Infarction Triage and Intervention Registry. Arch Intern Med 1992;152(5):972-6.

McGlynn EA, Naylor CD, Anderson GM, Leape LL, Park RE, Hilborne LH, et al. Comparison of the appropriateness of coronary angiography and coronary artery bypass graft surgery between Canada and New York State. JAMA 1994;272(12):934-40.

Mendelson G, Aronow WS. Underutilization of measurement of serum low-density lipoprotein cholesterol levels and of lipid-lowering therapy in older patients with manifest atherosclerotic disease. J Am Geriatr Soc 1998;46(9):1128-31.

Merlo J, Ranstam J, Rastam L, Wessling A, Melander A. Age standardisation of drug utilisation: comparisons of different methods using cardiovascular drug data from Sweden and Spain. Eur J Clin Pharmacol 1994;46(5):393-8.

Miller M, Byington R, Hunninghake D, Pitt B, Furberg CD. Sex bias and underutilization of lipid-lowering therapy in patients with coronary artery disease at academic medical centers in the United States and Canada. Prospective Randomized Evaluation of the Vascular Effects of Norvasc Trial (PREVENT) Investigators. Arch Intern Med 2000;160(3):343-7.

Miller TD, Roger VL, Hodge DO, Hopfenspirger MR, Bailey KR, Gibbons RJ. Gender differences and temporal trends in clinical characteristics, stress test results and use of invasive procedures in patients undergoing evaluation for coronary artery disease. J Am Coll Cardiol 2001;38(3):690-7

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

Naylor CD, Ugnat AM, Weinkauf D, Anderson GM, Wielgosz A. Coronary artery bypass grafting in Canada: What is its rate of use? Which rate is right? CMAJ 1992;146(6):851-9.

O'Shea EB. A study of the use of aspirin by general practitioners in suspected myocardial infarction. Ir Med J 2001;94(2):48-50, 52.

Oliver MF. Cholesterol and coronary disease--outstanding questions. Cardiovasc Drugs Ther 1992;6(2):131-6.

Onder G, Gambassi G, Landi F, Pedone C, Cesari M, Carbonin PU, et al. Trends in antihypertensive drugs in the elderly: the decline of thiazides. J Hum Hypertens 2001;15(5):291-7.

Orlandini A, Tuero E, Paolasso E, Vilamajo OG, Diaz R. Usefulness of pharmacologic stress echocardiography in a chest pain center. Am J Cardiol 2000;86(11):1247-50, A6.

Pagley PR, Yarzebski J, Goldberg R, Chen Z, Chiriboga D, Dalen P, et al. Gender differences in the treatment of patients with acute myocardial infarction. A multihospital, community-based perspective. Arch Intern Med 1993;153(5):625-9.

Petticrew M, McKee M, Jones J. Coronary artery surgery: are women discriminated against? BMJ 1993;306(6886):1164-6.

Pfeffer MA, Moye LA, Braunwald E, Basta L, Brown EJ, Jr., Cuddy TE, et al. Selection bias in the use of thrombolytic therapy in acute myocardial infarction. The SAVE Investigators. JAMA 1991;266(4):528-32.

Pfisterer M, Cox JL, Granger CB, Brener SJ, Naylor CD, Califf RM, et al. Atenolol use and clinical outcomes after thrombolysis for acute myocardial infarction: the GUSTO-I experience. Global Utilization of Streptokinase and TPA (alteplase) for Occluded Coronary Arteries. J Am Coll Cardiol 1998;32(3):634-40.

Philbin EF, McCullough PA, DiSalvo TG, Dec GW, Jenkins PL, Weaver WD. Underuse of invasive procedures among Medicaid patients with acute myocardial infarction. Am J Public Health 2001;91(7):1082-8.

Pilote L, Granger C, Armstrong PW, Mark DB, Hlatky MA. Differences in the treatment of myocardial infarction between the United States and Canada. A survey of physicians in the GUSTO trial. Med Care 1995;33(6):598-610.

Pilote L, Califf RM, Sapp S, Miller DP, Mark DB, Weaver WD, et al. Regional variation across the United States in the management of acute myocardial infarction. GUSTO-1 Investigators. Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries. N Engl J Med 1995;333(9):565-72.

Pocock SJ, McCormack V, Gueyffier F, Boutitie F, Fagard RH, Boissel JP. A score for predicting risk of death from cardiovascular disease in adults with raised blood pressure, based on individual patient data from randomised controlled trials. BMJ 2001;323(7304):75-81.

Pretre R, Turina MI. Analysis of trials of surgery vs angioplasty in myocardial revascularization. Semin Interv Cardiol 1999;4(4):235-43.

Raine RA, Crayford TJ, Chan KL, Chambers JB. Gender differences in the treatment of patients with acute myocardial ischemia and infarction in England. Int J Technol Assess Health Care 1999;15(1):136-46.

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

Ramsey DJ, Goff DC, Wear ML, Labarthe DR, Nichaman MZ. Sex and ethnic differences in use of myocardial revascularization procedures in Mexican Americans and non-Hispanic whites: the Corpus Christi Heart Project. J Clin Epidemiol 1997;50(5):603-9.

Rao AV. Coronary heart disease risk factors in women: focus on gender differences. J La State Med Soc 1998;150(2):67-72.

Rifkind BM. High-density lipoprotein cholesterol and coronary artery disease: survey of the evidence. Am J Cardiol 1990;66(6):3A-6A.

Rill V, Brown DL. Practice of coronary angioplasty in California in 1995 : comparison to 1989 and impact of coronary stenting. Circulation 1999;99(21):e12.

Rochon PA, Clark JP, Binns MA, Patel V, Gurwitz JH. Reporting of gender-related information in clinical trials of drug therapy for myocardial infarction. CMAJ 1998;159(4):321-7.

Roger VL, Farkouh ME, Weston SA, Reeder GS, Jacobsen SJ, Zinsmeister AR, et al. Sex differences in evaluation and outcome of unstable angina. Jama 2000;283(5):646-52.

Roger VL, Pellikka PA, Bell MR, Chow CW, Bailey KR, Seward JB. Sex and test verification bias. Impact on the diagnostic value of exercise echocardiography. Circulation 1997;95(2):405-10.

Rojas-Fernandez CH, Kephart GC, Sketris IS, Kass K. Underuse of acetylsalicylic acid in individuals with myocardial infarction, ischemic heart disease or stroke: data from the 1995 population-based Nova Scotia Health Survey. Can J Cardiol 1999;15(3):291-6.

Saha S, Stettin GD, Redberg RF. Gender and willingness to undergo invasive cardiac procedures. J Gen Intern Med 1999;14(2):122-5.

Sane DC, Stump DC, Topol EJ, Sigmon KN, Clair WK, Kereiakes DJ, et al. Racial differences in responses to thrombolytic therapy with recombinant tissue-type plasminogen activator. Increased fibrin(ogen)olysis in blacks. The Thrombolysis and Angioplasty in Myocardial Infarction Study Group. Circulation 1991;83(1):170-5.

Schneider EC, Leape LL, Weissman JS, Piana RN, Gatsonis C, Epstein AM. Racial differences in cardiac revascularization rates: does "overuse" explain higher rates among white patients? Ann Intern Med 2001;135(5):328-37.

Shahar E, Folsom AR, Romm FJ, Bisgard KM, Metcalf PA, Crum L, et al. Patterns of aspirin use in middle-aged adults: the Atherosclerosis Risk in Communities (ARIC) Study. Am Heart J 1996;131(5):915-22.

Shaw LJ, Miller DD, Romeis JC, Kargl D, Younis LT, Chaitman BR. Gender differences in the noninvasive evaluation and management of patients with suspected coronary artery disease. Ann Intern Med 1994;120(7):559-66.

Simons-Morton DG, Calfas KJ, Oldenburg B, Burton NW. Effects of interventions in health care settings on physical activity or cardiorespiratory fitness. Am J Prev Med 1998;15(4):413-30.

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

Sketris IS, Kephart GC, Hicks VA, Hubbard EJ, Brown MG, Chandler RF, et al. Prescribing patterns of antilipemic drugs and prevalence of hypercholesterolemia in the Nova Scotia population more than 65 years old. Ann Pharmacother 1995;29(6):576-81.

Steingart RM, Packer M, Hamm P, Coglianese ME, Gersh B, Geltman EM, et al. Sex differences in the management of coronary artery disease. Survival and Ventricular Enlargement Investigators. N Engl J Med 1991;325(4):226-30.

Stern MP, Haffner SM. Body fat distribution and hyperinsulinemia as risk factors for diabetes and cardiovascular disease. Arteriosclerosis 1986;6(2):123-30.

Strandberg TE, Pitkanen A, Larjo P, Hirvonen P, Kohvakka A. Attitude changes of general practitioners towards lowering LDL cholesterol. J Cardiovasc Risk 1998;5(1):43-6.

Strauss R, Pfeifer C, Muhlberger V, Ulmer H, Pfeiffer KP. Effects of morbidity, age, gender and region on percutaneous transluminal coronary angioplasty (PTCA) utilisation. Public Health 1999;113(2):79-87.

Sudano JJ, Jr., Baker DW. Antihypertensive medication use in Hispanic adults: a comparison with black adults and white adults. Med Care 2001;39(6):575-87.

Sullivan AK, Holdright DR, Wright CA, Sparrow JL, Cunningham D, Fox KM. Chest pain in women: clinical, investigative, and prognostic features. BMJ 1994;308(6933):883-6.

Swahn E. The care of patients with ischaemic heart disease from a gender perspective. Eur Heart J 1998;19(12):1758-65.

Tobin JN, Wassertheil-Smoller S, Wexler JP, Steingart RM, Budner N, Lense L, et al. Sex bias in considering coronary bypass surgery. Ann Intern Med 1987;107(1):19-25.

Toiber F, Murthy VS. Prescribing and usage patterns of two antihypertensive agents: a comparison of terazosin and enalapril. Hosp Formul 1991;26(10):811-3, 817-8.

Tsuyuki RT, Teo KK, Ikuta RM, Bay KS, Greenwood PV, Montague TJ. Mortality risk and patterns of practice in 2,070 patients with acute myocardial infarction, 1987-92. Relative importance of age, sex, and medical therapy. Chest 1994;105(6):1687-92.

Van de Werf F, Topol EJ, Lee KL, Woodlief LH, Granger CB, Armstrong PW, et al. Variations in patient management and outcomes for acute myocardial infarction in the United States and other countries. Results from the GUSTO trial. Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries. JAMA 1995;273(20):1586-91.

Wallenius S, Peura S, Klaukka T, Enlund H. Who is using antihypertensive drugs? A prescription analysis from Finland. Scand J Prim Health Care 1996;14(1):54-61.

Weaver WD, White HD, Wilcox RG, Aylward PE, Morris D, Guerci A, et al. Comparisons of characteristics and outcomes among women and men with acute myocardial infarction treated with thrombolytic therapy. GUSTO-I investigators. JAMA 1996;275(10):777-82.

Weintraub WS, Wenger NK, Jones EL, Craver JM, Guyton RA. Changing clinical characteristics of coronary surgery patients. Differences between men and women. Circulation 1993;88(5 Pt 2):II79-86.

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

White HD, Barbash GI, Califf RM, Simes RJ, Granger CB, Weaver WD, et al. Age and outcome with contemporary thrombolytic therapy. Results from the GUSTO-I trial. Global Utilization of Streptokinase and TPA for Occluded coronary arteries trial. Circulation 1996;94(8):1826-33.

Wilkinson P, Laji K, Ranjadayalan K, Parsons L, Timmis AD. Acute myocardial infarction in women: survival analysis in first six months. BMJ 1994;309(6954):566-9.

Yapp CK, Taylor LS, Ow CY, Jamrozik K, Puddey IB. Hypertension management: a comparison of urban versus rural general practitioners in Western Australia. Clin Exp Pharmacol Physiol 1995;22(6-7):447-9.

Yarzebski J, Col N, Pagley P, Savageau J, Gore J, Goldberg R.
Gender differences and factors associated with the receipt of thrombolytic therapy in patients with acute myocardial infarction: a community-wide perspective. Am Heart J 1996;131(1):43-50.

5.01 Troponins

Balk EM, Ioannidis JP, Salem D, Chew PW, Lau J. Accuracy of biomarkers to diagnose acute cardiac ischemia in the emergency department: a meta-analysis. Ann Emerg Med 2001;37(5):478-94.

Christenson RH, Duh SH. Evidence based approach to practice guides and decision thresholds for cardiac markers. Scand J Clin Lab Invest Suppl 1999;230:90-102.

Ebell MH, White LL, Weismantel D. A systematic review of troponin T and I values as a prognostic tool for patients with chest pain. J Fam Pract 2000;49(8):746-53.

Heidenreich PA, et al. The Prognostic Value of Troponin in Patients with Non-ST Elevation Acute Coronary Syndromes: A Meta-Analysis. J Am Coll Cardiol 2001;38(2):478-85.

Olatidoye AG, Wu AH, Feng YJ, Waters D. Prognostic role of troponin T versus troponin I in unstable angina pectoris for cardiac events with meta-analysis comparing published studies. Am J Cardiol 1998;81(12):1405-10.

Ottani F, Galvani M, Nicolini FA, Ferrini D, Pozzati A, Di Pasquale G, et al. Elevated cardiac troponin levels predict the risk of adverse outcome in patients with acute coronary syndromes. Am Heart J 2000;140(6):917-27.

Safstrom K, Lindahl B, Swahn E. Risk stratification in unstable coronary artery disease--exercise test and troponin T from a gender perspective. FRISC-Study Group. Fragmin during InStability in Coronary artery disease. J Am Coll Cardiol 2000;35(7):1791-800.

Wu AH, Lane PL. Metaanalysis in clinical chemistry: validation of cardiac troponin T as a marker for ischemic heart diseases. Clin Chem 1995;41(8 Pt 2):1228-33.

5.02 Creatine kinase MB

Balk EM, Ioannidis JP, Salem D, Chew PW, Lau J. Accuracy of biomarkers to diagnose acute cardiac ischemia in the emergency department: a meta-analysis. Ann Emerg Med 2001;37(5):478-94.

Christenson RH, Duh SH. Evidence based approach to practice guides and decision thresholds for cardiac markers. Scand J Clin Lab Invest Suppl 1999;230:90-102.

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

Olatidoye AG, Wu AH, Feng YJ, Waters D. Prognostic role of troponin T versus troponin I in unstable angina pectoris for cardiac events with meta-analysis comparing published studies. Am J Cardiol 1998;81(12):1405-10.

Wu AH, Lane PL. Metaanalysis in clinical chemistry: validation of cardiac troponin T as a marker for ischemic heart diseases. Clin Chem 1995;41(8 Pt 2):1228-33.

5.03 Myoglobin

Balk EM, Ioannidis JP, Salem D, Chew PW, Lau J. Accuracy of biomarkers to diagnose acute cardiac ischemia in the emergency department: a meta-analysis. Ann Emerg Med 2001;37(5):478-94.

Christenson RH, Duh SH. Evidence based approach to practice guides and decision thresholds for cardiac markers. Scand J Clin Lab Invest Suppl 1999;230:90-102.

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

1. Brown AD, Garber AM. Cost effectiveness of coronary heart disease prevention strategies in adults. Pharmacoeconomics 1998;14(1):27-48.
2. Castillo PA, Palmer CS, Halpern MT, Hatziandreu EJ, Gersh BJ. Cost-effectiveness of thrombolytic therapy for acute myocardial infarction. Ann Pharmacother 1997;31(5):596-603.
3. Cleland JG, Walker A. Is medical treatment for angina the most cost-effective option? Eur Heart J 1997;18(Suppl B):B35-42.
4. Davie AP. ACE inhibitors after myocardial infarction. Clinical and economic considerations. Pharmacoeconomics 2000;17(3):237-43.
5. 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.
6. Garber AM, Browner WS, Hulley SB. Cholesterol screening in asymptomatic adults, revisited. Part 2. Ann Intern Med 1996;124(5):518-31.
7. Goldman L, Coxson P, Hunink MG, Goldman PA, Tosteson AN, Mittleman M, et al. The relative influence of secondary versus primary prevention using the National Cholesterol Education Program Adult Treatment Panel II guidelines. J Am Coll Cardiol 1999;34(3):768-76.
8. Hillegass WB, Newman AR, Raco DL. Glycoprotein IIb/IIIa receptor therapy in percutaneous coronary intervention and non-ST-segment elevation acute coronary syndromes. Estimating the economic implications. Pharmacoeconomics 2001;19(1):41-55.
9. Hunink MG, Kuntz KM, Fleischmann KE, Brady TJ. Noninvasive imaging for the diagnosis of coronary artery disease: focusing the development of new diagnostic technology. Ann Intern Med 1999;131(9):673-80.
10. Kellett J, Clarke J. Comparison of "accelerated" tissue plasminogen activator with streptokinase for treatment of suspected myocardial infarction. Med Decis Making 1995;15(4):297-310.
11. 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.
12. Marine JE, Freedberg KA, Davidoff R. Cost-effectiveness of stress-echocardiography. Cardiol Clin 1999;17(3):583-95, x.
13. Mark DB, Hlatky MA, Califf RM, Naylor CD, Lee KL, Armstrong PW, et al. Cost effectiveness of thrombolytic therapy with tissue plasminogen activator as compared with streptokinase for acute myocardial infarction. N Engl J Med 1995;332(21):1418-24.
14. McGregor M, Brophy JM. Use of abciximab (c7E3 Fab, ReoPro) as an adjunct to balloon angioplasty. Can J Cardiol 1999;15(2):201-7.
15. Midgette AS, Wong JB, Beshansky JR, Porath A, Fleming C, Pauker SG. Cost-effectiveness of streptokinase for acute myocardial infarction: A combined meta-analysis and decision analysis of the effects of infarct location and of likelihood of infarction. Med Decis Making 1994;14(2):108-17.
16. Montagne O, Vedel I, Durand-Zaleski I. Assessment of the impact of fibrates and diet on survival and their cost-effectiveness: evidence from randomized, controlled trials in coronary heart disease and health economic evaluations. Clin Ther 1999;21(11):2027-35.
17. Moulds RF. Measurement of cost-effectiveness of drug therapy: a review of the treatment of hypertension. Med J Aust 1990;153(Suppl):S4-6.
18. Prosser LA, Stinnett AA, Goldman PA, Williams LW, Hunink MG, Goldman L, et al. Cost-effectiveness of cholesterol-lowering therapies according to selected patient characteristics. Ann Intern Med 2000;132(10):769-79.
19. Tice JA, Ross E, Coxson PG, Rosenberg I, Weinstein MC, Hunink MG, et al. Cost-effectiveness of vitamin therapy to lower plasma homocysteine levels for the prevention of coronary heart disease: effect of grain fortification and beyond. JAMA 2001;286(8):936-43.
20. van der Weijden T, Knottnerus JA, Ament AJ, Stoffers HE, Grol RP. Economic evaluation of cholesterol-related interventions in general practice. An appraisal of the evidence. J Epidemiol Community Health 1998;52(9):586-94.

Appendix E: Cost-effectiveness Analyses and Decision Analyses Articles (continued)

21. Wong JB, Sonnenberg FA, Salem DN, Pauker SG. Myocardial revascularization for chronic stable angina. Analysis of the role of percutaneous transluminal coronary angioplasty based on data available in 1989. Ann Intern Med 1990;113(11):852-71.

Appendix F: Clinical Practice Guidelines (N = 43)

1. 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.
2. Evaluation of technologies for identifying acute cardiac ischemia in emergency departments. Evid Rep Technol Assess (Summ) 2000(26):1-4.
3. Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, et al. ACC/AHA guidelines for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina). J Am Coll Cardiol 2000;36(3):970-1062.
4. Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, et al. ACC/AHA guidelines for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction: executive summary and recommendations. A report of the American College of Cardiology/American Heart Association task force on practice guidelines (committee on the management of patients with unstable angina). Circulation 2000;102(10):1193-209.
5. Eagle KA, Guyton RA, Davidoff R, Ewy GA, Fonger J, Gardner TJ, et al. ACC/AHA Guidelines for Coronary Artery Bypass Graft Surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1991 Guidelines for Coronary Artery Bypass Graft Surgery). American College of Cardiology/American Heart Association. J Am Coll Cardiol 1999;34(4):1262-347.
6. Eagle KA, Guyton RA, Davidoff R, Ewy GA, Fonger J, Gardner TJ, et al. ACC/AHA guidelines for coronary artery bypass graft surgery: executive summary and recommendations : A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to revise the 1991 guidelines for coronary artery bypass graft surgery). Circulation 1999;100(13):1464-80.
7. Eckel RH. Obesity and heart disease: a statement for healthcare professionals from the Nutrition Committee, American Heart Association. Circulation 1997;96(9):3248-50.
8. Eckel RH, Krauss RM. American Heart Association call to action: obesity as a major risk factor for coronary heart disease. AHA Nutrition Committee. Circulation 1998;97(21):2099-100.
9. Fletcher GF, Balady G, Blair SN, Blumenthal J, Caspersen C, Chaitman B, et al. Statement on exercise: benefits and recommendations for physical activity programs for all Americans. A statement for health professionals by the Committee on Exercise and Cardiac Rehabilitation of the Council on Clinical Cardiology, American Heart Association. Circulation 1996;94(4):857-62.
10. Fletcher GF, Balady GJ, Amsterdam EA, Chaitman B, Eckel R, Fleg J, et al. Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association. Circulation 2001;104(14):1694-740.
11. Gibbons RJ, Balady GJ, Beasley JW, Bricker JT, Duvernoy WF, Froelicher VF, et al. ACC/AHA guidelines for exercise testing: executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Exercise Testing). Circulation 1997;96(1):345-54.
12. Gibbons RJ, Chatterjee K, Daley J, Douglas JS, Fihn SD, Gardin JM, et al. ACC/AHA/ACP-ASIM guidelines for the management of patients with chronic stable angina: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients With Chronic Stable Angina). J Am Coll Cardiol 1999;33(7):2092-197.
13. Gibbons RJ, Chatterjee K, Daley J, Douglas JS, Fihn SD, Gardin JM, et al. ACC/AHA/ACP-ASIM guidelines for the management of patients with chronic stable angina: executive summary and recommendations. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients with Chronic Stable Angina). Circulation 1999;99(21):2829-48.

Appendix F: Clinical Practice Guidelines (continued)

14. Grundy SM, Balady GJ, Criqui MH, Fletcher G, Greenland P, Hiratzka LF, et al. Guide to primary prevention of cardiovascular diseases. A statement for healthcare professionals from the Task Force on Risk Reduction. American Heart Association Science Advisory and Coordinating Committee. Circulation 1997;95(9):2329-31.
15. Grundy SM, Balady GJ, Criqui MH, Fletcher G, Greenland P, Hiratzka LF, et al. When to start cholesterol-lowering therapy in patients with coronary heart disease. A statement for healthcare professionals from the American Heart Association Task Force on Risk Reduction. Circulation 1997;95(6):1683-5.
16. Grundy SM, Balady GJ, Criqui MH, Fletcher G, Greenland P, Hiratzka LF, et al. Primary prevention of coronary heart disease: guidance from Framingham: a statement for healthcare professionals from the AHA Task Force on Risk Reduction. American Heart Association. Circulation 1998;97(18):1876-87.
17. Grundy SM, Benjamin IJ, Burke GL, Chait A, Eckel RH, Howard BV, et al. Diabetes and cardiovascular disease: a statement for healthcare professionals from the American Heart Association. Circulation 1999;100(10):1134-46.
18. Hennekens CH, Dyken ML, Fuster V. Aspirin as a therapeutic agent in cardiovascular disease: a statement for healthcare professionals from the American Heart Association. Circulation 1997;96(8):2751-3.
19. Hirsh J, Anand SS, Halperin JL, Fuster V. AHA Scientific Statement: Guide to anticoagulant therapy: heparin: a statement for healthcare professionals from the American Heart Association. Arterioscler Thromb Vasc Biol 2001;21(7):E9-9.
20. Hirsh J, Anand SS, Halperin JL, Fuster V. Guide to anticoagulant therapy: Heparin : a statement for healthcare professionals from the American Heart Association. Circulation 2001;103(24):2994-3018.
21. Krauss RM, Winston M, Fletcher BJ, Grundy SM. Obesity : impact on cardiovascular disease. Circulation 1998;98(14):1472-6.
22. LaRosa JC. The clinical lipid specialist. Task Force on Cholesterol Issues, American Heart Association. Circulation 1990;82(4):1548.
23. LaRosa JC, Hunninghake D, Bush D, Criqui MH, Getz GS, Gotto AM, Jr., et al. The cholesterol facts. A summary of the evidence relating dietary fats, serum cholesterol, and coronary heart disease. A joint statement by the American Heart Association and the National Heart, Lung, and Blood Institute. The Task Force on Cholesterol Issues, American Heart Association. Circulation 1990;81(5):1721-33.
24. Malinow MR, Bostom AG, Krauss RM. Homocyst(e)ine, diet, and cardiovascular diseases: a statement for healthcare professionals from the Nutrition Committee, American Heart Association. Circulation 1999;99(1):178-82.
25. Milne R. HMG-CoA reductase inhibitor treatment in the prevention of coronary heart disease Southampton: Wessex Institute for Health Research and Development. Wessex Institute for Health Research and Development. DEC Report No. 72. 1997
26. Mosca L, Grundy SM, Judelson D, King K, Limacher M, Oparil S, et al. AHA/ACC scientific statement: consensus panel statement. Guide to preventive cardiology for women. American Heart Association/American College of Cardiology. J Am Coll Cardiol 1999;33(6):1751-5.
27. Mosca L, Grundy SM, Judelson D, King K, Limacher M, Oparil S, et al. Guide to Preventive Cardiology for Women.AHA/ACC Scientific Statement Consensus panel statement. Circulation 1999;99(18):2480-4.
28. NHS Centre for Reviews and Dissemination. Management of stable angina. Effective Health Care. 1997;3:1-8.
29. O'Rourke RA, Brundage BH, Froelicher VF, Greenland P, Grundy SM, Hachamovitch R, et al. American College of Cardiology/American Heart Association Expert Consensus document on electron-beam computed tomography for the diagnosis and prognosis of coronary artery disease. Circulation 2000;102(1):126-40.

Appendix F: Clinical Practice Guidelines (continued)

30. Ockene IS, Miller NH. Cigarette smoking, cardiovascular disease, and stroke: a statement for healthcare professionals from the American Heart Association. American Heart Association Task Force on Risk Reduction. Circulation 1997;96(9):3243-7.
31. Perras C, Baladi J. A clinical and economic review of HMG-CoA reductase inhibitors in coronary heart disease – summary. Ottawa: Canadian Coordinating Office for Health Technology Assessment/Office Canadien de Coordination de L'Evaluation des Technologies de la Sante. Canadian Coordinating Office for Health Technology Assessment (CCOHTA). 12039012. technology Overview. 1998.
32. Ramsay LE, Haq IU, Jackson PR, Yeo WW, Pickin DM, Payne JN. Targeting lipid-lowering drug therapy for primary prevention of coronary disease: an updated Sheffield table. Lancet 1996;348(9024):387-8.
33. Ryan TJ, Anderson JL, Antman EM, Braniff BA, Brooks NH, Califf RM, et al. ACC/AHA guidelines for the management of patients with acute myocardial infarction: executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction). Circulation 1996;94(9):2341-50.
34. Ryan TJ, Antman EM, Brooks NH, Califf RM, Hillis LD, Hiratzka LF, et al. 1999 update: ACC/AHA Guidelines for the Management of Patients With Acute Myocardial Infarction: Executive Summary and Recommendations: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction). Circulation 1999;100(9):1016-30.
35. Savoie I, Wright J, Bassett K. Lipid lowering therapy Vancouver: B.C. Office of Health technology Assessment, Centre for Health Services and Policy Research, University of British Columbia. Finnish Office for Health Care Technology Assessment (FinOHTA). 1896256112. BCOHTA 98:4J. 1998.
36. 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.
37. Smith SC, Jr., Blair SN, Criqui MH, Fletcher GF, Fuster V, Gersh BJ, et al. AHA consensus panel statement. Preventing heart attack and death in patients with coronary disease. The Secondary Prevention Panel. J Am Coll Cardiol 1995;26(1):292-4.
38. Smith SC, Jr., Dove JT, Jacobs AK, Kennedy JW, Kereiakes D, Kern MJ, et al. ACC/AHA guidelines of percutaneous coronary interventions (revision of the 1993 PTCA guidelines)--executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (committee to revise the 1993 guidelines for percutaneous transluminal coronary angioplasty). J Am Coll Cardiol 2001;37(8):2215-39.
39. Smith SC, Jr., Dove JT, Jacobs AK, Kennedy JW, Kereiakes D, Kern MJ, et al. ACC/AHA guidelines for percutaneous coronary intervention (revision of the 1993 PTCA guidelines)-executive summary: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee to revise the 1993 guidelines for percutaneous transluminal coronary angioplasty) endorsed by the Society for Cardiac Angiography and Interventions. Circulation 2001;103(24):3019-41.
40. Tracy CM, Akhtar M, DiMarco JP, Packer DL, Weitz HH. American College of Cardiology/American Heart Association clinical competence statement on invasive electrophysiology studies, catheter ablation, and cardioversion. A report of the American College of Cardiology/American Heart Association/American College of Physicians--American Society of Internal Medicine Task Force on clinical competence. J Am Coll Cardiol 2000;36(5):1725-36.
41. Tracy CM, Akhtar M, DiMarco JP, Packer DL, Weitz HH, Winters WL, et al. American College of Cardiology/American Heart Association Clinical Competence Statement on invasive electrophysiology studies, catheter ablation, and cardioversion: A report of the American College of Cardiology/American Heart Association/American College of Physicians-American Society of Internal Medicine Task Force on Clinical Competence. Circulation 2000;102(18):2309-20.

Appendix F: Clinical Practice Guidelines (continued)

42. U.S. Preventive Services Task Force. Guide to clinical preventive services, 2nd ed. Baltimore: Williams and Wilkins. 1996.
43. Wexler L, Brundage B, Crouse J, Detrano R, Fuster V, Maddahi J, et al. Coronary artery calcification: pathophysiology, epidemiology, imaging methods, and clinical implications. A statement for health professionals from the American Heart Association. Writing Group. Circulation 1996;94(5):1175-92.

Appendix G: Evidence Reports (N = 9)

1. Moderately elevated blood pressure. A report from SBU, the Swedish Council on Technology Assessment in Health Care. J Intern Med Suppl 1995;737:1-225.
2. An evaluation of beta-blockers, calcium antagonists, nitrates, and alternative therapies for stable angina. Evid Rep Technol Assess (Summ) 1999(10):1-2.
3. Berry E, Kelly S, Hutton J, Harris KM, Roderick P, Boyce JC, et al. A systematic literature review of spiral and electron beam computed tomography: with particular reference to clinical applications in hepatic lesions, pulmonary embolus and coronary artery disease. Health Technol Assess 1999;3(18):i-iv, 1-118.
4. Berry E, Kelly S, Hutton J, Lindsay HS, Blaxill JM, Evans JA, et al. Intravascular ultrasound-guided interventions in coronary artery disease: a systematic literature review, with decision-analytic modelling, of outcomes and cost-effectiveness. Health Technol Assess 2000;4(35):1-117.
5. Heidenreich P, Go A, Melsop K, et al. Prediction of risk for patients with unstable angina. Evidence Report/Technology Assessment No. 31(prepared by the UCSF-Stanford Evidence-based practice Center under Contract No. 290-97-0013). AHRQ Publication No. 01-E001. Rockville, MD: Agency for Healthcare Research and Quality. December 2000.
6. Lau J, Ioannidis J, Balk E, et al. Evaluation of Technologies for Identifying Acute Cardiac Ischemia in Emergency Departments. Evidence Report/technology Assessment Number 26. (Prepared by the New England Medical Center Evidence-based Practice Center under Contract No. 290-97-0019) AHRQ Publication No. 01-Eoo6, Rockville, MD: Agency for Healthcare Research and Quality. May 2001.
7. McDonagh MS, Bachmann LM, Golder S, Kleijnen J, ter Riet G. A rapid and systematic review of the clinical effectiveness and cost-effectiveness of glycoprotein IIb/IIIa antagonists in the medical management of unstable angina. Health Technol Assess 2000;4(30):1-95.
8. Meads C, Cummins C, Jolly K, Stevens A, Burls A, Hyde C. Coronary artery stents in the treatment of ischaemic heart disease: a rapid and systematic review. Health Technol Assess 2000;4(23):1-153.
9. Pignone M, Phillips C, Lannon C, et al. Screening for Lipid Disorders. Systematic Evidence Review. Research Triangle Institute – University of North Carolina, Evidence-based Practice Center. September 13, 2000.

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