

FINAL Key Questions and Background

Cardiac Stents – Re-Review

Background

Coronary artery disease (CAD), also referred to as coronary heart disease (CHD) or ischemic heart disease (IHD), is the single leading cause of death for both men and women in the U.S. and is the most common form of cardiovascular disease; thus the economic and public health burden of CAD is considerable. Atherosclerosis is the most common underlying cause of CAD. It is a disease process in which plaque (comprised of lipids, inflammatory cells, smooth muscle cells, and connective tissue) builds up on artery walls. Partial or complete blockage of coronary arteries can occur with plaque formation and may prevent the portions of the heart muscle from receiving blood, oxygen, and vital nutrients. Atherosclerosis can cause blockage by two mechanisms: 1) progressive narrowing of the artery due to the plaque narrowing the vessel lumen, and 2) thrombotic occlusion of the artery, which occurs when the hard surface of a plaque tears or breaks off, exposing the inner fatty pro-thrombotic, platelet-attracting components to the site, resulting in enlargement of the blockage. Coronary atherosclerotic plaque disruption and associated intraluminal platelet-fibrin thrombus formation are responsible for the acute coronary syndromes of acute MI, unstable angina (UA), and probably for sudden death.

Chest pain (angina) is the most common symptom of obstructive CAD and is the presenting symptom in at least 50% of patients with CAD. Because of the poor correlation between symptoms and CAD, clinicians must rely on a careful history and other modalities to detect and confirm a suspicion of CAD. Classic angina is characterized by retrosternal chest discomfort, often described as a crushing pressure. The discomfort may radiate to the jaw, neck, back, shoulder or arm. It can be accompanied with dyspnea, diaphoresis, nausea and syncope. If the discomfort presents (1) in a predictable pattern, (2) is brought on by physical or mental stress, and (3) subsides with rest or angina medication such as nitroglycerin, it is called stable angina, which is consistent with stable CAD. One can have stable CAD but not have angina with optimal medical therapy. Angina that occurs with less exertion, causes greater discomfort, or takes longer than 20 minutes to subside may be an ominous warning of critical ischemia and has been termed unstable angina. Unstable angina is classified as part of acute coronary syndrome (ACS).

In general, persons with angina already have CAD lesions with at least 75% obstruction and are at increased risk of MI, heart failure and sudden death due to plaque destabilization and thrombosis. Evidence-based recommendations for medical management are now advised for all persons with CAD. Optimal medical therapy, or the newer term, guideline directed medical therapy, includes lifestyle modifications (physical activity, smoking cessations, weight management and dietary changes) as well as treatment of secondary conditions within current guidelines (diabetes and hypertension), risk modification with antiplatelet drugs and management of lipid levels and treatment of angina symptoms if present. For patients with stable CAD with low risk for coronary events, guideline directed medical therapy may be the only treatment. For patients with stable CAD determined to be at high risk for coronary events, treatment may involve both medical therapy and revascularization therapy, with the goal of reducing mortality risk and/or improving symptoms. For patients considered at high risk of

coronary events, invasive coronary angiography for further risk stratification and assessment of appropriateness for revascularization may be the next logical steps in addition to medical therapy.

Overall, consideration of revascularization is based on the clinical presentation (acute coronary syndrome or stable angina), the severity of the angina (based on Canadian Cardiovascular Society Classification), the extent of ischemia on noninvasive testing, and the presence or absence of other prognostic factors including congestive heart failure, depressed left ventricular function, and diabetes, the extent of medical therapy, and the extent of anatomic disease. Revascularization methods include coronary artery bypass graft surgery (CABG) and percutaneous coronary interventions (PCI).

This report will focus on PCI with stenting. A stent is a stainless mesh tube that can be collapsed and attached to the end of a balloon catheter. When the catheter tip is floated to an area of stenosis, the balloon is inflated to expand the stent. The balloon is then deflated and detached from the stent. The stent remains in the artery permanently to act as a physical scaffold to help keep the artery open. There are two general types of stent that have been FDA approved: Bare metal stents (BMS) and Drug Eluting Stents (DES). DES are essentially BMS that have been coated with a polymer containing an antiproliferative drug. These drugs inhibit vascular smooth cell proliferation and migration and are intended to prevent the neo-intimal hyperplasia that appeared to cause the restenosis observed with BMS implantation. All three treatment approaches (medical therapy, PCI and CABG) have seen important improvements over the years. Only stenting and medical therapy are considered in this report.

Policy Context

This technology was originally reviewed May 2009 and was selected for re-review based on new literature identified, changing standards of practice.

Objectives

The aim of this assessment is to systematically review, critically appraise and analyze research evidence comparing the safety and efficacy of: 1) percutaneous coronary intervention with stenting (PCI) with medical therapy versus medical therapy alone in patients with stable CAD, and 2) percutaneous coronary intervention with newer generation FDA-approved drug eluting stents (DES) with bare metal stent (BMS).

Key Questions

KQ1: In patients with stable CAD:

- a. Is PCI with stenting and medical therapy more effective than medical therapy in reducing death and MI and/or improving symptoms, functional status and health-related quality of life? Does the effect vary by (a) BMS versus medical therapy (b) DES versus medical therapy?
- b. What is the comparative safety of PCI with stenting versus medical therapy (including evaluation of bleeding, renal insufficiency and serious adverse events such as nonfatal MI, death)?
- c. If there is benefit to PCI compared with medical therapy alone, is there evidence of differential benefit or harm based on specific patient characteristics or subgroups (e.g. sex, diabetes, left main CAD, age)?
- d. What is the evidence of cost-effectiveness of PCI with stenting versus medical therapy?

- KQ2:** In patients with CAD (*stable or unstable presentation*) is there updated evidence subsequent to the previous (May 2009) report that:
- Newer generation DES are more efficacious than BMS in reducing MI and death and/or improving symptoms, functional status and patient quality of life?
 - Newer generation DES are safer than BMS (including evaluation of thrombosis, serious adverse events)?
 - There is differential efficacy or safety of newer generation DES versus BMS based on specific patient characteristics or subgroups (e.g. sex, diabetes, left main CAD, age)?
 - Newer generation DES are more cost effective than BMS?

Scope

Population: For KQ 1, patients with stable CAD, for KQ 2, patients with CAD undergoing stenting of coronary vessels (stable or unstable presentation) for de novo lesions

Intervention: FDA approved bare-metal stent (BMS) or drug-eluting stent (DES)

Comparator(s): Medical therapy (KQ1), BMS versus DES (KQ2)

Outcomes:

- Efficacy/effectiveness

Primary outcomes:

- All-cause mortality and cardiac death
- Myocardial infarction (MI)
- Patient-reported outcomes: quality of life, symptom relief, functional status measured with standardized measures such as the Seattle Angina Questionnaire, Patient Health Questionnaire, Rose Dyspnea Score

Secondary or intermediate outcomes: Repeat revascularizations (KQ 2 only)

- Safety and harms outcomes

- Thrombosis
- Pharmacological, or procedural complications
- Bleeding
- Renal insufficiency
- Stent fracture, loss, perforation, dissection, or structural problems
- Serious adverse events (e.g. nonfatal MI, death, stroke, need for emergent CABG, vascular complications requiring intervention)

- Economic:

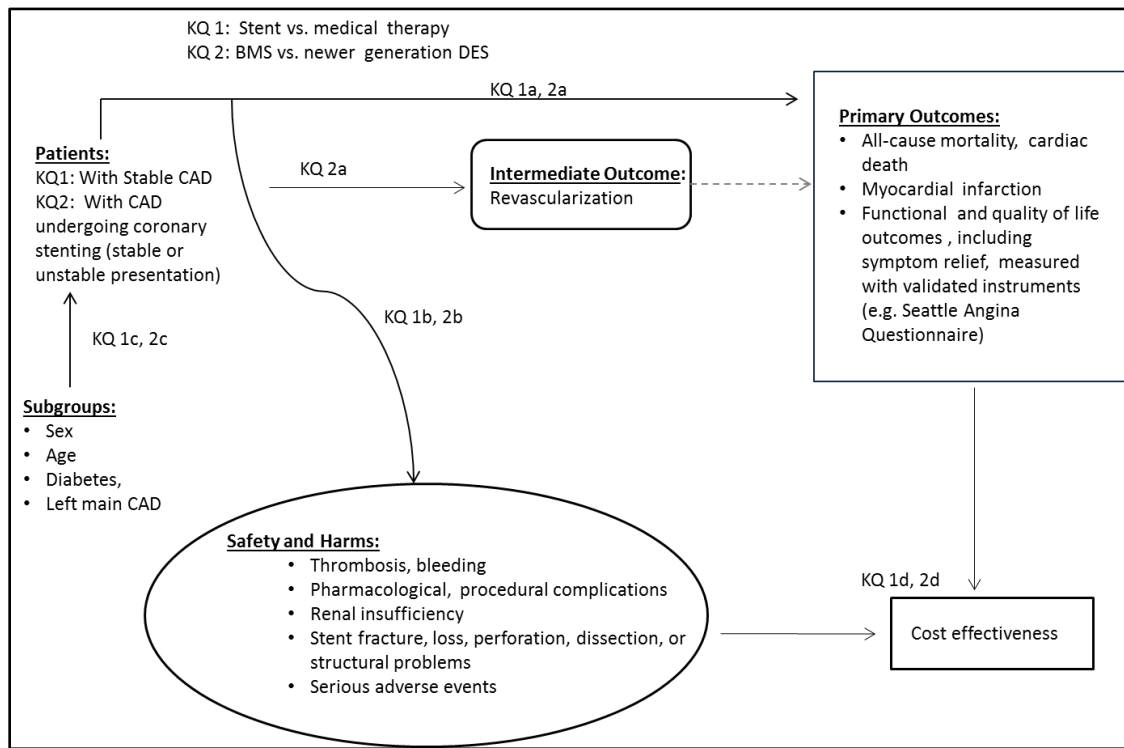
- Cost-effectiveness (e.g., cost per improved outcome), cost-utility (e.g., cost per quality adjusted life year (QALY), incremental cost effectiveness ratio (ICER)) outcomes

Study Design

This report will focus on evidence that evaluates efficacy and has the least potential for bias. High quality systematic reviews will be appraised and incorporated if feasible. RCTs and prospective comparative cohort studies with low risk of bias published subsequent to such reviews will be evaluated

based on the PICO inclusion/exclusion criteria. As Key Question Q 2 serves to update the 2009 assessment, only comparative studies published subsequent to that review which focus on newer generation, FDA-approved DES will be included and described; results will be described based on the context of previous findings. For Key Questions 1c and 2c, RCTs which stratify on patient or other characteristics and formally evaluate statistical interaction (effect modification) will be sought. For Key Questions 1d and 2d, only full, formal economic studies (i.e., cost-effectiveness, cost-utility, cost-minimization, and cost-benefit studies) will be considered.

Analytic Framework



Public Comment & Response

For additional information on [key questions and public comment](#).