

Health Technology Clinical Committee Findings and Coverage Decision

Topic: Cardiac Stent

Meeting Date: May 8, 2009

Final Adoption: October 30, 2009

Number and Coverage Topic

20090508A – Cardiac Stent: Drug Eluting Stents (DES) and Bare Metal Stents (BMS) for the treatment of coronary artery disease.

HTCC Coverage Determination

Cardiac Stent is a **covered benefit with conditions** consistent with the criteria identified in the reimbursement determination.

HTCC Reimbursement Determination

The committee reviewed the findings and decision, and amended the limitations of coverage to read as follows:

❖ **Limitations of Coverage**

- 1) Bare Metal Stents are covered without conditions.
- 2) Drug eluting stents are conditionally covered for:
 - a. Stent diameter of 3 mm or less;
 - b. Length of stent(s) of longer than 15 mm placed within a single vessel;
 - c. Patients with diabetes mellitus;
 - d. Stents placed to treat in stent restenosis; or
 - e. Treatment of left main coronary disease.

❖ **Non-Covered Indicators**

Drug eluting stents are not covered for other indications.

❖ **Agency Contact Information**

Agency	Contact Phone Number
Labor and Industries	1-800-547-8367
Public Employees Health Plan	1-800-762-6004
Health and Recovery Services Administration	1-800-562-3022

Health Technology Background

The Cardiac Stent topic was selected and published in August 2007 to undergo an evidence review process. Heart disease is the leading cause of death and disability in US: with 700,000 deaths. The most common heart disease in the US is coronary artery disease (CAD), which can lead to heart attack. CAD is a narrowing of one or more coronary arteries that result in an insufficient supply of oxygen to the heart muscle and is a leading cause of death in the US and developed countries. CAD may be asymptomatic or lead to chest pain (angina), heart attack, myocardial infarction (MI) or death. Prediction of which patients with CAD will have serious versus no or a mild symptom remains difficult.

Treatments include:

- Manage and reduce risk factors, such as: smoking, obesity, high blood pressure and cholesterol.
- Medication therapy – beta blockers, nitrates, statins, antiplatelet agents and calcium channel blockers.
- Surgical treatment by mechanically opening the artery with a catheter with or without stent (percutaneous coronary intervention – PCI) and bypass surgery.

Use of PCI has steadily risen over past decade while bypass remains relatively unchanged. PCI accounts for over 60% of surgical treatment. Unanswered questions remain about best use of each option, when and for what patient. Cardiac Stents are small tubes placed in an artery to keep it open. Stents are either not coated (bare metal stents) or coated with a drug (drug eluting stents). Cardiac Stent potential advantages: physically opening the artery and being less invasive than bypass surgery. Cardiac Stent potential disadvantages: targeted solution to widespread disease, unclear protocols, clotting and re-operation. Important, unanswered questions remain about whether, when, and what type of stent placement is appropriate versus other medical management or surgery.

In March 2009, the HTA posted a draft and then followed with a final report from a contracted research organization that reviewed publicly submitted information; searched, summarized, and evaluated trials, articles, and other evidence about the topic. The comprehensive, public and peer reviewed, Cardiac Stent report is 175 pages, identified 304 potentially relevant citations; 10 previous health technology assessments or similar reports; 12 meta-analyses or pooled analysis, one of which was of non-randomized studies; 13 reports of long-term follow-up or sub-analyses to previous RCTs or new RCTs found; 26 non-randomized or registry studies and 1 full economic study and one systematic review.

Upon circulation of the draft findings and decision, comments were received from a committee member and provider and professional groups expressing concerns or disagreement with the draft decision. At the August 28th HTCC public meeting, the clinical committee reviewed the draft findings and decision and public comments. Based on public input and committee discussion, the committee would like additional expert input prior to finalizing the conditional coverage criteria to ensure that additional high risk groups were not inadvertently left out.

Ad Hoc Advisory Group Scope and Role: Participate in a group of technical experts to identify groups at high risk of restenosis and the evidence supporting it that are not currently included in the draft criteria. Approve a report to the HTCC, in time for distribution prior to the October 30, 2009 scheduled meeting. Subject to discussion within the group, provide report or testimony to the HTCC. Two HTCC members; a hospital association and agency representative; the evidence vendor and four cardiologists formed the workgroup. The workgroup met publicly, twice - on October 5th and 16th and selected Dr. Mike Ring to serve as the clinical chair. The workgroup started with a review of the task and a discussion of the potential high risk categories that were included in public comment. The list was updated based on comments, and members submitted some articles and other information to a central repository; reviewed the information; and eventually provided a ranking from 0 to 10 of importance of certain risk categories. After second discussion, a report was produced summarizing the categories and rankings by the workgroup members.

An independent group of eleven clinicians who practice medicine locally meet in public to decide whether state agencies should pay for the health technology based on whether the evidence report and other presented information shows it is safe, effective and has value. The committee met on May 8th, reviewed the report, including peer and public feedback, and heard public and agency comments. Meeting minutes detailing the discussion are available through the HTA program or online at <http://www.hta.hca.wa.gov> in the committee section.

Committee Findings

Having considered the evidence based technology assessment report and the written and oral comments, the committee identified the following key factors and health outcomes, and evidence related to those health outcomes and key factors:

1. Evidence availability and technology features

The committee finds the following key factors relevant to the coverage decision:

- 1.1 The evidence based technology assessment report indicates that Coronary Artery Disease (CAD), a narrowing of the arteries that supply the heart with oxygen, is very common and is an important public health concern. Prediction of risk of serious complication is difficult: while the location and severity of obstructions are used, they do not always correlate with symptoms or outcome.
- 1.2 Treatment options for CAD to open the arteries include medical therapy and lifestyle management, percutaneous coronary intervention (PCI) a catheter with or without stenting, and coronary artery bypass grafting (CABG). Catheter based interventions that leave a stent to hold open the arteries can include bare metal stents (BMS) or drug eluting stents (DES).
- 1.3 The committee found that there was a large amount of randomized and observational studies available comparing DES and BMS on many of the important health outcomes they identified for stents. The committee relied most heavily, as did the evidence based technology assessment report, on one recent meta analysis of 38 trials including 18,000 patients, and summarized information from five previous health technology assessments, most conducted with their own meta-analysis, and one focusing on registry studies
- 1.4 The committee also considered additional evidence published after the draft and final evidence report. The final evidence report includes a brief summary of the study published after the draft which linked Medicare data with ACC registry data, *Douglas, et. al.* An uncorrected proof of this registry study contained summary information on data of 260,000

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over 65 year old Medicare patients for up to 30 months. Two additional study abstracts were published one day prior to the meeting. The studies were briefly reviewed by the evidence review vendor and made available to committee members. First, a registry follow-up study from Sweden (SCAAR 2) on 47,967 patients through 2006 that were followed from one to five years. A second randomized trial, *Stone, et al*, of 3006 patients comparing BMS and DES in patients with ST-segment elevation myocardial infarction.

2. Is the technology safe?

The committee found that stent thrombosis was the most significant safety outcome measure, and discussed briefly bleeding and stent fracture. The report identified the following evidence:

- 2.1. The evidence based technology assessment report indicated that stent thrombosis is a rare, but serious complication (generally occurring in about 1.5% of cases) with potentially higher rates in DES. This topic prompted a review of evidence by an FDA panel in 2006 that concluded DES used for approved indications (single, new lesion of certain size) and with anti-platelet therapy is prescribed for at least 1 year (instead of 3 to 6 months) were safe. From the most recent meta-analysis with four year follow up, thrombosis rates are low and not statistically different: 1.4% SES; 1.7%PES and 1.2%BMS; though the evidence review indicates that even large studies may be underpowered to detect statistically significant differences.
 - 2.1.1. The evidence based technology assessment report summarized seven HTA's, including one HTA of registry data: most concluded no statistically significant difference, though several indicated they may be underpowered, three reported there was a higher risk of stent thrombosis with DES.
 - 2.1.2. The evidence based technology assessment also included a summary from Stettler's more recent meta-analysis of randomized trials related to thrombosis (included 24 trials and 12,973 patients which showed an overall rate of thrombosis at 1.4% and no statistically significant difference between BMS and DES in up to four years, though some statistical differences were observed in subgroups comparing SES, PES and BMS and short versus longer time periods. Adherence and length of anti-platelet therapy are not well documented in trials, though a 2008 Stettler updated meta-analysis found no statistically significant difference in thrombosis rates, regardless of anti-platelet therapy regimen.
- 2.2. Stent Thrombosis in special populations (diabetics and acute MI): Most HTA's and the Stettler meta-analysis in specific subpopulations generally reported no statistically significant difference between BMS and DES in stent thrombosis rates. One HTA noted patients more likely to benefit from DES to be diabetic patients, small vessels, and chronic kidney disease, were at the same time at higher risk for developing late stent thrombosis. Although, one HTA of registry data indicated higher in-stent thrombosis with DES (2.4 to 4.4%) versus BMS (0.8%).
- 2.3. Bleeding and Stent Fracture: the evidence based technology assessment report reviewed these safety issues, however no randomized studies or HTA's compared DES to BMS for this outcome. One non-randomized study compared different DES patients, with overall rates of bleeding at 3.1%, patients on dual antiplatelet use and over age 65 were significant risk factors for major bleeding in DES patients.

3. Is the technology effective?

The committee found that there were four key health outcomes that were most significant in assessing the technology's effectiveness. The report identified the following evidence:

3.1. Freedom from Overall and Cardiac Mortality:

- 3.1.1. The evidence based technology report includes death, and specifically cardiac-related death, as a key health outcome in treatments for cardiac artery disease and core evidence indicates no difference between DES and BMS. It was noted both by the evidence review and committee members that the updated FDA recommendation to continue dual anti-platelet therapy for one year in DES patients may be a related factor that was not separately reported in many studies.
- 3.1.2. The evidence review of previous HTA and the meta-analysis report no statistically significant difference in overall or cardiac mortality between DES and BMS up to four years.
- 3.1.3. Studies including registry data cite the SCAAR (Sweeden) where authors found increased risk of death with DES at 6 months and 3 years (relative risk of 1.18%). In other registry studies, the findings were mixed, with six suggesting no difference; and three showing higher BMS risk.
- 3.1.4. Freedom from mortality in elderly subpopulation. The Douglas study (not critically appraised) of Medicare patients indicates a 3% higher risk of mortality from BMS than DES.
- 3.1.5. Freedom from mortality in acute MI subpopulation. The evidence based technology report summarized results from one recent HTA, a meta-analysis and three recent RCT's that concluded no statistically significant difference in DES and BMS groups with acute MI for mortality.
- 3.1.6. Freedom from mortality in diabetics subpopulation. The evidence based technology report indicates that diabetics tend to have multi-vessel disease, smaller coronary arteries, and longer lesions. Previous HTAs had only limited evaluation of diabetics, but recent meta-analysis reported a two fold increase in mortality for diabetic patients receiving less than 6 months of dual anti-platelet therapy. Three recent meta-analyses indicate that the overall mortality risk is similar between BMS and DES.

3.2. Freedom from MI

- 3.2.1. The evidence based technology report and committee agreed that subsequent myocardial infarction (MI or heart attack) is a key health outcome in treatments for cardiac artery disease, including stents and core evidence indicates no difference between DES and BMS.
- 3.2.2. The evidence review of previous HTAs, the Stettler meta-analysis and two other meta-analyses report no statistically significant difference in MI between DES and BMS in trials with two to five years follow up. One meta-analysis with follow up at 6 to 12 months reported lower MI with DES (3.3%) than BMS (4.2%).
- 3.2.3. Freedom from MI in diabetics subpopulation. The evidence based technology report focused on the recent meta-analysis with up to four years follow up indicating no difference in MI outcomes between BMS and DES diabetic patients.
- 3.2.4. Freedom from MI in acute MI subpopulation. The evidence based technology report focused on the recent meta-analysis with up to four years follow up indicating no difference in MI outcomes between BMS and DES in acute MI patients.
- 3.2.5. Freedom from MI in elderly subpopulation: The evidence report summarized the Douglas study (not critically appraised) finding a higher rate of MI (1.4% risk difference) in BMS patients.

3.3. Freedom or reduction of Target vessel revascularization/target lesion revascularization (TVR)

- 3.3.1. The evidence based technology report and committee agreed that TVR, or repeat procedures to open the same vessel, is a key health outcome in stent comparisons and that DES results in 11% fewer TVR than BMS.

- 3.3.2. The committee discussed the implication of dual anti-platelet therapy and whether that impacts revascularization rates.
- 3.3.3. The evidence review of previous HTAs, the Stettler meta-analysis and two other meta-analyses report a lower rate of TVR using DES compared to BMS. The Stettler meta-analysis reported a revascularization rate of DES at 6.9% to 9.0% and BMS at 19.0% with up to 4 year's follow up – this represents an 11.1% reduction.
- 3.3.4. Revascularization rates in studies of the Acute-MI subpopulation also reported decreased revascularization using DES (4.8% to 5.1%) versus BMS (12.0% to 13.1%).
- 3.3.5. Revascularization rates in HTA's and meta-analysis of the diabetic subpopulation also reported significant decreased revascularization using DES, regardless of use of dual anti platelet therapy, out to one year DES (6.3% to 11.3%) versus BMS (19.3% to 31.1%).
- 3.3.6. Revascularization rates in studies of the elderly subpopulation reported a no difference in revascularization rate between DES (23.5%) and BMS (23.4%) at 30 months.

3.4. Quality of Life

- 3.4.1. The evidence based technology report included quality of life as a key outcome, but studies did not report or define this measure. The committee commented that quality of life is important and future studies should include this outcome. Additionally, TVR is a part of a quality of life where less need for re-surgery would be positive but the metric is incomplete and it appears that short term results may favor DES but longer term results are similar.

4. Is the technology cost-effective?

The committee found that there was key information about cost and value:

- 4.1. There remains uncertainty regarding efficacy, effectiveness, and safety of DES versus BMS and differing assumptions contribute to variability in cost analysis. The incremental cost effectiveness ratios (ICER) were most influenced by the price premium of DES.
- 4.2. The evidence included 43 cost effectiveness studies, but focused on evidence from previous HTA's which concluded that DES might be cost effective in higher risk patients and not cost-effective with low risk patients; when more realistic assumptions and data values were used, DES may be cost effective only under very limited circumstances, and several studies were industry supported.
- 4.3. Price premium for DES in HTA's ranged from \$563 Euro to \$1,299. ICER for use of DES ranged from a low of \$27,540 to a high of \$1,099,858 QALY; with the four economic analyses performed as part of HTA's ranging from \$64,394 to over 1 million Euros. ICER's for repeat revascularizations ranged from \$1,650 to \$7,000.
- 4.4. Washington state use data from the COAP database which gathers information on all WA procedures, from 2004 to 2007, BMS was used 15% and DES 85%.
- 4.5. State agency cost data: Utilization at the three agencies over the same time period is 15% BMS and 83% DES.

Committee Conclusions

Having made findings as to the most significant and relevant evidence regarding health outcomes, key factors and identified evidence related to those factors, primarily based on the evidence based technology assessment report, the committee concludes:

5. Evidence availability and technology features

The committee concludes that the best available evidence on cardiac stents has been collected and summarized, and the overall quality of this evidence is high and robust as follows:

- 5.1. There was a large amount of high quality, randomized and observational studies available comparing DES and BMS on many of the important health outcomes they identified for stents. The committee relied most heavily on a recent meta analysis of 38 trials including 18,000 patients, and summarized information from five previous health technology assessments.
- 5.2. Randomized or well designed controlled trials provide the highest level of confidence for proving efficacy, especially with adequate participants, assessment of all patient centered health outcomes, and for sufficient duration. The very recent registry studies may provide additional information (e.g. rare complications and additional subpopulation data) but should not be relied upon as the basis to overturn the RCT results. Recently published articles not included in critical appraisal were considered, but would not be relied upon for final determination without seeking additional review by evidence vendor.
- 5.3. Heart disease is a burdensome condition with potentially significant and life threatening outcomes. It is widespread condition with imprecise measures of those at risk for life threatening outcomes and thus is a significant health concern to ensure the right treatment for those at high risk as well as low risk.
- 5.4. Many treatments, including non-invasive treatments, are covered by agencies. The type of stent selected (issue for current review) does not have an effect on mortality or heart attack – the two potentially life threatening outcomes, but may impact need for revascularization need and cost.

6. Is it safe?

The committee concludes that the comprehensive evidence reviewed shows that the DES and BMS have been proven equally safe. Key factors to the committee's conclusion included:

- 6.1. *Morbidity related to Stent Thrombosis:* The committee agreed with the evidence report conclusions that these are rare events, where even the larger RCT's and observational data may not be powered to detect. However, the best available meta analysis of RCT data shows difference relied heavily on the most recent meta-analysis with four year follow up: 1.4% SES; 1.7% PES and 1.2% BMS.
- 6.2. *Bleeding:* the committee concluded that bleeding is a very serious complication. Due to dual anti-platelet therapy proscribed with DES, this complication could be higher in DES; but not enough information and registry data, though lower quality, showed equivalence with 3.4% BMS vs 3.6% DES rate.
- 6.3. *Stent Fracture:* The committee agreed that this issue was not applicable since evidence was not obtainable on this outcome and no other reason to believe rates between the two stent types would be different.

7. Is it effective?

The committee concludes that the comprehensive evidence reviewed shows that the DES technology has been proven equally effective to BMS, and more effective than BMS in one area:

- 7.1. The committee identified four key health outcomes that impacted effectiveness; with three have high quality evidence available.

- 7.2. *Freedom from Cardiac Mortality*: the committee concluded that data from multiple RCTs demonstrated that there is no overall or cardiac related benefit with DES compared to BMS.
- 7.3. *Freedom from Myocardial Infarction (MI)*: the committee concluded that the data from multiple RCTs demonstrated that there is no benefit from DES compared to BMS in reducing rates of MI.
- 7.4. *Freedom or reduction of revascularization (TVR)*: the committee concluded that data from multiple RCTs demonstrates a benefit of an 11% reduction in the rate of revascularization with use of DES compared to BMS.
- 7.5. *Quality of Life*: the committee believes that quality of life is an important health outcome to demonstrate overall effect of treatment, but concluded that there was not reliable data to conclude whether DES provided a benefit over BMS. The committee discussed the previous revascularization reduction as a component of quality of life

8. Is it cost-effective?

The Committee concludes that the comprehensive evidence review shows that the DES technology is less cost-effective overall. However, the committee also addressed cost-effectiveness in a certain situation, for high risk patients, and was split with five finding that DES were more cost effective and five finding that DES was unproven or less cost-effective for this population.

- 8.1. The committee noted that the evidence review contained multiple cost effectiveness studies and agreed that the most important factors were the cost premium for DES, but also discussed the cost of medications, revascularization cost, issue of lack of ability to demonstrate higher overall efficacy, and the concept of measuring DES in terms of cost per revascularization versus cost per QALY (which takes revascularization and other factors into account).
- 8.2. The committee agreed that overall, DES is not cost-effective, especially considering the state's \$3,600 differential, where lower price premiums produced staggering cost per QALYs.
- 8.3. For certain subpopulations of high risk patients, some HTAs reported, and five committee members agreed that DES is cost-effective.

9. Medicare Decision and Expert Treatment Guidelines

The committee deliberations included a discussion of National Medicare Decisions and expert treatment guidelines, and an understanding that the committee must find substantial evidence to support a decision that is contrary. RCW 70.14.110. Based on the following, the Committee concludes that a decision consistent with two expert treatment guidelines and contrary to the National Medicare Coverage Decision and one treatment guideline is justified:

- 9.1. Centers for Medicare and Medicaid Services (2008) – there is no national coverage decision (NCD) relating to drug eluting versus bare metal stents. There is coverage memo on percutaneous intervention overall (PTA) which covers treatment with conditions: PTA (with and without a placement of a stent) is covered when used in accordance with FDA approved protocols for treatment of atherosclerotic lesions of a single coronary artery for patients for whom the likely alternative treatment is coronary bypass surgery and who exhibit the following characteristics: (1) angina refractory to optimal medical management; (2) objective evidence of myocardial ischemia; and (3) lesions amenable to angioplasty.
- 9.2. Guidelines -- No guidelines for clinical care or appropriateness have been published regarding the use of BMS versus DES. The most comprehensive guideline, a joint ACC/AHA guideline

addresses broader perspectives on setting and issues involved in the decisions leading to coronary stent placement as well as other treatments.

- 9.3. Two other organizations, England's NHS and Ontario's OHTAC have recommendations for use of DES in narrow lesions (<3.0 or 2.75mm) long lesions (>15 or 20 mm). Patients with diabetes and a price differential cap of \$300 pounds are additional limits.

Committee Decision

Based on the deliberations of key health outcomes, the committee decided that it had the most complete information: a comprehensive and current evidence report, public comments, additional just published studies, input from a clinical expert, and agency and state utilization information. The committee concluded that the current evidence on Cardiac Stents demonstrates that there is sufficient evidence of a health benefit to cover the use of cardiac stents, but limit the use of Drug eluting stents to certain circumstances. The committee considered all the evidence and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable. The committee found that drug eluting stents were proven to be equivalent to bare metal stents in safety and efficacy overall. The committee found that drug eluting stents were proven to be more effective in one area: reducing revascularization, and were proven to cost more.

Based on these findings, the committee voted to continue coverage for bare metal stents and voted 8 to 2 to cover drug eluting stents, with conditions: limited to patients with highest risk of revascularization (less than 3 millimeter vessel, or lesion longer than 15 millimeters, or diabetics).

Health Technology Clinical Committee Authority

Washington State's legislature believes it is important to use a scientific based, clinician centered approach for difficult and important health care benefit decisions. Pursuant to chapter 70.14 RCW, the legislature has directed the Washington State Health Care Authority, through its Health Technology Assessment program to engage in a process for evaluation process that gathers and assesses the quality of the latest medical evidence using a scientific research company and takes public input at all stages. Pursuant to RCW 70.14.110 a Health Technology Clinical Committee (HTCC) composed of eleven independent health care professionals reviews all the information and renders a decision at an open public meeting. The Washington State [Health Technology Clinical Committee \(HTCC\)](#), determines how selected health technologies are covered by several state agencies. RCW 70.14.080-140. These technologies may include medical or surgical devices and procedures, medical equipment, and diagnostic tests. HTCC bases their decisions on evidence of the technology's safety, efficacy, and cost effectiveness. Participating state agencies are required to comply with the decisions of the HTCC. HTCC decisions may be re-reviewed at the determination of the HCA Administrator.