Treatment Strategies for Women With Coronary Artery Disease
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None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

Preface

The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to organize knowledge and make it available to inform decisions about health care. As part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Congress directed AHRQ to conduct and support research on the comparative outcomes, clinical effectiveness, and appropriateness of pharmaceuticals, devices, and health care services to meet the needs of Medicare, Medicaid, and the Children’s Health Insurance Program (CHIP).

AHRQ has an established network of Evidence-based Practice Centers (EPCs) that produce Evidence Reports/Technology Assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care. The EPCs now lend their expertise to the Effective Health Care Program by conducting comparative effectiveness reviews (CERs) of medications, devices, and other relevant interventions, including strategies for how these items and services can best be organized, managed, and delivered.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews are useful because they define the strengths and limits of the evidence, clarifying whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about systematic reviews, see www.effectivehealthcare.ahrq.gov/reference/purpose.cfm.

AHRQ expects that CERs will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. In addition, AHRQ is committed to presenting information in different formats so that consumers who make decisions about their own and their family’s health can benefit from the evidence.

Transparency and stakeholder input from are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input. Comparative Effectiveness Reviews will be updated regularly.

We welcome comments on this CER. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to epc@ahrq.hhs.gov.

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Structured Abstract

**Objectives.** Although coronary artery disease (CAD) is the leading cause of death for women in the United States, treatment studies to date have primarily enrolled men and may not reflect the benefits and risks that women experience. Our systematic review of the medical literature assessed the comparative effectiveness of major treatment options for CAD specifically in women. The comparisons were (1) percutaneous coronary intervention (PCI) versus fibrinolysis/supportive pharmacologic therapy in ST elevation myocardial infarction (STEMI), (2) early invasive versus initial conservative management in non-ST elevation myocardial infarction (NSTEMI) or unstable angina, and (3) PCI versus coronary artery bypass surgery (CABG) versus optimal medical therapy in stable or unstable angina. The endpoints assessed were clinical outcomes, modifiers of effectiveness by demographic and clinical factors, and safety outcomes.

**Data Sources.** MEDLINE®, PubMed®, Embase®, and Cochrane Database of Systematic Reviews.

**Review Methods.** Randomized controlled trials published in English from January 1, 2001, to December 12, 2011, comparing the treatment options for CAD listed above and containing sex-specific outcomes. Clinical outcomes were classified as short term (≤30 days), intermediate term (1 year), or long term (>1 year). Random-effects meta-analysis was performed for studies with similar outcomes measured at similar time points.

**Results.** Twenty-eight comparative studies contributed evidence about effectiveness, modifiers of effectiveness, or safety for the comparisons described above. For women with STEMI, five studies showed a reduction in composite outcomes (primarily death/MI/stroke) at 30 days for PCI over fibrinolysis (odds ratio [OR] 0.50; 95% CI, 0.36 to 0.72; high strength of evidence [SOE]); there was insufficient evidence for assessing outcomes at 1 year. For women with NSTEMI or unstable angina, the included studies, although not showing statistical significance, suggested a benefit of early invasive over initial conservative management for the composite outcome of primarily death/MI at 6 months and 1 year (2 studies, OR 0.77; CI, 0.28 to 2.12; low SOE; 5 studies, OR 0.78; CI, 0.54 to 1.12; low SOE). Evidence, however, suggested a small benefit of initial conservative management at 5 years (2 studies, OR 1.05; CI, 0.81 to 1.35). Given the small suggested benefit at 5 years, the wide confidence interval crossing 1, and the trend favoring early invasive therapy suggested at earlier time points and across time points in men—we cannot support firm conclusions (insufficient SOE). For women with stable angina randomized to revascularization (PCI or CABG) or medical therapy, three studies showed a reduction in the composite outcome of death/MI/repeat revascularization at 5 years for revascularization with either PCI (OR 0.64; CI, 0.47 to 0.89; moderate SOE) or CABG (OR 0.56; CI, 0.32 to 0.96; low SOE). For stable and unstable angina trials comparing PCI with CABG, two studies suggested a nonsignificant benefit of PCI in mortality at 30 days (low SOE). At 1 year and beyond, although suggestive of a benefit of CABG in for the composite outcomes
of death/MI/stroke for women, this finding was not statistically significant and represented wide confidence intervals (low SOE at 1 year and at >2 years).

Five studies assessed modifiers of effectiveness in women due to demographic factors (≥65 or ≥80 years of age) or clinical factors (risk stratification or diabetes). Strength of evidence for modifiers of effectiveness for STEMI, NSTEMI, and stable/unstable angina was insufficient.

Four studies assessed safety outcomes in women: two STEMI studies (PCI versus fibrinolysis) and two NSTEMI studies (PCI versus CABG) assessed transfusion rates, incidence of intracranial hemorrhage, and bleeding rates. Strength of evidence for safety outcomes for all the CAD presentations was insufficient.

**Conclusions.** From a limited number of studies reporting results for women separately from the total study population, our findings confirm current practice and evidence for care in one of the three areas evaluated. For women with STEMI, we found that an invasive approach with immediate PCI is superior to fibrinolysis for reducing cardiovascular events, which is similar to findings in previous meta-analyses combining results for both women and men. For women with NSTEMI or unstable angina, evidence suggested that an early invasive approach reduces cardiovascular events; however, it was not statistically significant. Previous meta-analyses of studies comparing early invasive with initial conservative strategies on a combined population of men and women showed a significant benefit of early invasive therapy. We also found that the few trials reporting sex-specific data on revascularization compared with optimal medical therapy for stable angina showed a greater benefit with revascularization for women, while the men in the study fared equally well with either treatment. In contrast, previous meta-analyses that combined results for men and women found similar outcomes for either treatment.

Limitations include a small number of trials with data for women available for meta-analysis, varying definitions of composite outcomes, and variable timing of followup. Future studies should collect and report clinical outcomes and harms in women by treatment strategy and at each followup time point—including subgroup data on important demographic and clinical factors that may modify clinical effectiveness—so that firmer conclusions can be reached about the risk and benefit of these therapies in women.
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Executive Summary

Background

Cardiovascular disease remains the leading cause of death among women in the United States. More than 500,000 women die of cardiovascular disease each year, exceeding the number of deaths in men and the next seven causes of death in women combined. This translates into approximately one death every minute. Coronary artery disease (CAD)—which includes coronary atherosclerotic disease, myocardial infarction (MI), acute coronary syndrome, and angina—is the most prevalent form of cardiovascular disease and is the largest subset of this mortality. An estimated 16.3 million Americans 20 years of age and older have CAD, and the overall CAD prevalence is 7 percent in adults in the United States (8.3% for men, 6.1% for women). The prevalence of CAD is higher in men than in women across different age groups until they reach 75 years of age, giving the perception that CAD is a male-specific disease.

This report focuses on women because of the differences in clinical presentation and coronary anatomy, which affect the treatment options for CAD. Currently available guidelines and systematic reviews provide specific treatment recommendations for women only among a subset of treatment options and overall assume that treatment options are equally effective for both sexes when gender data are not available. However, women have a worse prognosis than men for manifestations of CAD such as acute myocardial infarction, and some data suggest that women and men do not respond equally to the same treatments. Further, women are more likely than men to experience bleeding complications.

In women, CAD is misdiagnosed or not treated as aggressively as in men or is underresearched. Multiple factors are likely to contribute to the lower use of evidence-based medicine (medical therapy and/or coronary revascularization) and the higher rate of cardiovascular complications among women with CAD. These factors include:

- Cardiovascular disease affects women later in life.
- At the time CAD is diagnosed, women are more likely to have comorbid factors such as diabetes mellitus, hypertension, hypercholesterolemia, peripheral vascular disease, and heart failure.
- Women present with angina-equivalent symptoms such as dyspnea or atypical symptoms more often than men.
- The coronary vessels in women tend to be smaller than those of men, which makes them more difficult to revascularize percutaneously and surgically, and microvascular disease of the coronary arteries is more common in women than in men.
- Women tend to have less extensive CAD and a higher proportion of nonobstructive CAD.
- Delay in hospitalization, symptom pattern and recognition, and higher frequency of nonobstructive CAD ultimately results in delay in diagnosis and effective treatment.
- Because of underrepresentation of women in randomized controlled trials (RCTs), a lack of solid data on cardiovascular disease in women leaves uncertainty about the risk–benefit ratio of treatment.
Thus, a better understanding of the evidence for the effectiveness of medical treatment and revascularization therapies specifically in women is needed in order to reduce cardiovascular events in women.

**Clinical Presentations of CAD**

Coronary artery disease is the presence of atherosclerosis in the epicardial coronary arteries. Atherosclerotic plaques may either rupture and cause acute ischemia or progressively narrow the coronary artery lumen, resulting in chronic stable angina. Acute myocardial ischemia occurs when an atheromatous plaque ruptures or splits. The reasons for why a specific plaque ruptures when it does are unclear but probably relate to plaque morphology, plaque calcium content, and plaque softening due to an inflammatory process. Rupture exposes collagen and other thrombogenic material, which activates platelets and the coagulation cascade, resulting in an acute thrombus that interrupts coronary blood flow and causes some degree of myocardial ischemia. The consequences of acute ischemia depend on the location and degree of obstruction and range from reversible ischemia (unstable angina) through partial obstruction and tissue damage (non-ST elevation myocardial infarction [NSTEMI]) to complete epicardial occlusions leading to possible transmural infarction of the heart muscle (ST elevation myocardial infarction [STEMI]). The constellation of clinical symptoms that are compatible with acute myocardial ischemia is usually referred to as acute coronary syndrome.26,27

Angina resulting from progressive narrowing of the coronary arteries is the initial manifestation of ischemic heart disease in approximately one-half of patients.28 Angina is a clinical syndrome characterized by discomfort in the chest, jaw, shoulder, back, or arm. It is typically aggravated by exertion or emotional stress and relieved by nitroglycerin. Angina usually occurs in patients with CAD that involves at least one large epicardial artery. However, angina can also occur in patients with valvular heart disease, hypertrophic cardiomyopathy, and uncontrolled hypertension. It can also be present in patients with normal coronary arteries and myocardial ischemia related to spasm or endothelial dysfunction. Most angina is a sign of significant CAD—defined angiographically as a stenosis with greater than 70 percent diameter in at least one major epicardial artery segment or with greater than 50 percent diameter in the left main coronary artery. However, some angina is caused by stenotic lesions of lesser diameters, which have much less prognostic significance.28

Unstable angina (UA) is defined as angina with at least one of three features: (1) it occurs at rest or with minimal exertion, (2) it is severe and of recent onset (within the past 4 to 6 weeks), and/or (3) it occurs in a crescento pattern (i.e., more severe, more prolonged, or more frequent than previously experienced). UA and NSTEMI have a fairly similar pathophysiology, mortality rate, and management strategy when compared with STEMI; therefore they are often grouped together as UA/NSTEMI in clinical guidelines and trial populations. Chronic stable angina is classified as pain that classically occurs with moderate to severe exertion, is milder in nature, and is relieved with rest or sublingual nitroglycerin.

**Treatment Options for Patients With CAD**

**Optimal Medical Therapy**

All patients with CAD—regardless of clinical presentation—should receive aggressive management of risk factors for progression of atherosclerosis (smoking, hypertension, hyperlipidemia, and diabetes) combined with pharmacological treatment (antiplatelets,
antianginals, beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists, and lipid-lowering drugs). Optimal medical therapy of CAD comprises the combinations of these treatments to reduce future cardiovascular events for all the clinical presentations outlined in the previous section. However, patients may not be able to receive optimal medical therapy if they have allergies to, or adverse effects from, individual medications (e.g., aspirin, beta blockers, or cholesterol-lowering drugs) or the combination of medications. Also, the definition of optimal medical therapy continues to evolve as new drugs are developed and as studies are conducted to assess the optimal blood pressure, blood sugar, and lipid goals needed to reduce future cardiovascular events. For medical therapy to be optimized, patients should be prescribed appropriate therapy to reach their therapeutic goal. The effectiveness of medical therapy is also affected by how adherent the patient is to the prescribed therapy.

**Coronary Revascularization**

Coronary revascularization falls broadly into two categories: coronary artery bypass grafting (CABG) and catheter-based percutaneous coronary intervention (PCI). Together, these coronary revascularization techniques are among the most common major medical procedures performed in North America and Europe. Since the introduction of bypass surgery in 1967 and PCI in 1977, it has become clear that both strategies can contribute to the effective treatment of patients with CAD. CABG and PCI (with or without stents) are alternative approaches in coronary revascularization, so their comparative effectiveness in terms of patient outcomes has been of great interest. The comparative effectiveness of CABG and PCI is an open question primarily for those patients for whom either procedure would be technically feasible or whose CAD is neither too limited nor too extensive.

CABG is generally preferred for patients with very high CAD burden—often described as left main CAD or severe triple-vessel disease with reduced left ventricular function—because CABG has previously been shown in RCTs to improve survival when compared with medical therapy. In contrast, PCI is generally preferred for patients with milder CAD burden—described as single- or double-vessel disease—when symptoms warrant coronary revascularization, in light of its lower procedural risk and evidence that PCI reduces angina and myocardial ischemia in this subset of patients. Uncertainty exists about the choice between PCI and CABG for patients with moderate CAD burden; namely, patients with disease of the proximal left anterior descending artery and less extensive forms of triple-vessel CAD. Most RCTs of PCI and CABG have been conducted in this middle segment of the patient population with CAD. The major advantage of PCI is its relative ease of use and avoidance of general anesthesia, thoracotomy, extracorporeal circulation, central nervous system complications, and prolonged convalescence. Repeat PCI can be performed more easily than repeat bypass surgery, and revascularization can be achieved more quickly in emergency situations. The disadvantages of PCI are early restenosis and the inability to relieve many totally occluded arteries or vessels with extensive atherosclerotic disease. CABG has the advantages of greater durability (graft patency rates exceeding 90% at 10 years with arterial conduits) and more complete revascularization regardless of the morphology of the obstructing atherosclerotic lesion.

Therefore, patients and clinicians have two or more major treatment approaches to consider for each presentation of CAD. In general, these fall into less invasive (i.e., more medical) approaches and more invasive approaches. Table A summarizes the major treatment options for each clinical scenario described in the sections that follow.
Table A. Comparisons of treatment strategies for women with CAD

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<th>CAD Presentation</th>
<th>Treatment Choices</th>
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</tr>
<tr>
<td>NSTEMI/unstable angina</td>
<td>Early invasive management (with PCI or CABG) vs. initial conservative management</td>
</tr>
<tr>
<td>Stable/unstable angina</td>
<td>PCI vs. CABG vs. optimal medical therapy</td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass grafting; CAD = coronary artery disease; NSTEMI = non-ST elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST elevation myocardial infarction

**STEMI**

Treatment for patients with ST-segment elevation is well established. Patients with STEMI are candidates for reperfusion therapy (either pharmacological or catheter-based) to restore blood flow promptly in the occluded epicardial infarct-related artery. Pharmacological therapy consists of fibrinolysis or conservative/supportive therapy with facilitated antithrombotic medications.27 Multiple randomized trials have demonstrated the benefit of PCI in reducing major cardiovascular adverse events when compared with fibrinolysis or conservative therapy; therefore, immediate revascularization with PCI is the preferred strategy when patients have close access to a catheterization facility. Otherwise, fibrinolysis is recommended (in facilities without access) since it also has been shown to improve cardiovascular outcomes. In older or unstable patients, the use of fibrinolytics can increase bleeding complications; therefore, trials comparing conservative medical therapy to PCI have been performed. In general, patients with STEMI are not treated with CABG (unless emergent from PCI complications) but do receive optimal medical therapy.

**UA/NSTEMI**

Patients with UA/NSTEMI are not candidates for immediate pharmacological reperfusion. The optimal management of UA/NSTEMI has the twin goals of the immediate relief of ischemia and the prevention of serious adverse outcomes (i.e., death or MI). Optimal management is best accomplished with an approach that includes anti-ischemic therapy, antithrombotic therapy, ongoing risk stratification, and in some cases the use of invasive procedures. In addition to aggressive medical therapy, two treatment pathways have emerged for treating patients without ST-segment elevation.26 An initial conservative strategy (also referred to as selective invasive management) calls for proceeding with an invasive evaluation only for those patients whose medical therapy fails (refractory angina or angina at rest or with minimal activity despite vigorous medical therapy) or in whom objective evidence of ischemia (dynamic electrocardiographic changes, high-risk stress test) is identified. An early invasive strategy triages patients to undergo an invasive diagnostic evaluation without first getting a noninvasive stress test or having medical treatment fail. Patients treated with an early invasive strategy generally will undergo coronary angiography within 4 to 24 hours of admission; however, these patients also are treated with the usual UA/NSTEMI medications, including appropriate anti-ischemic, antiplatelet, and anticoagulant therapy. Several RCTs have demonstrated improved clinical outcomes in patients with an invasive strategy, leading to guideline recommendations for invasive approaches to treat patients with NSTEMI and high-risk acute coronary syndrome. Patients with UA/NSTEMI also receive optimal medical therapy.
Angina

The treatment of stable angina has two major purposes. The first is to prevent MI and death and thereby increase the quantity of life. The second is to reduce symptoms of angina and occurrence of ischemia, which should improve the quality of life.28 All patients with stable angina are candidates for optimal medical therapy and may be candidates for PCI or CABG based on findings from coronary angiography and if symptoms persist despite optimal medical therapy.

Objectives of This Review

Although CAD is the leading cause of death for women in the United States, treatment studies to date have primarily enrolled men and may not reflect the benefits and risks that women experience. We conducted this systematic review of the medical literature to assess the comparative effectiveness of the major treatment options for CAD specifically in women, evaluating these comparisons:

1. PCI versus fibrinolysis or PCI versus conservative/supportive medical management in women with STEMI
2. Early invasive versus initial conservative management in women with UA/NSTEMI
3. PCI versus CABG versus optimal medical therapy in women with stable or unstable angina

The endpoints assessed were clinical outcomes, modifiers of effectiveness by demographic and clinical factors, and safety outcomes. The following Key Questions (KQs) were considered in this review:

KQ 1. In women presenting with ST elevation myocardial infarction (STEMI):
   a. What is the effectiveness of percutaneous coronary intervention (PCI) versus fibrinolysis/supportive therapy on clinical outcomes (nonfatal MI, death, stroke, repeat revascularization, recurrent unstable angina, heart failure, repeat hospitalization, length of hospital stay, angina relief, quality of life, or cognitive effects)?
   b. Is there evidence that the comparative effectiveness of PCI versus fibrinolysis/supportive therapy varies based on characteristics such as:
      • Age, race, or other demographic and socioeconomic risk factors?
      • Coronary disease risk factors such as diabetes, chronic kidney disease, or other comorbid disease?
      • Angiographic-specific factors (number of diseased vessels, vessel territory stenoses, left ventricular function, access site, or prior PCI or coronary artery bypass graft surgery [CABG] revascularization procedure)?
      • Hospital characteristics (hospital volume, setting, guideline-based treatment protocols)?
   c. What are the significant safety concerns associated with each treatment strategy (i.e., adverse drug reactions, radiation exposure, access site complications, renal dysfunction, anaphylaxis, arrhythmias, stent thrombosis, bleeding, infections)?

KQ 2. In women presenting with unstable angina or non-ST elevation myocardial infarction (UA/NSTEMI):
   a. What is the effectiveness of early invasive (PCI or CABG) versus initial conservative therapy on clinical outcomes (nonfatal MI, death, stroke, repeat revascularization, recurrent unstable angina, heart failure, repeat hospitalization, length of hospital stay, graft failure, angina relief, quality of life, or cognitive effects)?
b. Is there evidence that the comparative effectiveness of early invasive versus initial conservative therapy varies based on characteristics such as:
- Age, race, or other demographic and socioeconomic risk factors?
- Coronary disease risk factors such as diabetes, chronic kidney disease, or other comorbid disease?
- Angiographic-specific factors (number of diseased vessels, vessel territory stenoses, left ventricular function, access site, or prior PCI or CABG revascularization procedure)?
- Hospital characteristics (hospital volume, setting, guideline-based treatment protocols)?

c. What are the significant safety concerns associated with each treatment strategy (i.e., adverse drug reactions, radiation exposure, access site complications, renal dysfunction, anaphylaxis, arrhythmias, stent thrombosis, bleeding, infections)?

KQ 3. In women presenting with stable or unstable angina:

a. What is the effectiveness of the following treatment strategies on clinical outcomes (nonfatal MI, death, stroke, repeat revascularization, recurrent unstable angina, heart failure, repeat hospitalization, length of hospital stay, graft failure, angina relief, quality of life, or cognitive effects)?
- Revascularization (PCI or CABG) versus optimal medical therapy in women with stable angina
- PCI versus CABG in women with stable or unstable angina

b. Is there evidence that the comparative effectiveness of revascularization versus optimal medical therapy varies based on characteristics such as:
- Age, race, or other demographic and socioeconomic risk factors?
- Coronary disease risk factors such as diabetes, chronic kidney disease, or other comorbid disease?
- Angiographic-specific factors (number of diseased vessels, vessel territory stenoses, left ventricular function, access site, or prior PCI or CABG revascularization procedure)?
- CABG-specific factors such as type of surgery performed, cardiopulmonary bypass mode (normothermic versus hypothermic), on-pump versus off-pump, type of cardioplegia used (blood versus crystalloid), or use of saphenous vein grafts, single or bilateral internal mammary artery grafts, or other types of bypass grafts?
- Hospital characteristics (hospital volume, setting, guideline-based treatment protocols)?

c. What are the significant safety concerns associated with each treatment strategy (i.e., adverse drug reactions, radiation exposure, access site complications, renal dysfunction, anaphylaxis, arrhythmias, stent thrombosis, bleeding, infections)?

Analytic Framework

Figure A shows the analytic framework for the systematic review of treatment strategies for women with CAD.
Methods

Input From Stakeholders

During the topic refinement stage, the KQs were refined with the help of an eight-person Key Informant group representing clinicians (cardiology, primary care, cardiac surgery), patients, scientific experts, and Federal agencies. We solicited input from the Task Order Officer and an eight-person Technical Expert Panel (TEP) with experts knowledgeable in CAD, PCI, and CABG throughout our evidence review and followed, based on an a priori research protocol, the Effective Health Care Program’s Methods Guide for Effectiveness and Comparative Effectiveness Reviews (hereafter referred to as the Methods Guide) for literature search strategies, inclusion/exclusion of studies, abstract screening, data abstraction and management, assessment of methodological quality of individual studies, data synthesis, and grading of evidence for each KQ. All Key Informant and TEP participants were screened for conflicts of interest, and any potential conflicts were balanced or mitigated.

Data Sources and Selection

We included studies published in English from January 1, 2001, through December 12, 2011. Search strategies were specific to each database in order to retrieve the articles most relevant to the KQs. Our search strategy used the National Library of Medicine’s medical subject headings (MeSH) keyword nomenclature developed for MEDLINE® and adapted for use in other databases. In consultation with our research librarians, we used PubMed®, EMBASE®, the
Cochrane Database of Systematic Reviews, and the Cochrane Central Registry of Controlled Trials for our literature search. We also searched the grey literature of study registries and conference abstracts for relevant articles from completed RCTs. Grey literature databases included Clinicaltrials.gov; metaRegister of Controlled Trials; ClinicalStudyResults.org; WHO: International Clinical Trials Registry Platform Search Portal; and ProQuest COS Conference Papers Index. The exact search strings used in our strategy are given in Appendix A of the full report. The reference lists of articles applicable to the relevant KQs of two previous Agency for Healthcare Research and Quality (AHRQ) reports related to this topic\textsuperscript{32,33} and from identified systematic reviews and meta-analyses were manually hand-searched and cross-referenced against our library, and additional manuscripts were retrieved. All citations were imported into an electronic bibliographic database (EndNote\textsuperscript{\textregistered} Version X4; Thomson Reuters, Philadelphia, PA).

We developed a list of article inclusion and exclusion criteria for the KQs (Table B). This review focused on randomized controlled studies, since this is the strongest study design for evaluating treatment effectiveness and since observational studies contain potential biases (e.g., patient selection bias, intervention bias) that could affect the clinical outcome. The TEP approved this approach given that the number of abstracts identified in PubMed exceeded 5,000. This review focused on comparisons of treatment strategies; therefore, differences in specific drugs or devices were not investigated and were considered beyond the scope. Using the prespecified inclusion and exclusion criteria, titles and abstracts were examined independently by two reviewers for potential relevance to the KQs. Articles included by any reviewer underwent full-text screening. At the full-text screening stage, two independent reviewers read each article to determine if it met eligibility criteria. At the full-text review stage, paired researchers independently reviewed the articles and indicated a decision to “include” or “exclude” the article for data abstraction. When the paired reviewers arrived at different decisions about whether to include or exclude an article, they reconciled the difference through a third-party arbitrator. Articles meeting our eligibility criteria were included for data abstraction. Relevant review articles, meta-analyses, and methods articles were flagged for manual searching and cross-referencing against the library of citations identified through electronic database searching.

**Data Extraction and Quality Assessment**

The investigative team created forms for abstracting the data elements for the KQs. The abstraction forms were pilot tested with a sample of included articles to ensure that all relevant data elements were captured and that there was consistency and reproducibility between abstractors for accuracy. Based on their clinical and methodological expertise, two researchers were assigned to abstract data from the eligible articles pertaining to the research questions. One researcher abstracted the data, and the second overread the article and the accompanying abstraction form to check for accuracy and completeness. Disagreements were resolved by consensus or by obtaining a third reviewer’s opinion if consensus was not reached by the first two researchers. Guidance documents were drafted and given to the researchers as reference material to perform data abstraction, thus aiding in both reproducibility and standardization of data collection.
Table B. Summary of inclusion and exclusion criteria

<table>
<thead>
<tr>
<th>Study Characteristic</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
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<tr>
<td><strong>Population</strong></td>
<td>Adult women (≥18 years of age) with CAD and angiographically proven single- or multiple-vessel disease including STEMI, NSTEMI, and stable angina</td>
<td>Study population was composed entirely of patients without CAD, or the population also included patients with CAD but results were not reported separately for the subgroup with CAD. Study did not include women, or results were not reported by sex. All subjects under age 18, or some subjects under age 18, but results were not broken down by age. Study did not report any of the primary or secondary outcomes of interest.</td>
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<tr>
<td><strong>Interventions and comparators</strong></td>
<td>Article reported original data for any of the interventions compared with another treatment category; or a related methodology paper of an included article. Optimal medical therapy alone. PCI (bare-metal and drug-eluting stents) with optimal medical therapy. CABG with optimal medical therapy.</td>
<td>Intervention comparisons within the same treatment category such as: Medical therapy with medical therapy (e.g., one type of fibrinolysis drug compared with another fibrinolysis drug). PCI with PCI (e.g., bare-metal stent compared with drug-eluting stent). CABG with CABG (e.g., open sternotomy compared with minimally invasive CABG).</td>
</tr>
<tr>
<td><strong>Outcomes and effect modifiers</strong></td>
<td>Primary outcomes: major adverse cardiovascular events such as death, nonfatal myocardial infarction, stroke, and repeat revascularization. Other clinical outcomes: heart failure, repeat hospitalization, length of hospital stay, unstable angina, graft failure, angina relief, quality of life, cognitive effects. Adverse effects of interventions: adverse drug reactions, radiation exposure, access site complications, renal dysfunction, anaphylaxis, arrhythmias, stent thrombosis, bleeding, infections.</td>
<td>Outcomes of women not reported separately from total population. Study did not report any of the primary or secondary outcomes of interest.</td>
</tr>
<tr>
<td>Study Characteristic</td>
<td>Inclusion Criteria</td>
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| **Outcomes and effect modifiers (continued)** | Effect modifiers—individual characteristics including the following:  
Age, race, or other demographic and socioeconomic risk factors  
Coronary disease risk factors such as diabetes, chronic kidney disease, or other comorbid disease  
Angiographic-specific factors such as access site (radial or femoral), number of diseased vessels, vessel territory stenoses, left ventricular function, or prior PCI or CABG revascularization procedure  
CABG-specific factors such as type of surgery performed (traditional or robot-assisted), cardiopulmonary bypass mode (normothermic versus hypothermic), on-pump versus off-pump, type of cardioplegia used (blood versus crystalloid), or use of saphenous vein grafts, single or bilateral internal mammary artery grafts, or other types of bypass grafts  
Hospital characteristics (hospital patient volume, setting, guideline-based treatment protocols) | Outcomes of women not reported separately from total population |
| **Timing** | Short-term (≤30 days), intermediate-term (1 year), or long-term (>1 year) | None |
| **Setting** | Inpatient or outpatient, primarily primary care and cardiology clinics | None |
| **Study design** | Randomized controlled trial (strongest study design for evaluating treatment effectiveness) | Observational (retrospective or prospective cohort) studies, due to potential biases that could affect the clinical outcome (e.g., patient selection bias, intervention bias)  
Not a clinical study (e.g., editorial, nonsystematic review, letter to the editor, case series). Systematic reviews and meta-analyses were excluded from abstraction but hand-searched as potential sources of additional material if relevant to the topic. |
| **Publication languages** | English only | Given the high volume of English-language publications (including the majority of known important studies), non-English articles were excluded |

CABG = coronary artery bypass grafting; CAD = coronary artery disease; NSTEMI = non-ST elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST elevation myocardial infarction

To aid in both reproducibility and standardization of data collection, researchers received data abstraction instructions directly on each form created specifically for this project with the DistillerSR data synthesis software program (Evidence Partners Inc., Manotick, ON, Canada).
We designed the data abstraction forms for this project to collect the data required to evaluate the specified eligibility criteria for inclusion in this review as well as to collect demographics and outcomes. The safety outcomes abstracted included adverse drug reactions, radiation exposure, access-site complications, renal dysfunction, anaphylaxis, arrhythmias, stent thrombosis, bleeding, and infections—the more common adverse events resulting from medical therapy and revascularization. Data on the total population and women and men subgroups were collected. Appendix B of the full report lists the elements used in the data abstraction form. Appendix C contains a bibliography of all studies included in this review, organized alphabetically by author. When appropriate, methods articles providing additional detail were considered when abstracting data for an included study. If a methods article was used as a source for information in the abstraction of a study, it was included in the review and is listed in the bibliography in Appendix C.

Study quality was assessed on the basis of the reported methods and results and performed by two reviewers. We evaluated the quality of individual studies using the approach described in the Methods Guide. To evaluate methodological quality, we applied criteria for RCTs that were derived from the core elements described in the Methods Guide. To indicate the summary judgment of the quality of the individual studies, we used the summary ratings of Good, Fair, and Poor based on the study’s adherence to well-accepted standard methodologies and adequate reporting.

We used data abstracted on the population studied, the intervention and comparator, the outcomes measured, settings, and timing of assessments to identify specific issues that may have limited the applicability of individual studies or a body of evidence as recommended in the Methods Guide. We used these data to evaluate the applicability to clinical practice, paying special attention to study eligibility criteria, demographic features of the enrolled population (e.g., age, race/ethnicity, sex) in comparison with the target population, version or characteristics of the intervention used in comparison with therapies currently in use (e.g., specific components of treatments considered to be “optimal medical therapy,” plus advancements in PCI or CABG techniques that have changed over time), and clinical relevance and timing of the outcome measures. We summarized issues of applicability qualitatively. Appendix D of the full report summarizes our assessment of the quality and applicability for each included study.

**Data Synthesis and Analysis**

We synthesized the primary literature by continuous data (e.g., age, event rates) and categorical data (e.g., race/ethnicity, presence of coronary disease risk factors). We determined the feasibility of completing a quantitative synthesis (i.e., meta-analysis). The feasibility of a meta-analysis depended on the volume of relevant literature (two or more studies), and clinical and methodological homogeneity of the studies. When a meta-analysis was appropriate, we used random-effects models to quantitatively synthesize the available evidence (Review Manager software Version 5.1.; Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011). We tested for heterogeneity while recognizing that the ability of statistical methods to detect heterogeneity may be limited. When feasible, we used similar composite outcomes in the meta-analysis for two reasons: (1) a majority of studies reported a composite outcome (e.g., death/MI/stroke/revascularization) as their primary endpoint and (2) many of the studies reported results for women for the primary composite outcome but not for each individual (secondary) outcome. We presented summary odds ratio estimates, standard errors, and confidence intervals for women and men separately to show any similarity or differences.
The majority of outcomes within this report were binary or categorical; therefore, we summarized these outcomes by proportions. We summarized inherently continuous variables, such as age, by mean, median, and standard deviation.

**Grading the Body of Evidence**

The strength of evidence for each KQ was assessed by using the approach described in the Methods Guide. The evidence was evaluated by using the four required domains: risk of bias (low, medium, or high), consistency (consistent, inconsistent, or unknown/not applicable), directness (direct or indirect), and precision (precise or imprecise). Additionally, when appropriate, the studies were evaluated for the presence of confounders that would diminish an observed effect, the strength of association (magnitude of effect), and publication bias. The strength of evidence was assigned an overall grade of high, moderate, low, or insufficient according to the following four-level scale:

- **b. High**—High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.
- **c. Moderate**—Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
- **d. Low**—Low confidence that the evidence reflects the true effect. Further research is likely to change the confidence in the estimate of effect and is likely to change the estimate.
- **e. Insufficient**—Evidence either is unavailable or does not permit estimation of effect.

**Results**

The flow of articles through the literature search and screening process is depicted in Figure B. Of the 13,073 citations identified by our searches, 5,369 were duplicates. Manual searching identified an additional 173 citations for a total of 7,877 citations. After applying inclusion/exclusion criteria at the title/abstract level, 619 full-text articles were retrieved and screened. Of these, 547 articles were excluded at the full-text screening stage, with 72 articles (representing 28 studies) remaining for data abstraction. Appendix E of the full report provides a complete list of articles excluded at the full-text screening stage, with reasons for exclusion.
Summary of Key Findings

Our search identified 28 comparative studies (72 articles, including methodology and secondary analysis papers). Of the 28 studies, 24 were good quality and 4 were fair quality for their overall reporting of methodology and analysis. A total of 35,597 patients included 10,126 (28%) women. We grouped these by CAD presentation and type of comparison:

a. KQ 1: seven studies (six good quality, one fair) comparing PCI with fibrinolysis/supportive (five fibrinolysis, two supportive) in patients with STEMI
b. KQ 2: seven studies (six good quality, one fair) comparing early invasive (PCI or CABG) with initial conservative in patients with UA/NSTEMI
c. KQ 3: 5 studies (all good quality) comparing revascularization (PCI or CABG) with optimal medical therapy in patients with stable angina (Strategy 1) and 10 studies (8 good quality, 2 fair) comparing PCI with CABG in patients with either stable or unstable angina (Strategy 2). There were a total of 14 studies with 1 study containing data for both comparative strategies.
Table C summarizes the key findings for each KQ, including the modifiers of effectiveness and safety concerns, and provides a grade for the strength of supporting evidence. Detailed reporting of the risk of bias, consistency, directness, precision, and limits to applicability are described in the Summary and Discussion section of the full report.

Discussion

The findings from this systematic review on the treatment strategies for women across the spectrum of CAD presentations highlight areas for future research and for informing clinical practice. First, this review underscores the significant need for clinical researchers to provide study findings with women-specific data on the primary and secondary clinical outcomes. Overall, we were able to find only 28 relevant studies with data on either shorter term or longer term outcomes in women with CAD treated with invasive or conservative medical therapies. In addition, the representation of women enrolled in these trials was low. Melloni et al. found similarly low rates with sex-specific results discussed in only 31 percent of the 156 primary trial publications cited by the American Heart Association’s 2007 women’s prevention guidelines. In addition, they found that enrollment of women in randomized clinical trials had increased over time (18% in 1970 to 34% in 2006) but remained low relative to their overall representation in disease populations (e.g., 25% women representation in RCTs of CAD compared with 46% women representation in the CAD population).

Second, our findings confirm current practice and evidence for care in one of the three areas evaluated. For women patients with STEMI, we found that an invasive approach with immediate PCI is superior to fibrinolysis in reducing cardiovascular events in women. These findings are similar to a meta-analysis of 23 randomized trials comparing PCI with fibrinolysis for acute MI in combined populations of men and women. However, for patients with NSTEMI treated with an early invasive approach compared with a conservative or selective invasive approach, this review did not find statistically significant evidence about the benefit of an early invasive approach in reducing cardiovascular events in women—although our findings did suggest a benefit of early invasive therapy. In contrast, the meta-analysis for trials of early invasive versus conservative strategies in the overall population showed a statistically significant benefit of early invasive therapy. The results from this review suggest that such a benefit may also be true in women, but the confidence intervals are too wide to support a firm conclusion.

In addition, for medical therapy alone versus revascularization plus medical therapy for patients with stable angina or high CAD burden, the findings from the current analysis suggest a benefit of revascularization in women. These findings should be viewed with caution because they are based on a limited number of studies with data on 704 (17%) women; these analyses often have both PCI and CABG together in the revascularization group, and the overall findings from these studies do not show a significant benefit beyond angina or symptom reduction for revascularization. In these studies, it is possible that women who present later in life with CAD, and with higher CAD burden, may be obtaining a greater benefit with revascularization, and the findings from this analysis should prompt further research in this area and again encourage researchers to provide data specific on women. In contrast, previous meta-analyses that combined results for men and women found similar outcomes for either treatment. The higher proportion of men enrolled in these trials (83%) may have led to the masking of the women’s results by the men’s results within a pooled analysis.
Table C. Summary of key findings

<table>
<thead>
<tr>
<th>Key Question</th>
<th>Strength of Evidence</th>
<th>Conclusions</th>
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<tbody>
<tr>
<td><strong>KQ 1: Women with STEMI (PCI vs. fibrinolysis/supportive therapy)</strong></td>
<td></td>
<td>7 studies (6 good quality, 1 fair) compared PCI with or without supportive therapy with fibrinolysis or other routine medical care for women with STEMI and contributed evidence about the comparative effectiveness, modifiers of effectiveness, or safety for these interventions. These studies included a total of 4,527 patients, of which 1,174 (26%) were women.</td>
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<td></td>
<td><strong>Effectiveness of intervention</strong></td>
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<td></td>
<td>1. High (women and men) for short-term (30-day) composite outcomes</td>
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<td></td>
<td>2. Insufficient (women and men) for intermediate-term (1-year) composite outcomes</td>
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<td></td>
<td><strong>Modifiers of effectiveness</strong></td>
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<td></td>
<td><strong>Safety concerns</strong></td>
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### Table C. Summary of key findings (continued)

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<tr>
<th>Key Question</th>
<th>Strength of Evidence</th>
<th>Conclusions</th>
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<tr>
<td><strong>KQ 2: Women with UA/NSTEMI (early invasive vs. initial conservative)</strong></td>
<td></td>
<td>7 studies (6 good quality, 1 fair) compared early invasive (revascularization via PCI or CABG) with initial conservative therapy for women with UA/NSTEMI and contributed evidence about the comparative effectiveness, modifiers of effectiveness, or safety for these interventions. These studies included a total of 17,930 patients, of which 6,084 (34%) were women.</td>
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<tr>
<td>Effectiveness of interventions</td>
<td>1. Low (women) and high (men) for short-term (6-month) composite outcomes 2. Low (women and men) for intermediate-term (1-year) composite outcomes 3. Insufficient (women) and low (men) for long-term (5-year) composite outcomes</td>
<td><strong>Effectiveness of interventions:</strong> A meta-analysis of 2 good-quality studies reporting 6-month composite outcomes (death/MI) suggested a benefit of early invasive compared with initial conservative therapy in women (OR, 0.77; 95% CI, 0.28 to 2.12) that, however, was not statistically significant; early invasive therapy was superior to initial conservative therapy in men at 6 months (OR, 0.65; CI, 0.52 to 0.82; p=0.0002). At 1 year, a meta-analysis of 5 good-quality studies showed that the composite outcome (primarily death/MI) suggested a similar benefit in women who received early invasive therapy (OR, 0.78; CI, 0.54 to 1.12) as well as in men (OR, 0.88; CI, 0.64 to 1.20); however, this was not statistically significant. A meta-analysis of 2 good-quality studies with 5-year followup between early invasive and initial conservative therapy for the composite outcome of death/MI in both sexes suggested a small benefit of initial conservative therapy in women (1.05; CI, 0.81 to 1.35) while suggesting a benefit of early invasive therapy in men (0.91; CI, 0.53 to 1.56). Given the small suggested benefit at 5 years in women, the wide confidence interval crossing 1, and the trend favoring early invasive therapy suggested at earlier time points and across time points in men — we cannot support firm conclusions.</td>
</tr>
<tr>
<td>Modifiers of effectiveness</td>
<td>Insufficient</td>
<td><strong>Modifiers of effectiveness:</strong> 2 good-quality studies comparing initial conservative medical therapy with early invasive therapy with PCI reported a subgroup analysis by risk stratification and included a total of 4,030 patients, of which 1,439 (36%) were women. These studies revealed conflicting results—one showed no difference in treatment outcomes in the intermediate- and high-risk groups; the other showed a higher event rate in women in the groups with moderate-to-high risk for thrombolysis in myocardial infarction.</td>
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<tr>
<td>Safety concerns</td>
<td>Insufficient</td>
<td><strong>Safety concerns:</strong> 1 good-quality study (2,220 total patients, 757 [34%] women) reported the harms associated with treatment of UA/NSTEMI by sex group but not the rates of events by treatment group. Bleeding in women undergoing PTCA was higher compared with men (adjusted OR, 3.6; 95% CI, 1.6 to 8.3). However, bleeding related to CABG was similar in women and men, with rates of 12.6 and 15%, respectively. No studies systematically reported radiation exposure, contrast reactions, access site complications, stent thrombosis, or infection in women with UA/NSTEMI comparing early invasive with initial conservative therapy.</td>
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</table>
### Table C. Summary of key findings (continued)

<table>
<thead>
<tr>
<th>Key Question</th>
<th>Strength of Evidence</th>
<th>Conclusions</th>
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<tbody>
<tr>
<td><strong>KQ 3: Strategy 1—women with stable angina (revascularization vs. optimal medical therapy)</strong></td>
<td>Effectiveness of interventions 1. With the PCI strategy: Moderate (women) and low (men) for long-term (4- to 5-year) composite outcomes 2. With the CABG strategy: Low (women and men) for long-term (4- to 5-year) composite outcomes 3. With both types of revascularization: Moderate (women) and low (men) for long-term (4- to 5-year) composite outcomes</td>
<td>5 studies (all good quality) compared revascularization (PCI or CABG) with optimal medical therapy for women with stable angina and contributed evidence about the comparative effectiveness, modifiers of effectiveness, or safety for these interventions. These studies included a total of 6,851 patients, of which 1,285 (19%) were women. - Effectiveness of interventions: A meta-analysis of 3 good-quality studies with long-term followup on the composite outcomes (death/MI/revascularization) comparing PCI or CABG with optimal medical therapy showed that revascularization was significantly better than optimal medical therapy in women with stable angina (OR, 0.64; 95% CI, 0.47 to 0.89; p=0.008 for PCI strategy trials; OR, 0.56; CI, 0.32 to 0.96; p=0.04 for CABG strategy trials; and OR, 0.59; CI, 0.43 to 0.81; p=0.001 for either PCI or CABG). However, for men with stable angina, the analysis suggested a small benefit for optimal medical therapy when compared with PCI (OR, 1.03; CI, 0.79 to 1.33). This suggested small benefit however has a wide confidence interval crossing 1 and is not supported by additional time periods or by the evidence in women. Analyses suggested a benefit of CABG (OR, 0.62; CI, 0.31 to 1.24) or either PCI or CABG (OR, 0.71; CI, 0.49 to 1.02) in men with stable angina. These findings were not statistically significant and had very wide confidence intervals.</td>
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### Table C. Summary of key findings (continued)

<table>
<thead>
<tr>
<th>Key Question</th>
<th>Strength of Evidence</th>
<th>Conclusions</th>
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<tr>
<td>KQ 3: Strategy 2—women with stable/unstable angina (PCI vs. CABG)</td>
<td>Effectiveness of interventions</td>
<td>10 studies (8 good quality, 2 fair) compared PCI with CABG in women with stable/unstable angina and contributed evidence about the comparative effectiveness, modifiers of effectiveness, or safety for these interventions. These studies included a total of 6,289 patients, of which 1583 (25%) were women.</td>
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<td></td>
<td>Effectiveness of interventions</td>
<td>• Effectiveness of interventions: A meta-analysis of 2 good-quality studies reporting a 30-day death outcome showed no statistically significant difference between PCI and CABG in either men or women. The summary odds ratio in women was 0.68 (95% CI, 0.24 to 1.93) and in men was 1.36 (CI, 0.44 to 4.24). The odds ratios suggest a possible sex effect, with PCI showing more benefit in women and CABG showing more benefit in men, but the confidence intervals are too wide to support firm conclusions. For 1-year composite outcomes (death/MI/stroke), a meta-analysis of 2 good-quality studies showed lower events in the CABG group for both sexes, but this benefit was not statistically significant. The summary odds ratio in women was 1.30 (CI, 0.69 to 2.45) and in men was 1.19 (CI, 0.84 to 1.70). For long-term (&gt;2 years) composite outcomes (death/MI/stroke), a meta-analysis of 4 good-quality studies suggested lower events in the CABG group in women (OR, 1.17; CI, 0.90 to 1.54) although again this did not reach statistical significance; however in men, CABG was significantly better than PCI in lowering cardiovascular events (OR, 1.63; CI, 1.20 to 2.23; p=0.002).</td>
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<td></td>
<td>Insufficient</td>
<td>• Modifiers of effectiveness: 1 good-quality study evaluated the comparative effectiveness of PCI vs. CABG in diabetic patients with stable/unstable angina. The survival rate at 7 years was similar in diabetic women from both treatment groups. However in diabetic men, those treated with CABG had higher survival than those treated with PCI.</td>
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<tr>
<td></td>
<td>Safety concerns</td>
<td>• Safety concerns: 1 good-quality study reported harms associated with PCI compared with CABG among women with UA/NSTEMI and found that bleeding associated with PCI was higher in women compared with men (OR, 29.4; 95% CI, 5.3 to 500; p=0.001). No studies systematically reported radiation exposure, contrast reactions, access site complications, stent thrombosis or infection, in women with UA/NSTEMI undergoing PCI or CABG.</td>
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</table>

CABG = coronary artery bypass grafting; CI = confidence interval; MI = myocardial infarction; NSTEMI = non-ST elevation myocardial infarction; OR = odds ratio; PCI = percutaneous coronary intervention; SOE = strength of evidence; STEMI = ST elevation myocardial infarction; t-PA = tissue plasminogen activator; UA = unstable angina
Our stakeholder group advised us to assess the effectiveness of these therapies by sex on multiple important clinical outcomes such as nonfatal MI, death, stroke, repeat revascularization, recurrent unstable angina, heart failure, repeat hospitalization, length of hospital stay, angina relief, quality of life, or cognitive effects. A majority of sex-specific reporting was on the composite outcome of major cardiovascular adverse events (death, MI, or revascularization). Individual outcomes by sex were rarely reported, especially on heart failure, repeat hospitalization, length of hospital stay, angina relief, quality of life, or cognitive effects.

Based on the small number of studies that looked at demographic and clinical factors that influence response to treatment strategies in women, there was insufficient evidence that clinicians can use to determine if age, race/ethnicity, socioeconomic status, coronary risk factors, angiographic-specific factors, CABS-specific factors, or hospital-level characteristics should be taken into consideration when deciding a treatment strategy for women with CAD. Unfortunately, more studies are needed that evaluate the subgroups and various demographic and clinical characteristics to fully understand this evidence gap.

In addition, the safety concerns or harms of these treatment strategies are underreported for women enrolled in RCTs. It appears that the bleeding risk may be higher in women receiving fibrinolysis or PCI. Careful consideration should be given to the dose, timing, and duration of antiplatelet, antithrombotic, and anticoagulant therapies administered to women.

Limitations of the Review Process

With 28 studies meeting the inclusion criteria, this systematic review has several limitations. First, our search focused on comparative RCTs—the highest quality of evidence for determining the efficacy of different treatment modalities on cardiovascular outcomes. While this was adequate for evaluating the evidence to support the clinical outcomes by treatment strategy and by CAD presentation for the overall population, there were very few RCTs that reported subgroup analyses by demographic or clinical characteristics and also very few RCTs that reported the harms or risks of therapy. Most studies that reported results applicable to modifiers of effectiveness or safety did this for the overall population and did not separate the effects by sex. We are aware that there are several observational and noncomparator studies of each of the treatment modalities that address these issues in women. Because of the problems with confounding from observational studies and the difficulty of constructing reliable comparisons among single-arm studies, we did not include observational or noncomparator studies in our review.

Second, the sample size and low representation of women in most of the comparator studies may affect the study authors’ ability to analyze the results by sex, therefore reducing the number of studies reporting these findings separately (i.e., reporting bias). We excluded 355 articles due to lack of sex-specific reporting of the study results, which resulted in low numbers of studies available for analysis for each clinical presentation (STEMI, UA/NSTEMI, stable angina). Of these 355 articles, 116 were associated with the same 28 studies included in our review, but they did not report data on women separately. The remaining 239 articles were associated with 173 studies that did not report data on women. Figure C presents a graph of the number of articles reporting data on women per year. The percentage ranges from 0 percent (in 1992 and 1993) to 75 percent in 1995. On average, 17 percent of the articles comparing treatment strategies for CAD reported sex-specific outcomes. Of note, many articles included a multivariate analysis that included sex as a covariate in the model; the majority found no evidence of a sex effect. The result of a multivariable model is insufficient for incorporating into a meta-analysis; thus these
were excluded from the review. Reporting bias in these publications therefore resulted in selection bias in this review.

**Figure C. Number of articles reporting data on women by year**

Third, the strength of our meta-analysis is limited by the different definitions of the primary composite outcome and by the timing (short term and long term) of those clinical endpoints. We used our best judgment in choosing which composite outcomes (e.g., death/MI/stroke and death/MI/stroke/revascularization) and time points (e.g., in hospital and 30 days) to combine in the meta-analysis.

A final limitation is the change in PCI techniques and definition of optimal medical therapy over time. Most of the studies involved balloon angioplasty or bare-metal stents. The current era of drug-eluting stents and the use of dual antiplatelet therapy may be underrepresented. Nevertheless, the findings represent the best available evidence. While the treatment options continue to evolve over time, these older therapies (bare-metal stents, balloon angioplasty) are still being used in clinical practice, and therefore we did not downgrade the strength of evidence based on the availability of newer technologies. Medication adherence to beta blockers, angiotensin-converting enzyme inhibitors, aspirin, antiplatelet agents, and lipid-lowering agents were not reported in the studies included in this review. There was also variable reporting on the implementation of optimal medical therapy.

Many of these studies were multicenter, international RCTs with multiple countries represented. The generalizability of those studies to the United States may be of concern; however, the practice of revascularization and prescription of medical therapies are not dramatically different.
Conclusions

From a limited number of studies reporting results for women separately from the total study population, our findings confirm current practice and evidence for care in one of the three areas evaluated.

1. For women with STEMI, we found that an invasive approach with immediate PCI is superior to fibrinolysis for reducing cardiovascular events, which is similar to findings in previous meta-analyses combining results for both women and men.

2. For women with NSTEMI or unstable angina, we found that, although not statistically significant, the evidence suggests a benefit of an early invasive approach in reducing cardiovascular events, whereas previous meta-analyses of studies comparing early invasive with initial conservative strategies on a combined population of men and women showed a statistically significant benefit of early invasive therapy.

3. For women with stable angina, the few trials reporting sex-specific data on revascularization compared with optimal medical therapy showed a greater benefit with revascularization for women, while the men in the study fared equally well with either treatment. In contrast, previous meta-analyses that combined results for men and women found similar outcomes for either treatment.

Implications for Future Research

This comprehensive review of the comparative effectiveness of treatment modalities for women with CAD identified numerous gaps in evidence that would be suitable for future research and for improving the reporting of women findings of cardiovascular therapies in the published literature.

Studies With Sufficient Representation of Women

Sex subgroup analyses are often limited by the number of men or women in each treatment group to allow for adequate power to detect a statistically significant difference in outcome. While we were able to find RCTs that reported risk ratios in women, the enrollment numbers were insufficient to have adequate power to detect a difference, thus resulting in large confidence intervals that often crossed the null effect, with a potential type II error. To better understand the clinical outcomes of women treated by medical therapy or revascularization, trials should be either (1) women-only enrollment or (2) of large enough sample size with stratification of randomization by sex to allow for meaningful sex-based analyses. In order to assess sex differences in treatment modalities and their impact on clinical outcomes, a sufficient sample size is required in order to have adequate statistical power for subgroup analyses.

Patient-Level Meta-Analysis

Given the small representation of women in these RCTs, the heterogeneity of clinical outcomes (e.g., definition of composite outcome) and different measurement time points (e.g., 30 days or 6 weeks for short-term outcomes), we are aware that our group-level meta-analysis may be inadequate (when too few studies are available) to address the comparative effectiveness of medical therapy and revascularization. Therefore, patient-level analysis of trials comparing similar interventions for the same CAD presentation may be more appropriate for assessing the sex differences as well as for conducting subgroup analyses on demographic and clinical factors that influence treatment outcomes, or for evaluating safety concerns/harms of these treatment
strategies. Subgroup analyses across trials can be done similarly to a previous AHRQ report on the comparative effectiveness of PCI and CABG, which included an addendum study that pooled individual patient data from 10 randomized trials to compare the effectiveness of CABG with PCI according to patients’ baseline clinical characteristics (e.g., age, diabetes, sex, individual cardiac risk factors, angioplasty versus bare metal stents).32,36,37

**Reporting Sex by Treatment Results Separately**

Our review excluded trials that looked for a sex effect yet failed to provide results of women and men by treatment arm. An example is a trial that did a multivariate analysis to assess factors that influenced clinical outcomes and included male (or female) sex in the model, with a finding that it was nonsignificant or significant. We did not contact the corresponding authors of the articles that did not report sex results separately. It would aid future comparisons of treatment modalities if study authors were to report the primary data for women and men separately either within the article itself or in an online supplementary appendix. The 2010 report by the Institute of Medicine on Women’s Health Research recommended that funding agencies ensure adequate participation of women and reporting of sex-specific analyses in health research.38

**Reporting of Demographic and Clinical Factors That Influence Cardiovascular Outcomes**

We found a few studies that conducted subgroup analyses of age, diabetes, and risk stratification in women populations. We did not find any data specific to women on race/ethnicity, socioeconomic factors, chronic kidney disease, angiographic-specific factors, or CABG-specific factors that were listed in KQ 2. Knowing the influence of these factors on cardiovascular outcomes is important for determining the proper treatment strategy and prognosis of women patients who present with various risk factors and comorbidities.

**Reporting of Safety Concerns/Risks by Sex**

Medical therapy can result in adverse drug reactions, and use of fibrinolytics can result in bleeding or intracranial hemorrhage. PCI can cause access site complications, radiation exposure, contrast-related anaphylaxis, bleeding, and stent thrombosis. CABG can result in wound infections, renal dysfunction, and bleeding. Most studies reported the bleeding risk of revascularization strategies but not the other safety concerns. Systematic reporting of adverse events in publications—in total and by sex—should continue to clarify which treatment modalities are safe for use in clinical practice.

To summarize, these evidence gaps could be addressed in various ways. First, more primary research with adequate representation of women for any of the three CAD clinical presentations could be conducted to achieve adequate statistical power for a sex-based analysis. Second, authors of the comparative trials that were excluded for not reporting sex-based results could be contacted to provide results of women and men by treatment arm, and the group-level meta-analysis could be repeated with a larger number of trials. Alternatively, these authors could be contacted to provide compatible (deidentified) datasets that could be combined for a patient-level analysis to assess the comparative effectiveness, modifiers of effectiveness, and risks of the various treatment strategies available. Finally, the use of observational cohorts from electronic health records could inform the real-world effectiveness of the treatment strategies chosen by clinicians and patients in a nonrandom fashion.
Glossary

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tr>
<td>AHRQ</td>
<td>Agency for Healthcare Research and Quality</td>
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<tr>
<td>CABG</td>
<td>coronary artery bypass graft</td>
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<tr>
<td>CAD</td>
<td>coronary artery disease</td>
</tr>
<tr>
<td>CI</td>
<td>confidence interval</td>
</tr>
<tr>
<td>KQ</td>
<td>Key Question</td>
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<tr>
<td>MACE</td>
<td>major adverse cardiovascular events</td>
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<tr>
<td>MI</td>
<td>myocardial infarction</td>
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<tr>
<td>NSTEMI</td>
<td>non-ST elevation myocardial infarction</td>
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<tr>
<td>OR</td>
<td>odds ratio</td>
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<tr>
<td>PCI</td>
<td>percutaneous coronary intervention</td>
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<tr>
<td>RCT</td>
<td>randomized controlled trial</td>
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<tr>
<td>SOE</td>
<td>strength of evidence</td>
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<tr>
<td>STEMI</td>
<td>ST elevation myocardial infarction</td>
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<td>TEP</td>
<td>Technical Expert Panel</td>
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<tr>
<td>t-PA</td>
<td>tissue plasminogen activator</td>
</tr>
<tr>
<td>UA</td>
<td>unstable angina</td>
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</table>

References


Introduction

Background

Cardiovascular disease remains the leading cause of death among women in the United States. More than 500,000 women die of cardiovascular disease each year, exceeding the number of deaths in men and the next seven causes of death in women combined. This translates into approximately one death every minute. Coronary artery disease (CAD)—which includes coronary atherosclerotic disease, myocardial infarction, acute coronary syndrome, and angina—is the most prevalent form of cardiovascular disease and is the largest subset of this mortality. An estimated 16.3 million Americans 20 years of age and older have CAD, and the overall CAD prevalence is 7 percent in adults in the United States (8.3% for men, 6.1% for women). The prevalence of CAD is higher in men than in women across different age groups until they reach 75 years of age, thus giving the perception that CAD is a male-specific disease.

The morbidity associated with this disease is also considerable. The estimated annual incidence of myocardial infarction is 610,000 new heart attacks; the average age at first myocardial infarction is 64.5 years for men and 70.3 for women. Many more individuals are hospitalized for unstable angina and for evaluation and treatment of stable chest pain syndromes. Recent data have shown a decrease in mortality rate in women, but reductions are well behind those obtained in men and are mainly in older women—still leaving the greater discrepancy in mortality rate limited to younger patients.

This report focuses on women because of the differences in clinical presentation and coronary anatomy, which affect the treatment options for CAD. Currently available guidelines and systematic reviews provide specific treatment recommendations for women only among a subset of treatment options and overall assume that treatment options are equally effective for both sexes when gender data are not available. However, women have a worse prognosis than men for manifestations of CAD such as acute myocardial infarction, and some data suggest that women and men do not respond equally to the same treatments. Further, women are more likely than men to experience bleeding complications.

In women, CAD is misdiagnosed or not treated as aggressively as in men or is underresearched. Multiple factors are likely to contribute to the lower use of evidence-based medicine (medical therapy and/or coronary revascularization) and the higher rate of cardiovascular complications among women with CAD. These factors include:

- Cardiovascular disease affects women later in life.
- At the time CAD is diagnosed, women are more likely to have comorbid factors such as diabetes mellitus, hypertension, hypercholesterolemia, peripheral vascular disease, and heart failure.
- Women present with angina-equivalent symptoms such as dyspnea or atypical symptoms more often than men.
- The coronary vessels in women tend to be smaller than those of men, which makes them more difficult to revascularize percutaneously and surgically, and microvascular disease of the coronary arteries is more common in women than in men.
- Women tend to have less extensive CAD and a higher proportion of nonobstructive CAD.
Delay in hospitalization, symptom pattern and recognition, and higher frequency of nonobstructive CAD ultimately results in delay in diagnosis and effective treatment.  

Because of underrepresentation of women in RCTs, a lack of solid data on cardiovascular disease in women leaves uncertainty about the risk-benefit ratio of treatment. Thus, a better understanding of the evidence for the effectiveness of medical treatment and revascularization therapies specifically in women is needed in order to reduce cardiovascular events in women.

**Clinical Presentations of CAD**

Coronary artery disease is the presence of atherosclerosis in the epicardial coronary arteries. Atherosclerotic plaques may either rupture and cause acute ischemia or progressively narrow the coronary artery lumen, resulting in chronic stable angina. Acute myocardial ischemia occurs when an atheromatous plaque ruptures or splits. The reasons for why a specific plaque ruptures when it does are unclear but probably relate to plaque morphology, plaque calcium content, and plaque softening due to an inflammatory process. Rupture exposes collagen and other thrombogenic material, which activates platelets and the coagulation cascade, resulting in an acute thrombus that interrupts coronary blood flow and causes some degree of myocardial ischemia. The consequences of acute ischemia depend on the location and degree of obstruction and range from reversible ischemia (unstable angina) through partial obstruction and tissue damage (non-ST elevation myocardial infarction [NSTEMI]) to complete epicardial occlusions leading to possible transmural infarction of the heart muscle (ST elevation myocardial infarction [STEMI]). The constellation of clinical symptoms that are compatible with acute myocardial ischemia is usually referred to as acute coronary syndrome.

Angina resulting from progressive narrowing of the coronary arteries is the initial manifestation of ischemic heart disease in approximately one-half of patients. Angina is a clinical syndrome characterized by discomfort in the chest, jaw, shoulder, back, or arm. It is typically aggravated by exertion or emotional stress and relieved by nitroglycerin. Angina usually occurs in patients with CAD that involves at least one large epicardial artery. However, angina can also occur in patients with valvular heart disease, hypertrophic cardiomyopathy, and uncontrolled hypertension. It can also be present in patients with normal coronary arteries and myocardial ischemia related to spasm or endothelial dysfunction. Most angina is a sign of significant CAD—defined angiographically as a stenosis with greater than 70 percent diameter in at least one major epicardial artery segment or with greater than 50 percent diameter in the left main coronary artery. However, some angina is caused by stenotic lesions of lesser diameters, which have much less prognostic significance.

Unstable angina (UA) is defined as angina with at least one of three features: (1) it occurs at rest or with minimal exertion, (2) it is severe and of recent onset (within the past 4 to 6 weeks), and/or (3) it occurs in a crescendo pattern (i.e., more severe, more prolonged, or more frequent than previously experienced). UA and NSTEMI have a fairly similar pathophysiology, mortality rate, and management strategy when compared with STEMI; therefore they are often grouped together as UA/NSTEMI in clinical guidelines and trial populations. Chronic stable angina is classified as pain that typically occurs with moderate to severe exertion, is milder in nature, and relieved with rest or sublingual nitroglycerin.
Treatment Options for Patients With CAD

Optimal Medical Therapy

All patients with CAD—regardless of clinical presentation—should receive aggressive management of risk factors for progression of atherosclerosis (smoking, hypertension, hyperlipidemia, and diabetes) combined with pharmacological treatment (antiplatelets, antianginals, beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists, and lipid-lowering drugs). Optimal medical therapy of CAD comprises the combinations of these treatments to reduce future cardiovascular events for all the clinical presentations outlined in the previous section. However, patients may not be able to receive optimal medical therapy if they have allergies to, or adverse effects from, individual medications (e.g., aspirin, beta blockers, or cholesterol-lowering drugs) or the combination of medications. Also, the definition of optimal medical therapy continues to evolve as new drugs are developed and as studies are conducted to assess the optimal blood pressure, blood sugar, and lipid goals needed to reduce future cardiovascular events. For medical therapy to be optimized, patients should be prescribed appropriate therapy to reach their therapeutic goal. The effectiveness of medical therapy is also affected by how adherent the patient is to the prescribed therapy.

Coronary Revascularization

Coronary revascularization falls broadly into two categories: coronary artery bypass grafting (CABG) and catheter-based percutaneous coronary intervention (PCI). Together, these coronary revascularization techniques are among the most common major medical procedures performed in North America and Europe. Since the introduction of bypass surgery in 1967 and PCI in 1977, it has become clear that both strategies can contribute to the effective treatment of patients with CAD. CABG and PCI (with or without stents) are alternative approaches in coronary revascularization, so their comparative effectiveness in terms of patient outcomes has been of great interest. The comparative effectiveness of CABG and PCI is an open question primarily for those patients for whom either procedure would be technically feasible or whose CAD is neither too limited nor too extensive.

CABG is generally preferred for patients with very high CAD burden—often described as left main CAD or severe triple-vessel disease with reduced left ventricular function—because CABG has previously been shown in randomized controlled trials (RCTs) to improve survival when compared with medical therapy. In contrast, PCI is generally preferred for patients with milder CAD burden—described as single- or double-vessel disease—when symptoms warrant coronary revascularization, in light of its lower procedural risk and evidence that PCI reduces angina and myocardial ischemia in this subset of patients. Uncertainty exists about the choice between PCI or CABG for patients with moderate CAD burden; namely, patients with disease of the proximal left anterior descending artery and less extensive forms of triple-vessel CAD. Most RCTs of PCI and CABG have been conducted in this middle segment of the patient population with CAD. The major advantage of PCI is its relative ease of use and avoidance of general anesthesia, thoracotomy, extracorporeal circulation, central nervous system complications, and prolonged convalescence. Repeat PCI can be performed more easily than repeat bypass surgery, and revascularization can be achieved more quickly in emergency situations. The disadvantages of PCI are early restenosis and the inability to relieve many totally occluded arteries or vessels with extensive atherosclerotic disease. CABG has the advantages of greater durability (graft
patency rates exceeding 90% at 10 years with arterial conduits) and more complete revascularization regardless of the morphology of the obstructing atherosclerotic lesion. Therefore, patients and clinicians have two or more major treatment approaches to consider for each presentation of CAD. In general, these fall into less invasive (i.e., more medical) approaches and more invasive approaches. Table 1 summarizes the major treatment options for each clinical scenario described in the sections that follow.

<table>
<thead>
<tr>
<th>CAD Presentation</th>
<th>Treatment Choices</th>
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| STEMI            | PCI vs. fibrinolysis  
|                  | PCI vs. conservative/supportive medical management |
| NSTEMI/unstable angina | Early invasive management (with PCI or CABG) vs. initial conservative management |
| Stable/unstable angina | PCI vs. CABG vs. optimal medical therapy |

CABG = coronary artery bypass grafting; CAD = coronary artery disease; NSTEMI = non-ST elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST elevation myocardial infarction

**STEMI**

Treatment for patients with ST-segment elevation is well established. Patients with STEMI are candidates for reperfusion therapy (either pharmacological or catheter based) to restore blood flow promptly in the occluded epicardial infarct-related artery. Pharmacological therapy consists of fibrinolysis or conservative/supportive therapy with facilitated antithrombotic medications. Multiple randomized trials have demonstrated the benefit of PCI in reducing major cardiovascular adverse events when compared with fibrinolysis or conservative therapy; therefore, immediate revascularization with PCI is the preferred strategy when patients have close access to a catheterization facility. Otherwise, fibrinolysis is recommended (in facilities without access) since it also has been shown to improve cardiovascular outcomes. In older or unstable patients, the use of fibrinolytics can increase bleeding complications; therefore trials comparing conservative medical therapy with PCI have been performed. In general, patients with STEMI are not treated with CABG (unless emergent from PCI complications) but do receive optimal medical therapy.

**UA/NSTEMI**

Patients with UA/NSTEMI are not candidates for immediate pharmacological reperfusion. The optimal management of UA/NSTEMI has the twin goals of the immediate relief of ischemia and the prevention of serious adverse outcomes (i.e., death or MI). Optimal management is best accomplished with an approach that includes anti-ischemic therapy, antithrombotic therapy, ongoing risk stratification, and in some cases the use of invasive procedures. In addition to aggressive medical therapy, two treatment pathways have emerged for treating patients without ST-segment elevation. An initial conservative strategy (also referred to as selective invasive management) calls for proceeding with an invasive evaluation only for those patients whose medical therapy fails (refractory angina or angina at rest or with minimal activity despite vigorous medical therapy) or in whom objective evidence of ischemia (dynamic electrocardiographic changes, high-risk stress test) is identified. The early invasive strategy triages patients to undergo an invasive diagnostic evaluation without first getting a noninvasive stress test or having medical treatment fail. Patients treated with an early invasive strategy generally will undergo coronary angiography within 4 to 24 hours of admission; however, these
patients also are treated with the usual UA/NSTEMI medications, including appropriate anti-ischemic, antiplatelet, and anticoagulant therapy. Several RCTs have demonstrated improved clinical outcomes in patients with an invasive strategy, leading to guideline recommendations for invasive approaches to treat patients with NSTEMI and high-risk acute coronary syndrome. Patients with UA/NSTEMI also receive optimal medical therapy.

**Angina**

The treatment of stable angina has two major purposes. The first is to prevent MI and death and thereby increase the quantity of life. The second is to reduce symptoms of angina and incidence of ischemia, which should improve the quality of life. All patients with stable angina are candidates for optimal medical therapy and may be candidates for PCI or CABG based on findings from coronary angiography and if symptoms persist despite optimal medical therapy.

**Scope and Key Questions**

Although CAD is the leading cause of death for women in the United States, treatment studies to date have primarily enrolled men and may not reflect the benefits and risks that women experience. We conducted a systematic review of the medical literature to assess the comparative effectiveness of the major treatment options for CAD specifically in women, evaluating these comparisons:

1. PCI versus fibrinolysis or PCI versus conservative/supportive medical management in women with STEMI
2. Early invasive versus initial conservative management in women with UA/NSTEMI
3. PCI versus CABG versus optimal medical therapy in women with stable or unstable angina

The endpoints assessed were clinical outcomes, modifiers of effectiveness by demographic and clinical factors, and safety outcomes. The following Key Questions (KQs) were considered in this review:

**KQ 1.** In women presenting with ST elevation myocardial infarction (STEMI):

a. What is the effectiveness of percutaneous coronary intervention (PCI) versus fibrinolysis/supportive therapy on clinical outcomes (nonfatal MI, death, stroke, repeat revascularization, recurrent unstable angina, heart failure, repeat hospitalization, length of hospital stay, angina relief, quality of life, or cognitive effects)?

b. Is there evidence that the comparative effectiveness of PCI versus fibrinolysis/supportive therapy varies based on characteristics such as:
   - Age, race, or other demographic and socioeconomic risk factors?
   - Coronary disease risk factors such as diabetes, chronic kidney disease, or other comorbid disease?
   - Angiographic-specific factors (number of diseased vessels, vessel territory stenoses, left ventricular function, access site, or prior PCI or coronary artery bypass graft surgery [CABG] revascularization procedure)?
   - Hospital characteristics (hospital volume, setting, guideline-based treatment protocols)?

b. What are the significant safety concerns associated with each treatment strategy (i.e., adverse drug reactions, radiation exposure, access site complications, renal dysfunction, anaphylaxis, arrhythmias, stent thrombosis, bleeding, infections)?
KQ 2. In women presenting with unstable angina or non-ST elevation myocardial infarction (UA/NSTEMI):

a. What is the effectiveness of early invasive (PCI or CABG) versus initial conservative therapy on clinical outcomes (nonfatal MI, death, stroke, repeat revascularization, recurrent unstable angina, heart failure, repeat hospitalization, length of hospital stay, graft failure, angina relief, quality of life, or cognitive effects)?

b. Is there evidence that the comparative effectiveness of early invasive versus initial conservative therapy varies based on characteristics such as:
   • Age, race, or other demographic and socioeconomic risk factors?
   • Coronary disease risk factors such as diabetes, chronic kidney disease, or other comorbid disease?
   • Angiographic-specific factors (number of diseased vessels, vessel territory stenoses, left ventricular function, access site, or prior PCI or CABG revascularization procedure)?
   • Hospital characteristics (hospital volume, setting, guideline-based treatment protocols)?

c. What are the significant safety concerns associated with each treatment strategy (i.e., adverse drug reactions, radiation exposure, access site complications, renal dysfunction, anaphylaxis, arrhythmias, stent thrombosis, bleeding, infections)?

KQ 3. In women presenting with stable or unstable angina:

a. What is the effectiveness of the following treatment strategies on clinical outcomes (nonfatal MI, death, stroke, repeat revascularization, recurrent unstable angina, heart failure, repeat hospitalization, length of hospital stay, graft failure, angina relief, quality of life, or cognitive effects)?
   • Revascularization (PCI or CABG) versus optimal medical therapy in women with stable angina
   • PCI versus CABG in women with stable or unstable angina

b. Is there evidence that the comparative effectiveness of revascularization versus optimal medical therapy varies based on characteristics such as:
   • Age, race, or other demographic and socioeconomic risk factors?
   • Coronary disease risk factors such as diabetes, chronic kidney disease, or other comorbid disease?
   • Angiographic-specific factors (number of diseased vessels, vessel territory stenoses, left ventricular function, access site, or prior PCI or CABG revascularization procedure)?
   • CABG-specific factors such as type of surgery performed, cardiopulmonary bypass mode (normothermic versus hypothermic), on-pump versus off-pump, type of cardioplegia used (blood versus crystalloid), or use of saphenous vein grafts, single or bilateral internal mammary artery grafts, or other types of bypass grafts?
   • Hospital characteristics (hospital volume, setting, guideline-based treatment protocols)?

c. What are the significant safety concerns associated with each treatment strategy (i.e., adverse drug reactions, radiation exposure, access site complications, renal dysfunction, anaphylaxis, arrhythmias, stent thrombosis, bleeding, infections)?
Methods

Topic Development and Refinement

During the topic refinement stage, the Key Questions (KQs) were refined with the help of an eight-person Key Informant group representing clinicians (cardiology, primary care, cardiac surgery), patients, scientific experts, and Federal agencies. We solicited input from the Task Order Officer and an eight-person Technical Expert Panel (TEP) with experts knowledgeable in CAD, PCI, and CABG throughout our evidence review and followed, based on an a priori research protocol, the Effective Health Care Program’s Methods Guide for Effectiveness and Comparative Effectiveness Reviews (hereafter referred to as Methods Guide) for literature search strategies, inclusion/exclusion of studies, abstract screening, data abstraction and management, assessment of methodological quality of individual studies, data synthesis, and grading of evidence for each KQ. All Key Informant and TEP participants were screened for conflicts of interest, and any potential conflicts were balanced or mitigated.

Analytic Framework

Figure 1 shows the analytic framework for the systematic review of the comparative effectiveness of treatment strategies for women with CAD.

Figure 1. Analytic framework

CABG = coronary artery bypass graft; CAD = coronary artery disease; KQ = Key Question; MACE = major adverse cardiovascular events; MI = myocardial infarction; NSTEMI = non-ST elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST elevation myocardial infarction
Literature Search Strategy

Sources Searched

We included studies published in English from January 1, 2001, through December 12, 2011. Search strategies were specific to each database in order to retrieve the articles most relevant to the KQs. Our search strategy used the National Library of Medicine’s medical subject headings (MeSH) keyword nomenclature developed for MEDLINE® and adapted for use in other databases. In consultation with our research librarians, we used PubMed®, Embase®, the Cochrane Database of Systematic Reviews, and the Cochrane Central Registry of Controlled Trials for our literature search. We also searched the grey literature of study registries and conference abstracts for relevant articles from completed RCTs. Grey literature databases included Clinicaltrials.gov; metaRegister of Controlled Trials; ClinicalStudyResults.org; WHO: International Clinical Trials Registry Platform Search Portal; and ProQuest COS Conference Papers Index. The exact search strings used in our strategy are given in Appendix A. The reference list of articles applicable to the relevant KQs of two previous AHRQ reports related to this topic34,35 and from identified systematic reviews and meta-analyses was manually hand-searched and cross-referenced against our library, and additional manuscripts were retrieved. All citations were imported into an electronic bibliographic database (EndNote® Version X4; Thomson Reuters, Philadelphia, PA).

Process for Study Selection

Screening for Inclusion and Exclusion

We developed a list of article inclusion and exclusion criteria for the KQs (Table 2). This review focused on randomized controlled studies since this is the strongest study design for evaluating treatment effectiveness and since observational studies contain potential biases (e.g., patient selection bias, intervention bias) that could affect the clinical outcome. The TEP approved this approach given that the number of abstracts identified in PubMed exceeded 5,000. This review focused on comparisons of treatment strategies; therefore, differences in specific drugs or devices were not investigated and were considered beyond the scope. Using the prespecified inclusion and exclusion criteria, titles and abstracts were examined independently by two reviewers for potential relevance to the KQs. Articles included by any reviewer underwent full-text screening. At the full-text screening stage, two independent reviewers read each article to determine if it met eligibility criteria. At the full-text review stage, paired researchers independently reviewed the articles and indicated a decision to “include” or “exclude” the article for data abstraction. When the paired reviewers arrived at different decisions about whether to include or exclude an article, they reconciled the difference through a third-party arbitrator. Articles meeting our eligibility criteria were included for data abstraction. Relevant review articles, meta-analyses, and methods articles were flagged for manual searching and cross-referencing against the library of citations identified through electronic database searching.
Table 2. Summary of inclusion and exclusion criteria

<table>
<thead>
<tr>
<th>Study Characteristic</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
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<tbody>
<tr>
<td>Population</td>
<td>Adult women (≥18 years of age) with CAD and angiographically proven single- or multiple-vessel disease including STEMI, NSTEMI, and stable angina</td>
<td>• Study population was composed entirely of patients without CAD, or the population also included patients with CAD but results were not reported separately for the subgroup with CAD</td>
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<td></td>
<td></td>
<td>• Study did not include women, or results were not reported by sex</td>
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<td>• All subjects under age 18, or some subjects under age 18, but results were not broken down by age</td>
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<td></td>
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<td>• Study did not report any of the primary or secondary outcomes of interest</td>
</tr>
<tr>
<td>Interventions and comparators</td>
<td>Article reported original data for any of the interventions compared with another treatment category; or a related methodology paper of an included article</td>
<td>Intervention comparisons within the same treatment category such as:</td>
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<tr>
<td></td>
<td>• Optimal medical therapy alone</td>
<td>• Medical therapy with medical therapy (e.g., one type of fibrinolysis drug compared with another fibrinolysis drug)</td>
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<td></td>
<td>• PCI (bare-metal and drug-eluting stents) with optimal medical therapy</td>
<td>• PCI with PCI (e.g., bare-metal stent compared with drug-eluting stent)</td>
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<tr>
<td></td>
<td>• CABG with optimal medical therapy</td>
<td>• CABG with CABG (e.g., open sternotomy compared with minimally invasive CABG)</td>
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<tr>
<td>Outcomes and effect modifiers</td>
<td>• Primary outcomes: major adverse cardiovascular events such as death, nonfatal myocardial infarction, stroke, and repeat revascularization</td>
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<tr>
<td></td>
<td>• Other clinical outcomes: heart failure, repeat hospitalization, length of hospital stay, unstable angina, graft failure, angina relief, quality of life, cognitive effects</td>
<td>• Study did not report any of the primary or secondary outcomes of interest</td>
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<tr>
<td></td>
<td>• Adverse effects of interventions: adverse drug reactions, radiation exposure, access site complications, renal dysfunction, anaphylaxis, arrhythmias, stent thrombosis, bleeding, infections</td>
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Table 2. Summary of inclusion and exclusion criteria (continued)

<table>
<thead>
<tr>
<th>Study Characteristic</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
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<tbody>
<tr>
<td>Effect modifiers—individual characteristics including the following:</td>
<td></td>
<td>Outcomes of women not reported separately from total population</td>
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<tr>
<td>• Age, race, or other demographic and socioeconomic risk factors</td>
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<tr>
<td>• Coronary disease risk factors such as diabetes, chronic kidney disease, or other comorbid disease</td>
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<tr>
<td>• Angiographic-specific factors such as access site (radial or femoral), number of diseased vessels, vessel territory stenoses, left ventricular function, or prior PCI or CABG revascularization procedure</td>
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</tr>
<tr>
<td>• CABG-specific factors such as type of surgery performed (traditional or robot-assisted), cardiopulmonary bypass mode (normothermic vs. hypothermic), on-pump vs. off-pump, type of cardioplegia used (blood vs. crystalloid), or use of saphenous vein grafts, single or bilateral internal mammary artery grafts, or other types of bypass grafts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Hospital characteristics (hospital patient volume, setting, guideline-based treatment protocols)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outcomes and effect modifiers (continued)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Timing</td>
<td>Short-term (≤30 days), intermediate-term (1 year), or long-term (&gt;1 year)</td>
<td>None</td>
</tr>
<tr>
<td>Setting</td>
<td>Inpatient or outpatient, primarily primary care and cardiology clinics</td>
<td>None</td>
</tr>
<tr>
<td>Study design</td>
<td>Randomized controlled trial (strongest study design for evaluating treatment effectiveness)</td>
<td>• Observational (retrospective or prospective cohort) studies, due to potential biases that could affect the clinical outcome (e.g., patient selection bias, intervention bias)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Not a clinical study (e.g., editorial, nonsystematic review, letter to the editor, case series). Systematic reviews and meta-analyses were excluded from abstraction but hand-searched as potential sources of additional material if relevant to the topic.</td>
</tr>
<tr>
<td>Publication languages</td>
<td>English only</td>
<td>Given the high volume of English-language publications (including the majority of known important studies), non-English articles were excluded</td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass grafting; CAD = coronary artery disease; NSTEMI = non-ST elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST elevation myocardial infarction
Data Extraction and Data Management

The investigative team created forms for abstracting the data elements for the KQs. The abstraction forms were pilot tested with a sample of included articles to ensure that all relevant data elements were captured and that there was consistency and reproducibility between abstractors for accuracy. Based on their clinical and methodological expertise, two researchers were assigned to abstract data from the eligible articles pertaining to the research questions. One researcher abstracted the data, and the second overread the article and the accompanying abstraction form to check for accuracy and completeness. Disagreements were resolved by consensus or by obtaining a third reviewer’s opinion if consensus was not reached by the first two researchers. Guidance documents were drafted and given to the researchers as reference material to perform data abstraction, thus aiding in both reproducibility and standardization of data collection.

To aid in both reproducibility and standardization of data collection, researchers received data abstraction instructions directly on each form created specifically for this project with the DistillerSR data synthesis software program (Evidence Partners Inc., Manotick, ON, Canada). We designed the data abstraction forms for this project to collect the data required to evaluate the specified eligibility criteria for inclusion in this review as well as to collect demographics and outcomes. The safety outcomes abstracted included adverse drug reactions, radiation exposure, access-site complications, renal dysfunction, anaphylaxis, arrhythmias, stent thrombosis, bleeding, and infections—which are the more common adverse events resulting from medical therapy and revascularization.

Appendix B lists the elements used in the data abstraction form. Appendix C contains a bibliography of all studies included in this review, organized alphabetically by author. When appropriate, methods articles providing additional detail were considered when abstracting data for an included study. If a methods article was used as a source for information in the abstraction of a study, it was included in the review and is listed in the bibliography in Appendix C.

Individual Study Quality Assessment

Study quality was assessed on the basis of the reported methods and results and performed by two reviewers. We evaluated the quality of individual studies using the approach described in the Methods Guide.33 To evaluate methodological quality, we applied criteria for RCTs that were derived from the core elements described in the Methods Guide. To indicate the summary judgment of the quality of the individual studies, we used the summary ratings of Good, Fair, and Poor based on the study’s adherence to well-accepted standard methodologies and adequate reporting.

We used data abstracted on the population studied, the intervention and comparator, the outcomes measured, settings, and timing of assessments to identify specific issues that may have limited the applicability of individual studies or a body of evidence as recommended in the Methods Guide.33 We used these data to evaluate the applicability to clinical practice, paying special attention to study eligibility criteria, demographic features of the enrolled population (e.g., age, race/ethnicity, sex) in comparison with the target population, version or characteristics of the intervention used in comparison with therapies currently in use (e.g., specific components of treatments considered to be “optimal medical therapy,” plus advancements in PCI or CABG techniques that have changed over time), and clinical relevance and timing of the outcome
measures. We summarized issues of applicability qualitatively. Appendix D summarizes our assessment of the quality and applicability for each included study.

Data Synthesis

We synthesized the primary literature by continuous (e.g., age, event rates) and categorical data (e.g., race/ethnicity, presence of coronary disease risk factors). We determined the feasibility of completing a quantitative synthesis (i.e., meta-analysis). The feasibility of a meta-analysis depended on the volume of relevant literature (2 or more studies), and clinical and methodological homogeneity of the studies. When a meta-analysis was appropriate, we used random-effects models to quantitatively synthesize the available evidence (Review Manager software Version 5.1.; Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011). We tested for heterogeneity while recognizing that the ability of statistical methods to detect heterogeneity may be limited. When feasible, we used similar composite outcomes in the meta-analysis for two reasons: (1) a majority of studies reported a composite outcome (e.g., death, MI, stroke, revascularization) as their primary endpoint and (2) many of the studies reported results for women for the primary composite outcome but not for each individual (secondary) outcome. We presented summary odds ratio estimates, standard errors, and confidence intervals.

The majority of outcomes within this report were binary or categorical; therefore, we summarized these outcomes by proportions. We summarized inherently continuous variables, such as age, by mean, median, and standard deviation.

Grading the Body of Evidence

The strength of evidence for each KQ was assessed by using the approach described in the Methods Guide. The evidence was evaluated by using the four required domains: risk of bias (low, medium, or high), consistency (consistent, inconsistent, or unknown/not applicable), directness (direct or indirect), and precision (precise or imprecise). All the studies were randomized controlled trials and most were of good quality, resulting in a low risk of bias. To rate consistency, we looked at the test of heterogeneity and the $I^2$ value; any significant test of heterogeneity or $I^2$ value greater than 50 percent was rated as inconsistent. To rate directness, we looked at the composite outcome used in the meta-analysis; any inclusion of softer endpoints (e.g., revascularization or heart failure) in the composite outcome, or differences in the composite endpoint between studies, was rated as indirect. To rate precision, we looked at the effect sizes used in the power calculations of the trials to determine a clinically meaningful reduction in odds. For a negative finding, a confidence interval narrow enough to exclude a less than 30 percent reduction (or increase) was rated as precise. Additionally, when appropriate, the studies were evaluated for the presence of confounders that would diminish an observed effect, the strength of association (magnitude of effect), and publication bias.

The strength of evidence was assigned an overall grade of High, Moderate, Low, or insufficient according to the following four-level scale:

- **High**—High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.
- **Moderate**—Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
• Low—Low confidence that the evidence reflects the true effect. Further research is likely to change the confidence in the estimate of effect and is likely to change the estimate.
• Insufficient—Evidence either is unavailable or does not permit estimation of effect.

**Peer Review and Public Commentary**

The peer review process was our principal external quality-monitoring device. Nominations for peer reviewers were solicited from several sources, including the TEP and interested Federal agencies. The list of nominees was forwarded to AHRQ for vetting and approval. A list of reviewers submitting comments on the draft report is included in the Preface.
Results

The flow of articles through the literature search and screening process is depicted in Figure 2. Of the 13,073 citations identified by our searches, 5,369 were duplicates. Manual searching identified an additional 173 citations for a total of 7,877 citations. After applying inclusion/exclusion criteria at the title/abstract level, 619 full-text articles were retrieved and screened. Of these, 547 articles were excluded at the full-text screening stage, with 72 articles (representing 28 studies) remaining for data abstraction. Appendix E provides a complete list of articles excluded at the full-text screening stage, with reasons for exclusion.

Figure 2. Literature flow diagram

CABG = coronary artery bypass graft; CAD = coronary artery disease; KQ = Key Question; NSTEMI = non-ST elevation myocardial infarction; PCI = percutaneous coronary intervention; RCT = randomized controlled trial; STEMI = ST elevation myocardial infarction
Key Question 1: Women With STEMI (PCI Vs. Fibrinolysis)

In women presenting with ST elevation myocardial infarction (STEMI):

a. What is the effectiveness of percutaneous coronary intervention (PCI) versus fibrinolysis/supportive therapy on clinical outcomes (nonfatal MI, death, stroke, repeat revascularization, recurrent unstable angina, heart failure, repeat hospitalization, length of hospital stay, angina relief, quality of life, or cognitive effects)?

b. Is there evidence that the comparative effectiveness of PCI versus fibrinolysis/supportive therapy varies based on characteristics such as:
   - Age, race, or other demographic and socioeconomic risk factors?
   - Coronary disease risk factors such as diabetes, chronic kidney disease, or other comorbid disease?
   - Angiographic-specific factors (number of diseased vessels, vessel territory stenoses, left ventricular function, access site, or prior PCI or coronary artery bypass graft surgery [CABG] revascularization procedure)?
   - Hospital characteristics (hospital volume, setting, guideline-based treatment protocols)?

c. What are the significant safety concerns associated with each treatment strategy (i.e., adverse drug reactions, radiation exposure, access site complications, renal dysfunction, anaphylaxis, arrhythmias, stent thrombosis, bleeding, infections)?

Overview

STEMI is caused by the complete occlusion of an epicardial artery, leading to possible transmural infarction of the heart muscle. Treatment for patients with STEMI consists of reperfusion therapy (either pharmacological or catheter-based) to restore blood flow promptly in the occluded epicardial infarct-related artery. Pharmacological therapy consists of fibrinolysis or facilitated antithrombotic medications. In general, patients with STEMI are not treated with CABG (unless emergent from PCI complications) but do receive optimal medical therapy in addition to treatment directed at removing the clot. Studies assessing the effectiveness of immediate PCI compared with fibrinolytics or immediate PCI compared with conservative/supportive therapy were evaluated for KQ 1.
Key Points

- **Description of included studies:** Seven studies (6 good quality, 1 fair) evaluated PCI with or without supportive pharmacologic therapy versus fibrinolysis or other routine medical care for women with STEMI and included a total of 4,527 patients, of which 1,174 (26%) were women.

- **Effectiveness of interventions:** A meta-analysis of five studies (all good quality) reporting 30-day composite outcomes (primarily death/MI/stroke) showed that PCI was better than fibrinolysis in women (OR 0.50; 95% CI, 0.36 to 0.72) and men (OR 0.54; CI, 0.42 to 0.70). Strength of evidence favoring PCI over fibrinolysis was high at 30-day followup. However, there was insufficient evidence for assessing outcomes at 1 year. These findings also are limited in that all the studies were conducted with either balloon angioplasty or bare-metal stents. The current use of drug-eluting stents may lead to different practice patterns and, potentially, increase the effectiveness of PCI. Individual outcomes by sex were rarely reported for heart failure, repeat hospitalization, length of hospital stay, angina relief, quality of life, or cognitive effects.

- **Modifiers of effectiveness:** Two studies (1 good quality, 1 fair) reported subgroup analyses of demographic or clinical factors in women and included a total of 395 patients, of which 167 (32%) were women. Both studies assessed the influence of age on in-hospital mortality or composite clinical outcomes (death/heart failure/MI/stroke) and showed no age-related differences in PCI compared with optimal medical therapy. Therefore, there was insufficient evidence of the comparative effectiveness of treatment strategies among subgroups of women with STEMI, which precludes any meaningful conclusions.

- **Safety concerns:** Two good-quality studies reported safety concerns in women with STEMI and included a total of 1,532 patients, of which 367 (24%) were women. One study reported a lower nadir hematocrit in women receiving PCI versus fibrinolysis but no statistically significant differences in the requirement for blood transfusion. Another study reported the proportion of women with intracranial hemorrhage who received PCI versus accelerated tissue plasminogen activator (t-PA) (0% vs. 4.1%). No studies systematically collected radiation exposure, contrast reactions, access site complications, or stent thrombosis in women with STEMI undergoing PCI. Strength of evidence for safety concerns in STEMI studies was insufficient.

Detailed Synthesis

We identified seven studies\(^{36-42}\) that evaluated PCI with or without supportive pharmacologic therapy versus fibrinolysis or other routine medical care for women with STEMI. Of these seven studies, six were good quality, and one was fair quality. Table 3 presents a general description of these seven studies, including the study name, author, year, and related articles (i.e., study design and secondary papers); treatment comparisons evaluated; study population; and overall quality rating. Table 4 summarizes the women-specific outcomes (composite and individual) reported in these studies. Appendix F contains summary tables with sex-specific clinical outcomes for all followup time points.
<table>
<thead>
<tr>
<th>Study Author/Year Related Articles</th>
<th>Description of Study</th>
<th># Subjects</th>
<th>Quality</th>
</tr>
</thead>
</table>
| **CARESS-in-AMI** Di Mario et al., 2008\textsuperscript{36} and Di Mario et al., 2004\textsuperscript{43} | **Title:** Immediate angioplasty vs. standard therapy with rescue angioplasty after thrombolysis in the Combined Abciximab Reteplase Stent Study in Acute Myocardial Infarction (CARESS-in-AMI): an open, prospective, randomized, multicentre trial  
**Comparator:** Immediate PCI with fibrinolysis (reteplase) vs. fibrinolysis (reteplase) with rescue PCI  
**Components of medical therapy:** Clopidogrel (300 mg bolus on arrival, then 75 mg once daily 1 to 12 months after stent implantation). Beta blockers, angiotensin-converting enzyme inhibitors, and statins were administered to all patients unless contraindicated. | Total: 600 (Women: 128 (21%)) | Good |
| **DANAMI-2** Andersen et al., 2003\textsuperscript{37} and Mortensen et al., 2007\textsuperscript{44} Nielsen et al., 2010\textsuperscript{45} Busk et al., 2009\textsuperscript{46} Busk et al., 2008\textsuperscript{47} | **Title:** A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction  
**Comparator:** PCI vs. fibrinolysis (accelerated t-PA)  
**Components of medical therapy:** Aspirin 300 mg, IV beta-blocker (20 mg of metoprolol), IV unfractionated heparin (5000 U bolus, then 1000 U/hr). | Total: 1,572 (Women: 417 (27%)) | Good |
| **Dobrzycki et al., 2007\textsuperscript{40}** | **Title:** Transfer with GP Iib/IIa inhibitor tirofiban for primary percutaneous coronary intervention vs. on-site thrombolysis in patients with ST elevation myocardial infarction (STEMI): a randomized open-label study for patients admitted to community hospitals  
**Comparator:** Transfer with tirofiban for primary PCI vs. onsite fibrinolysis (streptokinase)  
**Components of medical therapy:** Aspirin 325 mg daily. Additional treatment was administered at the discretion of the physician. | Total: 401 (Women: 105 (26%)) | Good |
| **GUSTO II-B** Tamis-Holland et al., 2004\textsuperscript{39} | **Title:** Benefits of direct angioplasty for women and men with acute myocardial infarction: results of the Global Use of Strategies to Open Occluded Arteries in Acute Coronary Syndromes Angioplasty (GUSTO II-B) Angioplasty Substudy  
**Comparator:** PCI vs. fibrinolysis (accelerated t-PA)  
**Components of medical therapy:** Not reported. | Total: 1,137 (Women: 260 (23%)) | Good |
### Table 3. KQ 1: Study characteristics of RCTs evaluating women with STEMI (continued)

<table>
<thead>
<tr>
<th>Study Author/Year Related Articles</th>
<th>Description of Study</th>
<th># Subjects</th>
<th>Quality</th>
</tr>
</thead>
</table>
| Minai et al., 200241              | **Title:** Long-term outcome of primary percutaneous transluminal coronary angioplasty for low-risk acute myocardial infarction in patients older than 80 years: a single-center, open, randomized trial  
**Comparator:** PCI vs. optimal medical therapy (without fibrinolysis)  
**Components of medical therapy:** IV heparin; IV nitroglycerin (0.5 mg/min/kg) for 24 hours after admission. Aspirin, other cardiovascular medications (calcium channel blockers, beta-blockers, and angiotensin-converting enzyme inhibitors administered at the discretion of the physician. | Total: 120  
Women: 60 (50%) | Fair |
| PAMI Stone et al., 199542         | **Title:** Comparison of in-hospital outcome in men with outcome in women treated by either thrombolytic therapy or primary coronary angioplasty for acute myocardial infarction  
**Comparator:** PCI vs. fibrinolysis (t-PA)  
**Components of optimal medical therapy:** IV unfractionated heparin for 3 - 5 days, Nitroglycerin for at least 24 hours, followed by topical or oral nitrates. Aspirin 325 mg/daily, diltiazem 30 to 60 mg x 4 times a day; use of beta-blockers and IV lidocaine was left to investigator discretion. | Total: 395  
Women: 107 (27%) | Good |
| SHOCK Hochman et al., 200148 and  
Hochman et al., 199949  
Hochman et al., 199950 | **Title:** One-year survival following early revascularization for cardiogenic shock  
**Comparator:** Early invasive revascularization (PCI or CABG within 6 hours) vs. initial medical stabilization (thrombolysis, IABP)  
**Components of optimal medical therapy:** Aspirin, IV unfractionated heparin, as recommended by AHA/ACC guidelines and at discretion of local investigator. | Total: 302  
Women: 97 (32%) | Good |

CABG = coronary artery bypass graft; IABP = intra-aortic balloon pump; IV = intravenous; PCI = percutaneous coronary intervention; RCT = randomized controlled trial; STEMI = ST elevation myocardial infarction; t-PA = tissue plasminogen activator
<table>
<thead>
<tr>
<th>Study</th>
<th>Composite Outcome&lt;sup&gt;a&lt;/sup&gt; (Timing)</th>
<th>Anticipated Effect Size</th>
<th>Death&lt;sup&gt;a&lt;/sup&gt; (Timing)</th>
<th>MI (Timing)</th>
<th>Stroke (Timing)</th>
<th>Revascularization (Timing)</th>
<th>Other (Timing)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARESS-in-AMI&lt;sup&gt;36,43&lt;/sup&gt;</td>
<td>Total mortality/reinfarction/refractory MI (30 days)</td>
<td>Powered to detect &gt;50% RRR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DANAMI-2&lt;sup&gt;37,44-47&lt;/sup&gt;</td>
<td>Total mortality/nonfatal MI/stroke (30 days, 3 years; median 7.8 years)</td>
<td>Powered to detect 40% RRR</td>
<td>Yes (30 days, 3 years)</td>
<td></td>
<td></td>
<td></td>
<td>Angina (30 days, 1 year)</td>
</tr>
<tr>
<td>Dobrzycki et al.&lt;sup&gt;40&lt;/sup&gt;</td>
<td>Total mortality/nonfatal MI/stroke (30 days, 1 year)</td>
<td>Powered to detect 50% RRR</td>
<td>Yes (30 days, 1 year)</td>
<td></td>
<td></td>
<td></td>
<td>SF-36 (30 days, 1 year)</td>
</tr>
<tr>
<td>GUSTO II-B&lt;sup&gt;39&lt;/sup&gt;</td>
<td>Total mortality/nonfatal MI/nonfatal disabling stroke (30 days)</td>
<td>Powered to detect 40% RRR</td>
<td>Yes (30 days)</td>
<td>Yes (30 days)</td>
<td>Yes (30 days)</td>
<td>Intracranial hemorrhage (30 days)</td>
<td></td>
</tr>
<tr>
<td>Minai et al.&lt;sup&gt;41&lt;/sup&gt;</td>
<td>Total mortality/heart failure/repeat MI/stroke (3 years)</td>
<td>Primary outcome &amp; effect size not specified</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PAMI&lt;sup&gt;42&lt;/sup&gt;</td>
<td>Death/reinfarction (in hospital)</td>
<td>Powered to detect 50% RRR</td>
<td>Yes (in hospital)</td>
<td>Yes (in hospital)</td>
<td>Yes (in hospital)</td>
<td></td>
<td>Recurrent ischemia (in hospital)</td>
</tr>
<tr>
<td>SHOCK&lt;sup&gt;38,48-50&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yes (1 year)</td>
<td>Length of stay (in hospital)</td>
</tr>
</tbody>
</table>

MI = myocardial infarction; RRR = relative risk reduction; STEMI = ST elevation myocardial infarction

<sup>a</sup>Primary outcome in italics.
KQ 1a: Effectiveness of Interventions

A meta-analysis was performed on studies with similar composite outcomes measured at similar time points. This meta-analysis was divided into followup intervals of short term (≤30 days) and long term (>1 year). The SHOCK study, evaluating early revascularization versus medical stabilization, did not report 1-year data by sex, except for noting the lack of a treatment-by-sex interaction, and therefore was not included in the meta-analysis. Similarly, in the Minai study evaluating PCI versus no PCI, 3-year data reported no sex effect in a multivariate analysis; however, since the data were not reported by sex, this study also was excluded from the meta-analysis.

Short-Term Followup Studies

Five studies—CARESS-in-AMI, DANAMI-2, Dobrzycki, GUSTO II-B, and PAMI—were included in the meta-analysis based on comparable composite outcomes (primarily death/MI/stroke) and followup time points of 30 days or in-hospital. The published results from Dobrzycki et al. were inverted to change the reference arm to fibrinolysis. The PAMI study event rates by treatment group and sex were converted into odds ratios. Table 5 presents the outcomes, odds ratios, and confidence intervals for the meta-analysis.

<table>
<thead>
<tr>
<th>Study (Comparison)</th>
<th>Outcome</th>
<th>Women (95% CI)</th>
<th>Men (95% CI)</th>
<th>Overall (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARESS-in-AMI (immediate PCI with reteplase vs. reteplase with rescue PCI)</td>
<td>Death/MI/refractory ischemia (30 days)</td>
<td>0.40 (0.12 to 1.31)</td>
<td>0.39 (0.18 to 0.85)</td>
<td>0.40 (0.21 to 0.76)</td>
</tr>
<tr>
<td>DANAMI-2 (immediate PCI vs. accelerated t-PA)</td>
<td>Death/MI/stroke (30 days)</td>
<td>0.47 (0.27 to 0.81)</td>
<td>0.59 (0.39 to 0.90)</td>
<td>0.55 (0.38 to 0.76)</td>
</tr>
<tr>
<td>Dobrzycki (transfer for primary PCI vs. onsite streptokinase)</td>
<td>Death/MI/stroke (30 days)</td>
<td>0.49 (0.20 to 1.18)</td>
<td>0.56 (0.26 to 1.18)</td>
<td>0.51 (0.29 to 0.91)</td>
</tr>
<tr>
<td>GUSTO II-B (PCI vs. accelerated t-PA)</td>
<td>Death/MI/stroke (30 days)</td>
<td>0.69 (0.36 to 1.32)</td>
<td>0.56 (0.35 to 0.91)</td>
<td>0.67 (0.47 to 0.97)</td>
</tr>
<tr>
<td>PAMI (PCI vs. t-PA)</td>
<td>Death/MI (in-hospital)</td>
<td>0.30 (0.08 to 1.16)</td>
<td>0.47 (0.18 to 1.19)</td>
<td>0.40 (0.18 to 0.85)</td>
</tr>
</tbody>
</table>

CI = confidence interval; MI = myocardial infarction; PCI = percutaneous coronary intervention; t-PA = tissue plasminogen activator

Forest plots for the random-effects model are shown in Figure 3. The summary odds ratio in women was 0.50 (95% CI, 0.36 to 0.72) and in men was 0.54 (CI, 0.42 to 0.70). The test for heterogeneity was nonsignificant. These results show that PCI was better than fibrinolysis in reducing death/MI/stroke in both sexes (p=0.0001 women, p<0.00001 men) at 30 days.
Intermediate-Term Followup Studies

Two studies—DANAMI-2\(^44\) and Dobrzycki\(^{40}\)—reported sex-specific clinical outcomes at 1 year. Table 6 presents the outcomes, odds ratios, and confidence intervals for PCI compared with fibrinolysis by sex. Due to the heterogeneous clinical outcomes, a meta-analysis was not conducted.

Table 6. Sex results for STEMI on clinical outcomes (intermediate-term)

<table>
<thead>
<tr>
<th>Study (Comparison)</th>
<th>Women (95% CI)</th>
<th>Men (95% CI)</th>
<th>Overall (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DANAMI-2 (immediate PCI vs. accelerated t-PA)</td>
<td>0.86 (0.50 to 1.49)</td>
<td>0.86 (0.61 to 1.20)</td>
<td>NR</td>
</tr>
<tr>
<td>Dobrzycki (transfer for primary PCI vs. onsite streptokinase)</td>
<td>0.40 (0.17 to 0.94)</td>
<td>0.62 (0.35 to 1.09)</td>
<td>0.53 (0.33 to 0.84)</td>
</tr>
</tbody>
</table>

CI = confidence interval; NR = not reported; PCI = percutaneous coronary intervention; t-PA = tissue plasminogen activator

PCI Versus Fibrinolysis in High-Risk Groups

We identified two studies that evaluated a PCI or CABG strategy versus conservative/supportive medical therapy in high-risk groups.\(^{38,41}\) These studies were not included in the meta-analysis since the actual results by sex were not reported in the manuscript; instead both papers report the results of a multivariate analysis with sex as a covariate in the model. The SHOCK study\(^{38}\) was considered good quality and evaluated patients with cardiogenic shock and STEMI with a strategy of PCI or CABG within 6 hours versus initial medical stabilization that included fibrinolysis or insertion of an intra-aortic balloon pump (IABP). This study found that the early revascularization strategy was associated with a lower relative risk of death when compared with medical stabilization (risk ratio 0.72; 95% CI, 0.54 to 0.95). Analysis by sex did
not identify any significant interaction by treatment arm. The study by Minai et al.\textsuperscript{41} was considered fair quality and evaluated PCI versus routine medical therapy without reperfusion in patients 80 years of age and older. There was no difference in the number of patients with the composite outcome of death/heart failure/repeat MI/stroke at 3 years between the treatment arms. No analysis by sex was done; however, in a multivariate analysis to evaluate factors associated with the composite outcome, sex was not found to be significantly associated with the outcome in the overall study population. This study was limited by the small sample size of 120 patients enrolled.

**KQ 1b: Modifiers of Effectiveness**

Two studies\textsuperscript{41,42} evaluating women with STEMI assessed the characteristics of interest and included a total of 515 patients, of which 167 (32\%) were women. The PAMI study\textsuperscript{42} was considered good quality and evaluated patients randomized to PCI versus fibrinolysis with t-PA. No difference was found in in-hospital mortality among women receiving PCI versus t-PA who were under 65 years of age (0\% vs. 4\%; \textit{p}=0.42) nor among women 65 and older (5.9\% vs. 21.9\%; \textit{p}=0.58).

The study by Minai et al.\textsuperscript{41} evaluated PCI versus routine medical therapy without reperfusion in patients 80 years of age and older. The results are noted above. Appendix G contains a summary table with study data related to modifiers of effectiveness (subgroup analyses).

**KQ 1c: Safety Concerns**

Two good-quality studies reported safety concerns in women with STEMI and included a total of 1,532 patients, of which 367 (24\%) were women. In the PAMI study\textsuperscript{42} evaluating PCI versus t-PA in STEMI patients, the mean nadir hematocrit in women with PCI was 30 ± 5 percent versus 33 ± 5 percent in women with t-PA (\textit{p}=0.0002). However, there was no statistically significant difference in the requirement for blood transfusion in women with PCI versus t-PA (18\% vs. 8.8\%; \textit{p}=0.16). In the GUSTO II-B study\textsuperscript{39} the proportion of women with intracranial hemorrhage was reported in women who received PCI versus accelerated t-PA (0\% vs. 4.1\%), but statistical analysis for this comparison was not done. Appendix H contains a summary table with study data related to safety concerns (harms).
Key Question 2: Women With UA/NSTEMI (Early Invasive Vs. Initial Conservative Therapy)

In women presenting with unstable angina or non-ST elevation myocardial infarction (UA/NSTEMI):

a. What is the effectiveness of early invasive (PCI or CABG) versus initial conservative therapy on clinical outcomes (nonfatal MI, death, stroke, repeat revascularization, recurrent unstable angina, heart failure, repeat hospitalization, length of hospital stay, graft failure, angina relief, quality of life, or cognitive effects)?

b. Is there evidence that the comparative effectiveness of early invasive versus initial conservative therapy varies based on characteristics such as:
   - Age, race, or other demographic and socioeconomic risk factors?
   - Coronary disease risk factors such as diabetes, chronic kidney disease, or other comorbid disease?
   - Angiographic-specific factors (number of diseased vessels, vessel territory stenoses, left ventricular function, access site, or prior PCI or CABG revascularization procedure)?
   - Hospital characteristics (hospital volume, setting, guideline-based treatment protocols)?

c. What are the significant safety concerns associated with each treatment strategy (i.e., adverse drug reactions, radiation exposure, access site complications, renal dysfunction, anaphylaxis, arrhythmias, stent thrombosis, bleeding, infections)?

Overview

Unstable angina is caused by reversible ischemia of the epicardial arteries, whereas NSTEMI is caused by the partial obstruction of the epicardial arteries and results in myocardial tissue damage. Patients with UA/NSTEMI are not candidates for immediate pharmacological reperfusion (i.e., fibrinolysis). The optimal management of UA/NSTEMI has the twin goals of immediate relief of ischemia and the prevention of serious adverse outcomes (i.e., death or MI). Optimal management is best accomplished with aggressive medical therapy that includes anti-ischemic therapy, antithrombotic therapy, ongoing risk stratification, and in some cases the use of invasive procedures.

Following initiation of aggressive medical therapy, two treatment pathways have emerged for treating patients without ST-segment elevation.28 An “initial conservative strategy” calls for proceeding with an invasive evaluation only for those patients whose medical therapy fails (refractory angina or angina at rest or with minimal activity despite vigorous medical therapy) or in whom objective evidence of ischemia (dynamic electrocardiographic changes, high-risk stress
The early invasive strategy triages patients to undergo an invasive diagnostic evaluation without first having a noninvasive stress test or having medical treatment fail. Patients treated with an early invasive strategy generally will undergo coronary angiography within 4 to 24 hours of admission; however, these patients also are treated with the usual UA/NSTEMI medications, including appropriate anti-ischemic, antiplatelet, and anticoagulant therapy. Therefore, studies assessing the effectiveness of early invasive versus initial conservative therapy were evaluated for KQ 2.

**Key Points**

- **Description of included studies:** Seven studies (6 good quality, 1 fair) compared early invasive therapy (PCI or CABG) with initial conservative therapy for women with UA/NSTEMI and included a total of 17,930 patients, of which 6,084 (34%) were women.
- **Effectiveness of interventions:** A meta-analysis of two good-quality studies reporting 6-month composite outcomes (death/MI) suggested a benefit of early invasive compared with initial conservative therapy in women (OR 0.77; 95% CI, 0.28 to 2.12), but early invasive therapy was superior to initial conservative therapy in men (OR 0.65; CI, 0.52 to 0.82; p=0.0002). At 1 year, a meta-analysis of five good-quality studies showed that composite outcomes (primarily death or MI) suggested a benefit for women who received early invasive therapy (OR 0.78; CI, 0.54 to 1.12) as well as for men (OR 0.88; CI, 0.64 to 1.20); however this benefit was not statistically significant. Finally, a meta-analysis of two good-quality studies with 5-year followup comparing early invasive and initial conservative therapy for the composite outcome of death or MI did not reach statistical significance in either sex. The summary odds ratio in women was 1.05 (CI, 0.81 to 1.35) and in men was 0.91 (CI, 0.53 to 1.56). The long-term analysis is limited by the low number of studies. Strength of evidence favoring an early invasive approach was low for women and high for men at 6-month followup; low for women and men at 1-year followup; and insufficient for women and low for men at 5-year followup. Similar to the STEMI studies, individual outcomes by sex were rarely reported for heart failure, repeat hospitalization, length of hospital stay, quality of life, or cognitive effects.
- **Modifiers of effectiveness:** Two good-quality studies comparing early invasive treatment with PCI with initial conservative treatment reported a subgroup analysis by risk stratification and included a total of 4,030 patients, of which 1,439 (36%) were women. These studies revealed conflicting results—one showed no difference in treatment outcomes in the intermediate- and high-risk groups; the other showed a higher event rate in women in the groups with moderate-to-high risk for thrombolysis in myocardial infarction (TIMI). Strength of evidence for modifiers of effectiveness for early invasive versus initial conservative treatments was insufficient.
- **Safety concerns:** One good-quality study (2,220 total patients, 757 women, 34% women) reported the harms associated with treatment of UA/NSTEMI by sex group but not the rates of events by treatment group. Bleeding in women undergoing PTCA was higher compared with men (adjusted OR 3.6; 95% CI, 1.6 to 8.3). However, bleeding related to CABG was similar in women and men with rates of 12.6 and 15 percent respectively. No studies systematically reported radiation exposure, contrast reactions, access site complications, stent thrombosis or infection, in women with UA/NSTEMI comparing initial conservative with early invasive therapy. Strength of evidence for safety concerns in these populations was insufficient.
Detailed Synthesis

We identified seven studies\textsuperscript{22,52-57} that evaluated the effect of early invasive therapy compared with initial conservative therapy for UA/NSTEMI and reported results by sex. Of these seven studies, six were good quality, and one was fair. Table 7 presents a general description of these seven studies, including the study name, author, year, and related articles (i.e., study design and secondary papers); treatment comparisons evaluated; study population; and overall quality rating. Table 8 summarizes the women-specific outcomes (composite and individual) reported in these studies. Appendix F contains summary tables with sex-specific clinical outcomes for all followup time points.
<table>
<thead>
<tr>
<th>Study Author/Year Related Articles</th>
<th>Description of Study</th>
<th># of Subjects</th>
<th>Quality</th>
</tr>
</thead>
</table>
| **FRISC II** Lagerqvist et al., 2001<sup>52</sup> and Lagerqvist et al., 2006<sup>58</sup> Wallentin et al., 2000<sup>59</sup> Anonymous, 1999<sup>60</sup> | **Title:** Is early invasive treatment of unstable coronary artery disease equally effective for both women and men? FRISC II Study Group Investigators  
**Comparator:** Early invasive treatment with revascularization (PCI, type not specified, for 1- or 2-vessel CAD; CABG for 3-vessel CAD or left main disease) vs. initial conservative strategy  
**Components of optimal medical therapy:** Aspirin 300 to 600 mg (initial), then 75 to 320 mg daily. Beta blockade (unless contraindicated). Organic nitrates and calcium antagonists as needed. Lowering of cholesterol with statins, angiotensin converting-enzyme inhibitors for left-ventricular dysfunction, and aggressive antidiabetic treatment were recommended according to modern treatment guidelines. | Total: 2,457  
Women: 749 (30%) | Good |
| **GUSTO IV-ACS** Ottervanger et al., 2004<sup>53</sup> | **Title:** Association of revascularisation with low mortality in non-ST elevation acute coronary syndrome, a report from GUSTO IV-ACS  
**Comparator:** Early invasive management vs. initial conservative treatment within 30 days. A total of 2265 (30%) patients underwent revascularization: 789 patients CABG, 1450 patients PCI, and 26 both CABG and PCI. Type of PCI was not specified.  
**Components of optimal medical therapy:** Aspirin for 30 days if not contraindicated. IV unfractionated heparin as bolus and infusion for 48 hours or low molecular weight heparin (dalteparin) subcutaneously every 12 hours for 5 to 7 days or until a revascularisation procedure or discharge. Continuation of antithrombin therapy with unfractionated or low molecular weight heparin was left at the discretion of the investigator. | Total: 7,800  
Women: 2,896 (37%) | Good |
Table 7. KQ 2: Study characteristics of RCTs evaluating women with UA/NSTEMI (continued)

<table>
<thead>
<tr>
<th>Study Author/Year Related Articles</th>
<th>Description of Study</th>
<th># of Subjects</th>
<th>Quality</th>
</tr>
</thead>
</table>
| ICTUS de Winter et al., 2005 and Damman et al., 2010 | **Title:** Early invasive vs. selectively invasive management for acute coronary syndromes  
**Comparator:** Early invasive therapy with revascularization vs. selective invasive strategy (initial conservative)  
**Components of optimal medical therapy:** Aspirin (300 mg at randomization then 75 mg daily); enoxaparin (1 mg/kg twice daily subcutaneously for 48 hours), Clopidogrel (300 mg immediately, followed by 75 mg daily) in combination with aspirin was recommended after the drug was approved in 2002 for the indication of acute coronary syndromes; intensive lipid-lowering therapy, preferably 80 mg of atorvastatin daily or the equivalent. | Total: 1,200  
Women: 320 (27%) | Good |
| RITA-2 Anonymous, 1997 | **Title:** Coronary angioplasty vs. medical therapy for angina: the second Randomised Intervention Treatment of Angina (RITA-2) trial. RITA-2 trial participants  
**Comparator:** Early invasive therapy with PCI (primarily PTCA, but stent could be used if PTCA failed) vs. initial conservative  
**Components of optimal medical therapy:** Aspirin, unless contraindicated. Antianginal medication for symptom relief. Beta-adrenoceptor blocker with a calcium antagonist and/or long-acting nitrate in maximally tolerated doses. Lipid-lowering drugs prescribed at the discretion of the supervising clinician. | Total: 1,018  
Women: 183 (8%) | Fair |
| RITA-3 Clayton et al., 2004 and Fox et al., 2002 | **Title:** Do men benefit more than women from an interventional strategy in patients with unstable angina or non-ST elevation myocardial infarction? The impact of gender in the RITA-3 trial  
**Comparator:** Early invasive with PCI (type at discretion of investigator) vs. initial conservative  
**Components of optimal medical therapy:** Aspirin; enoxaparin 1 mg/kg twice daily subcutaneously for 2 to 8 days. Antianginal treatment chosen by the supervising clinician, including a beta-blocker unless contraindicated. | Total: 1,810  
Women: 682 (38%) | Good |
<table>
<thead>
<tr>
<th>Study Author/Year Related Articles</th>
<th>Description of Study</th>
<th># of Subjects</th>
<th>Quality</th>
</tr>
</thead>
</table>
| TACTICS TIMI-18 Cannon et al., 2001 and Glaser et al., 2002 Cannon et al., 1998 | Title: Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban  
 Comparator: Early invasive with PCI (type not specified) vs. initial conservative  
 Components of optimal medical therapy: Aspirin 325 mg daily (unless contraindicated); IV unfractionated heparin (5000 U bolus, then 1000 U/hour for 48 hours); tirofiban (loading dose 0.4 μg/kg per minute for a period of 30 minutes, then 0.1 μg/kg/min for 48 hours or until revascularization, and for at least 12 hours after PCI; beta blockers (82%), nitrates (94%), and lipid-lowering agents (52%). | Total: 2,220  
 Women: 757 (34%) | Good |
| TIMI III-B Anonymous, 1994 and Anderson et al., 1995 | Title: Effects of tissue plasminogen activator and a comparison of early invasive and conservative strategies in unstable angina and non-Q-wave myocardial infarction. Results of the TIMI IIIIB Trial  
 Comparator: Early invasive with PCI (type not specified) vs. initial conservative  
 Components of optimal medical therapy: Anti-ischemic therapy consisting of a beta-blocker (metoprolol 50 mg p.o. q 12 hours), a calcium antagonist (diltiazem 30 mg p.o. q 6 hours), and a long-acting nitrate (isosorbide dinitrate 10 mg p.o. q 8 hours) or larger doses and supplemented by sublingual nitroglycerin pm. IV heparin. Aspirin 325 mg daily was given on the second day and continued for 1 year. | Total: 1,425  
 Women: 497 (35%) | Good |

CABG = coronary artery bypass graft; PCI = percutaneous coronary intervention; NSTEMI = non-ST elevation myocardial infarction; PTCA: percutaneous transluminal coronary angioplasty; RCT = randomized controlled trial; UA = unstable angina
Table 8. Outcomes reported in RCTs evaluating women with UA/NSTEMI

<table>
<thead>
<tr>
<th>Study</th>
<th>Composite Outcome* (Timing)</th>
<th>Anticipated Effect Size</th>
<th>Death (Timing)</th>
<th>MI (Timing)</th>
<th>Stroke (Timing)</th>
<th>Revascularization (Timing)</th>
<th>Other (Timing)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRISC II 52,58-60</td>
<td>Death/MI or both (6 months, 1 year, 5 years)</td>
<td>Powered to detect 32% difference</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>GUSTO IV-ACS 53</td>
<td>Not reported by sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yes (1 year)</td>
</tr>
<tr>
<td>ICTUS 56,61</td>
<td>Death/MI/rehospitalization for angina (1 year)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>ICTUS 56,61</td>
<td>Death/spontaneous MI (5 years)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>ICTUS 56,61</td>
<td>Powered to detect 25% RRR</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>RITA-2 54</td>
<td>Death/MI (median followup of 2.7 years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Angina grade 2+ (6 months)</td>
<td></td>
</tr>
<tr>
<td>RITA-3 22,62</td>
<td>Death/MI (1 year)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Exercise time (6 months)</td>
<td></td>
</tr>
<tr>
<td>RITA-3 22,62</td>
<td>Death/MI/refractory angina (4 months, 1 year)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yes (1 year)</td>
<td></td>
</tr>
</tbody>
</table>
Table 8. Outcomes reported in RCTs evaluating women with UA/NSTEMI (continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Composite Outcome* (Timing)</th>
<th>Anticipated Effect Size</th>
<th>Death (Timing)</th>
<th>MI (Timing)</th>
<th>Stroke (Timing)</th>
<th>Revascularization (Timing)</th>
<th>Other (Timing)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TACTICS TIMI-18&lt;sup&gt;51,55,63&lt;/sup&gt;</td>
<td>Death/MI/rehospitalization for acute coronary syndrome (6 months)</td>
<td>Death (6 months)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Death/MI (6 months)</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Powered to detect 25% difference</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIMI III-B&lt;sup&gt;57,64&lt;/sup&gt;</td>
<td>Death/MI/failed symptom-limited exercise treadmill test (6 weeks)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Death/MI (6 weeks, 1 year)</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Powered to detect 30% RRR</td>
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</tr>
</tbody>
</table>

MI = myocardial infarction; RRR = relative risk reduction; NSTEMI = non-ST elevation myocardial infarction; UA = unstable angina

*Primary outcome in italics.
KQ 2a: Effectiveness of Interventions

A meta-analysis was performed on studies with similar composite outcomes measured at similar time points. This meta-analysis was divided into followup intervals of short term (6 months), intermediate term (1 year) and long term (5 years).

Short-Term Followup Studies

Two studies reporting 6-month outcomes—FRISC II\textsuperscript{60} and TACTICS TIMI-18\textsuperscript{51}—were included in the meta-analysis. The TIMI III-B study\textsuperscript{57} (good quality) reported a shorter followup time point of 6 weeks and therefore was not included in this meta-analysis. In TIMI III-B, the proportion of women with the composite outcome of death/MI at 6 weeks was 6.1 percent in the early invasive arm and 8.9 percent in the initial conservative arm (p=0.24). The proportion of men with the same composite outcome was 7.8 percent and 7.3 percent, respectively (p=0.73). The RITA-2 study\textsuperscript{54} (fair quality) reported outcomes for angina grade 2+ or exercise time and likewise was not included in the meta-analysis. In RITA-2, the proportion of women with angina graded 2 or higher at 6 months was 22.8 percent for the early invasive arm, and 39.8 percent for the initial conservative arm. In men, the proportion with angina graded 2 or higher was 20.5 percent and 31.4 percent, respectively. For the TACTICS TIMI-18 study, we used the adjusted odds ratio for the composite outcome of death/MI. Table 9 presents the outcomes, odds ratios, and confidence intervals for the meta-analysis.

Table 9. Sex results for UA/NSTEMI on composite outcomes (short-term)

<table>
<thead>
<tr>
<th>Study (Comparison)</th>
<th>Outcome</th>
<th>Women (95% CI)</th>
<th>Men (95% CI)</th>
<th>Overall (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRISC II (early invasive vs. initial conservative)</td>
<td>Death/MI</td>
<td>1.26 (0.80 to 1.97)</td>
<td>0.64 (0.49 to 0.84)</td>
<td>0.78 (0.62 to 0.98)</td>
</tr>
<tr>
<td>TACTICS TIMI-18 (early invasive vs. initial conservative)</td>
<td>Death/MI</td>
<td>0.45 (0.24 to 0.88)</td>
<td>0.68 (0.43 to 1.05)</td>
<td>0.74 (0.54 to 1.00)</td>
</tr>
</tbody>
</table>

CI = confidence interval; MI = myocardial infarction; PCI = percutaneous coronary intervention

Forest plots for the random-effects model are shown in Figure 4. The summary odds ratio in women was 0.77 (95% CI, 0.28 to 2.12) and in men was 0.65 (CI, 0.52 to 0.82). The test for heterogeneity was significant in women (p=0.01), but it was nonsignificant in men. These results for short-term outcomes suggested a non–statistically significant benefit of early invasive compared with initial conservative therapy in women but demonstrated that early invasive was superior to initial conservative therapy in men (p=0.0002). The two trials resulted in conflicting conclusions in women versus men, despite having similar results for the overall population.
Figure 4. UA/NSTEMI short-term (6 months) early invasive versus initial conservative

Intermediate-Term Followup Studies

Five studies with 1-year data—FRISC II, GUSTO IV-ACS, ICTUS, RITA-3, and TIMI III-B—were included in the meta-analysis. For the RITA-3 study, the adjusted odds ratio for the composite outcome of death/MI was selected for this analysis. For the ICTUS and TIMI III-B studies, event rates were converted to odds ratios. Table 10 presents the outcomes, odds ratios, and confidence intervals for the meta-analysis.

Table 10. Sex results for UA/NSTEMI on composite outcomes (intermediate-term)

<table>
<thead>
<tr>
<th>Study (Comparison)</th>
<th>Outcome</th>
<th>Women (95% CI)</th>
<th>Men (95% CI)</th>
<th>Overall (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRISC II (early invasive vs. initial conservative)</td>
<td>Death/MI</td>
<td>0.61 (0.47 to 0.79)</td>
<td>1.18 (0.79 to 1.76)</td>
<td>0.74 (0.60 to 0.92)</td>
</tr>
<tr>
<td>GUSTO IV-ACS (revascularization in 30 days vs. initial conservative)</td>
<td>Death</td>
<td>0.53 (0.28 to 1.00)</td>
<td>0.55 (0.35 to 0.85)</td>
<td>0.53 (0.37 to 0.77)</td>
</tr>
<tr>
<td>ICTUS (early invasive vs. selective invasive)</td>
<td>Death/MI/rehospitalization for angina</td>
<td>0.97 (0.59 to 1.60)</td>
<td>1.12 (0.81 to 1.56)</td>
<td>1.07 (0.87 to 1.33)</td>
</tr>
<tr>
<td>RITA-3 (early invasive vs. initial conservative)</td>
<td>Death/MI</td>
<td>1.79 (0.95 to 3.35)</td>
<td>0.63 (0.41 to 0.98)</td>
<td>0.91 (0.67 to 1.25)</td>
</tr>
<tr>
<td>TIMI III-B (early invasive vs. initial conservative)</td>
<td>Death/MI</td>
<td>0.60 (0.38 to 0.93)</td>
<td>1.07 (0.67 to 1.70)</td>
<td>0.88 (0.64 to 1.21)</td>
</tr>
</tbody>
</table>

CI = confidence interval; MI = myocardial infarction

Forest plots for the random-effects model are shown in Figure 5. The summary odds ratio in women was 0.78 (95% CI, 0.54 to 1.12) and in men was 0.88 (CI, 0.64 to 1.20). The test for heterogeneity was significant in women (p=0.01) and men (p=0.02). These results show trends favoring early invasive therapy in 1-year outcomes although these benefits were not statistically significant in either women or men.
Long-Term Followup Studies

Two studies with 5-year, long-term data were included in the analysis: FRISC II\(^5\) and ICTUS.\(^6\) Table 11 presents the outcomes, odds ratios, and confidence intervals for the meta-analysis.

Table 11. Sex results for UA/NSTEMI on composite outcomes (long-term)

<table>
<thead>
<tr>
<th>Study (Comparison)</th>
<th>Outcome</th>
<th>Women (95% CI)</th>
<th>Men (95% CI)</th>
<th>Overall (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRISC II (early invasive vs. initial conservative)</td>
<td>Death/MI</td>
<td>0.87 (0.53 to 1.43)</td>
<td>1.22 (0.87 to 1.71)</td>
<td>1.29 (1.00 to 1.66)</td>
</tr>
<tr>
<td>ICTUS (early invasive vs. selective invasive)</td>
<td>Death/MI</td>
<td>0.83 (0.59 to 0.86)</td>
<td>0.87 (0.69 to 0.95)</td>
<td></td>
</tr>
</tbody>
</table>

CI = confidence interval; MI = myocardial infarction

Forest plots for the random-effects model are shown in Figure 6. The summary odds ratio in women was 1.05 (95% CI, 0.81 to 1.35) and in men was 0.91 (CI, 0.53 to 1.56). The test for heterogeneity was significant in men (p=0.005) but not in women. Although these results demonstrate a slight trend favoring initial conservative therapy in women, given the small suggested benefit at 5 years, the wide confidence interval crossing 1, and the trend favoring early invasive therapy suggested at earlier time points and across time points in men — we cannot support firm conclusions. There was no evidence of a sex effect. The analysis is limited by the low number of studies.
Figure 6. UA/NSTEMI long-term (5 years) early invasive versus initial conservative

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odds Ratio IV, Random, 95% CI</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1.1 Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FRISC II, 2006</td>
<td>0.113</td>
<td>0.151</td>
<td>26.3%</td>
<td>1.12 [0.83, 1.51]</td>
<td></td>
</tr>
<tr>
<td>ICTUS, 2010</td>
<td>-0.139</td>
<td>0.253</td>
<td>18.2%</td>
<td>0.87 [0.53, 1.43]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>44.5%</td>
<td>1.05</td>
<td>[0.81, 1.35]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.00; Chi² = 0.73, df = 1 (P = 0.39); P = 0%</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.36 (P = 0.72)</td>
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<td></td>
</tr>
</tbody>
</table>

1.1.2 Men

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odds Ratio IV, Random, 95% CI</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRISC II, 2006</td>
<td>-0.357</td>
<td>0.098</td>
<td>30.3%</td>
<td>0.70 [0.58, 0.84]</td>
<td></td>
</tr>
<tr>
<td>ICTUS, 2010</td>
<td>0.199</td>
<td>0.172</td>
<td>24.5%</td>
<td>1.22 [0.87, 1.71]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>55.5%</td>
<td>0.91</td>
<td>[0.53, 1.56]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.14; Chi² = 7.97, df = 1 (P = 0.006); P = 07%</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Test for overall effect: Z = 0.35 (P = 0.73)</td>
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</tbody>
</table>

Total (95% CI) 100.0% 0.94 [0.70, 1.28] 

Heterogeneity: Tau² = 0.07; Chi² = 11.80, df = 3 (P = 0.006); I² = 75%

Test for overall effect: Z = 0.37 (P = 0.71)

Test for subgroup differences: Chi² = 0.22, df = 1 (P = 0.64), P = 0%

Some of the analyses above showed heterogeneity in clinical outcomes between the FRISC II and ICTUS studies. The major heterogeneity in these studies arises from the rates and threshold of invasive treatment in the conservative arm. In the FRISC II study, more conservative strategies were used, thus leading to lower rates of invasive treatment in the conservative groups. In the ICTUS study, the selective invasive group was more liberal with the rates of invasive therapy and almost as high as the invasive arms of the other studies, thus explaining some of the potential differences in the results.

KQ 2b: Modifiers of Effectiveness

We identified two good-quality studies examining the effect of early invasive therapy compared with initial conservative therapy in women by subgroup; these included a total of 4030 patients, of which 1439 (36%) were women. The TACTICS TIMI-18 study found that there was no significant benefit to the treatment of women with intermediate-risk (3 to 4) or high-risk (5 to 7) TIMI scores on the primary composite outcome of death/MI/rehospitalization for acute coronary syndrome with early invasive therapy (OR 0.72; 95% CI, 0.45 to 1.16) compared with initial conservative therapy (OR 0.56; CI, 0.23 to 1.32). There also was no significant benefit of early invasive therapy on the primary composite outcome for those presenting with ST-segment changes (OR 0.66; CI, 0.38 to 1.15). However, there did seem to be a reduced risk of the primary composite outcome among women who had an elevated troponin level and who underwent early invasive treatment compared with conservative treatment (OR 0.56; CI, 0.32 to 0.97). Men with ST-segment changes and elevated troponin levels also seemed to benefit from early invasive therapy but not those in intermediate- or high-risk groups based on TIMI risk scores.

The RITA-3 study also examined the effect of early invasive therapy compared with initial conservative therapy in women by subgroup based on risk, which was derived from components of the TIMI risk score and a couple other aspects of the participants’ presentation at randomization, including aspirin use and angina severity. This study, unlike the TACTICS TIMI-
18 study, found a higher event rate among women in moderate- and high-risk groups who underwent early invasive therapy compared with initial conservative therapy, with event rates of 13.4 percent versus 3.4 percent for those in the moderate-risk group and 11.7 percent versus 8.2 percent for those in the higher risk group. Men with moderate and higher risk had lower event rates if they were in the early invasive arm compared with the initial conservative arm, with 5.4 percent versus 9.4 percent for those in the moderate-risk group and 10.3 percent versus 17.9 percent for those in the higher risk group. This study also examined the effect of intervention group by body mass index group and found no effect of body mass index on treatment effect in either women or men. Appendix G contains a summary table with study data related to modifiers of effectiveness (subgroup analyses).

**KQ 2c: Safety Concerns**

We identified one good-quality study (2,220 total patients, 757 women, 34% women) that reported the harms associated with treatment of UA/NSTEMI by sex group but not the rates of events by treatment group. The TACTICS TIMI-18 study, comparing early invasive therapy with initial conservative therapy, found that bleeding in women undergoing PTCA was higher than in men (adjusted OR 3.6; 95% CI, 1.6 to 8.3). They found, however, that the bleeding related to CABG was similar in women and men with rates of 12.6 and 15 percent, respectively. Appendix H contains a summary table with study data related to safety concerns (harms).

**Key Question 3: Women With Stable or Unstable Angina**

In women with stable or unstable angina:

a. What is the effectiveness of the following treatment strategies on clinical outcomes (nonfatal MI, death, stroke, repeat revascularization, recurrent unstable angina, heart failure, repeat hospitalization, length of hospital stay, graft failure, angina relief, quality of life, or cognitive effects)?

   **Strategy 1. Revascularization (PCI or CABG) versus optimal medical therapy in women with stable angina**

   **Strategy 2. PCI versus CABG in women with stable or unstable angina**

b. Is there evidence that the comparative effectiveness of revascularization versus optimal medical therapy varies based on characteristics such as:

   - Age, race, or other demographic and socioeconomic risk factors?
   - Coronary disease risk factors such as diabetes, chronic kidney disease, or other comorbid disease?
   - Angiographic-specific factors (number of diseased vessels, vessel territory stenoses, left ventricular function, access site, or prior PCI or CABG revascularization procedure)?
• CABG-specific factors such as type of surgery performed, cardiopulmonary bypass mode (normothermic versus hypothermic), on-pump versus off-pump, type of cardioplegia used (blood versus crystalloid), or use of saphenous vein grafts, single or bilateral internal mammary artery grafts, or other types of bypass grafts?

• Hospital characteristics (hospital volume, setting, guideline-based treatment protocols)?

c. What are the significant safety concerns associated with each treatment strategy (i.e., adverse drug reactions, radiation exposure, access site complications, renal dysfunction, anaphylaxis, arrhythmias, stent thrombosis, bleeding, infections)?

Overview

Angina resulting from progressive narrowing of the coronary arteries is the initial manifestation of ischemic heart disease in approximately 50 percent of patients. Most angina is a sign of significant CAD, defined angiographically as a stenosis with ≥70 percent diameter in at least one major epicardial artery segment or with ≥50 percent diameter in the left main coronary artery. However, some angina is caused by stenotic lesions of lesser diameters, which have much less prognostic significance.

Chronic stable angina is classified as pain that classically occurs with moderate to severe exertion, is milder in nature, and relieved with rest or sublingual nitroglycerin. Unstable angina (UA) is defined as angina with at least one of three features: (1) it occurs at rest or with minimal exertion, (2) it is severe and of recent onset (within the past 4 to 6 weeks), and/or (3) it occurs in a crescendo pattern (i.e., more severe, more prolonged, or more frequent than previously experienced). UA and NSTEMI have a fairly similar pathophysiology, mortality rate, and management strategy when compared with STEMI; therefore they are often grouped together as UA/NSTEMI in clinical guidelines and trial populations.

The treatment of angina has two major purposes. The first is to prevent MI and death and thereby increase the quantity of life. The second is to reduce symptoms of angina and occurrence of ischemia, which should improve the quality of life. All patients with stable or unstable angina are candidates for optimal medical therapy and also may be candidates for PCI or CABG based on findings from coronary angiography or if symptoms persist despite optimal medical therapy.

For KQ 3, we evaluated two sets of treatment strategies:

1. Revascularization (PCI or CABG) versus optimal medical therapy in women with stable angina
2. PCI versus CABG in women with either stable or unstable angina
Strategy 1: Revascularization Versus Optimal Medical Therapy in Stable Angina

Key Points

- **Description of included studies:** Five studies (all good quality) compared revascularization (PCI or CABG) with optimal medical therapy for women with stable angina and included a total of 6,851 patients, of which 1,285 (19%) were women.

- **Effectiveness of interventions:** A meta-analysis of three good-quality studies with long-term (4- to 5-year) followup on the composite outcomes (death/MI/revascularization) comparing PCI or CABG with optimal medical therapy showed that revascularization was significantly better than optimal medical therapy in women with stable angina (OR 0.64; 95% CI, 0.47 to 0.89; p=0.008 for PCI strategy trials; OR 0.56 [CI, 0.32 to 0.96; p=0.04] for CABG strategy trials; and OR 0.59 [CI, 0.43 to 0.81; p=0.001] for either PCI or CABG). However, for men with stable angina, the analysis did not show statistically significant findings between revascularization and optimal medical therapy, though it demonstrated a trend favoring optimal medical therapy compared with PCI (OR 1.03; CI, 0.79 to 1.33 for PCI strategy trials). This suggested small benefit however has a wide confidence interval crossing 1 and is not supported by additional time periods or by the evidence in women. Conversely, evidence suggested that CABG or either PCI or CABG reduced outcomes compared with optimal medical therapy in men (OR 0.62; CI, 0.31 to 1.24 for CABG strategy trials; and OR 0.71; CI, 0.49 to 1.02 for either PCI or CABG)—again these findings were not statistically significant. Strength of evidence favoring revascularization for women was moderate in the PCI strategy, low in the CABG strategy, and moderate for both types of revascularization combined. In men, the strength of evidence was low for the PCI, CABG, and combined revascularization strategies.

- **Modifiers of effectiveness:** No studies were identified that evaluated women presenting with stable angina; therefore data are insufficient.

- **Safety concerns:** No studies were identified that evaluated women presenting with stable angina; therefore data are insufficient.

Detailed Synthesis

We identified five studies that reported outcomes for women with stable angina. Of these five studies, all were good quality. Two studies compared PCI with optimal medical therapy, one compared CABG with optimal medical therapy, and one compared medical management with transmyocardial revascularization (TMR). Table 12 presents a general description of these five studies, including the study name, author, year, and related articles (i.e., study design and secondary papers); treatment comparisons evaluated; study population; and overall quality rating. Table 13 summarizes the women-specific outcomes (composite and individual) reported in these studies. Appendix F contains summary tables with sex-specific clinical outcomes for all followup time points.
Table 12. KQ 3 Strategy 1: Study characteristics of RCTs evaluating women with stable angina (PCI/CABG vs. optimal medical therapy)

<table>
<thead>
<tr>
<th>Study Author/Year Related Articles</th>
<th>Description of Study</th>
<th># of Subjects</th>
<th>Quality</th>
</tr>
</thead>
</table>
| Allen et al., 2004<sup>69</sup> and Allen et al., 1999<sup>70</sup> | **Title:** Transmyocardial revascularization: 5-year follow-up of a prospective randomized multicenter trial  
**Comparator:** Surgical revascularization (CABG with transmyocardial revascularization) vs. optimal medical therapy  
**Components of optimal medical therapy:** Not reported. | Total: 222  
Women: 61 (27%) | Good |
| COURAGE Boden et al., 2007<sup>65</sup> and Mancini et al., 2009<sup>71</sup> Boden et al., 2006<sup>72</sup> | **Title:** Optimal medical therapy with or without PCI for stable coronary disease  
**Comparator:** PCI (type not specified) or CABG if PCI failed vs. optimal medical therapy  
**Components of optimal medical therapy:** Aspirin (81 to 325 mg per day) or 75 mg of clopidogrel per day, if aspirin intolerance was present. Metoprolol, amlodipine, and isosorbide mononitrate, alone or in combination, along with either lisinopril or losartan; aggressive therapy to lower low-density lipoprotein cholesterol levels (simvastatin alone or in combination with ezetimibe) with a target level of 60 to 85 mg per deciliter (1.55 to 2.20 mmol per liter). | Total: 2,287  
Women: 338 (15%) | Good |
| MASS II Hueb et al., 2010<sup>68</sup> and Hueb et al., 2004<sup>73</sup> Hueb et al., 2007<sup>74</sup> | **Title:** Ten-year follow-up survival of the Medicine, Angioplasty, or Surgery Study (MASS II): a randomized controlled clinical trial of 3 therapeutic strategies for multivessel coronary artery disease  
**Comparator:** PCI vs. optimal medical therapy; CABG vs. optimal medical therapy  
**Components of optimal medical therapy:** Nitrates, aspirin, beta blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, or a combination of these drugs unless contraindicated. Lipid-lowering agents, particularly statins, were also prescribed, along with a low-fat diet, on an individual basis. | Total: 611  
Women: 196 (32%) | Good |
Table 12. KQ 3 Strategy 1: Study characteristics of RCTs evaluating women with stable angina (PCI/CABG vs. optimal medical therapy) (continued)

<table>
<thead>
<tr>
<th>Study Author/Year Related Articles</th>
<th>Description of Study</th>
<th># of Subjects</th>
<th>Quality</th>
</tr>
</thead>
</table>
| **OAT** Hochman et al., 2006\(^{66}\) and Hochman et al., 2005\(^{75,76}\) | **Title:** Coronary intervention for persistent occlusion after myocardial infarction  
**Comparator:** PCI (or CABG if PCI failed) vs. optimal medical therapy  
**Components of optimal medical therapy:** Aspirin, anticoagulation if indicated, angiotensin-converting enzyme inhibition, beta blockade, and lipid-lowering therapy, unless contraindicated. Thienopyridine therapy was initiated before PCI and continued for 2 to 4 weeks after stenting. After reports of the efficacy of prolonged treatment with a thienopyridine after MI, the recommendation was changed to 1 year in both study groups. | Total: 2,166  
Women: 476 (22%) | Good |
| **STICH** Velazquez et al., 2011\(^{67}\) and Velazquez et al., 2007\(^{77}\) | **Title:** Coronary-artery bypass surgery in patients with left ventricular dysfunction  
**Comparator:** CABG vs. optimal medical therapy  
**Components of optimal medical therapy:** Unless contraindicated, optimal medical therapy included angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, or both; beta blocker; aldosterone antagonist; and antiplatelet agents adjusted to optimal doses within 30 days after randomization. Statin, diuretic, and digitalis use was individualized to patient-specific indications. The use of implantable defibrillators was encouraged as part of medical therapy and was used in compliance with standard guidelines. | Total: 1,212  
Women: 148 (12%) | Good |

CABG = coronary artery bypass graft; CAD = coronary artery disease; MI = myocardial infarction; PCI = percutaneous coronary intervention; PTCA = percutaneous transluminal coronary angioplasty
<table>
<thead>
<tr>
<th>Study</th>
<th>Composite Outcome* (Timing)</th>
<th>Anticipated Effect Size</th>
<th>Deatha (Timing)</th>
<th>MI (Timing)</th>
<th>CVA (Timing)</th>
<th>Revascularization (Timing)</th>
<th>Othera (Timing)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allen et al.69,70</td>
<td>Effect size not reported</td>
<td></td>
<td>Yes (5.7 years)</td>
<td></td>
<td></td>
<td></td>
<td>Angina relief</td>
</tr>
<tr>
<td>COURAGE65,71,72</td>
<td>Death/MI (median 4.6 years)</td>
<td>Powered to detect 22% RRR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MASS II68,73,74</td>
<td>Death/MI/angina requiring revascularization (10 years)</td>
<td>Powered to detect 2-fold difference</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OAT66,75,76</td>
<td>Death/MI/heart failure (4 years, 7 years)</td>
<td>Powered to detect 25% reduction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>STICH67,77</td>
<td>Powered to detect 25% reduction in mortality</td>
<td></td>
<td>Yes (5 years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass grafting; CVA = cerebrovascular accident; MI = myocardial infarction; PCI = percutaneous coronary intervention; RRR = relative risk reduction

*Primary outcome in italics.
KQ 3a: Effectiveness of Interventions

Long-Term Followup Studies

Three studies were included in a meta-analysis: COURAGE, MASS II and STICH. These studies had similar followup times (4 to 5 years, except a 10-year followup in the MASS II study) and comparable outcomes (composite, death). No results were available for the short- or intermediate-term outcomes. The TMR study by Allen et al. was excluded since the results were reported in a different fashion (i.e., whether sex had an impact on outcome for the TMR patients) and could not be incorporated into the meta-analysis. The OAT study was excluded from the meta-analysis since the study subjects were enrolled ≥7 days after an acute MI with revascularization or medical therapy for an occluded artery; the patient population was deemed to be quite different from those enrolled in the other studies. The MASS II study numbers were inverted to place PCI in the comparison group. Table 14 presents the outcomes, odds ratios, and confidence intervals for the meta-analyses.

Table 14. Sex results for stable angina on composite outcomes (long-term)

<table>
<thead>
<tr>
<th>Study (Comparison)</th>
<th>Outcome</th>
<th>Women (95% CI)</th>
<th>Men (95% CI)</th>
<th>Overall (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>COURAGE (PCI [or CABG if PCI failed] vs. optimal medical therapy)</td>
<td>Death/MI</td>
<td>0.65 (0.40 to 1.06)</td>
<td>1.15 (0.91 to 1.42)</td>
<td>1.05 (0.87 to 1.27)</td>
</tr>
<tr>
<td>MASS II (PCI vs. optimal medical therapy)</td>
<td>Death/MI/revascularization</td>
<td>0.64 (0.41 to 0.98)</td>
<td>0.88 (0.65 to 1.19)</td>
<td>0.79 (0.62 to 1.01)</td>
</tr>
<tr>
<td>MASS II (CABG vs. optimal medical therapy)</td>
<td>Death/MI/revascularization</td>
<td>0.43 (0.26 to 0.72)</td>
<td>0.43 (0.31 to 0.61)</td>
<td>0.43 (0.32 to 0.56)</td>
</tr>
<tr>
<td>STICH (CABG vs. optimal medical therapy)</td>
<td>Death</td>
<td>0.75 (0.42 to 1.31)</td>
<td>0.87 (0.72 to 1.06)</td>
<td>0.86 (0.72 to 1.04)</td>
</tr>
</tbody>
</table>

CI = confidence interval; CABG = coronary artery bypass graft; MI = myocardial infarction; PCI = percutaneous coronary intervention

Forest plots for the random-effects model are shown in Figures 7, 8, and 9. Separate analyses were created for (a) primarily PCI strategy, (b) primarily CABG strategy, and (c) either type of revascularization strategy compared with optimal medical therapy for the purposes of creating a sensitivity analysis given the subtle differences in patient populations and revascularization methods used in those studies.

The primarily PCI strategy (Figure 7) studies included COURAGE and MASS II (PCI). The summary odds ratio in women was 0.64 (95% CI, 0.47 to 0.89) and in men was 1.03 (CI, 0.79 to 1.33). The test for heterogeneity was not significant for women and men. The results showed that PCI reduced death/MI in women but not in men.
The primarily CABG strategy (Figure 8) studies included MASS II (CABG) and STICH. The summary odds ratio in women was 0.56 (CI, 0.32 to 0.96) and in men was 0.62 (CI, 0.31 to 1.24). The test for heterogeneity was not significant for women (p=0.15) but was significant for men (p=0.0004). These results show that CABG was significantly better in reducing cardiovascular events than optimal medical therapy was in women (effect size p=0.04) but not in men.
We then combined all studies utilizing both types of revascularization strategies (PCI or CABG)—COURAGE, MASS II, and STICH. Figure 9 shows the forest plot for the random-effects model using the MASS II (CABG) cohort. The summary odds ratio in women was 0.59 (CI, 0.43 to 0.81) and in men was 0.71 (CI, 0.49 to 1.02). The test for heterogeneity was not significant in women, but was significant in men. These results showed that revascularization was significantly better in reducing cardiovascular events than optimal medical therapy in women. Similar results were obtained if the model was run with the MASS II (PCI) cohort (figure not shown). For men, revascularization and optimal medical therapy were not statistically different.

**Figure 9. Stable angina, revascularization (combined) versus medical therapy**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1.1 Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>COURAGE, 2007</td>
<td>-0.431</td>
<td>0.249</td>
<td>13.7%</td>
<td>0.65 [0.40, 1.06]</td>
</tr>
<tr>
<td>MASS II (CABG), 2010</td>
<td>-0.844</td>
<td>0.26</td>
<td>13.2%</td>
<td>0.43 [0.26, 0.72]</td>
</tr>
<tr>
<td>STICH, 2011</td>
<td>-0.288</td>
<td>0.29</td>
<td>11.9%</td>
<td>0.75 [0.42, 1.32]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>38.8%</td>
<td>0.59</td>
<td>0.43, 0.81</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.01; Chi² = 2.31; df = 2 (P = 0.31); I² = 14%</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: Z = 3.24 (P = 0.001)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1.2 Men</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>COURAGE, 2007</td>
<td>-0.14</td>
<td>0.114</td>
<td>21.3%</td>
<td>0.87 [0.70, 1.09]</td>
</tr>
<tr>
<td>MASS II (CABG), 2010</td>
<td>-0.844</td>
<td>0.173</td>
<td>17.9%</td>
<td>0.43 [0.31, 0.60]</td>
</tr>
<tr>
<td>STICH, 2011</td>
<td>-0.139</td>
<td>0.093</td>
<td>22.0%</td>
<td>0.87 [0.72, 1.06]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>61.2%</td>
<td>0.71</td>
<td>0.49, 1.02</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.09; Chi² = 13.98; df = 2 (P = 0.0009); I² = 86%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.83 (P = 0.07)</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

| Total (95% CI)    | 100.0%          | 0.66  | 0.50, 0.86 |
| Heterogeneity: Tau² = 0.08; Chi² = 19.16; df = 6 (P = 0.002); I² = 74% |
| Test for overall effect: Z = 3.01 (P = 0.003) |
| Test for subgroup differences: Chi² = 0.53; df = 1 (P = 0.47); I² = 0% |

**KQ 3b: Modifiers of Effectiveness**

No studies were identified that evaluated women presenting with stable angina related to modifiers of the effectiveness of revascularization versus optimal medical therapy.

**KQ 3c: Safety Concerns**

No studies were identified that evaluated women presenting with stable angina related to safety concerns for revascularization versus optimal medical therapy.
Strategy 2: PCI Versus CABG in Stable/Unstable Angina

Key Points

- **Description of included studies:** 10 studies (8 good quality, 2 fair) compared PCI with CABG in women with stable/unstable angina and included a total of 6,289 patients, of which 1,583 (25%) were women.

- **Effectiveness of interventions:** A meta-analysis of two good-quality studies reporting 30-day death rates showed no statistically significant difference between PCI and CABG and therefore did not support evidence of a sex effect. The summary odds ratio in women was 0.68 (95% CI, 0.24 to 1.93) and in men was 1.36 (CI, 0.44 to 4.24). These two studies did, however, suggest a potentially greater benefit with PCI in women and with CABG in men. The low number of studies and wide confidence intervals made this a less robust finding and one that should be interpreted with caution. For 1-year outcomes (death/MI/stroke), a meta-analysis of two good-quality studies suggested potentially better outcomes in the CABG group for both sexes however this findings was not statistically significant (CI crosses 1). The summary odds ratio in women was 1.30 (CI, 0.69 to 2.45) and in men was 1.19 (CI, 0.84 to 1.70). For long-term (>2 years) outcomes (death/MI/stroke), a meta-analysis of four good-quality studies although not statistically significant, suggested better outcomes in the CABG group in women (OR 1.17; CI, 0.90 to 1.54); however in men, CABG was significantly better than PCI (OR 1.63; CI, 1.20 to 2.23, p= 0.002). Strength of evidence favoring CABG over PCI was low for women and men at 30-day and 1-year followups, and low for women and high for men at ≥2-year followup.

- **Modifiers of effectiveness:** One good-quality study (915 total patients, 249 [27%] women) evaluated the comparative effectiveness of PCI versus CABG in diabetic patients with stable/unstable angina. The survival rate at 7 years was similar in diabetic women from both treatment groups. However in diabetic men, those treated with CABG had higher survival than those who underwent PCI. Strength of evidence for modifiers of effectiveness for PCI versus CABG in stable/unstable angina was insufficient.

- **Safety concerns:** One good-quality study (1205 total patients, 283 [23%] women) reported harms associated with PCI compared with CABG among women with unstable angina or NSTEMI and found that bleeding associated with PCI was higher in women compared with men. Strength of evidence for safety concerns for PCI versus CABG in stable/unstable angina was insufficient.

Detailed Synthesis

We identified 10 studies that evaluated PCI versus CABG for women presenting with unstable angina or NSTEMI. Of these 10 studies, 8 were good quality, and 2 were fair quality. Table 15 presents a general description of these 10 studies, including the study name, author, year, and related articles (i.e., study design and secondary papers); treatment comparisons evaluated; study population; and overall quality rating. Table 16 summarizes the women-specific outcomes (composite and individual) reported in these studies. Appendix F contains summary tables with sex-specific clinical outcomes for all followup time points.
<table>
<thead>
<tr>
<th>Study Author/Year Related Articles</th>
<th>Description of Study</th>
<th># of Subjects</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ARTS I</strong> Vaina et al., 2009\textsuperscript{78} and van den Brand, et al., 2002\textsuperscript{87} Serruys et al., 1999\textsuperscript{88} Voudris et al., 2006\textsuperscript{89} Anonymous, 1999\textsuperscript{90}</td>
<td><strong>Title:</strong> Effect of gender differences on early and mid-term clinical outcome after percutaneous or surgical coronary revascularisation in patients with multivessel coronary artery disease: insights from ARTS I and ARTS II <strong>Comparator:</strong> PCI (BMS) vs. CABG <strong>Components of medical therapy:</strong> Not reported.</td>
<td>Total: 1,205 Women: 283 (23%)</td>
<td>Good</td>
</tr>
<tr>
<td><strong>BARI</strong> Jacobs et al., 1998\textsuperscript{79} and Gibbons et al., 2001\textsuperscript{91} Anonymous, 2007\textsuperscript{92} Lombardero et al., 2002\textsuperscript{93} Anonymous, 2000\textsuperscript{94} Hlatky et al., 1995\textsuperscript{95} Rogers et al., 1995\textsuperscript{96} Sutton-Tyrrell et al., 1998\textsuperscript{97} Mullany et al., 1999\textsuperscript{98} Anonymous, 1996\textsuperscript{99}</td>
<td><strong>Title:</strong> Better outcome for women compared with men undergoing coronary revascularization: a report from the bypass angioplasty revascularization investigation (BARI) <strong>Comparator:</strong> PCI (type not specified) vs. CABG <strong>Components of medical therapy:</strong> Not reported.</td>
<td>Total: 915 Women: 249 (27%)</td>
<td>Good</td>
</tr>
<tr>
<td><strong>CABRI</strong> Anonymous, 1995\textsuperscript{80}</td>
<td><strong>Title:</strong> First-year results of CABRI (Coronary Angioplasty vs. Bypass Revascularisation Investigation) <strong>Comparator:</strong> PCI (PTCA) vs. CABG <strong>Components of medical therapy:</strong> Aspirin; fish oils and lipid-lowering agent were allowed; individual patient management followed the established practice at each participating center.</td>
<td>Total: 1,054 Women: 234 (22%)</td>
<td>Good</td>
</tr>
<tr>
<td>Study Author/Year Related Articles</td>
<td>Description of Study</td>
<td># of Subjects</td>
<td>Quality</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>----------------------</td>
<td>---------------</td>
<td>---------</td>
</tr>
</tbody>
</table>
| **CARDia** Kapur et al., 2010<sup>84</sup> and Kapur et al., 2005<sup>100</sup> | **Title:** Randomized comparison of percutaneous coronary intervention with coronary artery bypass grafting in diabetic patients. 1-year results of the CARDia (Coronary Artery Revascularization in Diabetes) trial  
**Comparator:** PCI (BMS or DES) vs. CABG  
**Components of medical therapy:** Glycoprotein IIb/IIIa, clopidogrel, and aspirin. | Total: 510  
Women: 132 (26%) | Good |
| **EAST** King et al., 2000<sup>81</sup> and King et al., 1995<sup>101</sup> King et al., 1994<sup>102</sup> Zhao et al., 1996<sup>103</sup> | **Title:** Eight-year mortality in the Emory Angioplasty vs. Surgery Trial (EAST)  
**Comparator:** PCI (type not specified) vs. CABG  
**Components of medical therapy:** Not reported. | Total: 392  
Women: 103 (26%) | Good |
| **GABI** Kaehler et al., 2005<sup>86</sup> and Hamm et al., 1994<sup>104</sup> | **Title:** 13-year follow-up of the German angioplasty bypass surgery investigation  
**Comparator:** PCI (type not specified) vs. CABG  
**Components of medical therapy:** Not reported (discretion of treating provider). | Total: 359  
Women: 66 (18%) | Good |
| **MASS II** Hueb et al., 2010<sup>68</sup> and Hueb et al., 2004<sup>73</sup> Hueb et al., 2007<sup>74</sup> | **Title:** Ten-year followup survival of the Medicine, Angioplasty, or Surgery Study (MASS II): a randomized controlled clinical trial of 3 therapeutic strategies for multivessel coronary artery disease  
**Comparator:** PCI (type not specified) vs. CABG  
**Components of medical therapy:** Nitrates, aspirin, beta blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, or a combination of these drugs unless contraindicated. Lipid-lowering agents, particularly statins, were also prescribed, along with a low-fat diet, on an individual basis. | Total: 611  
Women: 196 (32%) | Good |
<table>
<thead>
<tr>
<th>Study Author/Year Related Articles</th>
<th>Description of Study</th>
<th># of Subjects</th>
<th>Quality</th>
</tr>
</thead>
</table>
| **PRECOMBAT**<br>Park et al., 2011<sup>85</sup> | Title: Randomized Trial of Stents versus Bypass Surgery for Left Main Coronary Artery Disease  
Comparitor: PCI (DES) vs. CABG  
Components of medical therapy: Before or during PCI: aspirin plus clopidogrel (loading dose, 300 mg) or ticlopidine (loading dose, 500 mg). After PCI: 100 mg/day aspirin indefinitely and 75 mg/day clopidogrel or 250 mg/day ticlopidine for at least 6 months. Medications after CABG were selected according to the policy of the institution or physician. | Total: 600  
Women: 141 (24%) | Good |
| **SOS**<br>Zhang et al., 2004<sup>62</sup> and Zhang et al., 2003<sup>105</sup>  
Stables et al., 1999<sup>106</sup> | Title: Relative benefit of coronary artery bypass grafting vs. stent-assisted percutaneous coronary intervention for angina pectoris and multivessel coronary disease in women vs. men (one-year results from the Stent or Surgery trial)  
Comparitor: PCI (BMS) vs. CABG  
Components of medical therapy: Not reported. | Total: 908  
Women: 206 (23%) | Fair |
| **SYNTAX**<br>Morice et al., 2010<sup>83</sup> | Title: Outcomes in patients with de novo left main disease treated with either percutaneous coronary intervention using paclitaxel-eluting stents or coronary artery bypass graft treatment in the Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery (SYNTAX) trial  
Comparitor: PCI (type not specified) vs. CABG  
Components of medical therapy: In the PCI arm, clopidogrel for 6 months, with aspirin therapy indefinitely. | Total: 705  
Women: 185 (26%) | Fair |

BMS = bare-metal stent; CABG = coronary artery bypass graft; CAD = coronary artery disease; DES = drug-eluting stent; PCI = percutaneous coronary intervention; PTCA = percutaneous transluminal coronary angioplasty; RCT = randomized controlled trial
<table>
<thead>
<tr>
<th>Study</th>
<th>Composite Outcome* (Timing)</th>
<th>Anticipated Effect Size</th>
<th>Death* (Timing)</th>
<th>MI (Timing)</th>
<th>CVA (Timing)</th>
<th>Revascularization (Timing)</th>
<th>Other (Timing)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARTS I</td>
<td>Death/CVA/MI/CABG/repeat PCI (30 days, 1 year, 3 years, 5 years)</td>
<td>Powered to detect 7% difference in favor of CABG</td>
<td>Yes (30 days, 1 year, 3 years, 5 years)</td>
<td>Yes (30 days, 1 year, 3 years, 5 years)</td>
<td>Yes (30 days, 1 year, 3 years, 5 years)</td>
<td>Yes (30 days, 1 year, 3 years, 5 years)</td>
<td>Quality of life (3 years)</td>
</tr>
<tr>
<td>BARI</td>
<td>Effect size not reported</td>
<td>Cumulative survival rate (5 year, 7 years, 10 years)</td>
<td>Yes (in hospital)</td>
<td>Yes (30 days, 1 year, 3 years, 5 years)</td>
<td>Yes (5 years) (30 days, 1 year, 3 years, 5 years)</td>
<td>Yes (10 years)</td>
<td>Angina status (4 years, 10 years)</td>
</tr>
<tr>
<td>CABRi</td>
<td>Powered to detect 60% reduction in mortality in PCI group</td>
<td>Yes (1 year)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Angina (1 year)</td>
</tr>
<tr>
<td>CARDiia</td>
<td>Death/MI/stroke repeat revascularization (1 year)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Death/MI/CVA (1 year)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Powered for OR of 0.69 in favor of PCI (upper CI 1.3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Composite Outcome (^a) (Timing)</td>
<td>Anticipated Effect Size</td>
<td>Death (^a) (Timing)</td>
<td>MI (Timing)</td>
<td>CVA (Timing)</td>
<td>Revascularization (Timing)</td>
<td>Other (Timing)</td>
</tr>
<tr>
<td>------------</td>
<td>----------------------------------</td>
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<td>------------------------</td>
<td>-------------</td>
<td>-------------</td>
<td>---------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>EAST(^81,101-103)</td>
<td>Powered for 25% reduction</td>
<td>Survival (3 years, 8 years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GABI(^86,104)</td>
<td>Powered for 15% difference in success rates as therapeutically equivalent</td>
<td>Yes (13 years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Primary outcome was freedom from angina (not reported by sex)</td>
</tr>
<tr>
<td>MASS II(^68,73,74)</td>
<td>Death/MI/angina requiring revascularization (10 years)</td>
<td>Powered to detect 2-fold difference</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRECOMBAT(^85)</td>
<td>Death/MI/stroke/ischemia-driven target-vessel revascularization (1 year, 2 years)</td>
<td>Powered to detect 7% difference</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOS(^82,105,106)</td>
<td>Powered for event rate of 5% in CABG arm and 10% in PCI arm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Primary outcome not reported by sex</td>
</tr>
<tr>
<td>SYNTAX(^83)</td>
<td>Death/MI/CVA/repeat revascularization (1 year)</td>
<td>Powered for clinically relevant difference of 5%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Quality of life (6 months, 1 year)</td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass grafting; CVA = cerebrovascular accident; MACE = major adverse cardiovascular event; MI = myocardial infarction; OR = odds ratio; PCI = percutaneous coronary intervention; RRR = relative risk reduction

\(^a\)Primary outcome in italics.
KQ 3a: Effectiveness of Interventions

A meta-analysis of studies was performed on those with similar composite outcomes measured at similar time points. This meta-analysis was divided into followup intervals of short term (≤30 days), intermediate term (1 year), and long term (≥2 years).

Short-Term Followup Studies

Two studies with short-term (30-day or in-hospital) outcomes—ARTS I\(^7\) and BARI\(^7\)—were included in the meta-analysis. For both studies, the reported event rates/percentages were converted into odds ratios. Table 17 presents the outcomes, odds ratios, and confidence intervals for the meta-analysis.

Table 17. Sex results for stable/unstable angina on composite outcomes (short-term)

<table>
<thead>
<tr>
<th>Study (comparison)</th>
<th>Outcome</th>
<th>Women (95% CI)</th>
<th>Men (95% CI)</th>
<th>Overall (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARTS I (PCI vs. CABG)</td>
<td>Death (30 days)</td>
<td>0.70 (0.19 to 2.51)</td>
<td>2.99 (0.60 to 14.91)</td>
<td>NR</td>
</tr>
<tr>
<td>BARI (PCI vs. CABG)</td>
<td>Death (in-hospital)</td>
<td>0.64 (0.11 to 3.86)</td>
<td>0.89 (0.34 to 2.31)</td>
<td>0.83 (0.36 to 1.93)</td>
</tr>
</tbody>
</table>

CI = confidence interval; CABG = coronary artery bypass graft; NR = not reported; PCI = percutaneous coronary intervention

Forest plots for the random-effects model are shown in Figure 10. The summary odds ratio in women was 0.68 (95% CI, 0.24 to 1.93) and in men was 1.36 (CI, 0.44 to 4.24). The test for heterogeneity was nonsignificant. The findings were not statistically significant for demonstrating a benefit in PCI and CABG, although the odds ratios suggested a possible sex effect, with PCI showing more benefit in women and CABG showing more benefit in men, but the confidence intervals are too wide to support firm conclusions.

Figure 10. Stable/unstable angina short-term (30 days) PCI versus CABG

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odds Ratio IV, Random, 95% CI</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1.1 Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ARTS I, 2009</td>
<td>-0.357</td>
<td>0.658</td>
<td>25.1%</td>
<td>0.70 [0.18, 2.54]</td>
<td></td>
</tr>
<tr>
<td>BARI, 1998</td>
<td>-0.446</td>
<td>0.908</td>
<td>13.2%</td>
<td>0.89 [0.34, 2.31]</td>
<td>0.83 [0.36 to 1.93]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>38.3%</td>
<td>0.68 [0.24, 1.93]</td>
</tr>
<tr>
<td>Heterogeneity: Tau^2 = 0.30; Chi^2 = 0.01, df = 1 (P = 0.94); I^2 = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.73 (P = 0.47)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1.1.2 Men

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odds Ratio IV, Random, 95% CI</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARTS I, 2009</td>
<td>1.095</td>
<td>0.62</td>
<td>16.4%</td>
<td>2.99 [0.60, 14.91]</td>
<td></td>
</tr>
<tr>
<td>BARI, 1998</td>
<td>-0.117</td>
<td>0.489</td>
<td>45.5%</td>
<td>0.89 [0.34, 2.32]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>61.7%</td>
<td>1.36 [0.44, 4.24]</td>
</tr>
<tr>
<td>Heterogeneity: Tau^2 = 0.28; Chi^2 = 1.61, df = 1 (P = 0.20); I^2 = 38%</td>
<td></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: Z = 0.54 (P = 0.59)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARTS I, 2009</td>
<td>1.095</td>
<td>0.62</td>
<td>16.4%</td>
<td>2.99 [0.60, 14.91]</td>
</tr>
<tr>
<td>BARI, 1998</td>
<td>-0.117</td>
<td>0.489</td>
<td>45.5%</td>
<td>0.89 [0.34, 2.32]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>61.7%</td>
</tr>
<tr>
<td>Heterogeneity: Tau^2 = 0.30; Chi^2 = 3.73, df = 3 (P = 0.50); I^2 = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.07 (P = 0.94)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for subgroup differences: Chi^2 = 0.79, df = 1 (P = 0.38), I^2 = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Intermediate-Term Followup Studies

Two studies with 1-year outcomes—ARTS I \cite{78} and CARDia \cite{84}—were included in the meta-analysis. In the SYNTAX study, \cite{83} there was no difference in the primary composite outcome (death/MI/stroke, or repeat revascularization) at 1 year between patients undergoing CABG and PCI (13.6% vs. 15.8%). No sex data by treatment in this fair-quality study were provided, but being female was a significant predictor of 1-year major adverse cardiovascular events (OR 0.50; 95% CI, 0.27 to 0.91; p=0.02 [interaction effect not reported]). The SYNTAX study was excluded from the meta-analysis since it did not report subgroup results by sex. The PRECOMBAT study \cite{85} did not report sex-specific data at 1 year, so this study was not included in this intermediate-term followup analysis (but data reported at 2 years are included in the long-term followup analysis below). Event data from the ARTS I study were transformed into risk ratios. Table 18 presents the outcomes, odds ratios, and confidence intervals for the meta-analysis.

<table>
<thead>
<tr>
<th>Study (Comparison)</th>
<th>Outcome</th>
<th>Women (95% CI)</th>
<th>Men (95% CI)</th>
<th>Overall (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARTS I (PCI vs. CABG)</td>
<td>Death/MI/stroke</td>
<td>1.05 (0.51 to 2.21)</td>
<td>1.27 (0.81 to 1.98)</td>
<td>NR</td>
</tr>
<tr>
<td>CARDia (PCI vs. CABG)</td>
<td>Death/MI/stroke</td>
<td>2.13 (0.68 to 6.68)</td>
<td>1.07 (0.59 to 1.93)</td>
<td>1.25 (0.75 to 2.09)</td>
</tr>
</tbody>
</table>

CI = confidence interval; CABG = coronary artery bypass graft; NR = not reported; PCI = percutaneous coronary intervention

Forest plots for the random effects model are shown in Figure 11. The summary odds ratio in women was 1.30 (95% CI, 0.69 to 2.45) and in men was 1.19 (CI, 0.84 to 1.70). The test for heterogeneity was nonsignificant. These results show lower events in the CABG group for both sexes, but this benefit was not statistically significant.

Figure 11. Stable/unstable angina intermediate-term (1 year) PCI versus CABG

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odds Ratio</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>I.1.1 Women</td>
<td></td>
<td></td>
<td></td>
<td>I, Random, 95% CI</td>
<td>I, Random, 95% CI</td>
</tr>
<tr>
<td>ARTS I, 2009</td>
<td>0.049</td>
<td>0.374</td>
<td>17.7%</td>
<td>1.05 [0.50, 2.19]</td>
<td></td>
</tr>
<tr>
<td>CARDia, 2010</td>
<td>0.756</td>
<td>0.583</td>
<td>7.3%</td>
<td>2.13 [0.68, 6.68]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>25.0%</td>
<td>1.30 [0.69, 2.45]</td>
</tr>
<tr>
<td>Heterogeneity: $\tau^2 = 0.01$; $\chi^2 = 1.04$, df = 1 ($P = 0.31$); $P = 4%$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: $Z = 0.81$ ($P = 0.42$)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

I.1.2 Men

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odds Ratio</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARTS I, 2009</td>
<td>0.239</td>
<td>0.228</td>
<td>47.7%</td>
<td>1.27 [0.81, 1.99]</td>
<td></td>
</tr>
<tr>
<td>CARDia, 2010</td>
<td>0.068</td>
<td>0.302</td>
<td>27.2%</td>
<td>1.07 [0.59, 1.93]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>75.0%</td>
<td>1.19 [0.84, 1.70]</td>
</tr>
<tr>
<td>Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 0.20$, df = 1 ($P = 0.65$); $P = 0%$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: $Z = 0.97$ ($P = 0.33$)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI) 100.0% 1.22 [0.89, 1.66]

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 1.29$, df = 3 ($P = 0.73$); $P = 0\%$ |
| Test for overall effect: $Z = 1.25$ ($P = 0.21$) |
| Test for subgroup differences: $\chi^2 = 0.05$, df = 1 ($P = 0.82$), $P = 0\%$ |
Long-Term Followup Studies

To assess the long-term effect at ≥2 years, four studies were included in the meta-analysis: ARTS I (3-year), BARI (5-year), MASS II (10-year), and PRECOMBAT (2-year). Results of the ARTS I and BARI studies were transformed into risk ratios. For the BARI study, the survival rates were converted into death rates. For women, the death rates for CABG and PCI were 24 percent of 240 and 26 percent of 249, respectively. For men, survival rates by treatment group were not reported. The MASS II results were inverted to hazard ratios <1 favoring PCI and hazard ratios >1 favoring CABG. The GABI study was excluded from the meta-analysis because it did not present data by sex. The GABI study randomized 359 patients (66 women) with angina CCS class II-IV, under age 75, and coronary multiple-vessel disease requiring revascularization of at least 2 major coronary vessels to either PCI or CABG. The authors report that the hazard ratio for death following PCI or CABG was not different between men and women at the 13-year followup. Table 19 presents the outcomes, odds ratios, and confidence intervals for the meta-analysis.

Table 19. Sex results for stable/unstable angina on composite outcomes (long-term)

<table>
<thead>
<tr>
<th>Study (Comparison)</th>
<th>Outcome</th>
<th>Women (95% CI)</th>
<th>Men (95% CI)</th>
<th>Overall (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARTS I (PCI vs. CABG)</td>
<td>Death/MI/CVA/revascularization</td>
<td>1.00 (0.57 to 1.76)</td>
<td>1.28 (0.88 to 1.86)</td>
<td>NR</td>
</tr>
<tr>
<td>BARI (PCI vs. CABG)</td>
<td>Death</td>
<td>1.11 (0.74 to 1.67)</td>
<td>NR</td>
<td>1.20 (0.92 to 1.59)</td>
</tr>
<tr>
<td>MASS II (PCI vs. CABG)</td>
<td>Death/MI/revascularization</td>
<td>1.47 (0.87 to 2.50)</td>
<td>2.04 (1.45 to 2.94)</td>
<td>1.89 (1.38 to 2.56)</td>
</tr>
<tr>
<td>PRECOMBAT (PCI vs. CABG)</td>
<td>Death/MI/CVA/revascularization</td>
<td>1.22 (0.48 to 3.08)</td>
<td>1.65 (0.88 to 3.07)</td>
<td>1.50 (0.90 to 2.52)</td>
</tr>
</tbody>
</table>

CI = confidence interval; CABG = coronary artery bypass graft; NR = not reported; PCI = percutaneous coronary intervention

Forest plots for the random effects model are shown in Figure 12. The summary odds ratio in women was 1.17 (95% CI, 0.90 to 1.54) and in men was 1.63 (CI, 1.20 to 2.23). The test for heterogeneity was nonsignificant. Similar to the intermediate-term outcomes, there was no definitive evidence of a sex effect. In men, CABG was significantly better than PCI (p=0.002); in women, results suggest lower events in the CABG group, but it was not statistically significant (p=0.24).
KQ 3b: Modifiers of Effectiveness

We identified one good-quality study (915 total patients, 249 [27%] women) in which the long-term survival rate (7 years) in diabetic women was addressed. In the BARI study, this subgroup analysis was not initially specified but was requested by the safety and monitoring board during the course of the trial on the basis of concurrent reports from another study. Survival rate at 7 years was significantly higher among diabetic patients (n=353) treated with CABG compared with those undergoing PCI (74.6% vs. 55.7%), a difference that remained significant in men (77.9% vs. 51.5%) but not in women (74.3% vs. 61.0%). Appendix G contains a summary table with study data related to modifiers of effectiveness (subgroup analyses).

KQ 3c: Safety Concerns

We identified one good-quality study (1,205 total patients, 283 [23%] women) that addressed significant safety concerns and, specifically, risk of major bleeding in women (n=283). The ARTS I study was designed to compare CABG with PCI combined with stent implantation for the treatment of patients with multiple-vessel disease. Major bleeding was higher in women undergoing PCI compared with men (7.2% vs. 0.2%, p<0.001) but not among those assigned to CABG (1.4% vs. 2.8%). After adjusting for baseline characteristics, major bleeding complications remained higher among women in the PCI group (OR 29.4; 95% CI, 5.3 to 500; p=0.001 women vs. men) compared with the CABG group (OR 1.5; CI, 0.4 to 10.1, p=0.58 women vs. men). Appendix H contains a summary table with study data related to safety concerns (harms).
Summary and Discussion

For this report, we conducted a systematic review of the medical literature for the comparative effectiveness of optimal medical therapy, PCI, and CABG in women with CAD. CAD presentations included stable angina and acute coronary syndrome; i.e., STEMI, NSTEMI, and unstable angina. This review assessed the comparative effectiveness of the three treatment strategies on (1) clinical outcomes, (2) outcomes by modifiers such as demographic and clinical factors, and (3) safety outcomes.

Our search identified 28 comparative studies (72 articles, including methodology and secondary analysis papers). Of the 28 studies, 24 were good quality and 4 were fair quality for their overall reporting of methodology and analysis. A total of 35,597 patients included 10,126 (28%) women. We grouped these by CAD presentation and type of comparison:

- KQ 1: 7 studies (6 good quality, 1 fair) comparing PCI with fibrinolysis/supportive medical therapy (5 fibrinolysis, 2 supportive) in patients with STEMI
- KQ 2: 7 studies (6 good quality, 1 fair) comparing early invasive (PCI or CABG) with initial conservative in patients with UA/NSTEMI
- KQ 3: 5 studies (all good quality) comparing revascularization with optimal medical therapy in patients with stable angina (Strategy 1) and 10 studies (8 good quality, 2 fair) comparing PCI with CABG in patients with either stable or unstable angina (Strategy 2).

There were a total of 14 studies with 1 study containing data for both comparative strategies.

Key Findings and Strength of Evidence

The main findings of the treatment strategies for women with CAD are summarized in the following sections. Table 20 summarizes the strength of evidence (SOE) by effectiveness outcome for the KQs.
<table>
<thead>
<tr>
<th>KQ: Presentation</th>
<th># Studies</th>
<th>N Total</th>
<th>Effect OR (95% CI)</th>
<th>Conclusions</th>
<th>Limitations to Applicability</th>
<th>Strength of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>KQ 1a: STEMI</strong></td>
<td>5^36,37,39,40,42</td>
<td>4,105</td>
<td>Women: 0.50 (0.36 to 0.72); p=0.0001</td>
<td>Women Favors PCI</td>
<td>PCI consisted of balloon angioplasty or bare-metal stents</td>
<td><strong>High</strong></td>
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<tr>
<td>PCI vs. fibrinolysis</td>
<td></td>
<td>Total: 1,017 (25%)</td>
<td>Men: 0.54 (0.42 to 0.70); p&lt;0.00001</td>
<td>Men Favors PCI</td>
<td></td>
<td></td>
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<tr>
<td>Death/MI/stroke</td>
<td></td>
<td>30 days (Figure 3)</td>
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<tr>
<td>30 days</td>
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<tr>
<td><strong>KQ 1a: STEMI</strong></td>
<td>2^40,44</td>
<td>1,973</td>
<td>Women: No summary estimate due to heterogeneous outcomes</td>
<td>Women Insufficient</td>
<td>PCI consisted of balloon angioplasty or bare-metal stents</td>
<td><strong>Insufficient</strong></td>
</tr>
<tr>
<td>PCI vs. fibrinolysis</td>
<td></td>
<td>Total: 523 (26%)</td>
<td>Men: No summary estimate due to heterogeneous outcomes</td>
<td>Men Insufficient</td>
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<tr>
<td>1 year</td>
<td></td>
<td>(No figure)</td>
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</tbody>
</table>

Study design/quality: RCT/good
Women
Risk of bias: Low
Consistency: Consistent
Directness: Direct
Precision: Precise

Men
Risk of bias: Low
Consistency: N/A
Directness: N/A
Precision: N/A

**SOE: High**

Study design/quality: RCT/good
Women
Risk of bias: Low
Consistency: N/A
Directness: N/A
Precision: N/A

Men
Risk of bias: Low
Consistency: N/A
Directness: N/A
Precision: N/A

**SOE: Insufficient**
Table 20. Strength of evidence by effectiveness outcome (continued)

<table>
<thead>
<tr>
<th>KQ: Presentation Comparison Outcome Time Point (Forest Plot #)</th>
<th># Studies</th>
<th>N Total N Women (%)</th>
<th>Effect OR (95% CI)</th>
<th>Conclusions</th>
<th>Limitations to Applicability</th>
<th>Strength of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>KQ 2a: UA/NSTEMI Early invasive vs. initial conservative Death/MI 6 months (Figure 4)</td>
<td>2(^{51,60})</td>
<td>Total: 4,677 Women: 1,506 (32%)</td>
<td>Women 0.77 (0.28 to 2.12) Men 0.65 (0.52 to 0.82); p=0.0002</td>
<td>Women Trend favoring early invasive Men Favors early invasive</td>
<td>FRISC II study had lower rates of invasive treatment in the initial conservative group.</td>
<td>SOE: Low</td>
</tr>
<tr>
<td>KQ 2a: UA/NSTEMI Early invasive vs. initial conservative Death/MI/rehospitalization 1 year (Figure 5)</td>
<td>5(^{22,53,56,59})</td>
<td>Total: 14,692 Women: 5,144 (35%)</td>
<td>Women 0.78 (0.54 to 1.12) Men 0.88 (0.64 to 1.20)</td>
<td>Women Trend favoring early invasive Men Trend favoring early invasive</td>
<td>FRISCII and RITA-3 studies had lower rates of invasive treatment in the initial conservative group. ICTUS allowed more liberal use of revascularization, therefore rates of invasive therapy were higher in initial conservative group.</td>
<td>Study design/quality: RCT/good Women Risk of bias: Low Consistency: Inconsistent Directness: Direct Precision: Precise SOE: Low</td>
</tr>
</tbody>
</table>

Study design/quality: RCT/good Risk of bias: Low Consistency: Inconsistent Directness: Direct Precision: Imprecise SOE: Low
Table 20. Strength of evidence by effectiveness outcome (continued)

<table>
<thead>
<tr>
<th>KQ: Presentation</th>
<th>Comparison</th>
<th>Outcome</th>
<th>Time Point (Forest Plot #)</th>
<th># Studies</th>
<th>N Total</th>
<th>N Women (%)</th>
<th>Effect OR (95% CI)</th>
<th>Conclusions</th>
<th>Limitations to Applicability</th>
<th>Strength of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>KQ 2a: UA/NSTEMI</strong></td>
<td>Early invasive vs. initial conservative</td>
<td>Death/MI/rehospitalization</td>
<td>5 years (Figure 6)</td>
<td>$2^{58,61}$</td>
<td>Total: 3,657</td>
<td>Women: 1,069 (29%)</td>
<td>Women: 1.05 (0.81 to 1.35)</td>
<td>Men: 0.91 (0.53 to 1.56)</td>
<td>Slight trend favoring initial conservative therapy. Given the small suggested benefit at 5 years, the wide confidence interval crossing 1, and the trend favoring early invasive therapy suggested at earlier time points and across time points in men, we cannot support firm conclusions.</td>
<td>At longer term followup, rate of PCI in initial conservative group approached that of early invasive group.</td>
</tr>
<tr>
<td><strong>KQ 3a: Stable angina</strong></td>
<td>PCI vs. medical therapy</td>
<td>Death/MI/revascularization</td>
<td>4–5 years (Figure 7)</td>
<td>$2^{55,68}$</td>
<td>Total: 2,898</td>
<td>Women: 556 (19%)</td>
<td>Women: 0.64 (0.47 to 0.89); p=0.008</td>
<td>Men: 1.03 (0.79 to 1.33)</td>
<td>Slight trend favoring medical therapy. This suggested small benefit, however, has a wide confidence interval crossing 1 and is not supported by additional time points or by the evidence in women.</td>
<td>None</td>
</tr>
</tbody>
</table>
Table 20. Strength of evidence by effectiveness outcome (continued)

<table>
<thead>
<tr>
<th>KQ: Presentation</th>
<th>Comparison Outcome</th>
<th>Time Point (Forest Plot #)</th>
<th># Studies</th>
<th>N Total</th>
<th>N Women (%)</th>
<th>Effect OR (95% CI)</th>
<th>Conclusions</th>
<th>Limitations to Applicability</th>
<th>Strength of Evidence</th>
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<tr>
<td>KQ 3a: Stable angina</td>
<td>CABG vs. medical therapy</td>
<td>Death/MI/ revascularization 4–5 years (Figure 8)</td>
<td>$2^{67,68}$</td>
<td>Total: 1,823</td>
<td>Women: 344 (19%)</td>
<td>Women: 0.56 (0.32 to 0.96); p=0.04</td>
<td>STICH study consisted of CABG in low EF patients.</td>
<td>Study design/quality: RCT/good</td>
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<tr>
<td>KQ 3a: Stable angina</td>
<td>Revascularization (PCI or CABG) vs. medical therapy</td>
<td>Death/MI/ revascularization 4–5 years (Figure 9)</td>
<td>$3^{65,67,68}$</td>
<td>Total: 4,110</td>
<td>Women: 704 (17%)</td>
<td>Women: 0.59 (0.43 to 0.81); p=0.001</td>
<td>STICH study consisted of CABG in low EF patients.</td>
<td>Study design/quality: RCT/good</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions**
- **Women**: Favors revascularization
- **Men**: Trend favoring revascularization

**Limitations to Applicability**
- **Women**: Consistency: Inconsistent, Directness: Indirect, Precision: Imprecise
- **Men**: Consistency: Inconsistent, Directness: Indirect, Precision: Imprecise

**Strength of Evidence**
- **SOE: Low**
Table 20. Strength of evidence by effectiveness outcome (continued)

<table>
<thead>
<tr>
<th>KQ: Presentation Comparison Outcome Time Point (Forest Plot #)</th>
<th># Studies</th>
<th>N Total N Women (%)</th>
<th>Effect OR (95% CI)</th>
<th>Conclusions</th>
<th>Limitations to Applicability</th>
<th>Strength of Evidence</th>
</tr>
</thead>
</table>
| KQ 3a: Stable/unstable angina PCI vs. CABG Death 30 days (Figure 10) | 2\(^78.79\) | Total: 2,120 Women: 530 (25%) | Women 0.68 (0.24 to 1.93)  
Men 1.36 (0.44 to 4.24) | Women Trend favoring PCI  
Men Trend favoring CABG | Type of PCI not specified in most studies. | Study design/quality: RCT/good  
Women Risk of bias: Low  
Consistency: Consistent  
Directness: Direct  
Precision: Imprecise  
SOE: Low  
Men Risk of bias: Low  
Consistency: Inconsistent  
Directness: Direct  
Precision: Imprecise  
SOE: Low |
| KQ 3a: Stable/unstable angina PCI vs. CABG Death/MI/stroke 1 year (Figure 11) | 2\(^78.80,84\) | Total: 1,715 Women: 415 (24%) | Women 1.30 (0.69 to 2.45)  
Men 1.19 (0.84 to 1.70) | Women Trend favoring CABG  
Men Trend favoring CABG | Type of PCI not specified in most studies. | Study design/quality: RCT/good  
Women Risk of bias: Low  
Consistency: Consistent  
Directness: Direct  
Precision: Imprecise  
SOE: Low  
Men Risk of bias: Low  
Consistency: Consistent  
Directness: Direct  
Precision: Imprecise  
SOE: Low |
<table>
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<tr>
<th>KQ: Presentation Comparison Outcome Time Point (Forest Plot #)</th>
<th># Studies</th>
<th>N Total N Women (%)</th>
<th>Effect OR (95% CI)</th>
<th>Conclusions</th>
<th>Limitations to Applicability</th>
<th>Strength of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>KQ 3a: Stable/unstable angina PCI vs. CABG Death/MI/stroke ≥2 years (Figure 12)</td>
<td>4668,78,79,85</td>
<td>Total: 3,331 Women: 866 (26%)</td>
<td>Women 1.17 (0.90 to 1.54) Men 1.63 (1.20 to 2.23); p=0.002</td>
<td>Women Trend favoring CABG Men Favors CABG</td>
<td>Type of PCI not specified in most studies.</td>
<td>Study design/quality: RCT/good Women Risk of bias: Low Consistency: Consistent Directness: Direct Precision: Imprecise <strong>SOE: Low</strong> Men Risk of bias: Low Consistency: Consistent Directness: Direct Precision: Precise <strong>SOE: High</strong></td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass grafting; CI = confidence interval; MI = myocardial infarction; EF = ejection fraction; NSTEMI = non-ST elevation myocardial infarction; OR = odds ratio; PCI = percutaneous coronary intervention; RCT = randomized controlled trial; SOE = strength of evidence; STEMI = ST elevation myocardial infarction; UA = unstable angina
Modifiers of Effectiveness

Five studies (four good, one fair quality) assessed variations in clinical outcomes in women due to demographic or clinical factors. One good-quality study evaluated the comparative effectiveness of PCI versus fibrinolysis in women under 65 years of age and women 65 and older and found no differences in in-hospital mortality among the treatment groups. One fair-quality study evaluated patients 80 years of age and older with STEMI. The study was limited by a small overall size, and it did not find significant differences in the composite outcome (death/heart failure/repeat MI/stroke) at 3 years in patients 80 years of age and older with STEMI undergoing PCI compared with conservative/supportive medical care.

Two good-quality UA/NSTEMI studies of early invasive versus initial conservative therapy showed conflicting results on risk stratification—one showed no difference in treatment outcomes in the intermediate- and high-risk groups (risk was derived from components of the TIMI risk score and a couple other aspects of the participants’ presentation at randomization, including aspirin use and angina severity). The other study showed a higher event rate in women in the groups at moderate-to-high risk for thrombolysis in myocardial infarction (TIMI).

One good-quality stable/unstable angina study comparing PCI with CABG showed no difference in survival rate in diabetic women receiving CABG although survival was higher for diabetic men and the total diabetic population (total population results were influenced by the higher proportion of men enrolled in the study).

Of note, we did not find any data specific to women on race, socioeconomic factors, chronic kidney disease, angiographic-specific factors, or CABG-specific factors. Strength of evidence for modifiers of effectiveness for all treatment comparisons was insufficient.

Safety Concerns

Four good-quality studies reported safety outcomes in women. Two good-quality STEMI studies comparing fibrinolysis with PCI showed no difference in transfusions and a higher incidence of intracranial hemorrhage in women who received accelerated t-PA versus PCI (4.1% vs. 0%), but statistical analysis for this comparison was not done. Two good-quality UA/NSTEMI studies showed higher in-hospital bleeding rates in women undergoing PCI (adjusted OR 3.6; 95% CI, 1.6 to 8.3) but not in those undergoing CABG. However, we did not find data specific to women on adverse drug reactions, radiation exposure, access site complications, renal dysfunction, anaphylaxis, arrhythmias, stent thrombosis, or infection. Strength of evidence for safety concerns for all treatment strategies was insufficient.

Discussion

The findings from this systematic review on the treatment strategies for women across the spectrum of CAD presentations highlight areas for future research and for informing clinical practice. First, this review underscores the significant need for clinical researchers to provide study findings with women-specific data on the primary and secondary clinical outcomes. Overall, we were able to find only 28 relevant studies with data on either shorter term or longer term outcomes in women with CAD treated with invasive or conservative medical therapies. In addition, the representation of women enrolled in these trials was low. Melloni et al. found similarly low rates with sex-specific results discussed in only 31 percent of the 156 primary trial publications cited by the American Heart Association’s 2007 women’s prevention guidelines. In
addition, they found that enrollment of women in randomized clinical trials had increased over time (18% in 1970 to 34% in 2006) but remained low relative to their overall representation in disease populations (e.g., 25% women representation in RCTs of CAD compared with 46% women representation in the CAD population).

Second, our findings confirm current practice and evidence for care in one of the three areas evaluated. For women patients with STEMI, we found that an invasive approach with immediate PCI is superior to fibrinolysis in reducing cardiovascular events. These findings are similar to a meta-analysis\textsuperscript{107} of 23 randomized trials comparing PCI with fibrinolysis for acute MI in combined populations of men and women. However, for patients with NSTEMI treated with an early invasive approach compared with a conservative or selective invasive approach, this review, while finding a trend favoring early invasive strategies, does not demonstrate a statistically significant benefit of an early invasive approach in reducing cardiovascular events in women. In contrast, the overall meta-analysis for trials of early invasive versus conservative strategies including both men and women showed a benefit of early invasive therapy.\textsuperscript{108} The results from this review suggest that such a benefit may also be true in women, but the confidence intervals are too wide to support a firm conclusion.

In addition, for medical therapy alone versus revascularization plus medical therapy for patients with stable angina or high CAD burden, the findings from the current analysis suggest a benefit of revascularization in women. These findings should be viewed with caution because they are based on a limited number of studies with data on 704 (17%) women; these analyses often have both PCI and CABG together in the revascularization group, and the overall findings from these studies do not show a significant benefit beyond angina or symptom reduction for revascularization. In these studies, it is possible that women who present later in life with CAD, and with higher CAD burden, may be obtaining a greater benefit with revascularization, and the findings from this analysis should prompt further research in this area and again encourage researchers to provide data specific on women. In contrast, previous meta-analyses that combined results for men and women found similar outcomes for either treatment. The higher proportion of men enrolled in these trials (83%) may have led to the masking of the women’s results by the men’s results within a pooled analysis.

Our stakeholder group advised us to assess the effectiveness of these therapies by sex on multiple important clinical outcomes, such as nonfatal MI, death, stroke, repeat revascularization, recurrent unstable angina, heart failure, repeat hospitalization, length of hospital stay, angina relief, quality of life, or cognitive effects. A majority of sex-specific reporting was on the composite outcome of major cardiovascular adverse events (death, MI, or revascularization). Individual outcomes by sex were rarely reported, especially on heart failure, repeat hospitalization, length of hospital stay, angina relief, quality of life, or cognitive effects.

Based on the small number of studies that looked at demographic and clinical factors that influence response to treatment strategies in women, there was insufficient evidence that clinicians can use to determine if age, race/ethnicity, socioeconomic status, coronary risk factors, angiographic-specific factors, CABG-specific factors, or hospital-level characteristics should be taken into consideration when deciding a treatment strategy for women with CAD. Unfortunately, more studies are needed that evaluate the subgroups and various demographic and clinical characteristics to fully understand this evidence gap.

In addition, the safety concerns or harms of these treatment strategies are underreported for women enrolled in RCTs. It appears that the bleeding risk may be higher in women receiving
fibrinolysis or PCI. Careful consideration should be given to the dose, timing, and duration of antiplatelet, antithrombotic, and anticoagulant therapies administered to women.

**Limitations of This Review**

With 28 studies meeting the inclusion criteria, this systematic review has several limitations. First, our search focused on comparative RCTs—the highest quality of evidence for determining the efficacy of different treatment modalities on cardiovascular outcomes. While this was adequate for evaluating the evidence to support the clinical outcomes by treatment strategy and by CAD presentation for the overall population, there were very few RCTs that reported subgroup analyses by demographic or clinical characteristics and also very few RCTs that reported the harms or risks of therapy. Most studies that reported results applicable to modifiers of effectiveness or safety did this for the overall population and did not separate the effects by sex. We are aware that there are several observational or noncomparator studies of each of the treatment modalities that address these issues in women. Because of the problems with confounding from observational studies and the difficulty of constructing reliable comparisons among single-arm studies, we did not include observational or noncomparator studies in our review.

Second, the sample size and low representation of women in most of the comparator studies may affect the study authors’ ability to analyze the results by sex, therefore reducing the number of studies reporting these findings separately (i.e., reporting bias). We excluded 355 articles due to lack of sex-specific reporting of the study results, which resulted in low numbers of studies available for analysis for each clinical presentation (STEMI, UA/NSTEMI, stable angina). Of these 355 articles, 116 were associated with the same 28 studies included in our review, but they did not report data on women separately. The remaining 239 articles were associated with 173 studies that did not report data on women. Figure 13 presents a graph of the number of articles reporting data on women per year. The percentage ranges from 0 percent (in 1992 and 1993) to 75 percent in 1995. On average, 17 percent of the articles comparing treatment strategies for CAD reported sex-specific outcomes. Of note, many articles included a multivariate analysis which included sex as a covariate in the model; the majority found no evidence of a gender effect. The result of a multivariable model is insufficient for incorporating into a meta-analysis, thus these were excluded from the review. Reporting bias in these publications therefore resulted in selection bias in this review.
Third, the strength of our meta-analysis is limited by the different definitions of the primary composite outcome and by the timing (short-term and long-term) of those clinical endpoints. We used our best judgment in choosing which composite outcomes (e.g., death/MI/stroke and death/MI/stroke/revascularization) and time points (e.g., in-hospital and 30 days) to combine in the meta-analysis.

A final limitation is the change in PCI techniques and definition of optimal medical therapy over time. Most of the studies involved balloon angioplasty or bare-metal stents. The current era of drug-eluting stents and the use of dual antiplatelet therapy may be underrepresented. Nevertheless, the findings represent the best available evidence. While the treatment options continue to evolve over time, these older therapies (bare-metal stents, balloon angioplasty) are still being used in clinical practice, and therefore we did not downgrade the strength of evidence based on the availability of newer technologies. Medication adherence to beta blockers, angiotensin-converting enzyme inhibitors, aspirin, antiplatelet agents, and lipid-lowering agents was not reported in the studies included in this review. There was also variable reporting on the implementation of optimal medical therapy.

Many of these studies were multicenter, international RCTs with multiple countries represented. The generalizability of those studies to the United States may be of concern; however, the practice of revascularization and prescription of medical therapies are not dramatically different.

**Conclusions**

From a limited number of studies reporting results for women separately from the total study population, our findings confirm current practice and evidence for care in one of the three areas evaluated.
1. For women with STEMI, we found that an invasive approach with immediate PCI is superior to fibrinolysis for reducing cardiovascular events, which is similar to findings in previous meta-analyses combining results for both women and men.

2. For women with NSTEMI or unstable angina, we found evidence suggestive of a benefit of early invasive strategies for reducing cardiovascular events; however, this benefit was not statistically significant. Previous meta-analyses of studies comparing early invasive with initial conservative strategies on a combined population of men and women showed a significant benefit of early invasive therapy.

3. For women with stable angina, the few trials reporting sex-specific data on revascularization compared with optimal medical therapy showed a greater benefit with revascularization for women, while the men in the study fared equally well with either treatment. In contrast, previous meta-analyses that combined results for men and women found similar outcomes for either treatment.
Future Research

This comprehensive review of the comparative effectiveness of treatment modalities for women with CAD identified numerous gaps in evidence that would be suitable for future research and for improving the reporting of women findings of cardiovascular therapies in the published literature.

Studies With Sufficient Representation of Women

Sex subgroup analyses are often limited by the number of men or women in each treatment group to allow for adequate power to detect a statistically significant difference in outcome. While we were able to find RCTs that reported risk ratios in women, the enrollment numbers were insufficient to have adequate power to detect a difference, thus resulting in large confidence intervals that often crossed the null effect, with a potential type II error. To better understand the clinical outcomes of women treated by medical therapy or revascularization, trials should be either (1) women-only enrollment or (2) of large enough sample size with stratification of randomization by sex to allow for meaningful sex-based analyses. In order to assess sex differences in treatment modalities and their impact on clinical outcomes, a sufficient sample size is required in order to have adequate statistical power for subgroup analyses.

Patient-Level Meta-Analysis

Given the small representation of women in these RCTs, the heterogeneity of clinical outcomes (e.g., definition of composite outcome) and different measurement time points (e.g., 30 days, 6 weeks for short-term outcomes), we are aware that our group-level meta-analysis may be inadequate (when too few studies are available) to address the comparative effectiveness of medical therapy and revascularization. Therefore, patient-level analysis of trials comparing similar interventions for the same CAD presentation may be more appropriate for assessing the sex differences as well as for conducting subgroup analyses on demographic and clinical factors that influence treatment outcomes, or for evaluating safety concerns/harms of these treatment strategies. Subgroup analyses across trials can be done similarly to a previous AHRQ report on the comparative effectiveness of PCI and CABG, which included an addendum study that pooled individual patient data from 10 randomized trials to compare the effectiveness of CABG with PCI according to patients’ baseline clinical characteristics (e.g., age, diabetes, sex, individual cardiac risk factors, angioplasty versus bare metal stents).

Reporting Sex by Treatment Results Separately

Our review excluded trials that looked for a sex effect yet failed to provide results of women and men by treatment arm. An example is a trial that did a multivariate analysis to assess factors that influenced clinical outcomes and included male (or female) sex in the model, with a finding that it was nonsignificant or significant. We did not contact the corresponding authors of the articles that did not report sex results separately. It would aid future comparisons of treatment modalities if study authors were to report the primary data for women and men separately either within the article itself or in an online supplementary appendix. The 2010 report by the Institute of Medicine on Women’s Health Research recommended that funding agencies ensure adequate participation of women and reporting of sex-specific analyses in health research.
Reporting of Demographic and Clinical Factors That Influence Cardiovascular Outcomes

We found a few studies that conducted subgroup analyses of age, diabetes, and risk stratification in women populations. We did not find any data specific to women on race, socioeconomic, chronic kidney disease, angiographic-specific factors, or CABG-specific factors that were listed in KQ 2. Knowing the influence of these factors on cardiovascular outcomes is important for determining the proper treatment strategy and prognosis of women patients who present with various risk factors and comorbidities.

Reporting of Safety Concerns/Risks by Sex

Medical therapy can result in adverse drug reactions, and use of fibrinolytics can result in bleeding or intracranial hemorrhage. PCI can cause access site complications, radiation exposure, contrast-related anaphylaxis, bleeding, and stent thrombosis. CABG can result in wound infections, renal dysfunction, and bleeding. Most studies reported the bleeding risk of revascularization strategies but not the other safety concerns. Systematic reporting of adverse events in publications—in total and by sex—should continue to clarify which treatment modalities are safe for use in clinical practice.

To summarize, these evidence gaps could be addressed in various ways. First, more primary research with adequate representation of women for any of the three CAD clinical presentations could be conducted to achieve adequate statistical power for a sex-based analysis. Second, authors of the comparative trials that were excluded for not reporting sex-based results could be contacted to provide results of women and men by treatment arm, and the group-level meta-analysis could be repeated with a larger number of trials. Alternatively, these authors could be contacted to provide compatible (deidentified) datasets that could be combined for a patient-level analysis to assess the comparative effectiveness, modifiers of effectiveness, and risks of the various treatment strategies available. Finally, the use of observational cohorts from electronic health records could inform the real-world effectiveness of the treatment strategies chosen by clinicians and patients in a nonrandom fashion.
References


### Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AHRQ</td>
<td>Agency for Healthcare Research and Quality</td>
</tr>
<tr>
<td>BMS</td>
<td>bare-metal stent</td>
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<tr>
<td>CABG</td>
<td>coronary artery bypass graft</td>
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<tr>
<td>CAD</td>
<td>coronary artery disease</td>
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<tr>
<td>CI</td>
<td>confidence interval</td>
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<tr>
<td>CVA</td>
<td>cerebrovascular accident</td>
</tr>
<tr>
<td>DES</td>
<td>drug-eluting stent</td>
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<tr>
<td>EF</td>
<td>ejection fraction</td>
</tr>
<tr>
<td>HCT</td>
<td>Hematocrit</td>
</tr>
<tr>
<td>HR</td>
<td>hazard ratio</td>
</tr>
<tr>
<td>IABP</td>
<td>intra-aortic balloon pump</td>
</tr>
<tr>
<td>ICH</td>
<td>intracranial hemorrhage</td>
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<tr>
<td>IV</td>
<td>Intravenous</td>
</tr>
<tr>
<td>KQ</td>
<td>Key Question</td>
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<tr>
<td>MACE</td>
<td>major adverse cardiovascular events</td>
</tr>
<tr>
<td>MI</td>
<td>myocardial infarction</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>non-ST elevation myocardial infarction</td>
</tr>
<tr>
<td>OR</td>
<td>odds ratio</td>
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<tr>
<td>PCI</td>
<td>percutaneous coronary intervention</td>
</tr>
<tr>
<td>PTCA</td>
<td>percutaneous transluminal coronary angioplasty</td>
</tr>
<tr>
<td>RCT</td>
<td>randomized controlled trial</td>
</tr>
<tr>
<td>RR</td>
<td>risk ratio</td>
</tr>
<tr>
<td>SOE</td>
<td>strength of evidence</td>
</tr>
<tr>
<td>STEMI</td>
<td>ST elevation myocardial infarction</td>
</tr>
<tr>
<td>TEP</td>
<td>Technical Expert Panel</td>
</tr>
<tr>
<td>TIMI</td>
<td>thrombolysis in myocardial infarction</td>
</tr>
<tr>
<td>TMR</td>
<td>transmyocardial revascularization</td>
</tr>
<tr>
<td>t-PA</td>
<td>tissue plasminogen activator</td>
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<td>UA</td>
<td>unstable angina</td>
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## Appendix A. Exact Search Strings

### PubMed® Search Strategy (December 12, 2011)

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<td>#6</td>
<td>#5 NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp]) NOT Animals[Mesh:noexp]</td>
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Limits: Human, English, Publication Date: 2001- Present
### Embase® Search Strategy (December 12, 2011)

**Platform:** Embase.com

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</tr>
<tr>
<td>#2</td>
<td>'transluminal coronary angioplasty'/exp OR 'percutaneous coronary intervention'/exp OR 'stent'/exp OR 'balloon dilatation'/exp OR 'percutaneous transluminal angioplasty'/exp OR 'atherectomy'/exp OR 'percutaneous transluminal angioplasty':ti OR pta:ti OR ('percutaneous coronary' NEXT/1 intervention*):ti OR pci:ti OR stent*:ti OR 'balloon angioplasty':ti OR 'balloon dilatation':ti OR 'balloon angioplasty':ab OR pta:ab OR ('percutaneous coronary' NEXT/1 intervention*):ab OR pci:ab OR stent*:ab OR 'balloon angioplasty':ab OR 'balloon dilatation':ab OR 'transluminal angioplasty':ab OR 'coronary atherectomy':ab OR 'coronary artery bypass graft'/exp OR 'heart muscle revascularization'/exp OR 'coronary artery bypass':ti OR cabg:ti OR 'aortocoronary bypass':ti OR 'coronary revascularization':ti OR 'myocardial revascularization':ti OR 'coronary artery revascularization'/exp</td>
</tr>
<tr>
<td>#3</td>
<td>'female'/exp OR exp female OR women OR woman OR females OR 'sex difference'/exp</td>
</tr>
<tr>
<td>#4</td>
<td>'randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR random* OR factorial* OR crossover* OR cross NEAR/1 over* OR placebo* OR double* NEAR/1 blind* OR singl* NEAR/1 blind* OR assign* OR allocat* OR volunteer*</td>
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<tr>
<td>#5</td>
<td>#1 AND #2 AND #3 AND #4</td>
</tr>
<tr>
<td>#6</td>
<td>#5 (AND [embase]/lim NOT [medline]/lim)</td>
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**Limits:** Human, English, Publication Date: 2001- Present

### Cochrane Search Strategy (December 12, 2011)

**Platform:** Wiley

**Databases searched:** Cochrane Central Registry of Controlled Trials and Cochrane Database of Systematic Reviews

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<tr>
<td>#1</td>
<td>cardiovascular diseases OR heart diseases OR heart OR cardiovas* OR cardiac* OR coronary OR myocardial OR acute coronary syndrome OR myocardial infarction OR unstable angina [in title-abstract-keywords]</td>
</tr>
<tr>
<td>#2</td>
<td>'percutaneous transluminal coronary angioplasty' OR PTCA OR &quot;percutaneous coronary intervention&quot; OR &quot;percutaneous coronary interventions&quot; OR &quot;percutaneous coronary intervention&quot; OR &quot;percutaneous coronary intervention&quot; OR PCI OR Stent* OR stents OR Balloon angioplasty OR Balloon dilatation OR Balloon dilatation OR Balloon angioplasty OR 'coronary atherectomy' OR Coronary Artery Bypass OR CABG OR aortocoronary bypass OR coronary revascularization OR myocardial revascularization [in title-abstract-keywords]</td>
</tr>
<tr>
<td>#3</td>
<td>women OR woman OR female OR females OR sex factors [in title-abstract-keywords]</td>
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<tr>
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<td>#1 AND #2 AND #3</td>
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**Limits:** 2001- Present
Grey Literature Searches

ClinicalTrials.gov
Search date: 12/16/2011

Search #1: PCI vs. CABG
Expert Search String:
( NOT ( “Recruiting” OR “Not yet recruiting” OR “Available” ) ) [OVERALL-STATUS] AND ( heart diseases OR cardiovascular diseases ) [DISEASE] AND ( ( percutaneous transluminal coronary angioplasty OR PTCA OR percutaneous coronary intervention OR PCI OR balloon OR stent ) AND ( coronary artery bypass OR CABG ) ) [TREATMENT]

Search #2: CABG vs. Medical Therapy
Expert Search String:
( NOT ( “Recruiting” OR “Not yet recruiting” OR “Available” ) ) [OVERALL-STATUS] AND ( heart diseases OR cardiovascular diseases ) [DISEASE] AND ( ( coronary artery bypass OR CABG ) AND ( medical management OR medical therapy OR OMT OR standard of care OR medical treatment OR standard therapy OR usual care ) ) [TREATMENT]

Search #3: PCI vs. Medical Therapy
Expert Search String:
( NOT ( “Recruiting” OR “Not yet recruiting” OR “Available” ) ) [OVERALL-STATUS] AND ( heart diseases OR cardiovascular diseases ) [DISEASE] AND ( ( percutaneous transluminal coronary angioplasty OR PTCA OR percutaneous coronary intervention OR PCI OR balloon OR stent ) AND ( medical management OR medical therapy OR OMT OR standard of care OR medical treatment OR standard therapy OR usual care ) ) [TREATMENT]

Processing of results
1. Total number of results: 117
2. Duplicates removed: 10
3. All Status categories other than Completed, Terminated, and Withdrawn removed: 39 removed
4. Final number for screening: 68

WHO: International Clinical Trials Registry Platform Search Portal
Search date: 12/16/2011

Condition: heart OR cardiovascular OR coronary artery disease OR CAD
Intervention: percutaneous transluminal coronary angioplasty OR PTCA OR percutaneous coronary intervention OR PCI OR balloon OR stent OR coronary artery bypass OR CABG OR coronary revascularization
Processing of results
1. Total number of results: 1157
2. Removed all entries with “Recruiting” status; retained entries with “Not recruiting” status: 253 removed, 904 remaining
3. Removed all entries with NCT designations (covered by a separate search of clinicaltrials.gov with a more refined search strategy): 531 removed, 373 remaining
4. Final number for screening: 373

ProQuest COS Conference Papers Index
Search date: 12/12/2011

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<td>(cardiovascular diseases or heart diseases or heart or cardiovas* or cardiac* or coronary or myocardial or acute coronary syndrome or myocardial infarction or unstable angina) [in all fields + text]</td>
</tr>
<tr>
<td>#2</td>
<td>(percutaneous transluminal coronary angioplasty or PTCA or percutaneous coronary intervention* or PCI or Stent* or stents or Balloon angioplasty or Balloon dilatation or Balloon dilation or Transluminal angioplasty or coronary atherectomy or Coronary Artery Bypass or CABG or aortocoronary bypass or coronary revascularization or myocardial revascularization) [in all fields + text]</td>
</tr>
<tr>
<td>#3</td>
<td>women OR woman OR female OR females OR sex OR gender [in all fields + text]</td>
</tr>
<tr>
<td>#4</td>
<td>#1 AND #2 AND #3 AND #4</td>
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</tbody>
</table>

Limits: 2001- Present
Appendix B. Data Abstraction Elements

I. Study Characteristics
- Study name and acronym
- Other articles used in this abstraction
- Study dates
- Date enrollment started (Mon and YYYY)
- Date enrollment ended (Mon and YYYY)
- Number of subjects screened/approached for study participation: Total. Female, Male
- Study site
- Single center, Multicenter, Not reported/Unclear
- Geographic location
  - If single center, enter City and State (if US) or City and Country (if outside US). If multicenter, enter number of sites. Enter NR if not reported.
  - If multicenter, specify applicable geographic regions
- Funding source: Government, Private foundation, Industry, Not reported, Other.
- Setting: Academic centers, Community hospitals, Outpatient, VA, Not reported/unclear, Other
- Were patients transported from the site of presentation to another location to receive PCI?
- Were patients transported from the site of presentation to another location to receive CABG?
- Qualifications of the study surgeons: Not specified, Minimum case volume (specify), Maximum mortality (specify), Other (specify)
- Qualifications of the study interventional cardiologists: Not specified, Minimum case volume (specify), Maximum mortality (specify), Minimum success rates (specify), Other (specify)
- Qualifications of the sites involved in the trial: Not specified, Minimum case volume (specify), Maximum mortality (specify), Minimum success rates (specify), Other (specify)
- Were guideline-based treatment protocols followed?
- Briefly describe use of guideline-based protocols.
- Length of followup
- Inclusion and exclusion criteria; Copy/paste criteria as reported in the article.
- Clinical presentation: STEMI NSTEMI/ Unstable angina Stable CAD
- Method for interpretation of angiograms: Central laboratory, Local site interpretation, Quantitative angiography, Unclear/Not reported Other
- Were study patients systematically enrolled in cardiac rehabilitation?
- Does the study report a composite primary endpoint?
- Indicate the components of the composite primary endpoint (check all that apply): Total mortality, Cardiac mortality, Nonfatal myocardial infarction, Stroke, TIA, Unstable angina, Angina/ recurrent symptoms, Angina class, Angina relief, Repeat revascularization, Heart failure, Graft failure, Hospitalization, Length of hospital stay, Bleeding, Quality of life, Cognitive effects, Adverse drug reactions, Radiation exposure, Access site complications, Renal dysfunction, Anaphylaxis, Arrhythmias, Stent thrombosis, Infections, Cost, Employment/productivity, Other (specify)
- Indicate timing of the components of the composite primary endpoint: Short-term (less than or equal to 30 days), Long-term (greater than 30 days), Mixture of short- and long-term outcomes
- Indicate all short-term (<30 days) primary and secondary endpoints separately reported (i.e. reported singly, rather than only reported as part of a composite primary endpoint): Total
mortality, Cardiac mortality, Nonfatal myocardial infarction, Stroke, TIA, Unstable angina, Angina/ recurrent symptoms, Angina class, Angina relief, Repeat revascularization, Heart failure, Graft failure, Hospitalization, Length of hospital stay, Bleeding, Quality of life, Cognitive effects, Adverse drug reactions, Radiation exposure, Access site complications, Renal dysfunction, Anaphylaxis, Arrhythmias, Stent thrombosis, Infections, Cost, Employment/ productivity, Other (specify)

- Indicate all long-term (>30 days) primary and secondary endpoints separately reported (i.e. reported singly, rather than only reported as part of a composite primary endpoint): Total mortality, Cardiac mortality, Nonfatal myocardial infarction, Stroke, TIA, Unstable angina, Angina/ recurrent symptoms, Angina class, Angina relief, Repeat revascularization, Heart failure, Graft failure, Hospitalization, Length of hospital stay, Bleeding, Quality of life, Cognitive effects, Adverse drug reactions, Radiation exposure, Access site complications, Renal dysfunction, Anaphylaxis, Arrhythmias, Stent thrombosis, Infections, Cost, Employment/ productivity, Other (specify)

- Describe how the short- and long-term outcome data is reported (e.g. Kaplan-Meier plots, Cox proportional hazards, hazard ratios, risk ratios, odds ratios, raw numbers, percentages, other methods), including whether p values, confidence intervals, etc. are provided.

- Include timing of outcomes (e.g. 1 yr, 5 yr)

- Comments (if needed)

II. Intervention characteristics

- Briefly indicate which population/intervention combination is reflected by the data abstracted on this instance of the form.

- PCI Procedural Characteristics
  - Describe the PCI intervention
  - Complete the below for Total, Female, and Male
    - Complete revascularization achieved
    - Vessels treated (mean): 1, 2, 3, or Unclear/ Not specified
    - Access site
      - Radial
      - Femoral
      - Unclear/ Not specified
    - Stents used (mean)
      - 0 stents
      - Bare metal stents
        - 1
        - 2
        - 3
        - More than 3
        - Unclear/ Not specified
      - Drug-eluting stents
        - 1
        - 2
        - 3
        - More than 3
        - Unclear/ Not specified
    - Interventional approach
      - Balloon
      - Atherectomy
      - Unclear/ Not specified
• Timing
  • Initial conservative strategy
  • Invasive strategy
  • Unclear/ Not specified
  o If applicable, specify type of bare metal stent used
  o If applicable, specify type of drug-eluting stent used:
• CABG Procedural Characteristics
  o Describe the CABG intervention:
  o Complete the below for Total, Female, and Male
    ▪ Bypass mode
      • None (beating heart)
      • Normothermic
      • Hypothermic
      • Unclear/ Not specified
    ▪ Cardioplegia type
      • Blood
      • Crystalloid
      • Other
      • Mixed
      • Unclear/ Not specified
    ▪ Incision type
      • Median sternotomy
      • Minimally invasive direct coronary bypass (Midcab)
      • Unclear/ Not specified
    ▪ Grafts used
      • 0 grafts
      • Saphenous vein (mean)
        o 1
        o 2
        o Greater than 2
        o Unclear/ Not specified
      • Mammary arteries (mean)
        o Left internal mammary artery
        o Right internal mammary artery
        o Both mammary arteries
        o Unclear/ Not specified
      • Radial artery (mean)
        o 1
        o 2
        o Unclear/ Not specified
    ▪ Transmyocardial laser revascularization (TMR)
      • Received
      • Not received
      • Unclear/ Not specified
    o If applicable, specify type of crystalloid cardioplegia agent used
  o If applicable, specify type of vein harvest (check all that apply): Endoscopic, Open, Unclear/ Not reported, Other (specify)
  o Mean cardiopulmonary bypass time
  o Mean cross-clamp time
Were concomitant procedures performed at the time of CABG surgery?

- If yes, describe the concomitant procedures

**Medical Therapy Intervention Characteristics**

- Describe the medical therapy intervention received by patients in the PCI arm (if applicable)
- Describe the medical therapy intervention received by patients in the CABG arm (if applicable)
- Describe the medical therapy intervention received by patients in the OMT arm (if applicable)
- Medications received in-hospital: record for PCI Subjects, CABG Subjects, and OMT Subjects; If ‘yes’ list drug name(s)/ dosage(s)
  - Acetylsalicylic acid (ASA)
  - Additional antiplatelet agents (e.g. clopidogrel, prasugrel, ticagrelor)
  - Antithrombin drugs (e.g. LMWH, unfractionated heparin, bivalirudin)
  - Glycoprotein IIb/IIIa inhibitors
  - Thrombolytic/ fibrinolytic drugs
  - Statins/ lipid-lowering drugs
  - Beta-blockers
  - ACEIs/ ARBs
  - Calcium channel blockers
  - Nitrates
  - Other #1 (specify)
  - Other #2 (specify)
  - Other #3 (specify)

**Discharge medications**

- Record for PCI Subjects, CABG Subjects, and OMT Subjects; If ‘yes’ list drug name(s)/ dosage(s)
  - Acetylsalicylic acid (ASA)
  - Additional antiplatelet agents (e.g. clopidogrel, prasugrel, ticagrelor)
  - Antithrombin drugs (e.g. LMWH, unfractionated heparin, bivalirudin)
  - Glycoprotein IIb/IIIa inhibitors
  - Thrombolytic/ fibrinolytic drugs
  - Statins/ lipid-lowering drugs
  - Beta-blockers
  - ACEIs/ ARBs
  - Calcium channel blockers
  - Nitrates
  - Other #1 (specify)
  - Other #2 (specify)
  - Other #3 (specify)

**Lifestyle modification**

- Indicate the components of lifestyle modification recommended to patients in the study (check all that apply): Smoking cessation, Diet modification, Exercise, Other (specify)
- If lifestyle modifications recommended were not consistent across all patients in the study, specify which groups received these recommendations and which did not.

**Therapeutic targets**

- Did the study include consideration of therapeutic target goals?
  - If yes, describe the therapeutic targets considered and whether interventions were adjusted for the purpose of meeting those specific goals.
- Compliance
  - If reported, provide data on in-hospital medication compliance (and lifestyle modification compliance, if available)
  - If reported, provide data on post-discharge medication compliance (and lifestyle modification compliance, if available) at the first followup visit after discharge. Include the time point of this followup visit (including units)
- Comments (if needed)

III. Outcomes
- Outcomes definitions
  - Authors’ definition of procedure-related outcomes
  - Authors’ definition of post-CABG MI
  - Authors’ definition of post-PCI MI
  - Check all outcomes for which gender-specific data is provided. Include an outcome if (1) data is reported specifically for women, or if (2) data is reported for men that can be used to calculate values for women (Total mortality, Cardiac mortality, Nonfatal myocardial infarction, Stroke, TIA, Unstable angina, Angina/ recurrent symptoms/ refractory angina/ refractory myocardial infarction, Angina class, Angina relief, Repeat revascularization (PCI or CABG), Heart failure, Graft failure, Hospitalization/ Re-hospitalization, Length of hospital stay, Bleeding, Quality of life, Cognitive effects, Adverse drug reactions, Radiation exposure, Access site complications, Renal dysfunction, Anaphylaxis, Arrhythmias, Stent thrombosis, Infections, Cost, Employment/ productivity, Other individual outcome #1 (e.g. CPR, cardioversion, respiratory failure, pulmonary edema), Other individual outcome #2, Other individual outcome #3.)
  - Comments (if needed)
- Composite outcome data
  - Are one or more composite outcomes reported in such a way that data for women can be abstracted or derived?
  - Is this a Primary or Secondary composite outcome?
  - Refer to the Intervention Characteristics forms completed; indicate which one applies to the outcome data recorded on this form:
  - Indicate the components that make up this composite outcome (check all that apply): Total mortality, Cardiac mortality, Nonfatal myocardial infarction, Stroke, TIA, Unstable angina, Angina/ recurrent symptoms/ refractory angina/ refractory myocardial infarction, Angina class, Angina relief, Repeat revascularization (PCI or CABG), Heart failure, Graft failure, Hospitalization/ Re-hospitalization, Length of hospital stay, Bleeding, Quality of life, Cognitive effects, Adverse drug reactions, Radiation exposure, Access site complications, Renal dysfunction, Anaphylaxis, Arrhythmias, Stent thrombosis, Infections, Cost, Employment/ productivity, Other individual outcome #1 (e.g. CPR, cardioversion, respiratory failure, pulmonary edema), Other individual outcome #2, Other individual outcome #3.
  - Complete tables to provide data for this outcome/ time point(s).
    - Timing of the outcome data reported in the table: Short term ≤ 30 days, Long-term > 30 days,
      - Specify timing of short-term outcome: 30 days, Other (specify)
      - Specify timing of long-term outcome: 6 weeks, 6 months, 1 year, 2 years, 3 years, 4 years, 5 years, Other (specify)
Indicate whether/how the results reported were adjusted (check all that apply): Results are not adjusted, RCT that did not adjust for any baseline difference, Age, Sex, Race, Comorbidity(ies) (specify), Other (specify all)

For each reported group (OMT, PCI, CABG, and/or Mixed Revascularization) record the following for Total, Female, and Male:

- N for Analysis
- Result
  - Mean
  - Median
  - Number of patients with outcome
  - % of patients with outcome
  - Relative risk
  - Relative hazard
  - Odds ratio
  - Risk difference
  - Other (specify)
- Variability
  - Standard Error (SE)
  - Standard Deviation (SD)
  - Other (specify)
- Confidence Interval (CI) or Interquartile Range (IQR)
  - 95% CI
  - Other %CI
  - IQR
- p-value between female and male data (within tx group)
- p-value between tx groups
- Reference group (for comparisons between tx groups)

- Comments (if needed)
- Individual outcome data
  - Select the outcome reported: Total mortality, Cardiac mortality, Nonfatal myocardial infarction, Stroke, TIA, Unstable angina, Angina/ recurrent symptoms/ refractory angina/ refractory myocardial infarction, Angina class, Angina relief, Repeat revascularization (PCI or CABG), Heart failure, Graft failure, Hospitalization/ Re-hospitalization, Length of hospital stay, Bleeding, Quality of life, Cognitive effects, Adverse drug reactions, Radiation exposure, Access site complications, Renal dysfunction, Anaphylaxis, Arrhythmias, Stent thrombosis, Infections, Cost, Employment/ productivity, Other individual outcome #1 (e.g. CPR, cardioversion, respiratory failure, pulmonary edema), Other individual outcome #2, Other individual outcome #3.
  - Complete tables to provide data for this outcome/ time point(s).
    - Timing of the outcome data reported in the table: Short term ≤ 30 days, Long-term > 30 days,
      - Specify timing of short-term outcome: 30 days, Other (specify)
      - Specify timing of long-term outcome: 6 weeks, 6 months, 1 year, 2 years, 3 years, 4 years, 5 years, Other (specify)
    - Indicate whether/how the results reported were adjusted (check all that apply): Results are not adjusted, RCT that did not adjust for any baseline difference, Age, Sex, Race, Comorbidity(ies) (specify), Other (specify all)
    - For each reported group (OMT, PCI, CABG, and/or Mixed Revascularization) record the following for Total, Female, and Male:
• N for Analysis
• Result
  o Mean
  o Median
  o Number of patients with outcome
  o % of patients with outcome
  o Relative risk
  o Relative hazard
  o Odds ratio
  o Risk difference
  o Other (specify)
• Variability
  o Standard Error (SE)
  o Standard Deviation (SD)
  o Other (specify)
• Confidence Interval (CI) or Interquartile Range (IQR)
  o 95% CI
  o Other %CI
  o IQR
• p-value between female and male data (within tx group)
• p-value between tx groups
• Reference group (for comparisons between tx groups)
  o Comments (if needed)

IV. Subgroup Analyses
• Does the article include subgroup analyses reported in a gender-specific way such that data for women can be abstracted or derived for any outcomes of interest?
• For each outcome record for Total, Female, and Male
• Indicate the nature of the subgroup analysis (i.e. the characteristic factor being considered): Age, Race, Other demographic or socioeconomic factor (specify), Diabetes, Chronic kidney disease, Other comorbid disease (specify), Angiographic-specific factor (specify), CABG-specific factor (specify), Hospital characteristic (specify)
• Specify the categories for this subgroup analysis. Columns are provided to capture up to 5 categories. Complete only the number needed to capture the data presented in the study.
  o Define the categories, then complete the tables with as much information as is provided in the study.
  o Provide data for each outcome. Clearly indicate units (number of patients, %, hazard ratio, etc.). Include values for confidence intervals, p values, standard error, standard deviation, etc. when available.
• Comments (if needed):

V. Quality Assessment
• Selection Bias
  o Was treatment adequately randomized (e.g. random number table, computer-generated randomization)?
  o Was the allocation of treatment adequately concealed (e.g. pharmacy-controlled randomization or use of sequentially numbered sealed envelopes)?
  o Did the strategy for recruiting participants into the study differ across study groups?
  o Are baseline characteristics similar between groups? If not, did the analysis control for differences?
• Performance Bias
  o Did researchers rule out any impact from a concurrent intervention or an unintended exposure that might bias results?
  o Did variation from the study protocol compromise the conclusions of the study?

• Attrition Bias
  o Was there a high rate of differential or overall attrition?
  o Did attrition result in a difference in group characteristics between baseline (or randomization) and followup?
  o Is the analysis conducted on an intention-to-treat (ITT) basis?

• Detection Bias
  o Were the outcome assessors blinded to the intervention status of participants?
  o Are the inclusion/exclusion criteria measured using valid and reliable measures?
  o Are the inclusion/exclusion criteria implemented consistently across all study participants?
  o Are interventions/exposures assessed using valid and reliable measures?
  o Are interventions/exposures implemented consistently across all study participants?
  o Are primary outcomes assessed using valid and reliable measures?
  o Are primary outcomes implemented consistently across all study participants?

• Reporting Bias
  o Are the potential outcomes pre-specified by the researchers? Are all pre-specified outcomes reported?

• Additional Comments

• Summary Judgment. Assign the study an overall quality rating based on the following definitions:
  o Good (low risk of bias). These studies have the least bias and results are considered valid. A study that adheres mostly to the commonly held concepts of high quality including the following: a formal randomized controlled study; clear description of the population, setting, interventions, and comparison groups; appropriate measurement of outcomes; appropriate statistical and analytic methods and reporting; no reporting errors; low dropout rate; and clear reporting of dropouts.
  o Fair. These studies are susceptible to some bias, but it is not sufficient to invalidate the results. They do not meet all the criteria required for a rating of good quality because they have some deficiencies, but no flaw is likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.
  o Poor (high risk of bias). These studies have significant flaws that imply biases of various types that may invalidate the results. They have serious errors in design, analysis, or reporting; large amounts of missing information; or discrepancies in reporting.

VI. Applicability
• Population (P) (select all that apply)
  o Study population not representative of community patients
  o Study population poorly specified
  o Key characteristics not reported

• Intervention (I) (select all that apply)
  o Monitoring practices or visit frequency not used in typical practice
  o Older versions of an intervention no longer in common use
  o Cointerventions that are likely to modify effectiveness of therapy
• Highly selected intervention team or level of training/proficiency not widely available

• Comparator (C) (select all that apply)
  o Inadequate comparison therapy

• Outcomes (O) (select all that apply)
  o Composite outcomes that mix outcomes of different significance
  o Data not stratified or adjusted for key predictors
  o Only short-term or surrogate outcomes reported

• Timing (T) (n/a)

• Setting (S) (select all that apply)
  o Resources available to providers for diagnosis and treatment of condition vary widely
  o Provider type/specialty varies across settings
  o Comparability of care in international settings unclear
  o Standards of care differ markedly from setting of interest
  o Specialty population or level of care differs from that seen in community

• Comments (if needed)
Appendix C. List of Included Studies


Hueb W, Lopes N, Gersh BJ, et al. Ten-year follow-up survival of the Medicine, Angioplasty, or Surgery


## Appendix D. Quality and Applicability of Included Studies

Table D-1. Quality and applicability for RCTs evaluating women with STEMI (KQ 1)

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Study Author/Year</th>
<th>Comparator</th>
<th>Quality</th>
<th>Limitations to Applicability</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARESS-in-AMI</td>
<td>Di Mario et al., 2008&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Immediate PCI with fibrinolysis (reteplase) vs. fibrinolysis (reteplase) with rescue PCI</td>
<td>Good</td>
<td>• None</td>
</tr>
<tr>
<td>DANAMI-2</td>
<td>Andersen et al., 2003&lt;sup&gt;2&lt;/sup&gt;</td>
<td>PCI vs. fibrinolysis (accelerated t-PA)</td>
<td>Good</td>
<td>• None</td>
</tr>
<tr>
<td>Dobrzycki</td>
<td>Dobrzycki et al., 2007&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Transfer with tirofiban for primary PCI vs. onsite fibrinolysis (streptokinase)</td>
<td>Good</td>
<td>• Comparability of care in international settings unclear</td>
</tr>
<tr>
<td>GUSTO II-B</td>
<td>Tamis-Holland et al., 2004&lt;sup&gt;4&lt;/sup&gt;</td>
<td>PCI vs. fibrinolysis (accelerated t-PA)</td>
<td>Good</td>
<td>• Comparability of care in international settings unclear</td>
</tr>
<tr>
<td>Minai</td>
<td>Minai et al., 2002&lt;sup&gt;5&lt;/sup&gt;</td>
<td>PCI vs. optimal medical therapy (without fibrinolysis)</td>
<td>Fair</td>
<td>• Comparability of care in international settings unclear</td>
</tr>
<tr>
<td>PAMI</td>
<td>Stone et al., 1995&lt;sup&gt;6&lt;/sup&gt;</td>
<td>PCI vs. fibrinolysis (t-PA)</td>
<td>Good</td>
<td>• Comparability of care in international settings unclear</td>
</tr>
<tr>
<td>SHOCK</td>
<td>Hochman et al., 2001&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Early invasive revascularization (PCI or CABG within 6 hours) vs. initial medical stabilization (thrombolysis, IABP)</td>
<td>Good</td>
<td>• None</td>
</tr>
</tbody>
</table>

Abbreviations: CABG = coronary artery bypass grafting; PCI = percutaneous coronary revascularization; STEMI = ST elevation myocardial infarction
Table D-2. Quality and applicability for RCTs evaluating women with UA/NSTEMI (KQ 2)

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Study Author/Year</th>
<th>Comparator</th>
<th>Quality</th>
<th>Limitations to Applicability</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRISC II</td>
<td>Lagerqvist et al., 2001$^8$</td>
<td>Early invasive treatment with revascularization vs. initial conservative strategy</td>
<td>Good</td>
<td>• Comparability of care in international settings unclear</td>
</tr>
<tr>
<td>GUSTO IV-ACS</td>
<td>Ottervanger et al., 2004$^9$</td>
<td>Early invasive management vs. initial conservative treatment within 30 days.</td>
<td>Good</td>
<td>• Older versions of an intervention no longer in common use</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Resources available to providers for diagnosis and treatment of condition varied widely</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Comparability of care in international settings unclear</td>
</tr>
<tr>
<td>ICTUS</td>
<td>de Winter et al., 2005$^{10}$</td>
<td>Early invasive therapy with revascularization vs. selective invasive strategy</td>
<td>Good</td>
<td>• Comparability of care in international settings unclear</td>
</tr>
<tr>
<td>RITA-2</td>
<td>Anonymous, 1997$^{11}$</td>
<td>Early invasive therapy with PCI vs. initial conservative</td>
<td>Fair</td>
<td>• Provider type/specialty varied across settings</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Comparability of care in international settings unclear</td>
</tr>
<tr>
<td>RITA-3</td>
<td>Clayton et al., 2004$^{12}$</td>
<td>Early invasive with PCI vs. initial conservative</td>
<td>Good</td>
<td>• None</td>
</tr>
<tr>
<td>TACTICS TIMI-18</td>
<td>Cannon et al., 2001$^{13}$</td>
<td>Early invasive with PCI vs. initial conservative</td>
<td>Good</td>
<td>• None</td>
</tr>
<tr>
<td>TIMI III-B</td>
<td>Anonymous, 1994$^{14}$</td>
<td>Early invasive with PCI vs. initial conservative</td>
<td>Good</td>
<td>• Older versions of an intervention no longer in common use</td>
</tr>
</tbody>
</table>

Abbreviations: CABG = coronary artery bypass grafting; PCI = percutaneous coronary revascularization
Table D-3. Quality and applicability for RCTs evaluating women with stable angina (KQ 3 Strategy 1)

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Study Author/Year</th>
<th>Comparator</th>
<th>Quality</th>
<th>Limitations to Applicability</th>
</tr>
</thead>
</table>
| Allen      | Allen et al., 2004<sup>15</sup> | Surgical revascularization vs. optimal medical therapy                       | Good    | • Older versions of an intervention no longer in common use  
• Cointerventions that were likely to modify effectiveness of therapy                                                |
| COURAGE    | Boden et al., 2007<sup>16</sup> | PCI (or CABG if PCI failed) vs. optimal medical therapy                      | Good    | • None                                                                                                           |
| MASS II    | Hueb et al., 2010<sup>17</sup> | PCI vs. optimal medical therapy  
CABG vs. optimal medical therapy | Good    | • Study population not representative of community patients  
• Cointerventions that were likely to modify effectiveness of therapy                                                |
| OAT        | Hochman et al., 2006<sup>18</sup> | PCI (or CABG if PCI failed) vs. optimal medical therapy                      | Good    | • None                                                                                                           |
| STICH      | Velazquez et al., 2011<sup>19</sup> | CABG vs. optimal medical therapy                                            | Good    | • Cointerventions that were likely to modify effectiveness of therapy  
• Comparability of care in international settings unclear                                                             |

Abbreviations: CABG = coronary artery bypass grafting; PCI = percutaneous coronary revascularization
Table D-4. Quality and applicability for RCTs evaluating women with stable/unstable angina (KQ 3 Strategy 2)

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Study Author/Year</th>
<th>Comparator</th>
<th>Quality</th>
<th>Limitations to Applicability</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARTS I</td>
<td>Vaina et al., 2009&lt;sup&gt;20&lt;/sup&gt;</td>
<td>PCI vs. CABG</td>
<td>Good</td>
<td>• None</td>
</tr>
</tbody>
</table>
| BARI       | Jacobs et al., 1998<sup>21</sup> | PCI vs. CABG | Good    | • Study population not representative of community patients  
  • Older versions of an intervention no longer in common use  
  • Cointerventions that were likely to modify effectiveness of therapy |
| CABRI      | Anonymous, 1995<sup>22</sup>    | PCI vs. CABG | Good    | • None                      |
| CARDia     | Kapur et al., 2010<sup>23</sup>| PCI vs. CABG | Good    | • Key characteristics not reported  
  • Provider type/specialty varied across settings |
| EAST       | King et al., 2000<sup>24</sup>| PCI vs. CABG | Good    | • Study population not representative of community patients  
  • Older versions of an intervention no longer in common use  
  • Cointerventions that were likely to modify effectiveness of therapy |
| GABI       | Kaehler et al., 2005<sup>25</sup> | PCI vs. CABG | Good    | • Cointerventions that were likely to modify effectiveness of therapy |
| MASS II    | Hueb et al., 2010<sup>17</sup> | PCI vs. CABG | Good    | • Study population not representative of community patients  
  • Cointerventions that were likely to modify effectiveness of therapy |
<p>| PRECOMBAT  | Park et al., 2011&lt;sup&gt;26&lt;/sup&gt;  | PCI vs. CABG | Good    | • Comparability of care in international settings unclear |</p>
<table>
<thead>
<tr>
<th>Study Name</th>
<th>Study Author/Year</th>
<th>Comparator</th>
<th>Quality</th>
<th>Limitations to Applicability</th>
</tr>
</thead>
</table>
| SOS        | Zhang et al., 2004$^{27}$ | PCI vs. CABG | Fair    | • Study population not representative of community patients  
• Cointerventions that were likely to modify effectiveness of therapy |
| SYNTAX     | Morice et al., 2010$^{28}$ | PCI vs. CABG | Fair    | • Data not stratified or adjusted for key predictors  
• Comparability of care in international settings unclear |

Abbreviations: CABG = coronary artery bypass grafting; PCI = percutaneous coronary revascularization
References Cited in Appendix D


Appendix E. List of Excluded Studies

All studies listed below were reviewed in their full-text version and excluded. Following each reference, in italics, is the reason for exclusion. Reasons for exclusion signify only the usefulness of the articles for this study and are not intended as criticisms of the articles.


Aaberge L, Rootwelt K, Blomhoff S, et al. Continued symptomatic improvement three to five years after transmyocardial revascularization with CO(2) laser: a late clinical follow-up of the Norwegian Randomized trial with transmyocardial revascularization. J Am Coll Cardiol. 2002;39(10):1588-93. PMID: 12020484. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Aaberge L, Rootwelt K, Smith HJ, et al. Effects of transmyocardial revascularization on myocardial perfusion and systolic function assessed by nuclear and magnetic resonance imaging methods. Scand Cardiovasc J. 2001;35(1):8-13. PMID: 11354578. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Aasa M, Dellborg M, Herlitz J, et al. Risk reduction for cardiac events after primary coronary intervention compared with thrombolysis for acute ST-elevation myocardial infarction (five-year results of the Swedish early decision reperfusion strategy [SWEDES] trial). Am J Cardiol. 2010;106(12):1685-91. PMID: 21126610. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Aasa M, Henriksson M, Dellborg M, et al. Cost and health outcome of primary percutaneous coronary intervention versus thrombolysis in acute ST-segment elevation myocardial infarction-Results of the Swedish Early Decision reperfusion Study (SWEDES) trial. Am Heart J. 2010;160(2):322-8. PMID: 20691839. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Anonymous. Arterial Revascularization Therapies Study (ARTS). Indian Heart J. 2001;53(2):239. PMID: 11428490. Exclude - Study type is not RCT, prospective or retrospective observational study, or registry.


Anonymous. Coronary angioplasty versus coronary artery bypass surgery: the Randomized Intervention Treatment of Angina (RITA) trial. Lancet. 1993;341(8845):573-80. PMID: 8094826. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Anonymous. Coronary artery bypass surgery versus percutaneous coronary intervention with stent implantation in patients with multivessel coronary artery disease (the Stent or Surgery trial): a randomised controlled trial. Lancet. 2002;360(9338):965-70. PMID: 12383664. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Anonymous. Does PCI added to drug therapy improve outcomes in stable CAD? J Fam Pract. 2007;56(7):529. PMID: 17612033. Exclude - Study type is not RCT, prospective or retrospective observational study, or registry.


Anonymous. Influence of diabetes on 5-year mortality and morbidity in a randomized trial comparing CABG and PTCA in patients with multivessel disease: the Bypass Angioplasty Revascularization Investigation (BARI). Circulation. 1997;96(6):1761-9. PMID: 9323059. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Anonymous. Little benefit to revascularization over intensive medical treatment in diabetes mellitus with coronary artery disease. J Natl Med Assoc. 2009;101(9):975-976. Exclude - Study type is not RCT, prospective or retrospective observational study, or registry.

Anonymous. One-year survival following early revascularization for cardiogenic shock (SCHOCK trial). Indian Heart J. 2001;53(2):240. PMID: 11428491. Exclude - Study type is not RCT, prospective or retrospective observational study, or registry.

Anonymous. Trial of invasive versus medical therapy in elderly patients with chronic symptomatic coronary-artery disease (TIME): a randomised trial. Lancet. 2001;358(9286):951-7. PMID: 11583747. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Aoki J, Ong AT, Arampatzis CA, et al. Comparison of three-year outcomes after coronary stenting versus coronary artery bypass grafting in patients with multivessel coronary disease, including involvement of the left anterior descending coronary artery proximally (a subanalysis of the arterial revascularization therapies study trial). Am J Cardiol. 2004;94(5):627-31. PMID: 15342295. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Armstrong PW. A comparison of pharmacologic therapy with/without timely coronary intervention vs. primary percutaneous intervention early after ST-elevation myocardial infarction: the WEST (Which Early ST-elevation myocardial infarction Therapy) study. Eur Heart J. 2006;27(13):1530-8. PMID: 16757491. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Aversano T, Aversano LT, Passamani E, et al. Thrombolytic therapy vs primary percutaneous coronary intervention for myocardial infarction in patients presenting to hospitals without on-site cardiac surgery: a randomized controlled trial. JAMA. 2002;287(15):1943-51. PMID: 11960536. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Banning AP, Westaby S, Morice MC, et al. Diabetic and nondiabetic patients with left main and/or 3-vessel coronary artery disease: comparison of outcomes with cardiac surgery and paclitaxel-eluting stents. J Am Coll Cardiol. 2010;55(11):1067-75. PMID: 2079596. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Bata I, Armstrong PW, Westerhout CM, et al. Time from first medical contact to reperfusion in ST elevation myocardial infarction: a Which Early ST Elevation Myocardial Infarction Therapy (WEST) substudy. Can J Cardiol. 2009;25(8):463-8. PMID: 19668780. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Berrocal DH, Cohen MG, Spinetta AD, et al. Early reperfusion and late clinical outcomes in patients presenting with acute myocardial infarction randomly assigned to primary percutaneous coronary intervention or streptokinase. Am Heart J. 2003;146(6):E22. PMID: 14661011. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes...

Bonnefoy E, Steg PG, Chabaud S, et al. Is primary angioplasty more effective than prehospital fibrinolysis in diabetics with acute myocardial infarction? Data from the CAPTIM randomized clinical trial. Eur Heart J. 2005;26(17):1712-8. PMID: 15840623. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Borges JC, Lopes N, Soares PR, et al. Five-year follow-up of angiographic disease progression after medicine, angioplasty, or surgery. J Cardiothorac Surg. 2010;5(91. PMID: 20977758. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Bourassa MG, Kip KE, Jacobs AK, et al. Is a strategy of intended incomplete percutaneous transluminal coronary angioplasty revascularization acceptable in nondiabetic patients who are candidates for coronary artery bypass graft surgery? The Bypass Angioplasty

E-4
Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Brener SJ, Galla JM, Bryant R, 3rd, et al. Comparison of percutaneous versus surgical revascularization of severe unprotected left main coronary stenosis in matched patients. Am J Cardiol. 2008;101(2):169-72. PMID: 18178401. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Brooks MM, Jones RH, Bach RG, et al. Predictors of mortality and mortality from cardiac causes in the bypass angioplasty revascularization investigation (BARI) randomized trial and registry. For the BARI Investigators. Circulation. 2000;101(23):2682-9. PMID: 10851204. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Buszman P, Tendera M, Bochenek A, et al. A prospective evaluation of early and late results of percutaneous and surgical revascularisation in patients with ischaemic left ventricular dysfunction. Kardiol Pol. 2002;56(1):57-61. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Buszman PE, Kiesz SR, Bochenek A, et al. Acute and late outcomes of unprotected left main stenting in comparison with surgical revascularization. J Am Coll Cardiol. 2008;51(5):538-45. PMID: 18237682. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Carver A, Elbaz S, Gershlick AH, et al. Longer-term follow-up of patients recruited to the REACT (Rescue Angioplasty Versus Conservative Treatment or Repeat Thrombolysis) trial. J Am Coll Cardiol. 2009;54(2):118-26. PMID: 19573727. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Chaitman BR, Hardison RM, Adler D, et al. The Bypass Angioplasty Revascularization Investigation 2 Diabetes randomized trial of different treatment strategies in type 2 diabetes mellitus with stable ischemic heart disease: impact of treatment strategy on cardiac mortality and myocardial infarction. Circulation. 2009;120(25):2529-40. PMID: 19920001. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Chung SC, Hlatky MA, Faxon D, et al. Primary direct stenting versus endoscopic atraumatic coronary artery bypass surgery in patients with proximal stenosis of the left anterior descending coronary artery--a prospective, randomised study. Kardiol Pol. 2004;61(9):253-61; discussion 262-4. PMID: 15531937. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Cleland JG, Calvert M, Freemantle N, et al. The Heart Failure Revascularisation Trial (HEART). Eur J Heart Fail. 2011;13(2):227-33. PMID: 21156659. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Cohen DJ. CABG and PCI did not differ clinically for angina relief in severe CAD. Ann Intern Med. 2011;155(2):JC1-10. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Daemen J, Kuck KH, Macaya C, et al. Multivessel coronary revascularization in patients with and without diabetes mellitus: 3-year follow-up of the ARTS-II (Arterial Revascularization Therapies Study-Part II) trial. J Am Coll Cardiol. 2008;52(24):1957-67. PMID: 19055986. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Dagenais GR, Lu J, Faxon DP, et al. Effects of optimal medical treatment with or without coronary revascularization on angina and subsequent revascularizations in patients with type 2 diabetes mellitus and stable ischemic heart disease. Circulation. 2011;123(14):1492-500. PMID: 21444887. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


de Boer MJ, Ottervanger JP, van ‘t Hof AW, et al. Reperfusion therapy in elderly patients with acute myocardial infarction: a randomized comparison of primary angioplasty and thrombolytic therapy. J Am Coll Cardiol. 2002;39(11):1723-8. PMID: 12039482. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Denardo SJ, Messerli FH, Gaxiola E, et al. Coronary revascularization strategy and outcomes according to blood pressure (from the International Verapamil SR-Trandolapril Study [INVEST]). Am J Cardiol. 2010;106(4):498-503. PMID: 20691307. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Devlin G, Reynolds HR, Mark DB, et al. Loss of short-term symptomatic benefit in patients with an occluded infarct artery is unrelated to non-protocol revascularization: results from the Occluded Artery Trial (OAT). Am Heart J. 2011;161(1):84-90. PMID: 21167338. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Di Pasquale P, Cannizzaro S, Parrinello G, et al. Is delayed facilitated percutaneous coronary intervention better than immediate in reperfused myocardial infarction? Six months follow up findings. J Thromb Thrombolysis. 2006;21(2):147-57. PMID: 16622610. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Diderholm E, Andren B, Frostfeldt G, et al. The prognostic and therapeutic implications of increased troponin T levels and ST depression in unstable coronary artery disease: the FRISC II invasive troponin T electrocardiogram substudy. Am Heart J. 2010;153(5):606-12. PMID: 21167338. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Diderholm E, Andreu B, Frostfeldt G, et al. ST depression in ECG at entry indicates severe coronary lesions and large benefits of an early invasive treatment strategy in unstable coronary artery disease; the FRISC II ECG substudy. The Fast Revascularisation during InStability in Coronary artery disease. Eur Heart J. 2002;23(1):41-9. PMID: 11741361. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Dieker HJ, van Horssen EV, Hersbach FM, et al. Transport for abciximab facilitated primary angioplasty versus on-site thrombolysis with a liberal rescue policy: the randomised Holland Infarction Study (HIS). J Thromb Thrombolysis. 2006;22(1):39-45. PMID: 16786231. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Dong-Bao L, Qi H, Hong-Wei L, et al. Effects of early angioplasty after fibrinolysis on prognosis of patients with ST-segment elevation acute myocardial infarction. African Journal of Biotechnology. 2011;10(70):15801-15804. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Dragu R, Behar S, Sandach A, et al. Should primary percutaneous coronary intervention be the preferred method of reperfusion therapy for patients with renal failure and ST-elevation acute myocardial infarction? Am J Cardiol. 2006;97(8):1142-5. PMID: 16616015. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Drenth DJ, Veeger NJ, Middel B, et al. Comparison of late (four years) functional health status between percutaneous transluminal angioplasty intervention and off-pump left internal mammary artery bypass grafting for isolated high-grade narrowing of the proximal left anterior descending coronary artery. Am J Cardiol. 2004;94(11):1414-7. PMID: 15566914. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Dryja T, Kornacewicz-Jach Z, Goracy J, et al. Treatment of acute ST-segment elevation myocardial infarction in West Pomerania province of Poland. Comparison between primary coronary intervention and thrombolytic therapy. Kardiol Pol. 2006;64(6):591-599. PMID: 16810577. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Dzavik V, Beanlands DS, Davies RF, et al. Effects of late percutaneous transluminal coronary angioplasty of an occluded infarct-related coronary artery on left ventricular function in patients with a recent (< 6 weeks) Q-wave acute myocardial infarction (Total Occlusion Post-Myocardial Infarction Intervention Study [TOMIIS]--a pilot study). Am J Cardiol. 1994;73(12):856-61. PMID: 8184807. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Dzavik V, Buller CE, Lamas GA, et al. Randomized trial of percutaneous coronary intervention for subacute infarct-related coronary artery occlusion to achieve long-term patency and improve ventricular function: the Total Occlusion Study of Canada (TOSCA)-2 trial. Circulation. 2006;114(23):2449-57. PMID: 17105848. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Dzavik V, Sleeper LA, Cocke TP, et al. Early revascularization is associated with improved survival in elderly patients with acute myocardial infarction complicated by cardiogenic shock: a report from the SHOCK Trial Registry. Eur Heart J. 2003;24(9):828-37. PMID: 12727150. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Dzavik V, Sleeper LA, Picard MH, et al. Outcome of patients aged >or=75 years in the SHould we emergently revascularize Occluded Coronaries in cardiogenic shock (SHOCK) trial: do elderly patients with acute myocardial infarction complicated by cardiogenic shock respond differently to emergent revascularization? Am Heart J. 2005;149(6):1128-34. PMID: 15976798. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Eefting F, Nathoe H, van Dijk D, et al. Randomized comparison between stenting and off-pump bypass surgery in patients referred for angioplasty. Circulation. 2003;108(23):2870-6. PMID: 14656913. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Erne P, Schoenenberger AW, Burchhardt D, et al. Effects of percutaneous coronary interventions in silent ischemia after myocardial infarction: the SWISSII II randomized controlled trial. JAMA. 2007;297(18):1985-91. PMID: 17488963. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Farkouh ME, Ramanathan K, Aymong ED, et al. An early revascularization strategy is associated with a survival benefit for diabetic patients in cardiogenic shock after acute myocardial infarction. Clin Cardiol. 2006;29(5):204-10. PMID: 16739392. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Favarato D, Hueb W, Gersh BJ, et al. Relative cost comparison of treatments for coronary artery disease: the First Year Follow-Up of MASS II Study. Circulation. 2003;108 Suppl 1:I121-3. PMID: 12970202. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Favarato ME, Hueb W, Boden WE, et al. Quality of life in patients with symptomatic multivessel coronary artery disease: a comparative post hoc analyses of medical, angioplasty or surgical strategies-MASS II trial. Int J Cardiol. 2007;116(3):364-70. PMID: 16876891. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Folland ED, Hartigan PM, Parisi AF. Percutaneous transluminal coronary angioplasty versus medical therapy for stable angina pectoris: outcomes for patients with double-vessel versus single-vessel coronary artery disease in a Veterans Affairs Cooperative randomized trial. Veterans Affairs ACME Investigators. J Am Coll Cardiol. 1997;29(7):1505-11. PMID: 9180111. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Fosbol EL, Thune JJ, Kelbaek H, et al. Long-term outcome of primary angioplasty compared with fibrinolysis across age groups: a Danish Multicenter Randomized Study on Fibrinolytic Therapy Versus Acute Coronary Angioplasty in Acute Myocardial Infarction (DANAMI-2) substudy. Am Heart J. 2008;156(2):391-6. PMID: 18657676. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Fox KA, Poole-Wilson P, Clayton TC, et al. 5-year outcome of an interventional strategy in non-ST-elevation acute coronary syndrome: the British Heart Foundation RITA 3 randomised trial. Lancet. 2005;366(9489):914-20. PMID: 16154018. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Fukunishi M, Nishigaki K, Okubo M, et al. J-SAP study 1-2: outcomes of patients with stable high-risk coronary artery disease receiving medical-preceding therapy in Japan. Circ J. 2006;70(8):1012-6. PMID: 16864934. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Gibbons RJ, Holmes DR, Reeder GS, et al. Immediate angioplasty compared with the administration of a thrombolytic agent followed by conservative treatment for myocardial infarction. The Mayo Coronary Care Unit and Catheterization Laboratory Groups. N Engl J Med. 1993;328(10):685-91. PMID: 8433727. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Graham MM, Ghali WA, Faris PD, et al. Survival after coronary revascularization in the elderly. Circulation. 2002;105(20):2378-84. PMID: 12021224. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Gray TJ, Burns SM, Clarke SC, et al. Percutaneous myocardial laser revascularization in patients with refractory angina pectoris. Am J Cardiol. 2003;91(6):661-6. PMID: 12633794. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Gruberg L, Mercado N, Milo S, et al. Impact of body mass index on the outcome of patients with multivessel disease randomized to either coronary artery bypass grafting or stenting in the ARTS trial: The obesity paradox II? Am J Cardiol. 2005;95(4):439-44. PMID: 15695125. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Gruberg L, Milo S, Ben Tzvi M, et al. Comparison of bypass surgery and stenting for the treatment of multivessel disease: results from the ARTS trial in Israel. Isr Med Assoc J. 2003;5(8):539-42. PMID: 12929288. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Hartigan PM, Giacomini JC, Folland ED, et al. Two-to-three-year follow-up of patients with single-vessel coronary artery disease randomized to PTCA or medical therapy (results of a VA cooperative study). Veterans Affairs Cooperative Studies Program ACME Investigators. Angioplasty Compared to Medicine. Am J Cardiol. 1998;82(12):1445-50. PMID: 9874045. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Henderson RA, Pocock SJ, Clayton TC, et al. Seven-year outcome in the RITA-2 trial: coronary angioplasty versus medical therapy. J Am Coll Cardiol. 2003;42(7):1161-70. PMID: 14522473. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Henriques JP, Zijlstra F, van’t Hof AW, et al. Primary percutaneous coronary intervention versus thrombolytic treatment: long term follow up according to infarct location. Heart. 2006;92(1):75-9. PMID: 15831596. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Hlatky MA, Bacon C, Boothroyd D, et al. Cognitive function 5 years after randomization to coronary angioplasty or coronary artery bypass graft surgery. Circulation. 1997;96(9 Suppl):II-11-4; discussion II-15. PMID: 9386068. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Hlatky MA, Boothroyd DB, Melsop KA, et al. Medical costs and quality of life 10 to 12 years after randomization to angioplasty or bypass surgery for multivessel coronary artery disease. Circulation. 2004;110(14):1960-6. PMID: 15451795. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Hlatky MA, Boothroyd DB, Melsop KA, et al. Economic outcomes of treatment strategies for type 2 diabetes mellitus and coronary artery disease in the


Holper EM, Brooks MM, Kim LJ, et al. Effects of heart failure and diabetes mellitus on long-term mortality after coronary revascularization (from the BARI Trial). Am J Cardiol. 2007;100(2):196-202. PMID: 17631069. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Hong SJ, Lim DS, Seo HS, et al. Percutaneous coronary intervention with drug-eluting stent implantation vs. minimally invasive direct coronary artery bypass (MIDCAB) in patients with left anterior descending coronary artery stenosis. Catheter Cardiovasc Interv. 2005;64(1):75-81. PMID: 15619278. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Horie H, Takahashi M, Minai K, et al. Long-term beneficial effect of late reperfusion for acute anterior myocardial infarction with percutaneous transluminal coronary angioplasty. Circulation. 1998;98(22):2377-82. PMID: 9832481. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Hueb WA, Bellotti G, de Oliveira SA, et al. The Medicine, Angioplasty or Surgery Study (MASS): a prospective, randomized trial of medical therapy, balloon angioplasty or bypass surgery for single proximal left anterior descending coronary artery stenoses. J Am Coll Cardiol. 1995;26(7):1600-5. PMID: 7594092. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Hueb WA, Soares PR, Almeida De Oliveira S, et al. Five-year follow-op of the medicine, angioplasty, or surgery study (MASS): A prospective, randomized trial of medical therapy, balloon angioplasty, or bypass surgery for single proximal left anterior descending coronary artery stenosis. Circulation. 1999;100(19 Suppl):I107-13. PMID: 10567287. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Idorn L, Hofsten DE, Wachtell K, et al. Prevalence and prognostic implications of ST-segment deviations from ambulatory Holter monitoring after ST-segment elevation myocardial infarction treated with either fibrinolysis or primary percutaneous coronary intervention (a Danish Trial in Acute Myocardial Infarction-2 Substudy). Am J Cardiol. 2007;100(6):937-43. PMID: 17826373. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Itoh T, Fukami K, Suzuki T, et al. Comparison of long-term prognostic evaluation between pre-intervention thrombolysis and primary coronary intervention: A prospective randomized trial - Five-year results of the IMPORTANT study. Circ J. 2010;74(8):1625-1634. PMID: 20571249. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

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. PMID: 11741360. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Janzon M, Levin LA, Swahn E. Invasive treatment in unstable coronary artery disease promotes health-related quality of life: results from the FRISC II trial. Am Heart J. 2004;148(1):114-21. PMID: 15215800. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Javaid A, Steinberg DH, Buch AN, et al. Outcomes of coronary artery bypass grafting versus percutaneous coronary intervention with drug-eluting stents for patients with multivessel coronary artery disease. Circulation. 2007;116(11 Suppl):I200-6. PMID: 17846304. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Jeger RV, Bonetti PO, Zellweger MJ, et al. Influence of revascularization on long-term outcome in patients > or =75 years of age with diabetes mellitus and angina pectoris. Am J Cardiol. 2005;96(2):193-8. PMID: 16018840. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Jeger RV, Harkness SM, Ramanathan K, et al. Emergency revascularization in patients with cardiogenic shock on admission: a report from the SHOCK trial and registry. Eur Heart J. 2006;27(6):664-70. PMID: 16423873. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Jeger RV, Lowe AM, Buller CE, et al. Hemodynamic parameters are prognostically important in cardiogenic shock but similar following early revascularization or initial medical stabilization: a report from the SHOCK Trial. Chest. 2007;132(6):1794-803. PMID: 17951622. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Jeger RV, Pfisterer ME. Revascularization in patients 75 years or older with diabetes mellitus and angina pectoris. Cardiol Rev. 2006;23(1):19-23. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Jeger RV, Tseng CH, Hochman JS, et al. Interhospital transfer for early revascularization in patients with ST-elevation myocardial infarction complicated by cardiogenic shock--a report from the SHOULD we revascularize Ocluded Coronaries for cardiogenic shockK? (SHOCK) trial and registry. Am Heart J. 2006;152(4):686-92. PMID: 16996836. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Johansen A, Hoilund-Carlsen PF, Christensen HW, et al. Use of myocardial perfusion imaging to predict...
the effectiveness of coronary revascularisation in patients with stable angina pectoris. Eur J Nucl Med Mol Imaging. 2005;32(12):1363-70. PMID: 15824925. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Kaiser C, Kuster GM, Erne P, et al. Risks and benefits of optimised medical and revascularisation therapy in elderly patients with angina--on-treatment analysis of the TIME trial. Eur Heart J. 2004;25(12):1036-42. PMID: 15191774. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Kapur A, Bartolini D, Finlay MC, et al. The Bypass Angioplasty Revascularization in Type 1 and Type 2 Diabetes Study: 5-year follow-up of revascularization with percutaneous coronary intervention versus coronary artery bypass grafting in diabetic patients with multivessel disease. J Cardiovasc Med (Hagerstown). 2010;11(1):26-33. PMID: 19797974. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Kasai T, Kajimoto K, Miyauchi K, et al. Propensity analysis of 12 years outcome after bypass graft or balloon angioplasty in patients with multivessel coronary artery disease. J Cardiol. 2008;52(3):186-194. PMID: 19027596. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Kawecki D, Kubiak G, Orszulik K, et al. Quality of life in patients with severe left ventricle dysfunction due to coronary artery disease. Central European Journal of Medicine. 2011;6(6):807-812. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


King SB, 3rd. The Emory Angioplasty vs Surgery Trial (EAST). Semin Interv Cardiol. 1999;4(4):185-90. PMID: 10738351. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.
for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Kip KE, Alderman EL, Bourassa MG, et al. Differential influence of diabetes mellitus on increased jeopardized myocardium after initial angioplasty or bypass surgery: bypass angioplasty revascularization investigation. Circulation. 2002;105(16):1914-20. PMID: 11997277. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Kjaergard HK, Nielsen PH, Andreasen JJ, et al. Coronary artery bypass grafting within 30 days after treatment of acute myocardial infarctions with angioplasty or fibrinolysis - a surgical substudy of DANAMI-2. Scand Cardiovasc J. 2004;38(3):143-6. PMID: 15223711. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Kleiman NS, Lakkis N, Cannon CP, et al. Prospective analysis of creatine kinase muscle-brain fraction and comparison with troponin T to predict cardiac risk and benefit of an invasive strategy in patients with non-ST-elevation acute coronary syndromes. J Am Coll Cardiol. 2002;40(6):1044-50. PMID: 12354426. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Kofoed KF, Madsen JK, Grande P, et al. Long-term effects of invasive treatment in patients with a post-thrombolytic Q-wave myocardial infarction. Scand Cardiovasc J. 2010;44(3):146-52. PMID: 20233135. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Kontny F. Improving outcomes in acute coronary syndromes--the FRISC II trial. Clin Cardiol. 2001;24(Suppl):13-7. PMID: 11286312. Exclude - Study type is not RCT, prospective or retrospective observational study, or registry.


Kruk M, Buller CE, Tcheng JE, et al. Impact of left ventricular ejection fraction on clinical outcomes over five years after infarct-related coronary artery recanalization (from the Occluded Artery Trial [OAT]). Am J Cardiol. 2010;105(1):10-6. PMID: 20102883. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Kruk M, Kadziela J, Reynolds HR, et al. Predictors of outcome and the lack of effect of percutaneous coronary revascularization procedures after the risk strata in patients with persistent total occlusion after myocardial infarction: Results from the OAT (Occluded Artery Trial) study. JACC Cardiovasc Interv. 2008;1(5):511-20. PMID: 19194534. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or
older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

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Exclude - No data for OMT/PCI/CABG comparison of interest.

Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.
Lansky AJ. Outcomes of percutaneous and surgical revascularization in women. Prog Cardiovasc Dis. 2004;46(4):305-19. PMID: 14961454. Exclude - Study type is not RCT, prospective or retrospective observational study, or registry.


Le May MR, Labinaz M, Davies RF, et al. Stenting versus thrombolysis in acute myocardial infarction trial (STAT). J Am Coll Cardiol. 2001;37(4):985-91. PMID: 11263625. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Lee MS, Kapoor N, Jamal F, et al. Comparison of coronary artery bypass surgery with percutaneous coronary intervention with drug-eluting stents for unprotected left main coronary artery disease. J Am Coll Cardiol. 2006;47(4):864-70. PMID: 16487857. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Lee MS, Kapoor N, Jamal F, et al. Comparison of bypass surgery with drug-eluting stents for diabetic patients with multivessel disease. Int J Cardiol. 2007;123(1):34-42. PMID: 17292983. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Lindholm MG, Boesgaard S, Thune JJ, et al. Percutaneous coronary intervention for acute MI does not prevent in-hospital development of cardiogenic shock compared to fibrinolysis. Eur J Heart Fail. 2008;10(7):668-74. PMID: 18571985. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Lopes NH, Paulitsch FdS, Gois AF, et al. Impact of number of vessels disease on outcome of patients with stable coronary artery disease: 5-year follow-up of the Medical, Angioplasty, and bypass Surgery study (MASS). Eur J Cardiothorac Surg. 2008;33(3):349-54. PMID: 18249128. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


MacK MJ, Banning AP, Serruys PW, et al. Bypass versus drug-eluting stents at three years in SYNTAX patients with diabetes mellitus or metabolic syndrome. Ann Thorac Surg. 2011;92(6):2140-2146. PMID: 21967819. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Madsen JK, Nielsen TT, Grande P, et al. Revascularization compared to medical treatment in patients with silent vs. symptomatic residual ischemia after thrombolysed myocardial infarction--the DANAMI study. Cardiology. 2007;108(4):243-51. PMID: 17114878. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Mahmariyan JJ, Dakik HA, Filipchuk NG, et al. An initial strategy of intensive medical therapy is comparable to that of coronary revascularization for suppression of scintigraphic ischemia in high-risk but stable survivors of acute myocardial infarction. J Am Coll Cardiol. 2006;48(12):2458-67. PMID: 17174182. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Malek LA, Reynolds HR, Forman SA, et al. Late coronary intervention for totally occluded left anterior descending coronary arteries in stable patients after myocardial infarction: Results from the Occluded Artery Trial (OAT). Am Heart J. 2009;157(4):724-32. PMID: 19332202. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Mancini GBJ, Bates ER, Maron DJ, et al. Quantitative results of baseline angiography and percutaneous coronary intervention in the courage trial. Circ Cardiovasc Qual Outcomes. 2009;2(4):320-327. PMID: 20031857. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Mark DB, Pan W, Clapp-Channing NE, et al. Quality of life after late invasive therapy for occluded arteries. N Engl J Med. 2009;360(8):774-83. PMID: 19228620. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

62. PMID: 19801024. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Martuscelli E, Clementi F, Gallagher MM, et al. Revascularization strategy in patients with multivessel disease and a major vessel chronically occluded; data from the CABRI trial. Eur J Cardiothorac Surg. 2008;33(1):4-8. PMID: 17988889. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Matteau A, Dorais M, Rinfret S, et al. Effectiveness of a change in reperfusion strategy to primary percutaneous coronary intervention in a nonselected population. Can J Cardiol. 2009;25(8):e279-83. PMID: 19668789. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

McCullough PA, Gibson CM, Dibattiste PM, et al. Timing of angiography and revascularization in acute coronary syndromes: an analysis of the TACTICS-TIMI-18 trial. J Interv Cardiol. 2004;17(2):81-6. PMID: 15104769. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


McKhann GM, Grega MA, Borowicz LM, Jr., et al. Is there cognitive decline 1 year after CABG? Comparison with surgical and nonsurgical controls. Neurology. 2005;65(7):991-9. PMID: 16107605. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Meliga E, Orzan F, Chiribiri A, et al. Surgical revascularization in the ischemic heart disease. Long-term results in a series of consecutive patients selected according to the principles. Minerva Cardioangiol. 2005;53(2):147-52. PMID: 15986009. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Menon V, Pearte CA, Buller CE, et al. Lack of benefit from percutaneous intervention of persistently occluded infarct arteries after the acute phase of myocardial infarction is time independent: insights from Occluded Artery Trial. Eur Heart J. 2009;30(2):183-91. PMID: 19028780. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Moreira AE, Hueb WA, Soares PR, et al. [Comparative study between the therapeutic effects of surgical myocardial revascularization and coronary angioplasty in equivalent ischemic situations: analysis through myocardial scintigraphy with 99mTc-Sestamibi]. Arq Bras Cardiol. 2005(2):92-9. PMID: 16113846. Exclude - Does not include outcome data reported in a gender-specific fashion
for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Morice MC, Feldman TE, Mack MJ, et al. Angiographic outcomes following stenting or coronary artery bypass surgery of the left main coronary artery: Fifteen-month outcomes from the synergy between PCI with TAXUS express and cardiac surgery left main angiographic substudy (SYNTAX-LE MANS). EuroIntervention. 2011;7(6):670-679. PMID: 21959312. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Nathoe HM, Van Dijk D, Jansen EWL, et al. Off-pump coronary artery bypass surgery compared with stent implantation and on-pump bypass surgery: Clinical outcome and cost-effectiveness at one year. Neth Heart J. 2005;13(7):259-268. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Nishigaki K, Yamazaki T, Kitabatake A, et al. Percutaneous coronary intervention plus medical therapy reduces the incidence of acute coronary syndrome more effectively than initial medical therapy only among patients with low-risk coronary artery disease a randomized, comparative, multicenter study. JACC Cardiovasc Interv. 2008;1(5):469-79. PMID: 19463347. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Nylaende M, Abdelmoor M, Stranden E, et al. The Oslo balloon angioplasty versus conservative treatment study (OBACT)--the 2-years results of a single centre, prospective, randomised study in patients with intermittent claudication. Eur J Vasc Endovasc Surg. 2007;33(1):3-12. PMID: 17055756. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Nylaende M, Kroese AJ, Morken B, et al. Beneficial effects of 1-year optimal medical treatment with and without additional PTA on inflammatory markers of atherosclerosis in patients with PAD. Results from the Oslo Balloon Angioplasty versus Conservative Treatment (OBACT) study. Vasc Med. 2007;12(4):275-83. PMID: 18048463. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


O'Donoghue M, Sabatine MS. Appropriate invasive and conservative treatment approaches for patients with ST-elevation MI. Curr Treat Options Cardiovasc Med. 2006;8(1):3-11. PMID: 16401379. Exclude - Study type is not RCT, prospective or retrospective observational study, or registry.


Ovbiagele B, Campbell S, Faiz A, et al. Relationship between non-specific prescription pill adherence and


Parisi AF, Hartigan PM, Folland ED. Evaluation of exercise thallium scintigraphy versus exercise electrocardiography in predicting survival outcomes and morbid cardiac events in patients with single- and double-vessel disease. Findings from the Angioplasty Compared to Medicine (ACME) Study. J Am Coll Cardiol. 1997;30(5):1256-63. PMID: 9350924. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Parodi G, Ndreppea G, Kastrati A, et al. Ability of mechanical reperfusion to salvage myocardium in patients with acute myocardial infarction presenting beyond 12 hours after onset of symptoms. Am Heart J. 2006;152(6):1133-9. PMID: 17161066. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Pell JP, Pell AC, Jeffrey RR, et al. Comparison of survival following coronary artery bypass grafting vs.
Percutaneous coronary intervention in diabetic and non-diabetic patients: retrospective cohort study of 6320 procedures. Diabet Med. 2004;21(7):790-2. PMID: 15209776. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Pfisterer M. Long-term outcome in elderly patients with chronic angina managed invasively versus by optimized medical therapy: four-year follow-up of the randomized Trial of Invasive versus Medical therapy in Elderly patients (TIME). Circulation. 2004;110(10):1213-8. PMID: 15337691. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Pfisterer M, Buser P, Osswald S, et al. Outcome of elderly patients with chronic symptomatic coronary artery disease with an invasive vs optimized medical treatment strategy: one-year results of the randomized TIME trial. JAMA. 2003;289(9):1117-23. PMID: 12622581. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Pfisterer M, Buser P, Osswald S, et al. Trial of Invasive versus Medical Therapy in the Elderly (TIME): Study protocol and patient outline. HeartDrug. 2001;1(3):144-147. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Pocock SJ, Henderson RA, Seed P, et al. Quality of life, employment status, and anginal symptoms after coronary angioplasty or bypass surgery. 3-year follow-up in the Randomized Intervention Treatment of Angina (RITA) Trial. Circulation. 1996;94(2):135-42. PMID: 8674171. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Poole-Wilson PA, Pocock SJ, Fox KA, et al. Interventional versus conservative treatment in acute non-ST elevation coronary syndrome: time course of patient management and disease events over one year in the RITA 3 trial. Heart. 2006;92(10):1473-9. PMID: 16621882. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Prasad A, Rihal C, Holmes DR, Jr. The COURAGE trial in perspective. Catheter Cardiovasc Interv. 2008;72(1):54-9. PMID: 18412271. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Exclude - No data for OMT/PCI/CABG comparison of interest.

Ramanathan KB, Weiman DS, Sacks J, et al. Percutaneous intervention versus coronary bypass surgery for patients older than 70 years of age with high-risk unstable angina. Ann Thorac Surg. 2005;80(4):1340-6. PMID: 16181866. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Rastan AJ, Boudriot E, Falk V, et al. Frequency and pattern of de-novo three-vessel and left main coronary artery disease; insights from single center enrolment in the SYNTAX study. Eur J Cardiothorac Surg. 2008;34(2):376-82; discussion 382-3. PMID: 18579392. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Ribeiro EE, Silva LA, Carneiro R, et al. Randomized trial of direct coronary angioplasty versus intravenous streptokinase in acute myocardial infarction. J Am Coll Cardiol. 1993;22(2):376-80. PMID: 8335807. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Riezebos RK, Ronner E, Ter Bals E, et al. Immediate versus deferred coronary angioplasty in non-ST-segment elevation acute coronary syndromes. Heart. 2009;95(10):807-12. PMID: 19098058. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Rihal CS, Sutton-Tyrrell K, Guo P, et al. Increased incidence of periprocedural complications among patients with peripheral vascular disease undergoing myocardial revascularization in the bypass angioplasty revascularization investigation. Circulation. 1999;100(2):171-7. PMID: 10402447. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Neurocognitive functioning in patients undergoing percutaneous coronary intervention benefit most from early intervention in high-risk patients with medically refractory ischemia. J Am Coll Cardiol. 2003;41(10):1732-8. PMID: 12767656. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Rott D, Behar S, Hod H, et al. Improved survival of patients with acute myocardial infarction with significant left ventricular dysfunction undergoing invasive coronary procedures. Am Heart J. 2001;141(2):267-76. PMID: 11174342. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Rodriguez AE, Baldi J, Fernandez Pereira C, et al. Five-year follow-up of the Argentine randomized trial of coronary angioplasty with stenting versus coronary bypass surgery in patients with multiple vessel disease and significant proximal LAD stenosis: results from the ERACI II study. Heart. 2003;89(2):184-8. PMID: 12527674. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Rodriguez A, Mele E, Peyregne E, et al. Three-year follow-up of the Argentine Randomized Trial of Percutaneous Transluminal Coronary Angioplasty Versus Coronary Artery Bypass Surgery in Multivessel Disease (ERACI). J Am Coll Cardiol. 1996;27(5):1178-84. PMID: 8609339. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Ryan TJ. Present-day PTCR versus CABG: a randomized comparison with a different focus and a new result. J Am Coll Cardiol. 2001;59-62. PMID: 11153773. Exclude - Study type is not RCT, prospective or retrospective observational study, or registry.

Rymuza H, Kowalik I, Drzewiecki A, et al. Successful primary coronary angioplasty improves early and long-term outcomes in ST segment elevation acute coronary syndromes in patients above 80 years of age. Kardiol Pol. 2011;69(4):346-354. PMID: 21523668. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Sabatine MS, Morrow DA, McCabe CH, et al. Combination of quantitative ST deviation and troponin elevation provides independent prognostic and therapeutic information in unstable angina and non-ST-elevation myocardial infarction. Am Heart J. 2006;151(1):25-31. PMID: 16368287. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Salem M, Rotevatn S, Stavnes S, et al. Usefulness and safety of percutaneous myocardial laser revascularization for refractory angina pectoris. Am J Cardiol. 2004;93(9):1086-91. PMID: 15110197. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Saw J, Topol EJ, Steinhubl SR, et al. Comparison of long-term usefulness of clopidogrel therapy after the first percutaneous coronary intervention or coronary artery bypass grafting versus that after the second or repeat intervention. Am J Cardiol. 2004;94(5):623-5. PMID: 15342293. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Scheller B, Hennen B, Hammer B, et al. Beneficial effects of immediate stenting after thrombolysis in
from symptom onset: a randomized controlled trial.

Mechanical reperfusion in patients with acute myocardial infarction. J Am Coll Cardiol. 2003;42(4):634-41. PMID: 12932593. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Scholten O, van Kuijk JP, Flu WJ, et al. Long-term outcome of prophylactic coronary revascularization in cardiac high-risk patients undergoing major vascular surgery (from the randomized DECREASE-V Pilot Study). Am J Cardiol. 2009;103(7):897-901. PMID: 19327412. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Schroter S, Lamping DL. Responsiveness of the coronary revascularisation outcome questionnaire compared with the SF-36 and Seattle Angina Questionnaire. Qual Life Res. 2006;15(6):1069-78. PMID: 16900287. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Schwartz L, Kip KE, Alderman E, et al. Baseline coronary angiographic findings in the Bypass Angioplasty Revascularization Investigation 2 Diabetes trial (BARI 2D). Am J Cardiol. 2009;103(5):632-8. PMID: 19231325. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Schweiger MJ, Cannon CP, Murphy SA, et al. Early coronary intervention following pharmacologic therapy for acute myocardial infarction (the combined TIMI 10B-TIMI 14 experience). Am J Cardiol. 2001;88(8):831-6. PMID: 11676942. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

PMID: 20960541. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Sedlis SP, Jurkovitz CT, Hartigan PM, et al. Optimal medical therapy with or without percutaneous coronary intervention for patients with stable coronary artery disease and chronic kidney disease. Am J Cardiol. 2009;104(12):1647-53. PMID: 19962469. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Sedlis SP, Morrison DA, Lorin JD, et al. Percutaneous coronary intervention versus coronary bypass graft surgery for diabetic patients with unstable angina and risk factors for adverse outcomes with bypass: outcome of diabetic patients in the AWESOME randomized trial and registry. J Am Coll Cardiol. 2002;40(9):1555-66. PMID: 12427406. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Sedlis SP, Ramanathan KB, Morrison DA, et al. Outcome of percutaneous coronary intervention versus coronary bypass grafting for patients with low left ventricular ejection fractions, unstable angina pectoris, and risk factors for adverse outcomes with bypass (the AWESOME Randomized Trial and Registry). Am J Cardiol. 2004;94(1):118-20. PMID: 15219521. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Sejersten M, Birnbaum Y, Ripa RS, et al. Influences of electrocardiographic ischaemia grades and symptom duration on outcomes in patients with acute myocardial infarction treated with thrombolysis versus primary percutaneous coronary intervention: results from the DANAMI-2 trial. Heart. 2006;92(11):1577-82. PMID: 16740918. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Sejersten M, Ripa RS, Maynard C, et al. Usefulness of quantitative baseline ST-segment elevation for predicting outcomes after primary coronary angioplasty or fibrinolysis (results from the DANAMI-2 trial). Am J Cardiol. 2006;97(5):611-6. PMID: 16490423. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Selnes OA, Grega MA, Borowicz LM, Jr., et al. Cognitive changes with coronary artery disease: a prospective study of coronary artery bypass graft patients and nonsurgical controls. Ann Thorac Surg. 2003;75(5):1377-84; discussion 1384-6. PMID: 12735550. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Serruys PW, Ong AT, van Herwerden LA, et al. Five-year outcomes after coronary stenting versus bypass surgery for the treatment of multivessel disease: the final analysis of the Arterial Revascularization Therapies Study (ARTS) randomized trial. J Am Coll Cardiol. 2005;46(4):575-81. PMID: 16098418. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Serruys PW, Onuma Y, Garg S, et al. 5-year clinical outcomes of the ARTS II (Arterial Revascularization Therapies Study II) of the sirolimus-eluting stent in the treatment of patients with multivessel de novo coronary artery lesions. J Am Coll Cardiol. 2010;55(11):1093-101. PMID: 20171036. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI or stable CAD.


Serruys PW, Unger F, Sousa JE. Stents had similar clinical outcomes but more repeated revascularisation than did bypass surgery in multivessel disease. Evidence-Based Medicine. 2001;6(6):174. Exclude - Study type is not RCT, prospective or retrospective observational study, or registry.


Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Silva JC, Rochitte CE, Junior JS, et al. Late coronary artery recanalization effects on left ventricular remodelling and contractility by magnetic resonance imaging. Eur Heart J. 2005;26(1):36-43. PMID: 15615797. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Singh SM, Alter DA. Is routine early invasive management of non-ST-segment elevation myocardial infarction beneficial in elderly patients? CMAJ. 2004;171(9):1046-7. PMID: 15546173. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Sinkovic A, Marinsek M, Svensek F. Women and men with unstable angina and/or non-ST-elevation myocardial infarction. Wien Klin Wochenschr. 2006;118 Suppl 2(52):79-83. PMID: 16817045. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Sinkovic A, Pehnec Z. In-hospital mortality and treatment in elderly patients with ST-elevation myocardial infarction. Journal fur Kardiologie. 2005;12(1):282-284. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Sleeper LA, Reynolds HR, White HD, et al. A severity scoring system for risk assessment of patients with cardiogenic shock: a report from the SHOCK Trial and Registry. Am Heart J. 2010;160(3):443-50. PMID: 20826251. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Soares PR, Hueb WA, Lemos PA, et al. Coronary revascularization (surgical or percutaneous) decreases mortality after the first year in diabetic subjects but not in nondiabetic subjects with multivessel disease: an analysis from the Medicine, Angioplasty, or Surgery Study (MASS II). Circulation. 2006;114(1 Suppl):420-4. PMID: 16820611. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Solomon DH, Stone PH, Glynn RJ, et al. Use of risk stratification to identify patients with unstable angina likeliest to benefit from an invasive versus conservative management strategy. J Am Coll Cardiol. 2001;38(4):969-76. PMID: 11583866. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


multicenter randomized trial. The VINO Study. Eur Heart J. 2002;23(3):230-8. PMID: 11792138. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Steg PG, Bonnefoy E, Chabaud S, et al. Impact of time to treatment on mortality after prehospital fibrinolysis or primary angioplasty: data from the CAPTIM randomized clinical trial. Circulation. 2003;108(23):2851-6. PMID: 14623806. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Stroupe KT, Morrison DA, Hlatky MA, et al. Cost-effectiveness of coronary artery bypass grafts versus percutaneous coronary intervention for revascularization of high-risk patients. Circulation. 2006;114(12):1251-7. PMID: 16966588. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Sutton AG, Campbell PG, Graham R, et al. One year results of the Middlesbrough early revascularisation to limit infarction (MERLIN) trial. Heart. 2005;91(10):1330-7. PMID: 16162629. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Svensson L, Aasa M, Dellborg M, et al. Comparison of very early treatment with either fibrinolysis or percutaneous coronary intervention facilitated with
abciximab with respect to ST recovery and infarct-related artery epicardial flow in patients with acute ST-segment elevation myocardial infarction: the Swedish Early Decision (SWEDES) reperfusion trial. Am Heart J. 2006;151(4):798 e1-7. PMID: 16569536. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Swahn E. Invasive strategy among women with Non-ST-Elevation Acute Coronary Syndrome. ACC Cardiosource Review Journal. 2007;16(10):29-30. Exclude - Study type is not RCT, prospective or retrospective observational study, or registry.


Takiuti ME, Hueb W, Hiscock SB, et al. Quality of life after surgical myocardial revascularization, angioplasty or medical treatment. Arq Bras Cardiol. 2007;88(5):537-44. PMID: 17589628. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Teo KK, Sedlis SP, Boden WE, et al. Optimal medical therapy with or without percutaneous coronary intervention in older patients with stable coronary disease: a pre-specified subset analysis of the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive druG Evaluation) trial. J Am Coll Cardiol. 2009;54(14):1303-8. PMID: 19778673. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Teo KK, Sedlis SP, Boden WE, et al. Optimal Medical Therapy With or Without Percutaneous Coronary Intervention in Older Patients With Stable Coronary Disease. A Pre-Specified Subset Analysis of the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive druG Evaluation) Trial. J Am Coll Cardiol. 2009;54(14):1303-1308. PMID: 19778673. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Thiele H, Scholz M, Engelmann L, et al. ST-segment recovery and prognosis in patients with ST-elevation myocardial infarction reperfused by prehospital combination fibrinolysis, prehospital initiated facilitated percutaneous coronary intervention, or primary percutaneous coronary intervention. Am J Cardiol. 2006;98(9):1132-9. PMID: 17056313. *Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.*


Thune JJ, Hoefsten DE, Lindholm MG, et al. Simple risk stratification at admission to identify patients with reduced mortality from primary angioplasty. Circulation. 2005;112(13):2017-21. PMID: 16186438. *Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.*


Udelson JE, Pearte CA, Kimmelstiel CD, et al. The Occluded Artery Trial (OAT) Viability Ancillary Study (OAT-NUC): influence of infarct zone viability on left ventricular remodeling after percutaneous coronary intervention versus optimal medical therapy alone. Am Heart J. 2011;161(3):611-21. PMID: 21392619. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Valeur N, Clemmensen P, Saunamaki K, et al. The prognostic value of pre-discharge exercise testing after myocardial infarction treated with either primary PCI or fibrinolysis: a DANAMI-2 sub-study. Eur Heart J. 2005;26(2):119-27. PMID: 15618067. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


van Gaal WJ, Arnold JR, Testa L, et al. Myocardial injury following coronary artery surgery versus angioplasty (MICASA): a randomised trial using biochemical markers and cardiac magnetic resonance imaging. EuroIntervention. 2011;6(6):703-10. PMID: 21205592. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


van Stel HF, Buskens E. Comparison of the SF-6D and the EQ-5D in patients with coronary heart disease. Health Qual Life Outcomes. 2006;4(20. PMID: 16563170. Exclude - Does not include
outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Vanasse A, Courteau J, Niyonsenga T. Revascularization and cardioprotective drug treatment in myocardial infarction patients: how do they impact on patients’ survival when delivered as usual care. BMC Cardiovasc Disord. 2006;6(21). PMID: 16674817. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Vermeer F, Oude Ophuis AJ, vd Berg EJ, et al. Prospective randomised comparison between thrombolysis, rescue PTCA, and primary PTCA in patients with extensive myocardial infarction admitted to a hospital without PTCA facilities: a safety and feasibility study. Heart. 1999;82(4):426-31. PMID: 10490554. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Vrachatis AD, Alpert MA, Georgulas VP, et al. Comparative efficacy of primary angioplasty with stent implantation and thrombolysis in restoring basal coronary artery flow in acute ST segment elevation myocardial infarction: quantitative assessment using the corrected TIMI frame count. Angiology. 2001;52(3):161-6. PMID: 11269778. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Wahrborg P. Quality of life after coronary angioplasty or bypass surgery. 1-year follow-up in the Coronary Angioplasty versus Bypass Revascularization investigation (CABRI) trial. Eur Heart J. 1999;20(9):653-8. PMID: 10208785. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Wahrborg P, Booth JE, Clayton T, et al. Neuropsychological outcome after percutaneous coronary intervention or coronary artery bypass grafting: results from the Stent or Surgery (SoS) Trial. Circulation. 2004;110(22):3411-7. PMID: 15557380. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Ward HB, Kelly RF, Thottapurathu L, et al. Coronary artery bypass grafting is superior to percutaneous coronary intervention in prevention of perioperative myocardial infarctions during subsequent vascular surgery. Ann Thorac Surg. 2006;82(3):795-800; discussion 800-1. PMID: 16928485. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Waters D. Comparison of aggressive lipid lowering with Atorvastatin vs. Revascularization Treatments (AVERT) and conventional care for the reduction of ischemic events in patients with stable coronary artery disease. Cardiovasc Rev Rep. 2000;21(1):26-31. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

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Exclude - Does not include outcomes of interest.

Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Exclude - No data for OMT/PCI/CABG comparison of interest.

Exclude - Study type is not RCT, prospective or retrospective observational study, or registry.

Exclude - No data for OMT/PCI/CABG comparison of interest.

Exclude - No data for OMT/PCI/CABG comparison of interest.

Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.
Widimsky P, Budesinsky T, Vorac D, et al. Long distance transport for primary angioplasty vs immediate thrombolysis in acute myocardial infarction. Final results of the randomized national multicentre trial--PRAGUE-2. Eur Heart J. 2003;24(1):94-104. PMID: 12559941. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Widimsky P, Groch L, Zelizko M, et al. Multicentre randomized trial comparing transport to primary angioplasty vs immediate thrombolysis vs combined strategy for patients with acute myocardial infarction presenting to a community hospital without a catheterization laboratory. The PRAGUE study. Eur Heart J. 2000;21(10):823-31. PMID: 10781354. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Widimsky P, Motovska Z, Simek S, et al. Clopidogrel pre-treatment in stable angina: for all patients > 6 h before elective coronary angiography or only for angiographically selected patients a few minutes before PCI? A randomized multicentre trial PRAGUE-8. Eur Heart J. 2008;29(12):1495-503. PMID: 18441320. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Yan AT, Yan RT, Cantor WJ, et al. Relationship between risk stratification at admission and treatment effects of early invasive management following fibrinolysis: Insights from the Trial of Routine ANgioplasty and Stenting after Fibrinolysis to Enhance Reperfusion in Acute Myocardial Infarction (TRANSFER-AMI). Eur Heart J. 2011;32(16):1994-2002. PMID: 21307037. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Yang SS, Li WM, Yin LL, et al. [Chronic effects of percutaneous transmyocardial laser revascularization in patients with refractory angina]. Zhonghua Xin Xue Guan Bing Za Zhi. 2007;51(4):1848-55. PMID: 19713656. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Yousef ZR, Redwood SR, Bucknall CA, et al. Late intervention after anterior myocardial infarction: effects on left ventricular size, function, quality of life, and exercise tolerance: results of the Open Artery Trial (TOAT Study). J Am Coll Cardiol. 2002;405;5;869-76. PMID: 12225709. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Zeymer U, Schroder R, Machnig T, et al. Primary percutaneous transluminal coronary angioplasty accelerates early myocardial reperfusion compared to thrombolytic therapy in patients with acute
myocardial infarction. Am Heart J. 2003;146(4):686-91. PMID: 14564324. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


Zhang Z, Mahoney EM, Spertus JA, et al. The impact of age on outcomes after coronary artery bypass surgery versus stent-assisted percutaneous coronary intervention: one-year results from the Stent or Surgery (SoS) trial. Am Heart J. 2006;152(6):1153-60. PMID: 17161069. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Zhang Z, Spertus JA, Mahoney EM, et al. The impact of acute coronary syndrome on clinical, economic, and cardiac-specific health status after coronary artery bypass surgery versus stent-assisted percutaneous coronary intervention: 1-year results from the stent or surgery (SoS) trial. Am Heart J. 2005;150(1):175-81. PMID: 16084166. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Zhao XQ, Kosinski AS, Barnhart HX, et al. Prediction of native coronary artery disease progression following PTCA or CABG in the Emory Angioplasty Versus Surgery Trial. Med Sci Monit. 2003;9(2):CR48-54. PMID: 12601286. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Ziegelstein RC, Hilbe JM, French WJ, et al. Magnesium use in the treatment of acute myocardial infarction in the United States (observations from the Second National Registry of Myocardial Infarction). Am J Cardiol. 2001;87(1):7-10. PMID: 11137825. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.


10547403. Exclude - Does not include outcome data reported in a gender-specific fashion for a study population that includes women 18 or older with angiographically proven CAD w/ STEMI, NSTEMI, or stable CAD.

Zijlstra F, Patel A, Jones M, et al. Clinical characteristics and outcome of patients with early (<2 h), intermediate (2-4 h) and late (>4 h) presentation treated by primary coronary angioplasty or thrombolytic therapy for acute myocardial infarction. Eur Heart J. 2002;23(7):550-7. PMID: 11922645.

Exclude - Study type is not RCT, prospective or retrospective observational study, or registry.


Exclude - No data for OMT/PCI/CABG comparison of interest.
## Appendix F. Summary Tables for Sex-Specific Clinical Outcomes

### Table F-1. Summary of RCTs reporting clinical outcomes for STEMI (KQ 1)

<table>
<thead>
<tr>
<th>Study Author/Year Related Articles</th>
<th>Population</th>
<th>Comparison</th>
<th># Subjects</th>
<th>Outcomes</th>
<th>Quality</th>
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<tr>
<td>CARESS-in-AMI Di Mario et al., 2008&lt;sup&gt;1&lt;/sup&gt; and Di Mario et al., 2004&lt;sup&gt;2&lt;/sup&gt;</td>
<td>STEMI</td>
<td>Fibrinolysis (reteplase) plus immediate PCI vs. fibrinolysis (reteplase) plus rescue PCI</td>
<td>Total: 600 Women: 128 (21%)</td>
<td>1) Composite outcome (total mortality/reinfarction/refractory MI within 30 days) HR (95%CI) Women: 0.4 (0.12 to 1.31) Men: 0.39 (0.18 to 0.85) Overall: 0.40 (0.21 to 0.76) 2) Cumulative event rate (total mortality/reinfarction/refractory MI within 30 days) Women: 6.2 vs. 14.5 Men: 3.9 vs. 9.7 Overall: 4.4 vs. 10.7</td>
<td>Good</td>
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<td>Study Author/Year Related Articles</td>
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<td>DANAMI-2 Andersen et al., 2003 and Mortensen et al., 2007</td>
<td>STEMI</td>
<td>Primary PCI vs. fibrinolysis (accelerated t-PA)</td>
<td>Total: 1,572 Women: 417 (27%)</td>
<td>1) Composite outcome (total mortality/nonfatal MI/stroke) 30 days OR (95% CI) Women: 0.47 (0.27 to 0.81) Men: 0.59 (0.39 to 0.90) Overall: 0.55 (0.39 to 0.76) 3 years HR (95% CI) Women: 0.62 (0.42 to 0.90) Men: 0.81 (0.63 to 1.04) Overall: 0.74 (0.60 to 0.92) Median 7.8 years HR (95% CI) Women: 0.73 (0.53 to 0.99) Men: 0.80 (0.66 to 0.97) Overall: 0.78 (0.66 to 0.92) 2) Angina (angina/recurrent symptoms/refractory angina/refractory MI) 30 days Women: 25.3% vs. 30.7% Men: 18.8% vs. 26.4% 1 year Women: 18.5% vs. 21.3% Men: 15.5% vs. 17.6% 3) General health SF-36 30 days Women: 62 vs. 61.1 Men: 69.2 vs. 65.1 1 year Women: 61.5 vs. 66.4 Men: 68.2 vs. 63.1</td>
<td>Good</td>
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<td>Study Author/Year Related Articles</td>
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<tr>
<td>Dobrzycki et al., 2007&lt;sup&gt;8&lt;/sup&gt;</td>
<td>STEMI</td>
<td>Fibrinolysis (streptokinase) onsite vs. tirofiban plus transfer for primary PCI</td>
<td>Total: 401 Women: 105 (26%)</td>
<td>1) Composite outcome (total mortality/nonfatal MI/stroke): 30 days RR (95% CI) Women: 2.04 (0.85 to 4.90) Men: 1.79 (0.85 to 3.79) Overall: 1.95 (1.1 to 3.45) 1 year Women: 2.48 (1.06 to 5.79) Men: 1.61 (0.92 to 2.85) Overall: 1.88 (1.18 to 3.00) 2) Total mortality 30 days RR (95% CI) Women: 2.19 (0.73 to 6.53) Men: 1.41 (0.50 to 3.96) Overall: 1.81 (0.86 to 3.82) 1 year Women: 2.41 (0.82 to 7.07) Men: 1.48 (0.68 to 3.22) Overall: 1.79 (0.96 to 3.35)</td>
<td>Good</td>
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<tr>
<td>GUSTO II-B Tamis-Holland et al., 2004&lt;sup&gt;9&lt;/sup&gt;</td>
<td>STEMI</td>
<td>PCI vs. fibrinolysis (accelerated t-PA)</td>
<td>Total: 1,137 Women: 260 (23%)</td>
<td>1) Composite outcome (30-day): (total mortality/nonfatal MI/nonfatal disabling stroke) OR (95% CI) Women: 0.685 (0.36 to 1.32) Men: 0.562 (0.35 to 0.91) Overall: 0.67 (0.47 to 0.97) 2) Total mortality (30-day) Women: 10.9% vs. 11.6% Men: 4% vs. 5.8% 3) Nonfatal MI (30-day): Women: 6.5% vs. 6.6% Men: 3.8% vs. 6.4% 4) Nonfatal disabling stroke (30-day): Women: 0 vs. 2.5% Men: 0.2% vs. 0.4%</td>
<td>Good</td>
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<td>Study Author/Year Related Articles</td>
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<td><strong>Minai et al., 2002</strong>&lt;sup&gt;10&lt;/sup&gt;</td>
<td>STEMI age ≥ 80 years</td>
<td>PCI vs. conservative/supportive medical therapy (without fibrinolysis)</td>
<td>Total: 120 Women: 60 (50%)</td>
<td>Composite outcome (total mortality/heart failure/repeat MI/stroke) 3 years 46 of the PCI subjects vs. 31 of the no PCI subjects; p = 0.06 Multivariate analysis was done to look at factors associated with the composite endpoint in the overall study (i.e., not treatment specific) and found that male gender was NOT a factor significantly associated with outcome in the overall population.</td>
<td>Fair</td>
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<td><strong>PAMI Stone et al., 1995</strong>&lt;sup&gt;11&lt;/sup&gt;</td>
<td>STEMI</td>
<td>PCI vs. fibrinolysis (t-PA)</td>
<td>Total: 395 Women: 107 (27%)</td>
<td>1) In-hospital death or reinfarction Women: 6% vs. 17.5%; p = 0.07 Men: 4.8% vs. 9.8%; p = 0.11 Overall: 5.1% vs. 12%; p = 0.02 2) In-hospital total mortality Women: 4.0% vs. 14%; p = 0.07 Men: 2.1% vs. 3.5%; p = 0.46 3) In-hospital nonfatal MI Women: 2.0% vs. 3.5%; p = 0.64 Men: 2.8% vs. 7.7%; p = 0.06 4) In-hospital recurrent ischemia Women: 16% vs. 28.1%; p = 0.14 Men: 8.2% vs. 28%; p = 0.001 5) In-hospital stroke Women: 0 vs. 5.3%; p = 0.10 Men: 0 vs. 2.8%; (p = 0.04 6) Length of stay Women: 7.8 ± 3.4 days vs. 8.5 ± 4.1 days; p = 0.34 Men: 7.4 ± 3.3 days vs. 8.3 ± 4.8 days; p = 0.05</td>
<td>Good</td>
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<td>Study Author/Year Related Articles</td>
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<td>SHOCK Hochman et al., 2001&lt;sup&gt;12&lt;/sup&gt; and Hochman et al., 2006&lt;sup&gt;13&lt;/sup&gt; Hochman et al., 1999&lt;sup&gt;14&lt;/sup&gt; Hochman et al., 1999&lt;sup&gt;15&lt;/sup&gt;</td>
<td>STEMI</td>
<td>Early revascularization (PCI or CABG within 6 hours) vs. initial medical stabilization (thrombolysis, IABP)</td>
<td>Total: 302 Women: 97 (32%)</td>
<td>Relative risk (95% CI) for death at 1 year with early revascularization vs. initial medical stabilization: 0.72 (0.54 to 0.95) There was no interaction between treatment effect and sex.</td>
<td>Good</td>
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Abbreviations: BMS = bare metal stent; CABG = coronary artery bypass graft; CAD = coronary artery disease; CI = confidence interval; DES = drug-eluting stent; HR = hazard ratio; IABP = intra-aortic balloon pump; MI = myocardial infarction; NSTEMI = non-ST elevation myocardial infarction; OR = odds ratio; PCI = percutaneous coronary intervention; PTCA = percutaneous transluminal coronary angioplasty; RCT = randomized controlled trial; RR = relative risk; UA = unstable angina
Table F-2. Summary of RCTs reporting clinical outcomes for UA/NSTEMI (KQ 2)

<table>
<thead>
<tr>
<th>Study Author/Year Related Articles</th>
<th>Population</th>
<th>Comparison</th>
<th># Subjects</th>
<th>Outcomes</th>
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<tr>
<td>FRISC II Lagerqvist et al., 2001\textsuperscript{16} \textit{and} Lagerqvist et al., 2006\textsuperscript{17} Wallentin et al., 2000\textsuperscript{18} Anonymous, 1999\textsuperscript{19}</td>
<td>UA/NSTEMI</td>
<td>Early invasive treatment with revascularization vs. initial conservative strategy</td>
<td>Total: 2,457 Women: 749 (30%)</td>
<td>Primary endpoint (death/MI or both) 6 months RR (95% CI) Invasive vs. conservative Women: 1.26 (0.80 to 1.97) Men: 0.64 (0.49 to 0.84) Overall: 0.78 (0.62 to 0.98); ( p = 0.031 ) 1 year Women: 12.4% vs. 10.5%; ( p = ) not significant Men: 9.6% vs. 15.8%; ( p &lt; 0.001 ) Overall: 0.74 (0.60 to 0.92); ( p = 0.005 ) Interaction by sex: ( p = 0.008 ) (significant) OR (95% CI) 0.91 (0.68 to 1.22) for effect of women on primary endpoint adjusted for treatment group Women did not benefit from early invasive strategy partly because of higher mortality related to CABG. 5 years OR (95% CI) Women: 1.12 (0.83 to 1.50) Men: 0.70 (0.59 to 0.86) Overall: 0.81 (0.69 to 0.95); ( p = 0.009 ) Interaction by sex ( p = 0.010 ) (significant)</td>
<td>Good</td>
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<td>GUSTO IV-ACS Ottervanger et al., 2004\textsuperscript{20}</td>
<td>NSTEMI Acute coronary syndrome</td>
<td>Revascularization within 30 days (early invasive) vs. initial conservative strategy</td>
<td>Total: 7,800 Women: 2896 (37%)</td>
<td>Death, 1 year Women: adjusted HR (95% CI) 0.53 (0.28 to 1.00) Men: adjusted HR (95% CI) 0.55 (0.35 to 0.85) Overall: adjusted RR (95% CI) 0.53 (0.37 to 0.77)</td>
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| ICTUS de Winter et al., 2005\(^{21}\) and Damman et al., 2010\(^{22}\) | NSTEMI-acute coronary syndrome | Early invasive therapy with revascularization vs. selective invasive strategy (initial conservative) | Total: 1,200 Women: 320 (27%) | 1) Death/MI/rehospitalization for angina 1 year  
Early invasive vs. selective  
Total: RR (95% CI) 1.07 (0.87 to 1.33); p = 0.33  
No significant difference among sex groups  
2) Death/spontaneous MI  
5 years HR (95% CI)  
Women: 0.87 (0.53 to 1.43); p = 0.59  
Men: 1.22 (0.87 to 1.71); p = 0.24  
Overall: 1.10 (0.83 to 1.45); p = 0.52 | Good |
| RITA-2 Anonymous, 1997\(^{23}\) | UA/stable CAD (no recent MI) | Early invasive therapy with PCI (PTCA) vs. initial conservative | Total: 1,018 Women: 183 (8%) | 1) Death/MI  
**Median followup of 2.7 years**  
PTCA vs. optimal medical therapy  
Total: RR (95% CI) 1.92 (1.08 to 3.41); p = 0.02  
No significant interaction by sex  
2) Secondary outcomes  
**Angina grade 2+ at 6 months**  
Women: 22.8% vs. 39.8%  
Men: 20.5% vs. 31.4%  
3) Exercise time  
**6 months mean (SE)**  
Women: 6.72 (0.25) vs. 6.52 (0.26);  
Men: 9.34 (0.13) vs. 8.90 (0.15) | Fair |
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<th>Study Author/Year Related Articles</th>
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<tr>
<td>RITA-3 Clayton et al., 2004\textsuperscript{24} and Fox et al., 2002\textsuperscript{25}</td>
<td>UA/NSTEMI</td>
<td>Early invasive (PCI) vs. initial conservative</td>
<td>Total: 1,810 Women: 682 (38%)</td>
<td>1) Primary outcome (death/MI/refractory angina) Early invasive vs. initial conservative 4 months Women: 10.9% vs. 9.6% (similar) Men: 8.8% vs. 17.3% Overall: 9.6% vs. 14.5% p = 0.001 RR (95% CI) 0.66 (0.51 to 0.85) Significant interaction by sex: p = 0.004 1 year Women: adjusted OR (95% CI) 1.14 (0.74 to 1.76) Men: adjusted OR (95% CI) 0.48 (0.34 to 0.67) Overall: RR (95% CI) 0.72 (0.58 to 0.90); p = 0.003 2) Secondary outcomes (death/MI) Early invasive vs. initial conservative 1 year Women: adjusted OR (95% CI) 1.79 (0.95 to 3.35) Men: adjusted OR (95% CI) 0.63 (0.41 to 0.98) Overall: RR (95% CI) 0.91 (0.67 to 1.25); p = 0.58 3) Death 1 year Women: adjusted OR (95% CI) 2.43 (1.01 to 5.84) Men: adjusted OR (95% CI) 0.78 (0.44 to 1.41) Overall: RR (95% CI) 1.16 (0.75 to 1.80); p = 0.50 Significant interaction by sex for all 3 outcomes 4) Risk stratification by TIMI risk score (death/MI/refractory angina) Early invasive vs. initial conservative Low risk Women: 2.3% vs. 3.8% Men: 6.1% vs. 5.1% Moderate risk Women: 13.4% vs. 3.4% Men: 5.4% vs. 9.5%</td>
<td>Good</td>
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<td>Study Author/Year</td>
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<td><strong>RITA-3 (continued)</strong></td>
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<td><strong>High risk</strong></td>
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<td>Women: 11.7% vs. 8.2%</td>
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<td>Men: 10.3% vs. 17.9%</td>
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<td><strong>Women in moderate- or high-risk TIMI groups had higher event rate in early invasive arm</strong></td>
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<td><strong>Men in moderate- or high-risk TIMI groups had benefit from early invasive therapy</strong></td>
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<td><strong>TACTICS TIMI-18</strong></td>
<td>UA./NSTEMI</td>
<td>Early invasive (PCI) vs. initial conservative</td>
<td>Total: 2,220 Women: 757 (34%)</td>
<td>1) Primary endpoint (death/MI/rehospitalization for acute coronary syndrome) Early invasive vs. initial conservative <strong>6 months</strong> Adjusted OR (95% CI) Women: 0.72 (0.47 to 1.11) Men: 0.64 (0.47 to 0.88) Overall: 0.78 (0.62 to 0.97) 2) Secondary outcomes (death/MI) Early invasive vs. initial conservative <strong>6 months</strong> Adjusted OR (95% CI) Women: 0.45 (0.24 to 0.88) Men: 0.68 (0.43 to 1.05) Overall: 0.74 (0.54 to 1.00); p &lt; 0.05 3) Death Early invasive vs. initial conservative <strong>6 months</strong> Adjusted OR (95% CI) Women: 0.94 (0.37 to 2.44) Men: 0.75 (0.36 to 1.56) Women less likely to undergo CABG even after adjustment for 3-vessel and left main disease</td>
<td>Good</td>
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<td>Study Author/Year Related Articles</td>
<td>Population</td>
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<td>TIMI III-B Anonymous, 1994&lt;sup&gt;29&lt;/sup&gt; and Anderson et al., 1995&lt;sup&gt;30&lt;/sup&gt;</td>
<td>UA/NSTEMI</td>
<td>Early invasive vs. initial conservative</td>
<td>Total: 1,425 Women: 497 (35%)</td>
<td>1) Primary endpoint (death/MI/failed symptom-limited exercise treadmill test) 6 weeks Overall: 16.2% vs. 18.1%; p = 0.33 2) Secondary outcomes (death/MI) Early invasive vs. initial conservative 6 weeks Women: 6.1% vs. 8.9%; p = 0.24 Men: 7.8% vs. 7.3%; p = 0.73 1 year Women: 9.7% vs. 15.4%; p = 0.06 Men: 11.3% vs. 10.6%; p = 0.68 Overall: 10.8% vs. 12.2%; p = 0.42 No interaction by sex</td>
<td>Good</td>
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</table>

Abbreviations: CABG = coronary artery bypass graft; CAD = coronary artery disease; CI = confidence interval; HR = hazard ratio; MI = myocardial infarction; NSTEMI = non-ST elevation myocardial infarction; OR = odds ratio; PCI = percutaneous coronary intervention; PTCA = percutaneous transluminal coronary angioplasty; RCT = randomized controlled trial; RR = risk ratio; SD = standard deviation; SE = standard error; t-PA = tissue plasminogen activator; UA = unstable angina
Table F-3. Summary of RCTs reporting clinical outcomes for stable angina (KQ 3 Strategy 1—revascularization vs. optimal medical therapy)

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<th>Study Author/Year Related Articles</th>
<th>Population</th>
<th>Comparison</th>
<th># Subjects</th>
<th>Outcomes</th>
<th>Quality</th>
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<tr>
<td>Allen et al., 2004 and Allen et al., 1999</td>
<td>Stable angina</td>
<td>Surgical revascularization (CABG with transmyocardial revascularization) vs. optimal medical therapy</td>
<td>Total: 222 Women: 61 (27%)</td>
<td>1) Death 5.7 years (SD 0.8) Men: OR (95% CI) 1.4 (0.4 to 5.0); p = 0.63 2) Angina relief 5.7 years (SD 0.8) Men: OR (95% CI) 1.1 (0.7 to 1.8); p = 0.41</td>
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<td>COURAGE Boden et al., 2007 and Mancini et al., 2009 Boden et al., 2006</td>
<td>Stable angina</td>
<td>PCI (type not specified) or CABG if PCI failed vs. optimal medical therapy</td>
<td>Total: 2,287 Women: 338 (15%)</td>
<td>1) Death/MI 4.6 years (median followup) PCI vs. optimal medical therapy: Women: 18% vs. 26% Men: 19% vs. 18% p = 0.03 Women: HR (95% CI) 0.65 (0.40 to 1.06) Men: HR (95% CI) 1.15 (0.93 to 1.42) Overall: HR (95% CI) 1.05 (0.87 to 1.27)</td>
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<td>Study Author/Year Related Articles</td>
<td>Population</td>
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<td><strong>MASS II</strong> Hueb et al., 2010&lt;sup&gt;36&lt;/sup&gt; and Hueb et al., 2004&lt;sup&gt;37&lt;/sup&gt; Hueb et al., 2007&lt;sup&gt;38&lt;/sup&gt;</td>
<td>Stable angina with multiple-vessel CAD</td>
<td>PCI vs. Optimal medical therapy CABG vs. optimal medical therapy</td>
<td>Total: 611 Women: 196 (32%)</td>
<td>Primary endpoint (death/MI/angina requiring mechanical revascularization) <strong>10 years</strong> Adjusted HR (95% CI) Women: Optimal medical therapy vs. PCI: 1.57 (1.01 to 2.46); p = 0.047 (favoring PCI) CABG vs. optimal medical therapy: 0.43 (0.26 to 0.72); p = 0.001 Men: Optimal medical therapy vs. PCI: 1.13 (0.84 to 1.53); p = 0.410 CABG vs. optimal medical therapy: 0.43 (0.31 to 0.60); p = 0.001 Overall: PCI vs. optimal medical therapy: 0.79 (0.62-1.01) CABG vs. optimal medical therapy: 0.43 (0.32 to 0.58) p &lt; 0.001</td>
<td>Good</td>
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<td>Study Author/Year Related Articles</td>
<td>Population</td>
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<td><strong>OAT</strong> Hochman et al., 2006(^{39}) and Hochman et al., 2005(^{40}) Hochman et al., 2011(^{41})</td>
<td>Stable angina</td>
<td>PCI (or CABG if PCI failed) vs. optimal medical therapy</td>
<td>Total: 2,166 Women: 476 (22%)</td>
<td>Primary endpoint (death/MI/heart failure) 4 years PCI vs. optimal medical therapy: Women: 18.3% vs. 22.9% Men: 16.8% vs. 13.5% p = 0.13 Women: HR &lt; 1.0 (favoring PCI, but not significant) Men: HR &gt; 1.0 (favoring optimal medical therapy, but not significant) Overall: HR 0.43 (0.32 to 0.56)</td>
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<td><strong>STICH</strong> Velazquez et al., 2011(^{42}) and Velazquez et al., 2007(^{43})</td>
<td>Stable angina</td>
<td>CABG vs. optimal medical therapy</td>
<td>Total: 1,212 Women: 148 (12%)</td>
<td>Death 5 years HR (95% CI) Women: 0.75 (0.42 to 1.31) Men: 0.87 (0.72 to 1.06) Overall: 0.86 (0.72 to 1.04) p = 0.61</td>
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Abbreviations: BMS = bare metal stent; CABG = coronary artery bypass graft; CAD = coronary artery disease; CI = confidence interval; DES = drug-eluting stent; HR = hazard ratio; MI = myocardial infarction; NSTEMI = non-ST elevation myocardial infarction; OR = odds ratio; PCI = percutaneous coronary intervention; PTCA = percutaneous transluminal coronary angioplasty; RCT = randomized controlled trial; SD = standard deviation; UA = unstable angina
**Table F-4. Summary of RCTs reporting clinical outcomes for stable/unstable angina (KQ 3 Strategy 2–PCI vs. CABG)**

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<th>Study Author/Year Related Articles</th>
<th>Population</th>
<th>Comparison</th>
<th># Subjects</th>
<th>Outcomes</th>
<th>Quality</th>
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</table>
| ARTS I                            | Unstable angina | PCI (BMS) vs. CABG | Total: 1,205 Women: 283 (23%) | 1) Composite outcome (death/CVA/MI/CABG/repeat PCI)  
30 days  
Women: PCI 13.0% vs. CABG 8.3%  
Men: PCI 8.0% vs. CABG 5.7%  
1 year  
Women: PCI 29.0% vs. CABG 14.5%  
Men: PCI 25.8% vs. CABG 10.7%  
3 years  
Women: PCI 35.5% vs. CABG 19.3%  
Men: PCI 33.5% vs. CABG 15.1%  
2) Composite death/CVA  
30 days  
Women: PCI 4.3% vs. CABG 4.8%  
Men: PCI 1.9% vs. CABG 1.5%  
1 year  
Women: PCI 8.0% vs. CABG 7.6%  
Men: PCI 3.5% vs. CABG 3.5%  
3 years  
Women: PCI 10.9% vs. CABG 9.7%  
Men: PCI 5.8% vs. 5.9% | Good |
<p>| Vaina et al., 2009 and van den Brand, et al., 2002 |  |  |  | | |
| Serruys et al., 1999 and Voudris et al., 2006 |  |  |  | | |
| Anonymous, 1999 |  |  |  | | |</p>
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<th>Study Author/Year Related Articles</th>
<th>Population</th>
<th>Comparison</th>
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<td>ARTS I (continued)</td>
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<td>3) Composite death/MI/CVA</td>
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<td>30 days</td>
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<td>Women: PCI 7.2% vs. 6.9%</td>
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<td>Men: PCI 4.5% vs. 5.0%</td>
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<td>Women: PCI 11.6% vs. 11.0%</td>
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<td>Men: PCI 8.9% vs. CABG 7.0%</td>
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<td>Women: PCI 14.5% vs. CABG 14.5%</td>
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<td>Men: PCI 12.3% vs. CABG 9.6%</td>
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<td>4) Death—5 years</td>
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<td>PCI: women 7.4% vs. men 9.0%; p = 0.29</td>
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<td>C:ABG: women 7.2% vs. men 10.1%; p = 0.48</td>
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<td>PCI: OR (95% CI) 1.1 (0.5 to 2.8); p = 0.86</td>
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<td>C:ABG: OR (95% CI) 1.4 (0.5 to 4.1); p = 0.54</td>
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<td>5) MI—5 years</td>
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<td>PCI: OR (95% CI) 1.4 (0.7 to 3.2); p = 0.44</td>
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<td>C:ABG: OR (95% CI) 0.6 (0.3 to 1.3); p = 0.17</td>
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<td>6) CVA—5 years</td>
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<td>PCI: OR (95% CI) 0.8 (0.3 to 2.2); p = 0.58</td>
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<td>C:ABG: OR (95% CI) 0.6 (0.3 to 1.9); p = 0.39</td>
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<td>7) Revascularization—5 years</td>
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<td>PCI: OR (95% CI) 1.0 (0.6 to 1.5); p = 0.92</td>
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<td>C:ABG: OR (95% CI) 0.7 (0.4 to 1.4); p = 0.32</td>
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<td>ARTS I (continued)</td>
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<td>8) Composite death/MI/CVA</td>
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<td>Men vs. women</td>
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<td>PCI: OR (95% CI) 1.2 (0.7 to 1.2); p = 0.57</td>
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<td>C:ABG: OR (95% CI) 0.8 (0.5 to 1.5); p = 0.57</td>
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<td>9) Composite MI/CVA/PTCA</td>
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<td>Men vs. women</td>
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<td>PCI: OR (95% CI) 0.9 (0.6 to 1.4); p = 0.77</td>
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<td>C:ABG: OR (95% CI) 0.8 (0.5 to 1.3); p = 0.38</td>
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<td>Study Author/Year Related Articles</td>
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<td>10) In-hospital outcomes</td>
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<td>PCI: OR 95% CI 0.6 (0.3 to 1.2); p = 0.14</td>
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<td>CABG: OR 95%CI 1.8 (0.7 to 6.2); p = 0.29</td>
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<td>11) In-hospital MI</td>
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<td>PCI: OR 95% CI 0.7 (0.2 to 2.6); p = 0.58</td>
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<td>CABG: OR 95%CI 1.2 (0.4 to 4.3); p = 0.72</td>
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<td>12) In-hospital CVA</td>
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<td>PCI: OR 95% CI 0.6 (0.1 to 12.5); p = 0.65</td>
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<td>CABG: OR 95%CI 1.8 (0.3 to 34.9); p = 0.57</td>
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<td>13) Quality of life—3 years</td>
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<td>Euro-QoL summary:</td>
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<td>PCI: Men 86 ± 16 vs. women 83 ± 19</td>
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<td>P = 0.08</td>
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<td>CABG: Men 86 ± 20 vs. women 82 ± 20</td>
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<td>P = 0.02</td>
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<td>14) Composite outcome</td>
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<td>PCI: OR (95%CI) 0.9 (0.6 to 1.4); p = 0.77</td>
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<td>CABG: OR (95%CI) 0.8 (0.5 to 1.3) p = 0.38</td>
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<td>Study Author/Year Related Articles</td>
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<td>ARTS I (continued)</td>
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<td>15) Individual outcomes</td>
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<td>Death:</td>
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<td>Women: PCI 2.9% vs. CABG 4.1%</td>
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<td>Men: PCI 1.3% vs. CABG 0.4%</td>
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<td>CVA:</td>
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<td>Women: PCI 2.2% vs. CABG 0.7%</td>
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<td>Men: PCI 0.6% vs. CABG 1.1%</td>
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<td>Women: PCI 3.6% vs. CABG 4.1%</td>
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<td>Men: PCI 3.2% vs. CABG 3.7%</td>
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<td>Women: PCI 7.2% vs. CABG 1.4%</td>
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<td>Men: PCI 5.2% vs. CABG 0.7%</td>
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<td>Women: PCI 87.0% vs. CABG 91.7%</td>
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<td>Men: PCI 92.0% vs. CABG 94.3%</td>
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<td>Study Author/Year Related Articles</td>
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<td>Women: PCI 20.3% vs. CABG 4.1%</td>
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<td>Men: PCI 21.2% vs. CABG 4.2%</td>
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<td>Women: PCI 71.0% vs. CABG 85.5%</td>
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<td>Men: PCI 74.2% vs. CABG 89.3%</td>
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<td>Women: PCI 5.8% vs. CABG 7.6%</td>
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<td>Men: PCI 7.1% vs. CABG 4.2%</td>
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<td>Revascularization:</td>
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<td>Women: PCI 24.6% vs. CABG 6.2%</td>
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<td>Men: PCI 26.8% vs. CABG 6.6%</td>
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<td>Major cardiovascular adverse event- free survival:</td>
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<td>Women: PCI 64.5% vs. CABG 80.7%</td>
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<td>Men: PCI 66.5% vs. CABG 84.9%</td>
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<td>Study Author/Year Related Articles</td>
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<td><strong>BARI</strong></td>
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<td>1) 5-year cumulative survival rate</td>
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<td>Jacobs et al., 1998&lt;sup&gt;49&lt;/sup&gt;</td>
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<td>PCI (type not specified) vs. CABG</td>
<td>Total: 915</td>
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<td>Women: PCI 86.3% vs. CABG 89.3%</td>
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<td>Gibbons et al., 2001&lt;sup&gt;50&lt;/sup&gt;</td>
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<td>Men: PCI 86% vs. CABG 89%</td>
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<td>Anonymous, 2007&lt;sup&gt;51&lt;/sup&gt;</td>
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<td>Survival free of MI:</td>
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<td>Lombardero et al., 2002&lt;sup&gt;52&lt;/sup&gt;</td>
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<td>Women: PCI 74% vs. CABG 76%</td>
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<td>Anonymous, 2000&lt;sup&gt;53&lt;/sup&gt;</td>
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<td>In-hospital death: PCI 1.1% vs. CABG 1.3%</td>
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<td>Hlatky et al., 1995&lt;sup&gt;54&lt;/sup&gt;</td>
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<td>Women: PCI 0.8% vs. CABG 1.3%</td>
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<td>Rogers et al., 1995&lt;sup&gt;55&lt;/sup&gt;</td>
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<td>Men: PCI 1.2% vs. CABG 1.4%</td>
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<td>Sutton-Tyrrell et al., 1998&lt;sup&gt;56&lt;/sup&gt;</td>
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<td>Q-waves MI:</td>
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<td>Mullany et al., 1999&lt;sup&gt;57&lt;/sup&gt;</td>
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<td>Women : PCI 1.2% vs. CABG 4.7%</td>
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<td>Anonymous, 1996&lt;sup&gt;58&lt;/sup&gt;</td>
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<td>Men : PCI 2.4% vs. CABG 4.6%</td>
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<td>BARI (continued)</td>
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<td>Congestive heart failure:</td>
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<td>Women: PCI 4.8% vs. CABG 9.8%</td>
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<td>Men: PCI 1.4% vs. CABG 1.8%</td>
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<td>2) 7-year survival rate</td>
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<td>Women: PCI 79.2% vs. CABG 82.6%</td>
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<td>Men: PCI 81.6% vs. CABG 85.1%</td>
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<td>3) 10-year survival rate</td>
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<td>Women: PCI 70.2% vs. CABG 67.8%</td>
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<td>Men: PCI 71.3% vs. CABG 75.5%</td>
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<td>4) 4-year angina status</td>
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<td>Women: PCI 23.3% vs. CABG 18.8%</td>
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<td>Men: PCI 19.7% vs. CABG 13.2%</td>
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<td>At 5 years, anginal status was not significantly different between men and women</td>
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<td>5) Repeat revascularization</td>
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<td>CABG: Women RR 1.74 p = 0.043</td>
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<td>PCI: Women RR 0.74 p = 0.011</td>
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<td>Women were less likely than men to undergo repeat revascularization with an initial strategy of CABG compared with PTCA (11.2% vs. 51.9%, respectively; p &lt; 0.001)</td>
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<td>Study Author/Year Related Articles</td>
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<td><strong>CABRI</strong> Anonymous, 1995&lt;sup&gt;59&lt;/sup&gt;</td>
<td>Stable/unstable angina with multiple-vessel disease</td>
<td>PCI (PTCA) vs. CABG</td>
<td>Total: 1,054 Women: 234 (22%)</td>
<td>1) Primary endpoint of mortality, 1 year PTCA 3.9% vs. CABG 2.7% RR 95%CI 1.42 (0.731 to 2.74); p = 0.297 Women had higher risk of 1-year mortality RR (95% CI) 2.07 (1.07 to 4.01); p=0.031 2) Angina, 1 year PTCA 13.9% vs. CABG 10.1% RR (95% CI) 1.54 (1.09 to 2.16) Women: 3.12 (1.41 to 6.54) p = 0.002 Men: 1.25 (0.85 to 1.85); p = 0.256 3) Crude absolute risk of angina, 1 year PTCA Women: 0.214 Men: 0.131 CABG Women: 0.069 Men: 0.104</td>
<td>Good</td>
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<td><strong>CARDia</strong> Kapur et al., 2010&lt;sup&gt;60&lt;/sup&gt; and Kapur et al., 2005&lt;sup&gt;61&lt;/sup&gt;</td>
<td>UA/NSTEMI Stable angina Diabetic Multiple-vessel disease or complex single lesion</td>
<td>PCI (BMS or DES) vs. CABG</td>
<td>Total: 510 Women: 132 (26%)</td>
<td>1) Primary endpoint, 1 year (death/MI/stroke) HR (95%CI) Women: 2.13 (0.68 to 6.68) Men: 1.07 (0.59 to 1.93) Overall: 1.25 (0.75 to 2.09) 2) Secondary endpoint, 1 year (death/MI/stroke/repeat revascularization) HR (95%CI) Women: 2.4 (0.87 to 6.61) Men: 1.62 (0.95 to 2.74) Overall: 1.77 (1.11 to 2.09)</td>
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<td>Study Author/Year Related Articles</td>
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<td><strong>EAST</strong>&lt;br&gt;King et al., 2000(^{62})&lt;br&gt;and&lt;br&gt;King et al., 1995(^{63})&lt;br&gt;King et al., 1994(^{64})&lt;br&gt;Zhao et al., 1996(^{65})</td>
<td>Stable angina with multiple-vessel disease</td>
<td>PCI (type not specified) vs. CABG</td>
<td>Total: 392&lt;br&gt;Women: 103 (26%)</td>
<td>Single outcome survival&lt;br&gt;3 years&lt;br&gt;CABG 93.8% vs. PTCA 92.9%&lt;br&gt;8 years&lt;br&gt;CABG 82.7% vs. PTCA 79.3%&lt;br&gt;Comparisons were made for other baseline variables including sex, and no survival differences by treatment assignment were seen</td>
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<td><strong>GABI</strong>&lt;br&gt;Kaehler et al., 2005(^{66})&lt;br&gt;and&lt;br&gt;Hamm et al., 1994(^{67})</td>
<td>Stable angina</td>
<td>PCI (type not specified) vs. CABG</td>
<td>Total: 359&lt;br&gt;Women: 66 (18%)</td>
<td>Death&lt;br&gt;13 years&lt;br&gt;No significant sex differences in hazard ratio for death</td>
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<td><strong>MASS II</strong>&lt;br&gt;Hueb et al., 2010(^{36})&lt;br&gt;and&lt;br&gt;Hueb et al., 2004(^{37})&lt;br&gt;Hueb et al., 2007(^{38})</td>
<td>Stable angina with multiple-vessel coronary artery disease</td>
<td>PCI (type not specified) vs. CABG</td>
<td>Total: 611&lt;br&gt;Women: 196 (32%)</td>
<td>Primary endpoint&lt;br&gt;(death/MI/angina requiring mechanical revascularization)&lt;br&gt;10 years&lt;br&gt;Adjusted HR (95% CI)&lt;br&gt;Women:&lt;br&gt;CABG vs. PCI: 0.68 (0.40 to 1.15); p = 0.015&lt;br&gt;Men:&lt;br&gt;CABG vs. PCI: 0.49 (0.34 to 0.69); p = 0.001&lt;br&gt;Overall:&lt;br&gt;CABG vs. PCI: 0.53 (0.39 to 0.72); p &lt; 0.001</td>
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<td>Study Author/Year Related Articles</td>
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<tr>
<td>PRECOMBAT Park et al., 2011⁶⁸</td>
<td>Stable/unstable angina</td>
<td>PCI (DES) vs. CABG</td>
<td>Total: 600 Women: 141 (24%)</td>
<td>1) Composite endpoint, 1 year (death/MI/stroke/ischemia-driven target-vessel revascularization) PCI 8.7% vs. CABG 6.7% 2) Composite endpoint, 2 years PCI 12.2% vs. CABG 8.1% HR (95% CI) 1.50 (0.90 to 2.52); p = 0.12 Women: PCI 13.9% vs. CABG 11.7% HR (95% CI) 1.22 (0.48 to 3.08); p = 0.68 Men: PCI 11.7% vs. CABG 7.0% HR (95% CI) 1.65 (0.88 to 3.07); p = 0.12 Overall: HR 1.50 (0.90 to 2.52)</td>
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<td>Study Author/Year Related Articles</td>
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<td>SOS Zhang et al., 2004&lt;sup&gt;69&lt;/sup&gt; and Zhang et al., 2003&lt;sup&gt;70&lt;/sup&gt; Stables et al., 1999&lt;sup&gt;71&lt;/sup&gt;</td>
<td>Stable angina</td>
<td>PCI (BMS) vs. CABG</td>
<td>Total: 908 Women: 206 (23%)</td>
<td>1) Quality of life (adjusted relative difference of CABG vs. PCI) 6 months Women: 39.3 Men: 18.3 &lt;br&gt;1 year Women: 0.6 Men: 15.3 &lt;br&gt;2) Angina frequency (adjusted relative difference of CABG vs. PCI) 6 months Women: 43.2 Men: 31.3 &lt;br&gt;1 year Women: 11.1 Men: 19.7 &lt;br&gt;3) Physical limitation (adjusted relative difference of CABG vs. PCI) 6 months Women: 11.6 Men: 54.7 &lt;br&gt;1 year Women: 1.6 Men: 50.6</td>
<td>Fair</td>
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<td>SYNTAX Morice et al., 2010&lt;sup&gt;72&lt;/sup&gt;</td>
<td>Triple-vessel or left main coronary artery disease</td>
<td>PCI (type not specified) vs. CABG</td>
<td>Total: 705 Women: 185 (26%)</td>
<td>1) Primary endpoint, 1 year (death/MI/stroke/repeat revascularization) CABG vs. PCI 13.6% vs. 15.8% OR (95% CI) 2.1 (-3.2 to 7.4); p = 0.44 &lt;br&gt;2) Predictors of 1-year major adverse cardiovascular events OR (95% CI) Women: 0.50 (0.27 to 0.91); p = 0.02</td>
<td>Fair</td>
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</table>

Abbreviations: BMS = bare metal stent; CABG = coronary artery bypass graft; CAD = coronary artery disease; CI = confidence interval; CVA = cerebrovascular accident; DES = drug-eluting stent; HR = hazard ratio; MI = myocardial infarction; NSTEMI = non-ST elevation myocardial infarction; OR = odds ratio; PCI = percutaneous coronary intervention; PTCA = percutaneous transluminal coronary angioplasty; RCT = randomized controlled trial; UA = unstable angina


# Appendix G. Summary Table for Modifiers of Effectiveness

## Table G-1. Summary of RCTs reporting modifiers of effectiveness (subgroup analyses)

<table>
<thead>
<tr>
<th>Study Author/Year Related Articles</th>
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<th>Comparison</th>
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<th>Subgroup Analyses</th>
<th>Quality</th>
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<tr>
<td><strong>BARI</strong> Jacobs et al., 1998&lt;sup&gt;1&lt;/sup&gt; and Gibbons et al., 2007&lt;sup&gt;2&lt;/sup&gt; Anonymous, 2007&lt;sup&gt;3&lt;/sup&gt; Lombardero et al., 2002&lt;sup&gt;4&lt;/sup&gt; Anonymous, 2000&lt;sup&gt;5&lt;/sup&gt; Hlatky et al., 1995&lt;sup&gt;6&lt;/sup&gt; Rogers et al., 1995&lt;sup&gt;7&lt;/sup&gt; Sutton-Tyrrell et al., 1998&lt;sup&gt;8&lt;/sup&gt; Mullany et al., 1999&lt;sup&gt;9&lt;/sup&gt; Anonymous, 1996&lt;sup&gt;10&lt;/sup&gt;</td>
<td>Stable/unstable angina Diabetics</td>
<td>PCI vs. CABG</td>
<td>Total: 915 Women: 249 (27%)</td>
<td>7-year survival rates Women: PCI 61.0% vs. CABG 74.3% Men: PCI 51.5% vs. CABG 77.9%</td>
<td>Good</td>
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<td><strong>Minai et al., 2002&lt;sup&gt;11&lt;/sup&gt;</strong></td>
<td>STEMI age ≥ 80 years</td>
<td>PCI vs conservative/supportive therapy</td>
<td>Total: 120 Women: 60 (50%)</td>
<td>No difference in composite outcome (death/congestive heart failure/repeat MI/cerebrovascular accident at 3 years between treatment groups)</td>
<td>Fair</td>
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<td><strong>PAMI</strong> Stone et al., 1995&lt;sup&gt;12&lt;/sup&gt;</td>
<td>STEMI</td>
<td>PCI vs. fibrinolysis (t-PA)</td>
<td>Total: 395 Women: 107 (27%)</td>
<td>In-hospital mortality Women aged &lt;65: 0% vs. 4%; p = 0.42 Women aged ≥65: 5.9% vs. 21.9%; p = 0.58 Men aged &lt;65: 0.9% vs. 0%; p = 0.74 Men aged ≥65: 5.6% vs. 10.4%; p = 0.42</td>
<td>Good</td>
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<tr>
<td>Study Author/Year Related Articles</td>
<td>Population</td>
<td>Comparison</td>
<td># Subjects</td>
<td>Subgroup Analyses</td>
<td>Quality</td>
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<td>RITA-3 Clayton et al., 2004&lt;sup&gt;13&lt;/sup&gt; and Fox et al., 2002&lt;sup&gt;14&lt;/sup&gt;</td>
<td>UA/NSTEMI</td>
<td>Early invasive (PCI) vs. initial conservative</td>
<td>Total: 1,810  Women: 682 (38%)</td>
<td>Lower TIMI risk scores, both men and women had similar event rates in early invasive vs. initial conservative treatment arms.  In those with moderate to high risk, men had lower event rates in intervention arm compared with conservative arm while women had higher even rates in the intervention arm.  Moderate risk (women)  Invasive: 13.4%  Conservative: 3.4%  High risk (women)  Invasive: 11.7%  Conservative: 8.2%  Moderate risk (men)  Invasive: 5.4%  Conservative: 9.4%  High risk (men)  Invasive: 10.3%  Conservative: 17.9%  No benefit of intervention was seen in any BMI group for women.</td>
<td>Good</td>
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<td>TACTICS TIMI-18 Cannon et al., 2001&lt;sup&gt;15&lt;/sup&gt; and Glaser et al., 2002&lt;sup&gt;16&lt;/sup&gt; Cannon et al., 1998&lt;sup&gt;17&lt;/sup&gt;</td>
<td>UA/NSTEMI</td>
<td>Early invasive (PCI) vs. initial conservative</td>
<td>Total: 2,220  Women: 757 (34%)</td>
<td>Primary endpoint (death/MI/rehospitalization for acute coronary syndrome by risk)  Women with intermediate (3–4) and high (5–7) TIMI risk scores did not have significantly different outcomes in early invasive vs. initial conservative group.  OR (95% CI) 0.72 (0.45 to 1.16) vs. 0.56 (0.23 to 1.32)</td>
<td>Good</td>
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</table>

Abbreviations: BMS = bare metal stent; CABG = coronary artery bypass graft; CAD = coronary artery disease; CI = confidence interval; DES = drug-eluting stent; HCT = hematocrit; MI = myocardial infarction; NSTEMI = non-ST elevation myocardial infarction; OR = odds ratio; PCI = percutaneous coronary intervention; PTCA = percutaneous transluminal coronary angioplasty; RCT = randomized controlled trial; TIMI = thrombolysis in myocardial infarction; t-PA = tissue plasminogen activator; UA = unstable angina
References Cited in Appendix G


# Appendix H. Summary Table for Safety Concerns

## Table H-1. Summary of RCTs reporting safety concerns (harms)

<table>
<thead>
<tr>
<th>Study Author/Year Related Articles</th>
<th>Population</th>
<th>Comparison</th>
<th># Subjects</th>
<th>Harms</th>
<th>Quality</th>
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<td><strong>ARTS I</strong></td>
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<tr>
<td>Vaina et al., 2009¹</td>
<td>UA/NSTEMI</td>
<td>PCI vs. CABG</td>
<td>Total: 1,205</td>
<td>Major bleeding</td>
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<td>and van den Brand, et al., 2002²</td>
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<td>Serruys et al., 1999³</td>
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<td>Voudris et al., 2006⁴</td>
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<td>Anonymous, 1999⁵</td>
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<td><strong>GUSTO II-B</strong></td>
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<td>Tamis-Holland et al., 2004⁶</td>
<td>STEMI</td>
<td>PCI vs. fibrinolysis (accelerated t-PA)</td>
<td>Total: 1,137</td>
<td>Intracranial hemorrhage</td>
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<td><strong>PAMI</strong></td>
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<tr>
<td>Stone et al., 1995⁷</td>
<td>STEMI</td>
<td>PCI vs. fibrinolysis (t-PA)</td>
<td>Total: 395</td>
<td>Nadir HCT (PCI vs. fibrinolysis)</td>
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<tr>
<td><strong>TACTICS TIMI-18</strong></td>
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<tr>
<td>Cannon et al., 2001⁸</td>
<td>UA/NSTEMI</td>
<td>Early invasive vs. initial conservative</td>
<td>Total: 2,220</td>
<td>Bleeding in women undergoing PTCA was higher compared to men; adjusted OR (95% CI) 3.6 (1.6 to 8.3).</td>
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<td>and</td>
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<td>Glaser et al., 2002⁹</td>
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<td>Cannon et al., 1998¹⁰</td>
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</table>

**Abbreviations:** BMS = bare metal stent; CABG = coronary artery bypass graft; CAD = coronary artery disease; CI = confidence interval; DES = drug-eluting stent; HCT = hematocrit; NSTEMI = non-ST elevation myocardial infarction; OR = odds ratio; PCI = percutaneous coronary intervention; PTCA = percutaneous transluminal coronary angioplasty; RCT = randomized controlled trial; t-PA = tissue plasminogen activator; UA = unstable angina
References Cited in Appendix H


