HEALTH EVIDENCE REVIEW COMMISSION (HERC)

COVERAGE GUIDANCE: CORONARY ARTERY REVASCULARIZATION FOR STABLE ANGINA

Approved 5/7/2015

HERC COVERAGE GUIDANCE

Coronary revascularization (with percutaneous coronary intervention (PCI) or coronary artery bypass surgery (CABG)) is recommended for coverage in patients with stable angina whose symptoms are not controlled with optimal medical therapy[1] or who cannot tolerate such therapy *(weak recommendation).*

CABG is recommended for coverage for patients with stable angina who have left main coronary artery stenosis or three-vessel coronary artery stenosis, with or without a trial of optimal medical therapy *(strong recommendation).*

[1]Optimal medical therapy for angina symptom control is defined as two or more antianginals (in addition to standard treatment for coronary artery disease). Antianginals are defined as: beta-blocker, nitrate, calcium channel blocker, or ranolazine.

Note: Definitions for strength of recommendation are provided in Appendix A GRADE Element Description

RATIONALE FOR GUIDANCE DEVELOPMENT

The HERC selects topics for guideline development or technology assessment based on the following principles:

- Represents a significant burden of disease
- Represents important uncertainty with regard to efficacy or harms
- Represents important variation or controversy in clinical care
- Represents high costs, significant economic impact
- Topic is of high public interest

Coverage guidance development follows to translate the evidence review to a policy decision. Coverage guidance may be based on an evidence-based guideline developed by the Evidence-based Guideline Subcommittee or a health technology assessment developed by the Heath Technology Assessment Subcommittee. In addition, coverage guidance may utilize an existing evidence report produced by one of HERC's trusted sources, generally within the last three years.

EVIDENCE SOURCES

Trusted sources

Dolor, R.J., Melloni, C., Chatterjee, R., Allen LaPointe, N.M., Williams, J.B., Coeytaux, R.R., et al. (2012). *Treatment strategies for women with coronary artery disease*. Rockville, MD: AHRQ. Accessed on October 2, 2014, from http://effectivehealthcare.ahrq.gov/ehc/products/218/1227/CER66_Treatment-Coronary-Artery-Disease_FinalReport_20120816.pdf

Greenhalgh, J., Hockenhull, J., Rao, N., Dundar, Y., Dickson, R. C., & Bagust, A. (2010). Drug-eluting stents versus bare metal stents for angina or acute coronary syndromes. *The Cochrane Database of Systematic Reviews,* Issue 5. Accessed on March 6, 2015, from DOI:10.1002/14651858.CD004587.pub2.

Skinner, J.S., & Cooper, A. (2011). Secondary prevention of ischemic cardiac events. *BMJ Clinical Evidence*, 8 (206), 1-66. Accessed on March 6, 2015, from http://www.ncbi.nlm.nih.gov/pubmed/21875445

Additional sources

Fihn, S. D., Gardin, J. M., Abrams, J., Berra, K., Blankenship, J. C., Douglas, P. S, et al. (2012). 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *Journal of the American College of Cardiology*, *60*(24), e44-e164. DOI:10.1016/j.jacc.2012.07.013. Accessed on October 27, 2014 from, http://content.onlinejacc.org/data/Journals/JAC/926038/07013.pdf

Fihn, S.D., Blankenship, J.C., Alexander, K.P., Bittl, J.A., Byrne, J.G., Fletcher, B.J., et al. (2014). 2014 ACC/AHA/ AATS/PCNA/SCAI/STS Focused Update of the Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease. *Journal of the American College of Cardiology*, *64*(18):1929-1949. DOI: 10.1161/CIR.0000000000000095. Accessed on October 27, 2014 from, http://content.onlinejacc.org/article.aspx?articleid=1891717&resultClick=3

Pursnani, S., Korley, F., Gopaul, R., Kanade, P., Chandra, N., Shaw, R.E., et. al. (2012). Percutaneous coronary intervention versus optimal medical therapy in stable coronary artery disease: A systematic review and meta-analysis of randomized clinical trials. *Circulation Cardiovascular Interventions*, *5*(4), 476-490. Accessed on March 6, 2015, from DOI: 10.1161/CIRCINTERVENTIONS.112.970954.

Thomas, S., Gokhal, R., Boden, W.E., & Devereaux, P.J. (2012). A meta-analysis of randomized control trials comparing percutaneous coronary interventions with medical therapy in stable angina pectoris. *The Canadian Journal of Cardiology, 29*(4), 472-482. Accessed on March 6, 2015, from DOI: 10.1016/j.cjca.2012.07.010.

Windecker, S., Stortecky, S., Stefanini, G.G., da Costa, B.R., Rutjes, A.W., Di Nisio, M., et. al. (2014). Revascularization versus medical treatment in patients with stable coronary artery disease: network meta-analysis. *British Medical Journal (Clinical Research Edition)*, 23(348), g3859. Accessed on March 6, 2015, from DOI: 10.1136/bmj.g3859.

The summary of evidence in this document is derived directly from these evidence sources, and portions are extracted verbatim.

EVIDENCE OVERVIEW

Clinical background

Coronary artery disease (CAD) 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.

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. 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.

Indications

Treatment options for secondary prevention include medical therapy (antiplatelet agents, statins, blood pressure reduction if indicated, beta-blockers and angiotensin converting enzyme inhibitors), coronary artery bypass grafting (CABG) and a number of less invasive methods, including percutaneous transluminal coronary angioplasty (PTCA), in which a small elongated balloon is inflated at the site of the plaque, effectively compacting the deposited material against the vessel wall. This is often accompanied by a coronary artery stent.

Technology description

Coronary artery stents are expandable devices resembling a tubular wire mesh used to 'scaffold' vessels open during PTCA procedures to relieve coronary obstructions in patients. The first of these were metal and are referred to as bare metal stents (BMS). Restenosis (re-narrowing of the treated vessel), which may require a repeat intervention, is a significant limitation of PTCA with the use of stents; rates of restenosis are recorded as ranging between 20 and 50 per cent, depending on the size, location and complexity of the lesion. In order to improve results and reduce restenosis, developments in stent design have been augmented by new drug-eluting technologies. Drug-eluting stents (DES) release anti-proliferative agents from their surface with the objective of limiting cell growth around the stent using cytotoxic, cytostatic and other agents (sirolimus, paclitaxel, everolimus, tacrolimus). Percutaneous coronary intervention (PCI) is an umbrella term that includes PTCA, with and without the additional use of stents.

This report is limited to individuals with stable angina or non-acute coronary heart disease (CHD); it does not address coronary interventions used in the setting of acute coronary syndrome. It is also limited to a comparison to optimal medical therapy to either PCI or CABG. There is a large body of evidence comparing PCI to CABG that is not included in this report.

Oregon utilization

Data from the Dartmouth Atlas of Health Care demonstrate that in Oregon, utilization of PCI is low compared to the national average and in proportion to utilization of CABG.

Table 1. Percutaneous Coronary Interventions (PCI) versus Inpatient Coronary Artery Bypass Grafting (CABG) Utilization per 1,000 Medicare Enrollees in 2012

	Male		Female		Overall	
	PCI	CABG	PCI	CABG	PCI	CABG
Oregon	5.6	3.9	2.9	1.2	4.1	2.4
Washington	6.9	3.5	3.4	1.3	4.9	2.3
National Average	8.4	4.1	4.5	1.4	6.2	2.6
90th Percentile	10.7	5.4	6.1	2.0	8.1	3.4
10th Percentile	5.8	3.1	3.0	0.9	4.3	1.9

Adapted from The Dartmouth Atlas of Health Care Website, http://www.dartmouthatlas.org/

Evidence review

Percutaneous coronary intervention vs. optimal medical therapy in stable coronary heart disease

It is unclear whether PTCA with or without stenting is more effective than medical treatment alone at reducing mortality, cardiac death, composite outcomes including mortality and cardiovascular morbidity, non-fatal MI, need for revascularization, or heart failure in people with non-acute CHD (low quality evidence). Populations and interventions (particularly the use of stents) varied between trials, and results varied by the specific analysis undertaken, outcome assessed, and population included (low-quality evidence).

Four systematic reviews comparing PTCA with or without stenting versus medical treatment alone (Jeremias 2009, Katritsis 2005, Ioannidis 2007, Trikalinos 2009) and three subsequent reports of RCTs included in the reviews (Boden 2009, Malek 2009, Mark 2009) were identified in the initial search of trusted sources. There was a large overlap in the RCTs meta-analyzed in the systematic reviews. However, each review combined different RCTs in their analysis and therefore all four reviews are reported on here.

The first review (Katrisis 2005, search date 2004, 11 RCTs, 2950 people with angiographically documented coronary stenosis in non-acute coronary artery disease settings) compared PTCA versus medical treatment. People with an acute coronary syndrome within the past week were excluded. However, in two RCTs all people had an MI within the past 3 months, but not in the past week. Most RCTs mainly included people with single-vessel or two-vessel disease, but one included people with multi-vessel disease only. The use of stents in people receiving PTCA varied among RCTs, and no RCT used drug-eluting stents. The review found no significant difference between PTCA and medical treatment in mortality (11 RCTs; 95/1476 [6%] with PTCA v 101/1474 [7%] with medical management; RR 0.94, 95% CI 0.72 to 1.24), non-fatal MI (11 RCTs; 87/1476 [6%] with PTCA v 65/1474 [4%] with medical management; RR 1.28, 95% CI 0.94 to 1.75), cardiac death or MI (11 RCTs; 126/1476 [8%] with PTCA v 109/1474 [7%] with medical management; RR 1.17, 95% CI 0.88 to 1.57), need for CABG (11 RCTs; 109/1476 [7.4%] with PTCA v 106/1474 [7.2%] with medical management; RR 1.03, 95% CI 0.80 to 1.33), or need for PTCA during follow-up (11 RCTs; 219/1476 [15%] with PTCA v 243/1474 [16%] with medical management; RR 1.23, 95% CI 0.80 to 1.90). However, there was considerable heterogeneity among trials.

Pre-specified subgroup analyses found that there was no significant difference in the end points considered in RCTs whether stents were available or not, and in trials with follow-up exceeding 2 years there was no difference in end points between PTCA and medical treatment. However, in RCTs with a mean follow-up <2 years, PTCA was associated with significantly higher rates of the composite outcome of cardiac mortality or MI compared with medical treatment (RR 1.82, 95% CI 1.10 to 2.99; absolute numbers not reported), although the confidence intervals overlapped with those from longer-term trials in which the difference was not significant (RCTs with follow-up exceeding 2 years, cardiac mortality or MI; RR 0.99, 95% CI 0.68 to 1.46). The review found that, in the two RCTs that exclusively included people with a relatively recent MI (more than one week but less than three months), PTCA significantly reduced mortality (RR 0.40, 95% CI 0.17 to 0.95) and need for PTCA during follow-up (RR 0.42, 95% CI 0.20 to 0.91;

absolute numbers not reported) compared with medical treatment. The largest RCT (Pocock 2000) identified by the review (1018 people) found that, compared with medical treatment, PTCA improved physical functioning (P <0.001), vitality (P = 0.01), and general health (P = 0.008) at 1 year (proportion of people rating their health "much improved": 33% with PTCA v 22% with medical treatment; P = 0.008), but found no significant difference at 3 years. The improvements were related to breathlessness, angina, and treadmill tolerance. High transfer (27%) to PTCA by people initially randomized to medical treatment may partly explain the lack of significant difference between groups at 3 years. The review found no significant difference between groups for death or MI (including procedure-related events) at 5 years (9% with PTCA v 8% with medical treatment; ARR +1.8%, 95% CI –1.7% to +5.2%).

The second review (Ioannidis 2007, search date 2007, 6 RCTs and 1 sub study, 2617 people that were stable and had an occluded coronary artery, 1–45 days from the onset of acute MI symptoms [mean 8 days], most RCTs with a mean ejection fraction between 44% and 53%, 1 RCT with a mean ejection fraction of 36%) compared PTCA versus medical treatment. Three RCTs had long-term follow up (mean: range 34–50 months), while the others were limited to 4 to 12 months. Three RCTs used stents in people receiving PTCA. The review found no significant difference between PTCA and medical treatment in mortality (99/1310 with PTCA v 106/1317 with medical management; RR 0.95, 95% CI 0.73 to 1.23; P = 0.69), non-fatal MI (70/1310 with PTCA v 55/1317 with medical management; RR 1.26, 95% CI 0.86 to 1.78; P = 0.19), death or MI (161/1310 with PTCA v 141/1317 with medical management; RR 0.99, 95% CI 0.57 to 1.70; P = 0.96), or heart failure (51/1310 with PTCA v 67/1317 with medical management; RR 0.67, 95% CI 0.36 to 1.22; P = 0.19). The review found no significant heterogeneity among RCTs for any of the summary effects (P >0.10 for all outcomes).

The third review (Jeremias 2009, search date 1997–2008), which included RCTs of coronary revascularization versus medical treatment in people with non-acute coronary artery disease, included a total of 28 RCTs, of which 17 RCTs were confined to PTCA versus medical treatment with a further 2 RCTs randomizing to PTCA, CABG, and medical treatment. In total, 8052 people were included in the trials comparing percutaneous coronary intervention (PCI) versus medical therapy, and the RCTs ranged in follow-up from 1 to 10.2 years. The population in the RCTs included people with stable angina, exercise-induced ischemia, post-thrombolytic therapy for MI, asymptomatic single vessel coronary artery disease, and ischemia post MI, among others. Most RCTs compared balloon angioplasty without stenting versus medical treatment, although in 5 RCTs bare metal stents were implanted in 72% to 100% of cases. The review found that PTCA significantly reduced all-cause mortality compared with medical treatment (OR 0.82, 95% CI 0.68 to 0.99; results presented graphically; absolute numbers not reported).

The fourth review (Trikalinos 2009, search date 2008, people with symptomatic or asymptomatic non-acute coronary artery disease) first compared PTCA without stents versus medical management (7 RCTs, number of people [median] 201, follow-up [median] 60 months, age [mean] 56 years, percentage men [median] 85%, 0% with multivessel disease). The review found no significant difference between PTCA and medical treatment in mortality (7 RCTs, 1991 people; RR 0.82, 95% CI 0.59 to 1.15), non-fatal MI (7 RCTs, 1991 people; RR 1.09, 95% CI 0.59 to 1.99), CABG (5 RCTs, 1646 people; RR 1.10, 95% CI 0.81 to 1.49), and any revascularization (7 RCTs, 1991 people; RR 1.08, 95% CI 0.74 to 1.56; absolute numbers not

reported for any outcome). Significant heterogeneity among RCTs was found for the outcomes of non-fatal MI and any revascularization. The review also compared PTCA with bare metal stents versus medical management (4 RCTs, number of people [median] 1134, follow-up [median] 30 months, age [mean] 60 years, percentage men [median] 83%, 60% with multivessel disease). The review found no significant difference between PTCA with bare metal stents and medical treatment in mortality (3 RCTs, 4518 people; RR 0.96, 95% CI 0.79 to 1.18), non-fatal MI (4 RCTs, 4619 people; RR 1.18, 95% CI 0.97 to 1.43), CABG (2 RCTs, 2267 people; RR 0.97, 95% CI 0.63 to 1.50), and any revascularization (3 RCTs, 4518 people; RR 0.78, 95% CI 0.58 to 1.05; absolute numbers not reported for any outcome). Significant heterogeneity among RCTs was found for the outcome of any revascularization. No RCTs directly compared PTCA with drug-eluting stents versus optimal medical therapy.

The first subsequent report (Boden 2009, 2287 people with initially severe angina [CCS grade 4] stabilized medically and at least 70% stenosis in at least one proximal epicardial coronary artery, and either objective evidence of myocardial ischemia or at least one coronary stenosis of at least 80% and classic angina without provocative testing) reported prespecified tertiary outcomes of one RCT included in a systematic review. The initial report of the RCT (the COURAGE trial) had reported on primary and major secondary end points. This report assessed the impact of PCI when added to optimal medical therapy on major, cause-specific cardiovascular outcomes (i.e., prespecified tertiary end points) during long-term follow-up. PTCA was attempted in 1077 of the 1149 people randomized to PTCA and 94% received at least one stent, the majority being bare metal stents. The RCT found no significant difference between PTCA and medical treatment in cardiac death (39/1149 [3.4%] with PTCA v 44/1138 [3.9%] with medical treatment; HR 0.87, 95% CI 0.56 to 1.33; P = 0.51), the composite outcome of cardiac death and MI (172/1149 [15.0%] with PTCA v 162/1138 [14.2%] with medical treatment; HR 1.07, 95% CI 0.86 to 1.33; P = 0.62), the composite outcome of cardiac death, MI, and acute coronary syndrome (270/1149 [23.5%] with PTCA v 257/1138 [22.6%] with medical treatment; HR 1.07, 95% CI 0.91 to 1.27; P = 0.60), the composite outcome of cardiac death, MI, and stroke (188/1149 [16%] with PTCA v 173/1138 [15%] with medical treatment; HR 1.10, 95% CI 0.89 to 1.35; P = 0.45), and the composite outcome of cardiac death, MI, acute coronary syndrome, and stroke (313/1149 [27.2%] with PTCA v 305/1138 [26.8%] with medical treatment; HR 1.05, 95% CI 0.89 to 1.22; P = 0.51).

The second and third subsequent reports were follow-ups from RCTs included in three systematic reviews (Malek 2009, Mark 2009). Malek 2009 compared PTCA with stenting versus optimal medical therapy in people with total occlusion of the infarct-related artery (793 left anterior descending [LAD group], 1408 left circumflex or right coronary artery [non-LAD group]). On days 3 to 28 (minimum of 24 hours) after MI, people were randomized to PTCA and stenting with optimal medical therapy (1101 people) or to optimal medical therapy alone (1100 people). People with LAD infarct-related artery were significantly older than people with non-LAD infarct-related artery (mean: 59.5 years with LAD v 58.1 years with non-LAD; P = 0.005) and the proportion of men was significantly lower (591/793 [75%] with LAD v 1126/1408 [80%] with non-LAD; P = 0.003). The RCT found that the 5-year cumulative primary composite outcome of first occurrence of MI, admission to hospital for heart failure, or all-cause mortality occurred more frequently in people with LAD infarct-related artery compared with people with non-LAD infarct-

related artery (19.5% with LAD v 16.4% with non-LAD; HR 1.34, 99% CI 1.00 to 1.81; P = 0.01). The RCT found that in people with LAD infarct-related artery, PTCA did not significantly reduce the primary outcome compared with medical treatment (22.7% with PTCA v 16.4% with medical treatment; HR 1.35, 99% CI 0.86 to 2.31; P = 0.09). Similarly, it found that in people with non-LAD infarct-related artery, PTCA did not significantly reduce the primary outcome compared with medical treatment (16.9% with PTCA v 15.8% with medical treatment; HR 1.03, 99% CI 0.70 to 1.52; P = 0.83). It also reported that there was no significant difference between people with LAD infarct-related artery and people with non-LAD infarct related artery for the secondary outcomes of death or non-fatal re-infarction, fatal and non-fatal reinfarction, or admission to hospital for heart failure or stroke. It reported that there was no significant difference for PTCA versus medical treatment for these secondary outcomes in either people with LAD infarct-related artery or in people with non-LAD infarct-related artery.

Mark 2009 (a substudy of 951 of 2166 people in original trial enrolled in the quality-of-life assessment, 3–28 days post MI) compared PTCA versus medical treatment for the outcome of quality of life at 4, 12, and 24 months' follow-up. The RCT found that PTCA significantly improved quality of life as assessed on the Duke Activity Status Index at 4 months' follow up compared with medical treatment (P = 0.008), whereas there was no significant difference between groups at 12 months' (P = 0.36) or 24 months' follow-up (P = 0.29). It found that there was no significant difference for PTCA versus medical treatment in quality of life as assessed by the Mental Health Inventory 5 at any follow-up.

This information is summarized in Table 1.

Table 1. Percutaneous coronary interventions vs. optimal medical therapy

Review or Trial	Outcomes	Sub-group Information
Katrisis 2005 (SR – no DES)	No difference in: • Mortality • Non-fatal MI • Composite of cardiac death or MI • Need for CABG • Need for PTCA	No difference with or without stents Mean F/U < 2 years: higher rates of composite in PTCA Recent (< 3 mos, > 1 week) MI: lower mortality, need for PTCA in PTCA F/U > 5 years: no diff in death or MI
Ioannidis 2007 (SR)	No difference in: • Mortality • Non-fatal MI • Composite of cardiac death or MI • Heart failure	
Jeremias 2009 (SR – no DES)	PTCA reduced all-cause mortality	

Trikalinos 2009 (SR – no DES)	No difference in: • Mortality • Non-fatal MI • Any revascularization • CABG	Same results comparing PTCA without stents and with bare metal stents
Boden 2009 (RCT – most stented, some DES)	No difference in: • Cardiac death • Composite of cardiac death or MI • Composite of cardiac death, MI or ACS • Composite of cardiac death, MI or stroke • Composite of cardiac death, MI, ACS or stroke	
Malek 2009 (RCT – recent MI, most stented)	No difference in: • Composite (5 year F/U) of MI, admit to hospital for heart failure, or all-cause mortality • Death or non-fatal reinfarction • Any reinfarction • Admit to hospital for heart failure or stroke	Same results comparing LAD and non-LAD infarct related arteries
Mark 2009 (RCT – recent MI, most stented)	PTCA improved quality of life at 4 months, but not 12 or 24 months	
TIME Investigators 2001 (RCT)	PTCA reduced all adverse cardiac events and angina severity No difference in deaths or non-fatal MI	Patients > 75
Dolor 2012 (SR)	PCI reduced composite of death, MI or repeat revascularization at 5 year F/U	Women

Subgroups

Age

One systematic review (Jeremias 2009) which included one RCT (TIME investigators 2001) was identified. The RCT (305 people aged >75 years, 44% female, with chronic refractory angina) compared PTCA versus medical treatment alone. It found that PTCA reduced all adverse cardiac events (death, non-fatal MI, hospital admissions for ACS) and decreased anginal severity compared with medical treatment, but had no significant effect on deaths or non-fatal MI after 6 months (adverse cardiac events, AR: 19% with PTCA v 49% with medical treatment; P <0.0001; change in angina class: –2.0 with PTCA v –1.6 with medical treatment; P <0.0001;

deaths, AR: 9% with PTCA v 4% with medical treatment; P = 0.15; non-fatal infarctions, AR: 8% with PTCA v 12% with medical treatment; P = 0.46).

Gender

One SR examined treatment of women with coronary disease (Dolor 2012). For women with stable angina, meta-analysis of three good quality studies (all women less than age 75) showed a reduction in the composite outcome of death/MI/repeat revascularization at 5 years for revascularization with PCI compared to optimal medical therapy (OR 0.64; CI, 0.47 to 0.89; p=0.008, moderate SOE). In one of these trials, patients had multivessel disease.

Evidence from additional sources

Because the initial search of trusted sources may not have identified the most recent and relevant information, staff undertook an additional MEDLINE search through February 2015, duplicating the strategy used in Dolor 2012 but without specifying women. This search identified three relevant reviews. Two of the three are of good quality, and found no benefit to PCI over medical therapy for management of stable angina, but their search dates ended in November 2011 and January 2012, respectively. The most recent review, of fair quality, found a benefit in overall mortality only with new generation drug eluting stents, as well as a reduction in revascularization and a nonsignificant reduction in subsequent MI. Findings are described in detail below.

Thomas and colleagues (2013) performed a systematic review and study-level meta-analysis of randomized controlled trials of patients with stable angina comparing PCI vs medical therapy for each of the following individual outcomes: all-cause mortality, cardiovascular (CV) mortality, myocardial infarction (MI), and angina relief. Staff rated this systematic review as good quality. Authors searched bibliographic databases through November 2011, and included ten prospective randomized controlled trials encompassing a total of 6,752 patients. This review did not detect differences between PCI vs medical therapy for all-cause mortality (663 events; relative risk [RR], 0.97 [confidence interval (CI), 0.84-1.12]; I^2 = 0%), CV mortality (214 events; RR, 0.91 [CI, 0.70-1.17]; I^2 = 0%), MI (472 events; RR, 1.09 [CI, 0.92-1.29]; I^2 = 0%), or angina relief at the end of follow-up (2016 events; RR, 1.10 [CI, 0.97-1.26]; I^2=85%). PCI was not associated with reductions in all-cause or CV mortality, MI, or angina relief. Considering the cost implication and the lack of clear clinical benefit, authors conclude that these findings continue to support existing clinical practice guidelines that medical therapy be considered the most appropriate initial clinical management for patients with stable angina.

A second systematic review and meta-analysis (Pursnani 2012) searched through January 2012 for randomized clinical trials comparing revascularization with PCI to optimal medical therapy (OMT) in patients with stable coronary artery disease. Staff also rated this a good quality review. The primary outcome was all-cause mortality, and secondary outcomes included cardiovascular death, nonfatal myocardial infarction, subsequent revascularization, and freedom from angina. Primary analyses were based on longest available follow-up with secondary analyses stratified by trial duration, with short-term (≤1 year), intermediate (1-5 years), and long-term (≥5 years) time points. Authors identified 12 randomized clinical trials enrolling 7,182 participants. For the primary analyses, when compared with OMT, PCI was associated with no significant improvement in mortality (risk ratio [RR], 0.85; 95% CI, 0.71-1.01), cardiac death (RR, 0.71;

95% CI, 0.47-1.06), nonfatal myocardial infarction (RR, 0.93; 95% CI, 0.70-1.24), or repeat revascularization (RR, 0.93; 95% CI, 0.76-1.14), with consistent results over all follow-up time points. Sensitivity analysis restricted to studies in which there was >50% stent use showed attenuation in the effect size for all-cause mortality (RR, 0.93; 95% CI, 0.78-1.11) with PCI. However, for freedom from angina, there was a significant improved outcome with PCI, as compared with the OMT group (RR, 1.20; 95% CI, 1.06-1.37), evident at all of the follow-up time points.

A network meta-analysis by Windecker and colleagues (2014) was the most recent and comprehensive review, although it was rated of fair quality by staff due to indirectness of evidence. Randomized controlled trials from 1980 through June 2013 were included if they had a clinical follow-up duration of at least six months and had randomized at least 100 patients per trial arm. Patients had to be randomized to medical treatment, coronary artery bypass grafting, or percutaneous coronary intervention using balloon angioplasty, bare metal stents, early generation stent systems (paclitaxel eluting Taxus stent [Boston Scientific, Natick, MA], sirolimus eluting Cypher stent [Cordis, Miami Lakes, FL], zotarolimus eluting Endeavor stent [Medtronic Cardiovascular, Santa Rosa, CA]) or new generation stent systems (zotarolimus eluting Resolute stent [Medtronic Cardiovascular, Santa Rosa, CA] and everolimus eluting Xience/Promus stent [Abbott Vascular, Santa Clara, CA and Boston Scientific, Natick, MA]) approved by the FDA. The review excluded trials in patients with acute myocardial infarction (ST segment elevation myocardial infarction or non-ST segment elevation myocardial infarction) and symptom onset less than 72 hours, trial arms with polymer or carbon coated bare metal stents, and trial arms with non-FDA approved drug eluting stents. Authors considered studies in general to be of high quality. Ninety five trials including 93,553 randomized patients and 5,346 accumulated events contributed to the analysis of all cause mortality for all interventions including CABG.

Percutaneous coronary intervention with the new generation everoliumus eluting stent, but no other percutaneous coronary intervention technology, was associated with reduced mortality compared with medical treatment (0.75, 0.59 to 0.96 17 trials, N = 13,272). There was also a trend toward reduced mortality with the new generation zotarolimus eluting (Resolute) stent (0.65, 0.42 to 1.00 four trials, N = 2,285). The estimated rate ratios for mortality were below 1, but inconclusive for revascularization with balloon angioplasty (0.85, 0.68 to 1.04, 29 trials, N = 7,609), bare metal stents (0.92, 0.79 to 1.05, 50 trials, N = 16,042), and early generation drug eluting stents (paclitaxel eluting: 0.92, 0.75 to 1.12, 27 trials, N = 11,541; sirolimus eluting: 0.91, 0.75 to 1.10, 39 trials, N = 19,781; zotarolimus eluting [Endeavor]: 0.88, 0.69 to 1.10, 8 trials, N = 8,937).

In the analysis of myocardial infarction, 5,796 events were reported during 243,031 patient years. All percutaneous coronary interventions, except bare metal stent (1.04, 0.84 to 1.27) and paclitaxel eluting stent (1.18, 0.88 to 1.54), showed evidence for a relevant but inconclusive reduction of myocardial infarction, with point estimates below 1 for balloon angioplasty (0.88, 0.70 to 1.11), sirolimus eluting stent (0.94, 0.71 to 1.22), zotarolimus eluting (Endeavor) stent (0.80, 0.56 to 1.10), zotarolimus eluting (Resolute) stent (0.82, 0.52 to 1.26), and everolimus eluting stent (0.75, 0.55 to 1.01).

Revascularization using coronary stents was associated with a reduction in subsequent revascularization for bare metal stent (0.44, 0.59 to 0.82), paclitaxel eluting stent (0.44, 0.35 to 0.55), sirolimus eluting stent (0.29, 0.24 to 0.36), zotarolimus eluting (Endeavor) stent (0.38, 0.29 to 0.51), zotarolimus eluting (Resolute) stent (0.26, 0.17 to 0.40), and everolimus eluting stent (0.27, 0.21 to 0.35). Revascularization with balloon angioplasty showed similar risks of subsequent revascularization compared with medical treatment (0.97, 0.82 to 1.16).

In summary, this network meta-analysis (Windecker 2014) found that percutaneous coronary intervention with the new generation everoliums eluting stents reduced mortality compared to medical management. The new generation zotarolimus eluting (Resolute) stent had only four trials contributing data, but also showed a trend toward reduced mortality. No other percutaneous coronary intervention technology was associated with reduced mortality when compared with medical management. All percutaneous coronary interventions, except bare metal stent and paclitaxel eluting stent, showed evidence for a relevant but inconclusive reduction of myocardial infarction. Revascularization using coronary stents was associated with a reduction in subsequent revascularization by 56-74%.

Summary

In summary, based on multiple trusted source and good quality systematic reviews, there is no clear advantage of an initial routine strategy of PTCA with or without stenting compared with medical treatment to reduce mortality and MI in patients with stable coronary disease and no recent MI. The exception, based on one recent fair quality meta-analysis, is a finding of reduced mortality with the new generation everolimus drug-eluting stent. There may be short-term improvement based on two RCTs in quality of life, and for women and older individuals, one systematic review suggests PCI may result in a reduction in angina symptoms and adverse cardiac events. Finally, one meta-analysis found that a strategy of PCI reduced need for subsequent revascularization by 56-74% over medical management.

Coronary artery bypass graft vs. optimal medical therapy

Two systematic reviews comparing CABG versus medical treatment were identified. In the first systematic review (Yusuf 1994, search date not reported, 7 RCTs, 2649 people with CHD, mostly male, aged 41–60 years, 80% with ejection fraction >50%, 60% with prior MI; and 83% with 2–3 vessel disease), people assigned to CABG also received medical treatment, and 37% initially assigned to medical treatment underwent CABG in the following 10 years. It found that, compared with medical treatment, CABG significantly reduced mortality at 5 and 10 years (5 years: RR 0.61, 95% CI 0.48 to 0.77; 10 years: RR 0.83, 95% CI 0.70 to 0.98). Most trials did not collect data on quality of life; neither did they report detailed information about long-term medication use. However, at one year, 66% of the medical treatment group and 20% of the CABG group were treated with beta-blockers, and 19% of the medical treatment group and 26% of the CABG group were treated with antiplatelet agents. The review found that, of the 1240 people who had CABG, 40 (3%) died and 88 (7%) had non-fatal MI within 30 days of the procedure. At 1 year, rates of the combined outcome of mortality or MI were significantly higher with CABG compared with medical treatment (12% with CABG v 8% with medical treatment; RR 1.45, 95% CI 1.18 to 2.03).

The second systematic review (Jeremias 2009, search date 1977–2008) included RCTs of coronary revascularization (CABG/PCI/mixed) versus medical treatment in people with non-acute coronary artery disease. It included 28 RCTs in total, of which 6 RCTs evaluated CABG (largely with saphenous vein grafts) versus medical treatment (all of which were included in the first review) and it included a further two RCTs evaluating PCI or CABG (the majority with internal thoracic artery graft). The 8 RCTs comparing CABG versus medical treatment included 3098 people, who were mostly male, and follow-up in the RCTs was from 1 to 5 years. The 8 RCTs included people with stable angina, disabling angina, mild stable angina, or free of angina post MI, and no symptoms; the year of publication of the RCTs varied from 1977 to 2004. The review found that CABG significantly reduced all-cause mortality compared with medical treatment (8 RCTs; OR 0.62, 95% CI 0.50 to 0.77; results presented graphically; absolute numbers not reported).

No harms were reported in either SR.

The efficacy of revascularization versus medical treatment has been evaluated in people with stable ischemia in one additional RCT (Davies 1997). The RCT (558 people with ischemia identified by exercise test or ambulatory ECG, who were either asymptomatic or whose angina was able to be controlled with medications) compared three interventions: revascularization (90 selected for CABG, 11 later refused and 1 had the procedure outside the specified time window; 102 selected for PTCA, 8 later refused and 2 had the procedure outside the time window), angina-guided medical treatment, and ischemia-guided medical treatment. In the angina-guided treatment group, drug treatment was sufficient to control angina. In the ischemia-guided group, additional drug therapy was added if ischemia was still present on ambulatory ECG recording. At 2 years, the rate of mortality or MI was lower with revascularization (angina-guided treatment: 12%; ischemia-guided treatment: 9%; revascularization: 5%). The difference between angina-guided treatment and revascularization was significant (P <0.01), but the differences between ischemia-guided treatment and revascularization (P = 0.12) and angina-guided treatment and ischemia-guided treatment (P = 0.3) were not significant. There was a tendency for the benefit of revascularization to be concentrated in those with proximal LAD artery disease, and in those with three-vessel disease compared with one- or two-vessel disease.

Subgroups

Reduced left ventricular function

The Yusuf 1994 systematic review described above found that the relative benefits of CABG were similar in people with normal compared with reduced left ventricular function (death: OR 0.61, 95% CI 0.46 to 0.81, with normal left ventricular function; OR 0.59, 95% CI 0.39 to 0.91, with reduced left ventricular function). The absolute benefit of CABG was greater in people with a reduced left ventricular function because the baseline risk of death was higher.

Multiple vessel disease

Yusuf 1994 found that CABG reduced mortality compared with medical treatment in people with single-vessel, two-vessel, three-vessel, and left main stem disease. Change in mortality was not significant for people with single-vessel and two-vessel disease; however, this may have been because the number of deaths was small. The risk of mortality was 0.54 (95% CI 0.22 to 1.33) with single-vessel disease, 0.84 (95% CI 0.54 to 1.32) with two-vessel disease, 0.58 (95% CI

0.42 to 0.80) with three-vessel disease, and 0.32 (95% CI 0.15 to 0.70) with left main stem disease.

Gender

One SR examined treatment of women with coronary disease (Dolor 2012). For women with stable angina, meta-analysis of two good quality studies showed a reduction in the composite outcome of death/ MI/repeat revascularization at 5 years for revascularization with CABG compared to OMT (OR 0.56; CI, 0.32 to 0.96; p=0.04; low SOE). However, patients in these two trials either had multivessel disease or left ventricular dysfunction.

Evidence from additional sources

Similar to the process used for PCI v OMT, because the initial search of trusted sources may not have identified the most recent and relevant information, staff undertook an additional MEDLINE search through February 2015, duplicating the strategy used in Dolor 2012 but without specifying women. This search identified one relevant network meta-analysis of CABG versus medical management (Windecker 2014), the details of which are described above. In patients with stable symptomatic or asymptomatic coronary artery disease, compared with a strategy of initial medical treatment, revascularization using coronary artery bypass grafting reduced all cause mortality by 20% (rate ratio 0.80, 95% confidence interval 0.70 to 0.91, 22 trials, N = 8,920). Revascularization using coronary artery bypass grafting compared with medical treatment reduced myocardial infarction during the observational period by 21% (0.79, 0.63 to 0.99). Compared with medical treatment, revascularization with coronary artery bypass grafting was effective in reducing subsequent revascularization by 84% (0.16, 0.13 to 0.20).

Summary

In summary, CABG plus medical treatment may be more effective than medical treatment alone at reducing mortality in the long run in people (mostly male) aged 41 to 60 years, most with previous MI and two to three-vessel disease and also in people with non-acute coronary artery disease (low quality evidence). However, it may increase the estimated incidence of the composite outcome of death or MI at 1 year. Further analysis in people (mostly male) aged 41 to 60 years, most with previous MI and two- to three-vessel disease, found that CABG may reduce mortality compared with medical treatment both in people with normal left ventricular function or with reduced left ventricular function, and may reduce mortality in people with three-vessel and left main stem disease, although the effect of CABG in those with single- or two-vessel disease are unclear, as the number of deaths in these groups was small (low-quality evidence).

A recent fair quality network meta-analysis of patients with symptomatic or asymptomatic stable CAD found a significant reduction in mortality, MI, and need for subsequent revascularization with CABG as compared to medical management.

Limitations of the evidence on coronary artery bypass grafting compared to optimal medical therapy

The results of the systematic reviews may not be easily generalized to current practice. People were generally aged 65 years or younger, but >50% of CABG procedures are now performed on people >65 years of age. In addition, almost all were male, and high-risk people (such as those with severe angina and left main coronary artery stenosis) were under represented. Internal thoracic artery grafts were largely confined to two more recent trials. In the first systematic review lipid lowering agents (particularly statins) and aspirin were used infrequently (aspirin used in 3% of people at enrollment, about 22% at 1 year). Only about 50% of people were taking beta-blockers at baseline. The first systematic review (Yusuf 1994) evaluated the efficacy of an initial strategy of CABG compared with medical treatment, although there was considerable crossover to surgery in those assigned to medical treatment; in the three larger trials, 25% by 5 years, 33% by 7 years, and 41% by 10 years. However, some general observations can be made, and those with more-extensive CHD and impaired left ventricular function are likely to derive the greatest absolute benefit with improved survival from CABG. One RCT (Hueb 2007) included in the second systematic review (Jeremias 2001) in those with preserved left ventricular function and multivessel disease more accurately reflects contemporary clinical practice with the use of more arterial conduits, although the mean age of participants was still only 60 years. The RCT was not powered to detect differences in survival, but CABG reduced the need for additional revascularization procedures and improved angina-free survival at 5 years. People with prior CABG have not been studied in RCTs, although they now represent a growing proportion of those undergoing CABG.

EVIDENCE SUMMARY

Evidence suggests that, compared to optimal medical therapy, PCI does not result in improvement in mortality or most other cardiac outcomes (non-fatal MI, need for revascularization, heart failure, composite outcomes), based on low quality evidence (multiple conflicting SRs). However, most studies utilized only PTCA or bare metal stents, and only a few trials included drug eluting stents. A network meta-analysis incorporating new generation drug-eluting stents found evidence that the everolimus eluting stent, but not other modalities, reduces mortality compared to medical treatment (low quality evidence, based on one fair quality metanalysis). Some subgroups appear to have differential outcomes; PCI may result in short-term benefit in mortality in patients with a recent MI (very low quality evidence, based on three conflicting RCTs), as well as in women (moderate quality evidence, based on one SR). In addition, PCI may improve physical functioning and quality of life in the short-term compared to OMT (very low quality evidence, based on one RCT), and for patients over age 75, may reduce anginal severity (very low quality evidence, based on one RCT).

On the contrary, CABG does appear to result in improved mortality compared to OMT, at least at five years follow up, although short-term risks are higher (low quality evidence). This benefit is present regardless of left ventricular function or gender, but may be limited to patients with three-vessel or left main stem disease.

There are a number of limitations to the evidence base, including the fact that most trials were limited to patients age 65 or younger, few trials included DE stents and OMT in many trials was suboptimal compared to current standards. In addition, for CABG trials, most did not utilize internal thoracic artery grafts. Lastly, there was considerable cross-over to surgery in those assigned to OMT (up to 41% by 10 years).

GRADE-INFORMED FRAMEWORK

The HERC develops recommendations by using the concepts of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. GRADE is a transparent and structured process for developing and presenting evidence and for carrying out the steps involved in developing recommendations. There are four elements that determine the strength of a recommendation, as listed in the table below. The HERC reviews the evidence and makes an assessment of each element, which in turn is used to develop the recommendations presented in the coverage guidance box. Balance between desirable and undesirable effects, and quality of evidence, are derived from the evidence presented in this document, while estimated relative costs, values and preferences are assessments of the HERC members.

Indication/ Intervention	Balance between desirable and undesirable effects	Quality of evidence*	Resource allocation	Variability in values and preferences	Coverage recommendation	Rationale
PCI vs. OMT (patients with non-acute coronary heart disease)	No difference in mortality (except with 1 out of 2 new generation drug-eluting stents), MI, MACE. PCI caused reduction in subsequent revascularization by 56-74%	Low based on multiple conflicting SRs*	Moderate	LOW most patients would not want a semi-invasive intervention without some assurance of proven significant benefit	Recommended for coverage in patients with stable angina whose symptoms are not controlled with optimal medical therapy[1] or who cannot tolerate such therapy *(weak recommendation)*	While the evidence is weak, it would be appropriate to cover PCI for symptomatic relief if optimal medical therapy has been tried and is ineffective at controlling symptoms, and coronary anatomy is appropriate. PCI cannot be recommended for coverage for improvement in MACE or mortality given the lack of consistent evidence of benefit for these critical outcomes.
	Possible short-term improvement in physical functioning, QOL, angina	Low based on 2 RCTs[#]				

Indication/ Intervention	Balance between desirable and undesirable effects	Quality of evidence*	Resource allocation	Variability in values and preferences	Coverage recommendation	Rationale
CABG vs. OMT	Short-term worse mortality, long-term benefit in mortality (benefit possibly limited to three vessel or left main stem disease) 21% reduction in MI and 84% reduction in subsequent revascularization compared with OMT in patients with stable disease	Low based on multiple SRs*	High	MODERATE Long term benefit is appealing but this is a major cardiac surgery and increased short-term mortality is concerning	Recommended for coverage in those with three vessel or left main stem disease *(strong recommendation)* Recommended for coverage in patients with stable angina whose symptoms are not controlled with optimal medical therapy[1] or who cannot tolerate such therapy *(weak recommendation)*	There is low quality evidence but with significant improvements in long-term mortality. CABG is recommended for coverage for those who have failed optimal medical therapy and for those with stable CHD but with appropriate anatomy, regardless of failure of OMT.

*The Quality of Evidence rating was assigned by the primary evidence source, not the HERC Subcommittee

[#]The Quality of Evidence rating was assigned by the HERC Subcommittee

[1]Optimal medical therapy for angina symptom control is defined as two or more antianginals (in addition to standard treatment for coronary artery disease). Antianginals are defined as: beta-blocker, nitrate, calcium channel blocker, or ranolazine.

Note: GRADE framework elements are described in Appendix A

POLICY LANDSCAPE

Quality measures

Nine potentially relevant quality measures were identified when searching the National Quality Measures Clearinghouse. Six were measures developed by the Agency for Healthcare Research and Quality, and three were developed by the Canadian Institute for Health Information. Seven of the measures quantified utilization of either PCI or CABG (area rate, volume), while there was one measure for each PCI and CABG documenting the mortality rate associated with the procedure.

Professional society guidelines

The 2012 ACC/AHA/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease addresses diagnosis, risk assessment, treatment and follow up of patients with known or suspected SIHD. While the guideline developers have been meticulous in maintaining and documenting editorial independence, the guideline overall receives a poor rating, primarily because study selection criteria are not specified, and no assessment of study quality is taken into account when developing recommendations.

Treatment is the section of the guideline that pertains to this coverage guidance document. Selected background and recommendations that are pertinent to stable disease from this section are presented below.

Factors That Should Not Influence Treatment Decisions

The 2 medical indications for revascularization are to prevent death and cardiovascular complications and to improve symptoms and quality of life. Nonetheless, the use of revascularization has risen dramatically in the past 3 decades. Much of this increase appears to be for indications for which benefits in survival or symptoms in comparison with noninvasive therapies are unlikely. National data suggest that about 12% of PCIs could be inappropriate because they lack evident potential to improve either survival or symptoms. Several reasons influence patients and physicians to prefer revascularization when the likelihood of benefit is less than the potential risk of the procedure. An ingrained preference for action (i.e., revascularization) over perceived inaction (i.e., medical therapy alone) likely often influences the decision making of both patients and physicians. Moreover, some healthcare professionals are unduly pessimistic about survival with conservative medical therapy and inaccurately optimistic about the survival benefits of revascularization procedures. As indicated earlier, patients often believe mistakenly that PCI has the potential to prevent AMI and prolong survival. In addition, the attendant expense and risk of combined antiplatelet therapy for an uncertain period of time might not be fully considered. Physicians are professionally obligated to provide accurate estimates of the risks, benefits, and costs of various therapeutic options that are based on the best available scientific data. Other factors can induce physicians to recommend revascularization. These include medicolegal concerns (often exaggerated) and feeling compelled to satisfy the expectations of patients and referring physicians (which are sometimes misinformed or unrealistic). Additionally, there are well-

documented regional variations in the use and appropriateness of cardiac procedures that appear to reflect local practice styles. This might partly reflect a mistaken belief by some physicians that “more care is better care”.

Although successful procedures can be psychologically satisfying to the physician and the patient, this does not justify the attendant economic costs and risk of complications of procedures that offer minimal, if any, genuine benefit. Although rarely discussed explicitly, financial incentives seem to affect the willingness of a minority of physicians and institutions to recommend certain procedures or drug therapies. Strong incentives created by the payment system encourage overutilization. Also, a small number of physicians might have financial relationships with the manufacturers of devices or drugs that might represent apparent conflicts that ought to be disclosed to patients. At a higher level, those responsible for the payment system, the manufacturers of devices and drugs, and physicians making clinical decisions must commit to supporting guideline based interventions. Any and all conflicts of interest must be revealed to patients in the process of informed consent before any invasive or noninvasive procedure.

Revascularization to Improve Survival: Recommendations

Left Main CAD Revascularization

CLASS I Recommendations

1. CABG to improve survival is recommended for patients with significant (≥50% diameter stenosis) left main coronary artery stenosis. (Level of Evidence: B)

CLASS IIa Recommendations

1. PCI to improve survival is reasonable as an alternative to CABG in selected stable patients with significant (≥50% diameter stenosis) unprotected left main CAD with: 1) anatomic conditions associated with a low risk of PCI procedural complications and a high likelihood of good long-term outcome (e.g., a low SYNTAX score [≤22], ostial or trunk left main CAD); and 2) clinical characteristics that predict a significantly increased risk of adverse surgical outcomes (e.g., STS-predicted risk of operative mortality ≥5%). (Level of Evidence: B)

CLASS IIb Recommendations

1. PCI to improve survival may be reasonable as an alternative to CABG in selected stable patients with significant (≥50% diameter stenosis) unprotected left main CAD with: a) anatomic conditions associated with a low to intermediate risk of PCI procedural complications and an intermediate to high likelihood of good long-term outcome (e.g., low–intermediate SYNTAX score of <33, bifurcation left main CAD); and b) clinical characteristics that predict an increased risk of adverse surgical outcomes (e.g., moderate–severe chronic obstructive pulmonary disease, disability from previous stroke, or previous cardiac surgery; STS-predicted risk of operative mortality >2%). (Level of Evidence: B)

CLASS III Recommendations: Harm

1. PCI to improve survival should not be performed in stable patients with significant (≥50% diameter stenosis) unprotected left main CAD who have unfavorable anatomy for PCI and who are good candidates for CABG. (Level of Evidence: B)

Non–Left Main CAD Revascularization

CLASS I Recommendations

1. CABG to improve survival is beneficial in patients with significant (≥70% diameter) stenoses in 3 major coronary arteries (with or without involvement of the proximal LAD artery) or in the proximal LAD artery plus 1 other major coronary artery. (Level of Evidence: B)

2. CABG or PCI to improve survival is beneficial in survivors of sudden cardiac death with presumed ischemia-mediated ventricular tachycardia caused by significant (≥70% diameter) stenosis in a major coronary artery. (CABG Level of Evidence: B ; PCI Level of Evidence: C)

CLASS IIa Recommendations

1. CABG to improve survival is reasonable in patients with significant (≥70% diameter) stenoses in 2 major coronary arteries with severe or extensive myocardial ischemia (e.g., high-risk criteria on stress testing, abnormal intracoronary hemodynamic evaluation, or >20% perfusion defect by myocardial perfusion stress imaging) or target vessels supplying a large area of viable myocardium. (Level of Evidence: B)

2. CABG to improve survival is reasonable in patients with mild–moderate LV systolic dysfunction (EF 35% to 50%) and significant (≥70% diameter stenosis) multi-vessel CAD or proximal LAD coronary artery stenosis, when viable myocardium is present in the region of intended revascularization. (Level of Evidence: B)

3. CABG with a left internal mammary artery (LIMA) graft to improve survival is reasonable in patients with significant (≥70% diameter) stenosis in the proximal LAD artery and evidence of extensive ischemia. (Level of Evidence: B)

4. It is reasonable to choose CABG over PCI to improve survival in patients with complex 3-vessel CAD (e.g., SYNTAX score >22), with or without involvement of the proximal LAD artery who are good candidates for CABG. (Level of Evidence: B)

5. CABG is probably recommended in preference to PCI to improve survival in patients with multivessel CAD and diabetes mellitus, particularly if a LIMA graft can be anastomosed to the LAD artery. (Level of Evidence: B)

CLASS IIb Recommendations

1. The usefulness of CABG to improve survival is uncertain in patients with significant (70%) diameter stenoses in 2 major coronary arteries not involving the proximal LAD artery and without extensive ischemia. (Level of Evidence: C)

2. The usefulness of PCI to improve survival is uncertain in patients with 2- or 3-vessel CAD (with or without involvement of the proximal LAD artery) or 1-vessel proximal LAD disease. (Level of Evidence: B)

3. CABG might be considered with the primary or sole intent of improving survival in patients with SIHD with severe LV systolic dysfunction (EF<35%) whether or not viable myocardium is present. (Level of Evidence: B)

4. The usefulness of CABG or PCI to improve survival is uncertain in patients with previous CABG and extensive anterior wall ischemia on noninvasive testing. (Level of Evidence: B)

CLASS III Recommendations: Harm

1. CABG or PCI should not be performed with the primary or sole intent to improve survival in patients with SIHD with 1 or more coronary stenoses that are not anatomically or functionally significant (e.g., <70% diameter non–left main coronary artery stenosis, FFR >0.80, no or only mild ischemia on noninvasive testing), involve only the left circumflex or right coronary artery, or subtend only a small area of viable myocardium. (Level of Evidence: B)

Revascularization to Improve Symptoms: Recommendations

CLASS I Recommendations

1. CABG or PCI to improve symptoms is beneficial in patients with 1 or more significant (≥70% diameter) coronary artery stenoses amenable to revascularization and unacceptable angina despite guideline directed medical therapy (GDMT). (Level of Evidence: A)

CLASS IIa Recommendations

1. CABG or PCI to improve symptoms is reasonable in patients with 1 or more significant (≥70% diameter) coronary artery stenoses and unacceptable angina for whom GDMT cannot be implemented because of medication contraindications, adverse effects, or patient preferences. (Level of Evidence: C)

2. PCI to improve symptoms is reasonable in patients with previous CABG, 1 or more significant (≥70% diameter) coronary artery stenoses associated with ischemia, and unacceptable angina despite GDMT. (Level of Evidence: C)

3. It is reasonable to choose CABG over PCI to improve symptoms in patients with complex 3-vessel CAD (e.g., SYNTAX score >22), with or without involvement of the proximal LAD artery, who are good candidates for CABG. (Level of Evidence: B)

CLASS IIb Recommendations

1. CABG to improve symptoms might be reasonable for patients with previous CABG, 1 or more significant (≥70% diameter) coronary artery stenoses not amenable to PCI, and unacceptable angina despite GDMT. (Level of Evidence: C)

2. Transmyocardial revascularization (TMR) performed as an adjunct to CABG to improve symptoms may be reasonable in patients with viable ischemic myocardium that is perfused by arteries that are not amenable to grafting. (Level of Evidence: B)

CLASS III Recommendations: Harm

1. CABG or PCI to improve symptoms should not be performed in patients who do not meet anatomic (≥50% diameter left main or ≥70% non–left main stenosis diameter) or physiological (e.g., abnormal FFR) criteria for revascularization. (Level of Evidence: C)

The 2014 ACC/AHA/AATS/PCNA/SCAI/STS Focused Update of the Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease updates the 2012 guideline described above. The areas addressed, where new evidence was found or recommendations were revised, were there following:

- Diagnosis of SIHD
- Treatment: Chelation therapy
- Treatment: Enhanced external counterpulsation
- CAD Revascularization: Revascularization to improve survival

Only the last area pertains to this guidance document, and will be discussed further. The 2012 recommendation was as follows:

Class IIa

CABG is probably recommended in preference to PCI to improve survival in patients with multivessel CAD and diabetes mellitus, particularly if a LIMA graft can be anastomosed to the left anterior descending (LAD) artery. (Level of Evidence: B)

The 2014 focused update makes the following new recommendation:

Class I

1. A Heart Team approach to revascularization is recommended in patients with diabetes mellitus and complex multivessel CAD. (Level of Evidence: C)

2. CABG is generally recommended in preference to PCI to improve survival in patients with diabetes mellitus and multivessel CAD for which revascularization is likely to improve survival (3-vessel CAD or complex 2-vessel CAD involving the proximal LAD), particularly if a LIMA graft can be anastomosed to the LAD artery, provided the patient is a good candidate for surgery. (Level of Evidence: B)

Coverage guidance is prepared by the Health Evidence Review Commission (HERC), HERC staff, and subcommittee members. The evidence summary is prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to guide public and private purchasers in Oregon in making informed decisions about health care services.

The Center is not engaged in rendering any clinical, legal, business or other professional advice. The statements in this document do not represent official policy positions of the Center. Researchers involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

APPENDIX A. GRADE ELEMENT DESCRIPTIONS

Element	Description
Balance between desirable and undesirable effects	The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted
Quality of evidence	The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted
Resource allocation	The higher the costs of an intervention—that is, the greater the resources consumed—the lower the likelihood that a strong recommendation is warranted
Values and preferences	The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted

Strong recommendation

In Favor: The subcommittee is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences.
Against: The subcommittee is confident that the undesirable effects of adherence to a recommendation outweigh the desirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences.

Weak recommendation

In Favor: The subcommittee concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences, but is not confident.
Against: The subcommittee concludes that the undesirable effects of adherence to a recommendation probably outweigh the desirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences, but is not confident.

Quality or strength of evidence rating across studies for the treatment/outcome[1]

High: The subcommittee is very confident that the true effect lies close to that of the estimate of the effect. Typical sets of studies are RCTs with few or no limitations and the estimate of effect is likely stable.
Moderate: The subcommittee is moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Typical sets of studies are RCTs with some limitations or well-performed nonrandomized studies with additional strengths that guard against potential bias and have large estimates of effects.
***Low*:** The subcommittee's confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. Typical sets of studies are RCTs with serious limitations or nonrandomized studies without special strengths.
***Very low*:** The subcommittee has very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect. Typical sets of studies are nonrandomized studies with serious limitations or inconsistent results across studies.

[1] Includes risk of bias, precision, directness, consistency and publication bias

APPENDIX B. APPLICABLE CODES

CODES	DESCRIPTION
ICD-9 Diagnosis Codes	
413.0	Angina decubitus
413.1	Prinzmetal angina
413.9	Other and unspecified angina pectoris
414.0	Coronary atherosclerosis
414.2	Chronic total occlusion of coronary artery
414.8-9	Other specified and unspecified forms of chronic ischemic heart disease
ICD-10 Diagnosis Codes	
I20.1	Angina pectoris with documented spasm
I20.8	Other forms of angina pectoris
I20.9	Angina pectoris, unspecified
I20.10	Atherosclerotic heart disease of native coronary artery without angina pectoris
I25.82	Chronic total occlusion of coronary artery
I25.89	Other forms of chronic ischemic heart disease
I25.9	Chronic ischemic heart disease, unspecified
ICD-9 Volume 3 (Procedure Codes)	
36.0	Removal of coronary obstruction and insertion of stent(s)
36.1	Bypass anastomosis for heart revascularization
CPT Codes	
33510-33516	Coronary artery bypass – venous grafting only
33517-33530	Combined arterial-venous grafting for coronary bypass
33533-33548	Arterial grafting for coronary artery bypass
92920-92944	Percutaneous revascularization procedures
HCPCS Level II Codes	
	None

Note: Inclusion on this list does not guarantee coverage

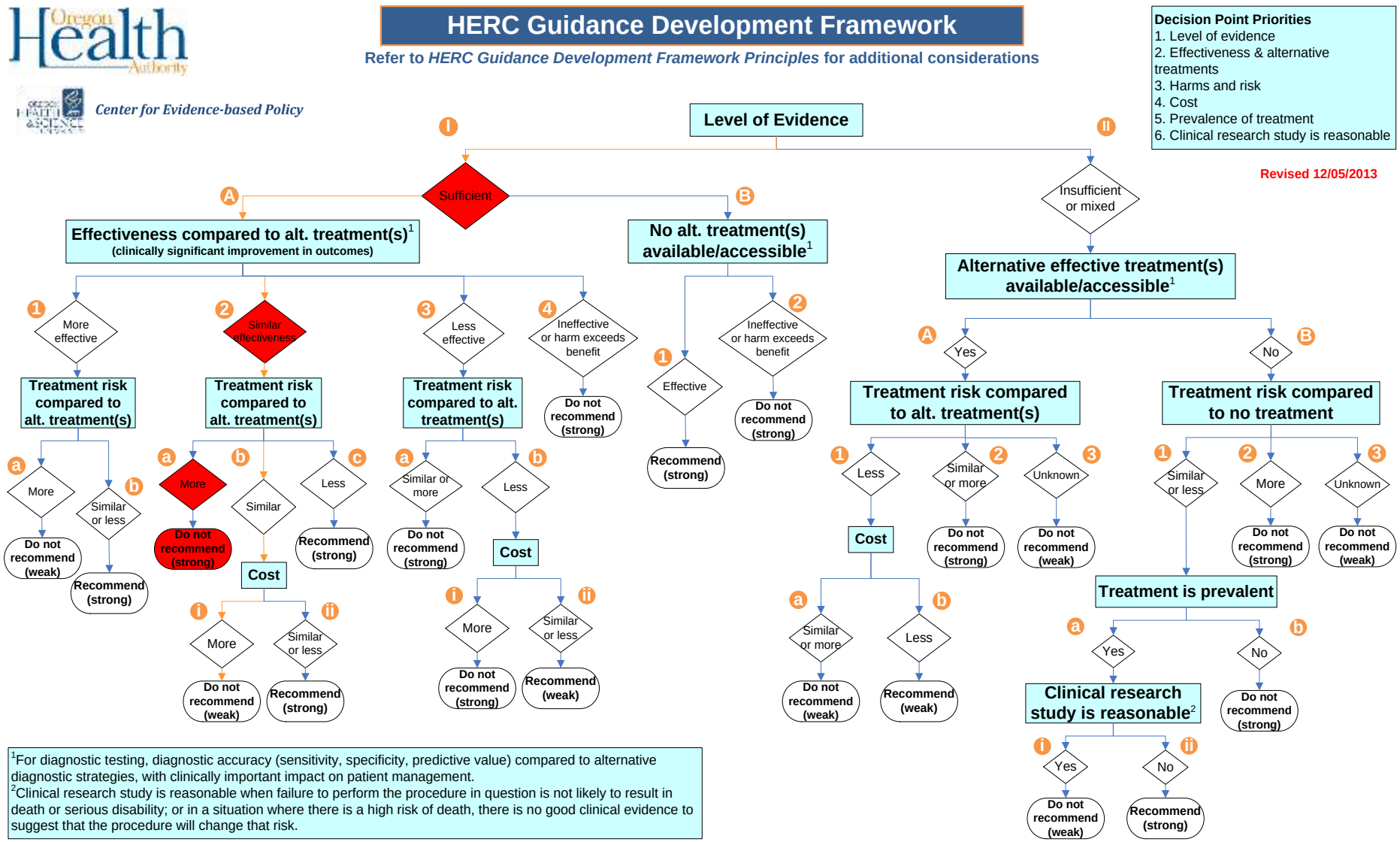
APPENDIX C. HERC GUIDANCE DEVELOPMENT FRAMEWORK

HERC Guidance Development Framework Principles

This framework was developed to assist with the decision making process for the Oregon policy-making body, the HERC and its subcommittees. It is a general guide, and must be used in the context of clinical judgment. It is not possible to include all possible scenarios and factors that may influence a policy decision in a graphic format. While this framework provides a general structure, factors that may influence decisions that are not captured on the framework include but are not limited to the following:

- Estimate of the level of risk associated with the treatment, or any alternatives;
- Which alternatives the treatment should most appropriately be compared to;
- Whether there is a discrete and clear diagnosis;
- The definition of clinical significance for a particular treatment, and the expected margin of benefit compared to alternatives;
- The relative balance of benefit compared to harm;
- The degree of benefit compared to cost; e.g., if the benefit is small and the cost is large, the committee may make a decision different than the algorithm suggests;
- Specific indications and contraindications that may determine appropriateness;
- Expected values and preferences of patients.

PCI for chronic stable angina vs. OMT – Based on mortality, MI



[1]For diagnostic testing, diagnostic accuracy (sensitivity, specificity, predictive value) compared to alternative diagnostic strategies, with clinically important impact on patient management.
[2]Clinical research study is reasonable when failure to perform the procedure in question is not likely to result in death or serious disability; or in a situation where there is a high risk of death, there is no good clinical evidence to suggest that the procedure will change that risk.

PCI for chronic stable angina vs. OMT based on quality of life

Oregon Health Authority

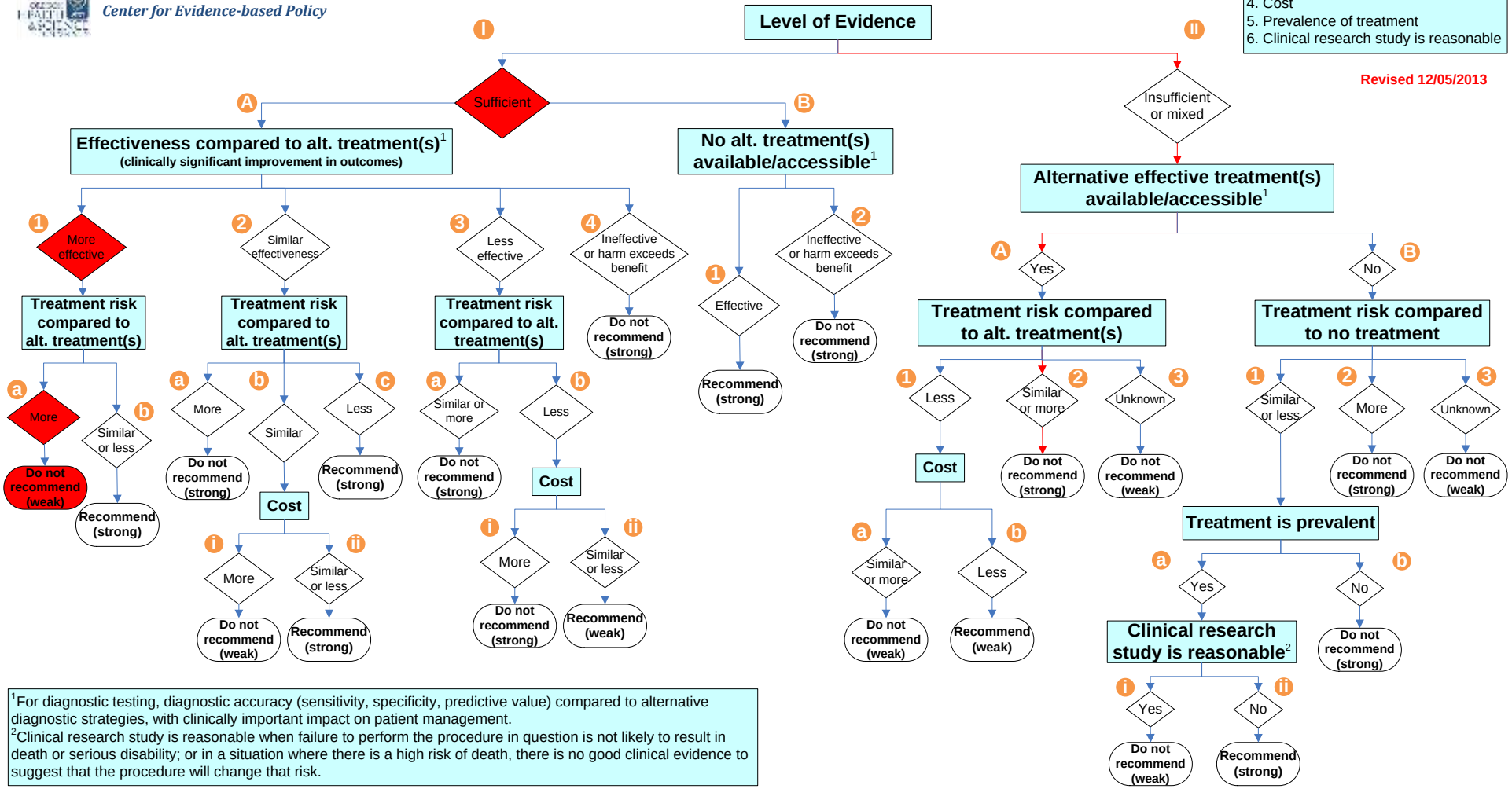
Center for Evidence-based Policy

HERC Guidance Development Framework

Refer to *HERC Guidance Development Framework Principles* for additional considerations

Decision Point Priorities
1. Level of evidence
2. Effectiveness & alternative treatments
3. Harms and risk
4. Cost
5. Prevalence of treatment
6. Clinical research study is reasonable

Revised 12/05/2013



[1]For diagnostic testing, diagnostic accuracy (sensitivity, specificity, predictive value) compared to alternative diagnostic strategies, with clinically important impact on patient management.
[2]Clinical research study is reasonable when failure to perform the procedure in question is not likely to result in death or serious disability; or in a situation where there is a high risk of death, there is no good clinical evidence to suggest that the procedure will change that risk.

CABG for chronic stable angina vs. OMT in 3-vessel and left main disease, based on mortality, MI, MACE

Oregon Health Authority

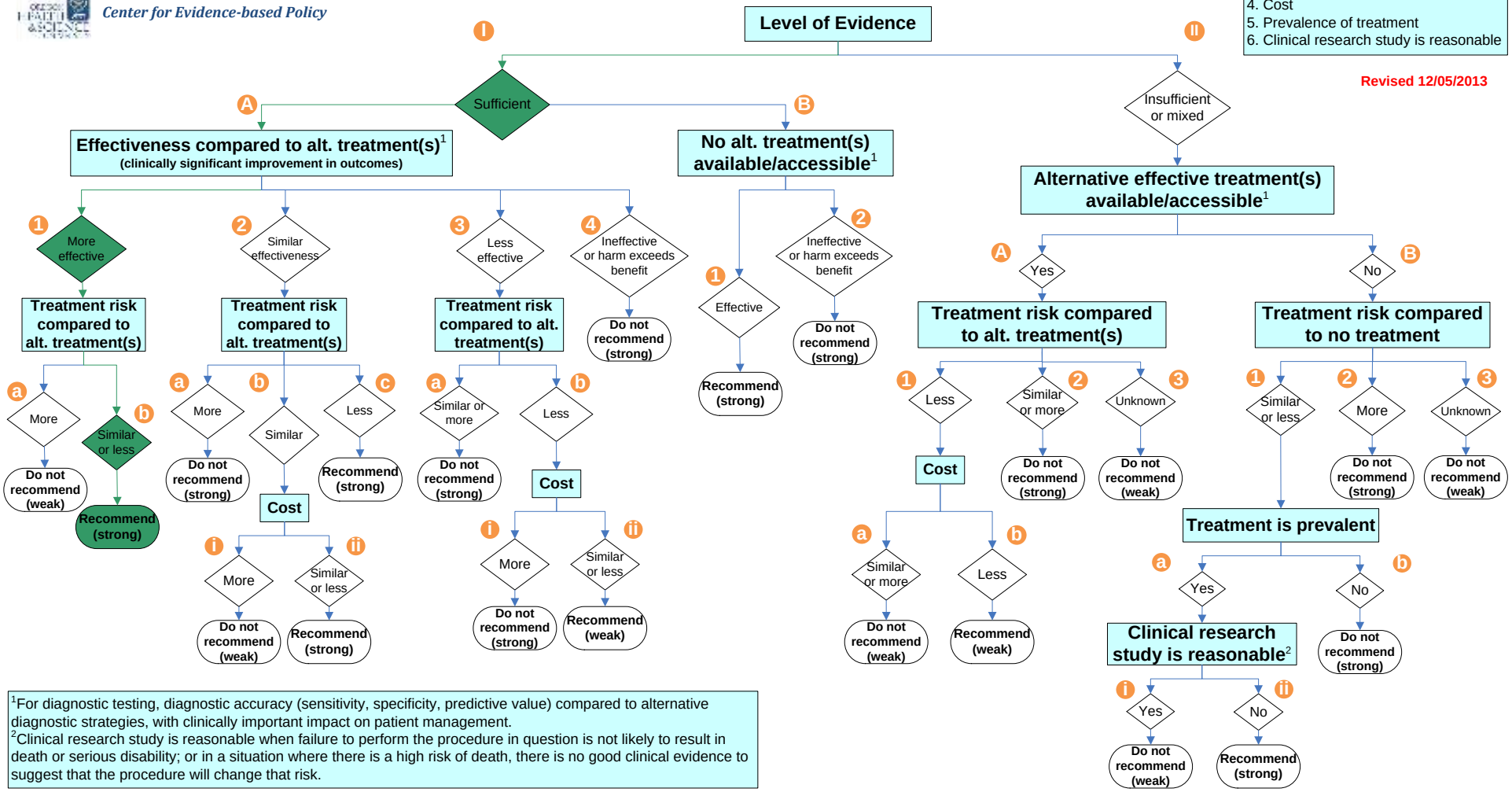
Center for Evidence-based Policy

HERC Guidance Development Framework

Refer to *HERC Guidance Development Framework Principles* for additional considerations

Decision Point Priorities
1. Level of evidence
2. Effectiveness & alternative treatments
3. Harms and risk
4. Cost
5. Prevalence of treatment
6. Clinical research study is reasonable

Revised 12/05/2013



[1]For diagnostic testing, diagnostic accuracy (sensitivity, specificity, predictive value) compared to alternative diagnostic strategies, with clinically important impact on patient management.
[2]Clinical research study is reasonable when failure to perform the procedure in question is not likely to result in death or serious disability; or in a situation where there is a high risk of death, there is no good clinical evidence to suggest that the procedure will change that risk.

CABG for chronic stable angina vs. OMT in 1- or 2-vessel, not left main, based on mortality, MI, MACE

Oregon Health Authority

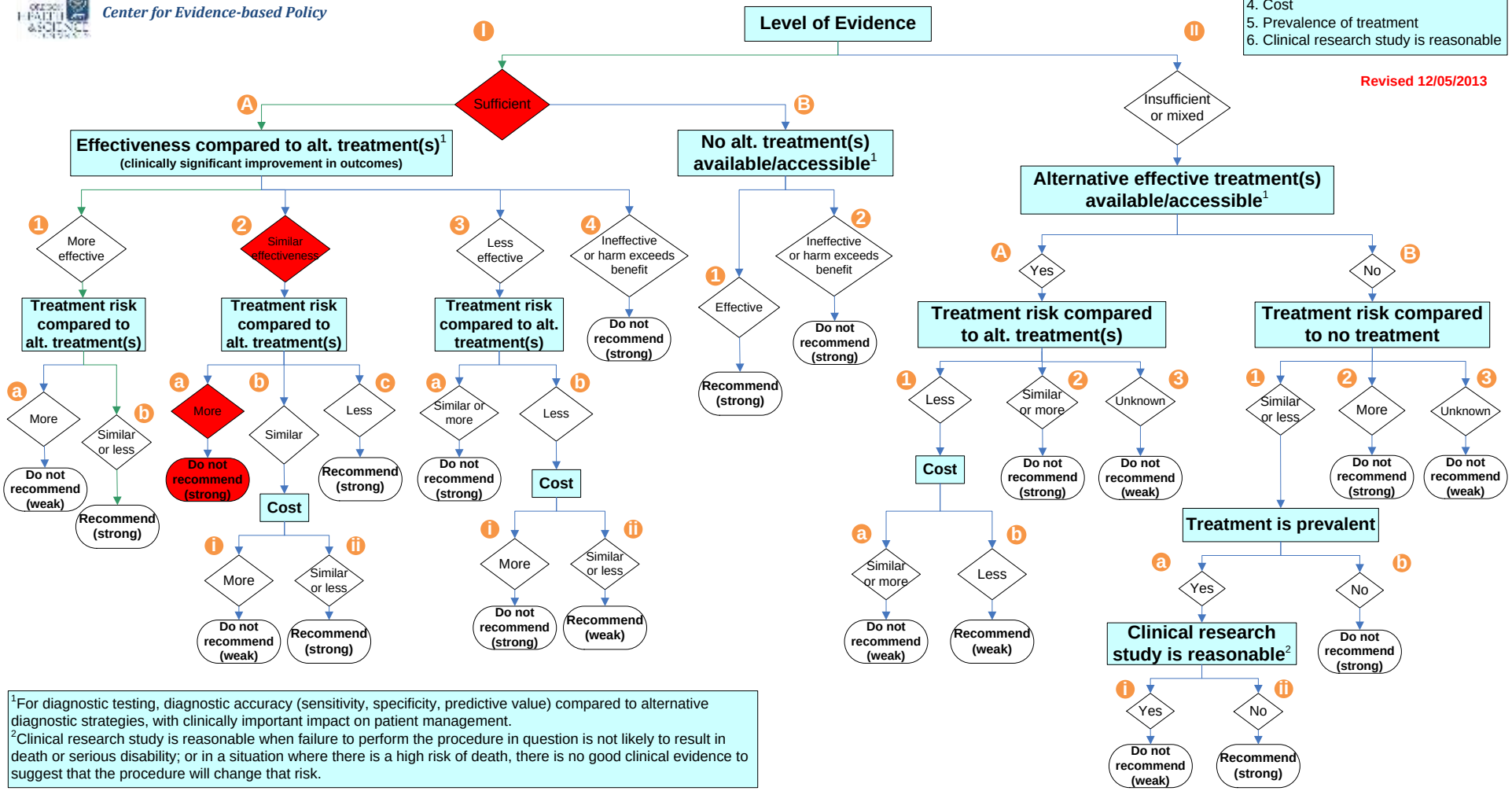
Center for Evidence-based Policy

HERC Guidance Development Framework

Refer to *HERC Guidance Development Framework Principles* for additional considerations

Decision Point Priorities
1. Level of evidence
2. Effectiveness & alternative treatments
3. Harms and risk
4. Cost
5. Prevalence of treatment
6. Clinical research study is reasonable

Revised 12/05/2013



[1]For diagnostic testing, diagnostic accuracy (sensitivity, specificity, predictive value) compared to alternative diagnostic strategies, with clinically important impact on patient management.
[2]Clinical research study is reasonable when failure to perform the procedure in question is not likely to result in death or serious disability; or in a situation where there is a high risk of death, there is no good clinical evidence to suggest that the procedure will change that risk.