

# ***AHRQ Comparative Effectiveness Review Surveillance Program***

## **CER #9:**

**Comparative Effectiveness of Percutaneous Coronary Interventions and Coronary Artery Bypass Grafting for Coronary Artery Disease**

## **Original release date:**

**October 2007**

## **Surveillance Report:**

**May 2013**

## **Key Findings:**

- New RCT and cohort studies further delineate which patients have improved outcomes when treated with CABG instead of PCI

## **Summary Decision**

This CER's priority for updating is **Medium**

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# **Comparative Effectiveness of Percutaneous Coronary Interventions and Coronary Artery Bypass Grafting for Coronary Artery Disease**

## **1. Introduction**

Comparative Effectiveness Review (CER) #9, Comparative Effectiveness of Percutaneous Coronary Interventions and Coronary Artery Bypass Grafting for Coronary Artery Disease, was released in October 2007.<sup>1</sup> An individual patient data meta-analysis was published in March 2009 and was considered by the CER program to be an update.<sup>2</sup> It was therefore due for a surveillance assessment in September 2009. When the Surveillance program began in Summer 2011 this CER was not part of the first wave of reports for surveillance and was added to our list a few months ago. At that time, we contacted experts involved in the original CER and subject experts to get their opinions as to whether the conclusions had changed and need to be updated. We also conducted an update electronic literature search.

## **2. Methods**

### **2.1 Literature Searches**

Using the search strategy employed for the original report, we conducted a limited literature search of Medline for the years January 1, 2006-January 23, 2013. This search included five high-profile general medical interest journals (Annals of Internal Medicine, British Medical Journal, Journal of the American Medical Association, Lancet, and the New England Journal of Medicine) and five specialty journals (American Journal of Cardiology, Annals of Thoracic Surgery, Catheterization and Cardiovascular Interventions, Circulation, and the Journal of the American College of Cardiology). The specialty journals were the most highly represented among the references for the original report. Appendix A includes the search methodology for this topic.

### **2.2 Study selection**

In general we used the same inclusion and exclusion criteria as the original CER.

### **2.3 Expert Opinion**

We shared the conclusions of the original report with 3 experts in the field (including the original project leader and local content experts) for their assessment of the need to update the report and their recommendations of any relevant new studies; 3 subject matter experts responded, including the project lead. Appendix C shows the questionnaire matrix that was sent to the experts.

## 2.4 Check for qualitative and quantitative signals

After abstracting the study conditions and findings for each new included study into an evidence table, we assessed whether the new findings provided a signal according to the Ottawa Method and/or the RAND Method, suggesting the need for an update. The criteria are listed in the table below.<sup>3,4</sup>

<b>Ottawa Method</b>	
<b>Ottawa Qualitative Criteria for Signals of Potentially Invalidating Changes in Evidence</b>	
A1	Opposing findings: A pivotal trial or systematic review (or guidelines) including at least one new trial that characterized the treatment in terms opposite to those used earlier.
A2	Substantial harm: A pivotal trial or systematic review (or guidelines) whose results called into question the use of the treatment based on evidence of harm or that did not proscribe use entirely but did potentially affect clinical decision making.
A3	A superior new treatment: A pivotal trial or systematic review (or guidelines) whose results identified another treatment as significantly superior to the one evaluated in the original review, based on efficacy or harm.
<b>Criteria for Signals of Major Changes in Evidence</b>	
A4	Important changes in effectiveness short of “opposing findings”
A5	Clinically important expansion of treatment
A6	Clinically important caveat
A7	Opposing findings from discordant meta-analysis or nonpivotal trial
<b>Quantitative Criteria for Signals of Potentially Invalidating Changes in Evidence</b>	
B1	A change in statistical significance (from nonsignificant to significant)
B2	A change in relative effect size of at least 50 percent
<b>RAND Method Indications for the Need for an Update</b>	
1	Original conclusion is still valid and this portion of the original report does not need updating
2	Original conclusion is possibly out of date and this portion of the original report may need updating
3	Original conclusion is probably out of date and this portion of the original report may need updating
4	Original conclusion is out of date

## 2.5 Compilation of Findings and Conclusions

For this assessment we constructed a summary table that included the key questions, the original conclusions, and the findings of the new literature search, the expert assessments, and any FDA reports that pertained to each key question. To assess the conclusions in terms of the evidence that they might need updating, we used the 4-category scheme described in the table above for the RAND Method.

In making the decision to classify a CER conclusion into one category or another, we used the following factors when making our assessments:

- If we found no new evidence or only confirmatory evidence and all responding experts assessed the CER conclusion as still valid, we classified the CER conclusion as still valid.

- If we found some new evidence that might change the CER conclusion, and /or a minority of responding experts assessed the CER conclusion as having new evidence that might change the conclusion, then we classified the CER conclusion as possibly out of date.
- If we found substantial new evidence that might change the CER conclusion, and/or a majority of responding experts assessed the CER conclusion as having new evidence that might change the conclusion, then we classified the CER conclusion as probably out of date.
- If we found new evidence that rendered the CER conclusion out of date or no longer applicable, we classified the CER conclusion as out of date. Recognizing that our literature searches were limited, we reserved this category only for situations where a limited search would produce prima facie evidence that a conclusion was out of date, such as the withdrawal of a drug or surgical device from the market, a black box warning from FDA, etc.

## **2.6 Determining Priority for Updating**

We used the following two criteria in making our final conclusion for this CER:

- How much of the CER is possibly, probably, or certainly out of date?
- How out of date is that portion of the CER? For example, would the potential changes to the conclusions involve refinement of original estimates or do the potential changes mean some therapies are no longer favored or may not exist? Is the portion of the CER that is probably or certainly out of date an issue of safety (a drug withdrawn from the market, a black box warning) or the availability of a new drug within class (the latter being less of a signal to update than the former)?

## **3. Results**

### **3.1 Search**

The literature search identified 250 titles. We further reviewed the full text of eight journal articles included in this search. The remaining titles were rejected because they clearly did not meet inclusion criteria for any of the review questions or were unlikely to impact the CER conclusions. In addition to the electronic database searches, we followed up suggestions from the topic experts for studies not already included in the original report.

Thus, 12 articles went on to full text review. Of these, 2 articles were rejected because they did not meet the inclusion criteria of the original report. The 10 remaining articles, were abstracted into an evidence table (Appendix B) for this assessment.<sup>5-14</sup>

### **3.2 Expert Opinion**

Two of three experts responded that the broad conclusion of the 2009 individual patient meta-analysis were still valid but that new evidence further refined the patient populations for which

Percutaneous Coronary Intervention (PCI) was an acceptable alternative to Coronary Artery Bypass Grafting (CABG).

### **3.3 Identifying qualitative and quantitative signals**

Table 1 shows the original key questions, the conclusions of the original report, the results of the literature and drug database searches, the experts' assessments, the recommendations of the Southern California Evidence-based Practice Center (SCEPC) regarding the need for update, and qualitative signals.



**Table 1: Summary Table**

Conclusions From CER Executive Summary	RAND Literature Search	FDA / Health Canada / MHRA (UK)	Expert Opinion EPC Investigator Other Experts	Conclusion from SCEPC
<b>Conclusion taken from Hlatky, 2009<sup>2</sup></b>				
<p>Long-term mortality is similar after CABG and PCI in most patient subgroups with multivessel coronary artery disease, so choice of treatment should depend on patient preferences for other outcomes. CABG might be a better option for patients with diabetes and patients aged 65 years or older because we found mortality to be lower in these subgroups.</p>	<p>1 RCT at 3 followup times <sup>6, 7, 12</sup> found that CABG was superior to PCI for patients with multivessel coronary artery disease, although patients with more favorable and less severe disease did equally well with PCI.</p> <p>2 RCTs<sup>10, 13</sup> and a meta-analysis<sup>11</sup> established that in certain circumstances PCI was acceptable in patients with unprotected left main disease.</p> <p>2 RCTs<sup>9, 14</sup> further established that CABG is the preferred treatment in patients with diabetes.</p> <p>2 cohort studies<sup>5, 8</sup> supported the general conclusion about the superiority of CABG over PCI and one of these included patients with heart failure and a history of tobacco use.<sup>5</sup></p>	<p>N/A</p>	<p>All 3 experts identified additional evidence that further delineated patient subgroups who might be more appropriate for one for of treatment or the other</p>	<p>This conclusion, while still generally valid, is probably out of date with respect to more detailed specifics of identification of patient subgroups who would be more appropriate for CABG or PCI</p>

Legend: CABG: Coronary Artery Bypass Grafting; PCI: Percutaneous Coronary Intervention; RCT: Randomized Controlled Trial; SCEPC: Southern California Evidence-based Practice Center

## References

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# **Appendices**

**Appendix A: Search Methodology**

**Appendix B: Evidence Tables**

**Appendix C: Questionnaire Matrix**

# Appendix A. Search Methodology

## **DATABASE SEARCHED & TIME PERIOD COVERED:**

Medline on OVID – 1/1/2006-1/23/2013

## **LANGUAGE:**

English

## **SEARCH STRATEGY:**

((angioplasty, balloon or balloon) adj2 angioplasty).af. OR ((balloon adj2 dilation) or (balloon adj2 dilatation) and coronary).af. OR ((atherectomy, coronary or atherectom\*) and coronary).af. OR angioplasty, transluminal, percutaneous coronary.af. OR (percutaneous and coronary and transluminal and angioplast\*).af. OR ptca.af. OR (transluminal coronary angioplasty or pci).af. OR (percutaneous adj2 coronary adj2 intervention\*).af. OR ("percutaneous coronary intervention" or stents or stent or stenting).af. OR "internal mammary".af.

AND

((coronary artery bypass or coronary) adj4 bypass) or cabg or coronary artery bypass surgery or "coronary artery bypass graft").af.

AND

(randomized controlled trial pt or controlled clinical trial pt or randomized controlled trials or random allocation or double blind method or single blind method or (((singl\* or double\* or trebl\* or tripl\*) adj25 blind\*) or mask) or (((clinical trial\* or clinical trials or clin\*) adj25 trial\*) or placebo\* or random\* or "research design")).af.

**NUMBER OF RESULTS: 907**

## **LIMITED BY THE FOLLOWING JOURNALS:**

ANNALS OF INTERNAL MEDICINE

BMJ

JAMA

LANCET

NEW ENGLAND JOURNAL OF MEDICINE

AMERICAN JOURNAL OF CARDIOLOGY

ANNALS OF THORACIC SURGERY

CATHETERIZATION AND CARDIOVASCULAR INTERVENTIONS

CIRCULATION

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

**NUMBER OF RESULTS AFTER FILTERING FOR JOURNALS: 250**

## Appendix B. Evidence Table

Author, year	Study design	Comparison	Sample size	Results
Serruys, 2009 <sup>12</sup> (SYNTAX)	RCT	Patients with 3 vessel disease or left main coronary artery disease were randomized CABG or PCI with drug-eluting stents	1800	Patients treated with PCI had a greater rate of repeat revascularization (13.5% vs. 5.9%, $p < 0.001$ ) than did patients treated with CABG at one followup. Rates of death and myocardial infarction were not statistically different between groups. Stroke occurred more often in patients treated with CABG
Kappetein, 2011 <sup>6</sup> (SYNTAX)	RCT	Patients with 3 vessel disease or left main coronary artery disease were randomized CABG or PCI with drug-eluting stents	1800	At 3 years of followup, rates of major adverse cardiac and cerebrovascular events continued to favor treatment with CABG compared to PCI (20.2% vs. 28.0%, $p < 0.001$ ). Differences in stroke were no longer statistically significant
Mohr, 2013 <sup>7</sup> (SYNTAX)	RCT	Patients with 3 vessel disease or left main coronary artery disease were randomized CABG or PCI with drug-eluting stents	1800	At 5 years of followup, overall rates of major adverse cardiac and cerebrovascular events continued to favor CABG over PCI. Rates of stroke were not statistically different between groups certain patients with a low SYNTAX score on angiography (less complex disease) had more similar outcomes whether treated with PCI or CABG, and either might be appropriate for such patients
Weintraub, 2012 <sup>8</sup> (ASCERT)	Cohort	Patients 65 years or older with 2 vessel or 3 vessel coronary artery disease who underwent CABG or PCI	86,244 for CABG 103,549 for PCI	At 1 year followup, there was no statistically significant difference in adjusted mortality. At 4 years of followup, patients treated with CABG had lower mortality than those treated with PCI (16.4% vs. 20.8%)
Farkouh, 2012 <sup>14</sup> (FREEDOM)	RCT	Patients with diabetes and multivessel coronary artery disease were randomized to CABG or PCI with drug-eluting stents	1900	The composite outcome of death from any cause, myocardial infarction, and stroke was higher at 5 years in patients treated with PCI than patients treated with CABG (26.6% vs. 18.7%, $p = 0.005$ ). Stroke was made common in patients treated with CABG (5.2% vs. 2.4%, $p = 0.03$ )

Kapur, 2010 <sup>9</sup> (CARDIa)	RCT	Patient with diabetes and symptomatic multivessel coronary artery disease were randomized to CABG or PCI, initially bare metal stents but later drug-eluting stents	510	The rate of death, myocardial infarction, stroke, or repeat revascularization at one year was higher in patients treated with PCI compared with patients treated with CABG (19.3% vs. 11.3%, p=0.02)
Park, 2011 <sup>13</sup> (PRECOMBAT)	RCT	Patients with unprotected left main coronary artery disease were randomized to CABG or PCI with drug-eluting stents	600	The composite rate of death, myocardial infarction, or stroke at 2 years was not statistically different between the two groups. The rates of revascularization was higher in PCI-treated patients (9.0% vs. 4.2%, p=0.02)
Boudriot, 2011 <sup>10</sup>	RCT	Patients with unprotected left main coronary artery disease were randomized to CABG or PCI with drug eluting stents	201	The combined rate of death and myocardial infarction at 1 year was similar between groups (7.9% vs. 5%) but repeat revascularization was more common in patients treated with PCI (14.0% vs. 5.9%)
Capodanno, 2011 <sup>11</sup>	Meta-analysis	Patients with left main coronary artery disease treated with CABG or PCI	4 RCTs including 1,611 patients	Target vessel revascularization was higher in patients treated with PCI compared to patients treated with CABG (11.4% vs. 5.4%, p<0.001). Stroke was less common among patients treated with PCI (0.1% vs. 1.7%, p=0.013). There were no statistically significant differences in stroke or myocardial infarction.
Hlatky, 2013 <sup>5</sup>	Cohort	Patients 66 years and older who received multivessel CABG or multivessel PCI	105,156	Patients treated with CABG had lower mortality at 5 years than patients treated with PCI (Hazard ratio=0.92, 95% CI 0.90-0.95). This difference was accentuated in patients with diabetes, a history of tobacco use, heart failure, and peripheral arterial disease.

Legend: CABG: Coronary Artery Bypass Grafting; CI: Confidence Interval; PCI: Percutaneous Coronary Intervention; RCT: Randomized Controlled Trial

## Appendix C. Questionnaire Matrix

### Surveillance and Identification of Triggers for Updating Systematic Reviews for the EHC Program

**Title:** Comparative Effectiveness of Percutaneous Coronary Interventions and Coronary Artery Bypass Grafting for Coronary Artery Disease

<b>Conclusions From CER Executive Summary</b>	<b>Is this conclusion almost certainly still supported by the evidence?</b>	<b>Has there been new evidence that may change this conclusion?</b>	<b>Do Not Know</b>
<b>Conclusion taken from Hlatky, 2009</b>			
Long-term mortality is similar after CABG and PCI in most patient subgroups with multivessel coronary artery disease, so choice of treatment should depend on patient preferences for other outcomes. CABG might be a better option for patients with diabetes and patients aged 65 years or older because we found mortality to be lower in these subgroups.	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
<b>Are there new data that could inform the key questions that might not be addressed in the conclusions?</b>			