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June 3, 2009

Leah Hole-Curry, JD
Program Director
Health Technology Assessment Program
Washington State Health Care Authority
P.O. Box 42712
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Re: HTCC Cardiac Stent Coverage Decision

Dear Leah,

Since our Health Technology Clinical Committee meeting of May 8, 2009, I have spent considerable time perusing relevant peer-reviewed literature and reflecting upon the HTCC decision on Drug-eluting Stents (DES), and I remain quite troubled with our HTCC decision.

As you are aware, the HTCC voted to restrict the use of DES to include:

- Patients with diabetes mellitus **OR**
- Target lesion <3 mm diameter **OR**
- target lesion >15 mm length

My concerns with our HTCC decision are multiple, as addressed below.

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1. HTCC Coverage Decision Conflicts with FDA approved Indications.
Our DES stent decision is in conflict with current FDA "on-label" licensing approved indications. This conflict between HTCC target lesion standards and approved license standards of the FDA for DES implies that Washington State will not cover some patients whose 'on-label' indications are approved by the FDA.

Stent Device	***Year***	***FDA Licensed Target Lesion Standards***	
		Caliber	**Length**
Cypher® Sirolimus	2003	≥2.5 mm to ≤3.5 mm	≤ 30 mm
Taxus® Paclitaxel	2004	≥2.5 mm to ≤3.75 mm	< 28 mm
Endeavor® Zotarolimus	2007	≥2.5 mm to ≤3.5 mm	≤ 27 mm
Xience V® Everolimus	2008	≥2.5 mm to ≤4.25 mm	≤ 28 mm
HTCC Recommendation	2009	<3.0 mm	> 15 mm

2. **Threshold benchmark criteria are not entirely evidence-based.**
Of some consternation to me is that these coverage target lesion thresholds that the HTCC adopted are not entirely evidence-based and are only partially supported by clinical trials evidence. In both Ontario OHTAC recommendations[1] and British NICE assessments for DES,[2] these thresholds were developed in negotiations unique to each country's health system. The NICE Assessment committee vessel lesion threshold standards (which the HTCC adopted) are based upon evidence from clinical trials, from risk factors derived from a British registry (the Liverpool Cardiothoracic Centre audit data), and *significantly* from testimony from British clinical specialists. Based on essentially the same set of clinical trials, Britain's NICE did not endorse DES in diabetics, whereas Ontario supports coverage for some diabetic patients, and the HTCC endorsed DES coverage for all diabetics.

Entity	*Year*	*Diabetes*	*Endorsed Target Lesion Standards*	
			Caliber	Length
British NHS (NICE)	2008	NO	<3.0 mm	>15 mm
Washington HTCC	2009	YES-All	<3.0 mm	>15 mm
Canadian OHTAC	2007	YES-Optional	<2.75 mm	>20 mm

3. **Safety Issues surrounding ISR-related TVR not addressed.**
The Health Technology Assessment report did not address safety issues surrounding the need for Target Vessel Revascularization (TVR) for In-Stent Restenosis (ISR), and this issue was not discussed in the HTCC meeting. Part of the reason is that the Spectrum HTA report treated TVR as an outcome benchmark of stent procedures rather than a separate safety measure. Safety issues such as cardiac and non-cardiac death, Myocardial Infarction (MI), and Stent Thrombosis (ST) after stent implants were discussed but other safety issues related to ISR-related TVR were never addressed.

Early BMS vs. DES clinical trials included scheduled angiograms as part of RCT protocols, and endpoints of these trials included angiographic evidence of restenosis with/without clinical symptoms. Angiographic confirmation of ISR is generally confirmed by using either 1) *Binary Restenosis* – (% of lesions with $\geq$50% stenosis) or 2) *Late Lumen Loss* – (difference in mm between the Minimal Lumen Diameter [MLD] at stent placement and at time of follow-up exam). Binary Restenosis in most HTA clinical trials impressively favor DES stents with 20% - 30% absolute differences in ISR in some clinical trials. 4-year (and some 5-year) follow-up clinical stent data validate earlier patterns of Binary Restenosis and Late Lumen Loss differences.

TVR is a complementary but more clinically relevant measure of the restenosis problem because evidence of myocardial ischemia is required in addition to the angiographic confirmation of ISR. Probably half of all patients with binary restenosis have myocardial ischemia, which is why TVR is a more valid endpoint of stent performance and why critics often point out that measures of ISR alone may misrepresent stent performance. With ischemic symptoms and angiographic findings as a measure of stent performance, TVR is required 50-75% less often with DES than BMS.

Safety data related to TVR are best obtained from cohort studies since the small numbers of TVR available in clinical trials are insufficient to reach adequately statistically powered conclusions. Observational studies indicate that the presentation of TVR patients with ISR is not a benign event.[3] A Cleveland Clinic study of all 984 patients undergoing TVR who represented with ISR after stenting with BMS between 1999 and 2003 revealed that over one-third (35.9%) of patients presented with Acute Coronary Syndrome (7.3% - NSTEMI, 2.2% - STEMI, and 26.4% - Unstable Angina) and required hospitalization for stabilization and angiography. 64.1% developed exertional angina. Except for death and MI associated with the clinical presentations with TVR, these safety risks were not addressed in the HTA report or discussed at the HTCC meeting.

Clinical Trials that were included in the HTA report provide 4-year and 5-year follow-up data that suggest that patient pools receiving BMS will undergo greater numbers of repeat procedures. Although not included in the analysis, common sense would suggest that the pool of BMS patients face a greater aggregate risk than the pool of patients receiving DES. The HTCC was aware of the greater number of repeat procedures associated with BMS but was not provided relevant safety data from observational studies addressing ISR-related TVR events.

The safety risks associated with ISR-related revascularization requirements are central to my disagreement with our current coverage solution. A decision not to cover DES will subject these PCI patients receiving BMS to increased numbers of revascularization procedures and increased safety risks that likely dominate the increased DES costs.

4. Special 'Off-Label' Sub-group Populations Not Addressed

The ACC-NCDR registry indicates that nearly 70% of all DES use is 'Off-label',[4] and some of these special population sub-groups were not included in clinical trial data that were reviewed. Clinical trial data addressing diabetes, acute myocardial infarction, small vessels, long lesions, and other subgroups were included in the Spectrum HTA report, but only small vessels, long lesions, and the diabetic sub-groups were discussed at our meeting. Excluding these three subgroup, the HTCC coverage decision did not adequately address the issue of DES in sub-groups where clinical evidence indicates differences in outcomes between DES and BMS.

My independent and critical review of relevant peer-reviewed literature on these subgroups reveals that some were not included in the Spectrum HTA report. I believe that evidence strongly supports use of DES over BMS for some … but not all … of them. As our coverage decision currently stands, *all of the following special situations, whether included in the HTA report or not,* are subject to the DES coverage decision.

- Restenosis of stented lesion
- Bypass graph related to prior CABG
- Unprotected Left Main Coronary Artery
- Ostial lesions

- Bifurcation Lesions
- Total occlusion lesions
- Acute Coronary Syndrome including:
  - ST-segment Elevation Myocardial Infarction (STEMI)
  - Non ST-segment Elevation Myocardial Infarction (NSTEMI)
  - Unstable Angina

Amplifying upon my concern, I would suggest that in the above list, one would find it extremely difficult to find any Interventionalist who would propose and defend treatment of a BMS-related restenosis with another BMS rather than a DES or who would propose and defend treatment of an unprotected Left Main Coronary Artery with a BMS rather than a DES.

5. Coverage Decision applies to populations not included in HTA.

In addition to subgroup populations that should have been separately addressed within the DES coverage solution, there are other subgroup populations *for whom the DES coverage solution equally applies*, even though they were not included in the original scope of the HTA and did not appear in the submitted HTA Stent report.

- Multi-lesion single vessel coronary artery disease
- Multivessel (2-3 vessel) coronary artery disease
- Lesions in non-candidates for Coronary Artery Bypass Graph (CABG) surgery and/or alternative therapy

These subgroup populations were not considered in the HTA report since they fundamentally address a different scope from the HTA report, i.e., … Stent vs. Surgery rather than a BMS vs. DES. While some of these special sub-groups are addressed in clinical trials, data on others are only available in cohort studies and cardiac registries.

Applying the stent coverage decision to these subgroups extends an *ex officio* endorsement to existing clinical practices without consideration of evidence-based data unique to these subgroup populations. I would suggest that applying the stent coverage decision to these subgroup populations reflects a disconnect between policy implementation (i.e., coverage decision) and HTA program methodology that promulgates evidence-based analysis as the basis for those coverage decisions.

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For the reasons I have outlined above, the defensibility of the current HTCC coverage decision is problematic and tenuous. The medical literature and number of relevant clinical trials, meta-analyses, observational studies, cohort studies, and dedicated stent registries on this HTA topic is overwhelming. I believe we have over-simplified our synthesis of complex data and/or made a decision with insufficient time/resources to assess *all* these data.

It is obvious that the current coverage decision is contrary to existing Interventional Cardiology stent use in the State of Washington, and I have no doubt that most Interventional Cardiologists with support of their professional societies (ACC and SCAI) will continue to deploy DES stents supported by their reading of evidence-based literature and independent of (or more likely, …. oblivious to and ignorant of…) patient coverage.

Physicians will never agree to provide two standards of care based on differing insurance coverage requirements, and many Interventionalists will not violate personal and medical ethics standards by complying with a coverage decision they oppose.

The consequences of our current coverage decision for stakeholders are predictable. Powerless to resist enforcement of the HTCC coverage decision, many PCI Interventionalists will continue to provide their standards of stent care utilization. (Paradoxically should Interventionalists change their behavior to comply with the coverage decision, they would benefit financially by performing greater numbers of BMS stent procedures, which are remunerated identically to DES stent procedures). Independent of physician compliance, hospitals, who are remunerated only for BMS stenting in non-coverage situations, will be left to absorb the uncovered costs of DES. Cost savings, if any, will accrue to the State, albeit hypothetical increases in yet-unknown *real-life* TVR rates after BMS-specific stent utilization could increase overall PCI costs. The health care consumer may also be affected. Patients who are selected for PCIs and do not meet coverage conditions will be subjected to increased numbers of repeat procedures and increased safety risks due to increased risks of ISR in BMS-related TVRs.

Last I want to affirm my strong belief in and support for the mission of the State of Washington to reduce health care costs. However, the inflexibility of the current HTA selection process provides the HTCC with a limited scope in which to make evidence-based decisions that might aggressively address cost issues. For example, at the HTCC stent meeting Jeff Thompson MD, Medical Director of Medicaid, intimated opportunities for potential stent cost savings by addressing

- limits to the number of stented lesions that are covered in a given vessel
- limits to coverage of stents in treatment of multivessel disease
- limits to coverage of stents in treatment of high-risk populations where alternatives might be better

I do not disagree with this perspective, but the HTCC committee was never provided the opportunity to address these issues since the topic provided to us was BMS vs. DES….. not Stent vs. Medical Therapy …. not Stent vs. Surgery, etc. In addition, the committee is sometimes challenged to make these decisions based upon evidence that is often tangential to the central decision issues.

Lacking any ability to influence formulation of topics that are provided to the HTCC and fully aware of limitations specified in the legislation that created the HTA program, I concede that my second guessing the design of the current stent HTA is moot and unproductive. Nonetheless, there remain opportunities to effect *evidence-based* cost savings within this current HTA with the broad support of stakeholders.

Please do not interpret this critique as an indictment of the HTA researchers or my colleagues on the Health Technology Clinical Committee. I believe the HTA was well-researched and well-presented, and I believe our committee has worked in good faith to decipher a very large amount of very complex information to develop a workable coverage decision.

Please contact me if you have questions or need clarification regarding my comments. Thank you for your consideration.

Sincerely yours,

Richard C. Phillips, MD MS MPH FACS
Member, Health Technology Clinical Committee

Definition of Terms

TERM	DEFINITION
ACC	American College of Cardiology is a professional society for heart care specialists.
ACC-NCDR	American College of Cardiology – National Cardiovascular Data Registry collects data on PCI procedures and other heart and vascular procedures. In Washington State, selected data elements from the NCDR are collected for all PCI procedures performed in all hospitals by the Clinical Outcome Assessment Program (COAP).
Binary Restenosis	Binary Restenosis or binary angiographic restenosis is a measure of recurrent narrowing following stent placement that is defined as a lesion that exceeds 50% of the Minimum Lumen Diameter at follow-up angiography.
BMS	Bare Metal Stent is a metal tube or "scaffold" that is inserted during balloon angioplasty of a narrowed coronary artery lesion to prevent elastic recoil of the dilated lesion to its pre-dilation narrowed caliber.
CABG	Coronary Artery Bypass Graph surgery is a revascularization procedure requiring a chest incision
DES	Drug-eluting stent is similarly to a bare metal stent (BMS) except that it is impregnated with a substance that inhibits neointimal hyperplasia in coronary vessels that cause recurrent narrowing of the stented coronary lesion.
HTA	Health Technology Assessment is the evidence-based report that was provided to the HTCC.
ISR	In-Stent Restenosis is the recurrent narrowing of a lesion that undergoes a PCI with placement of either a BMS or DES. ISR is generally measured as binary restenosis or as Lumen Late Loss
LLL	Lumen Late Loss reflects the change in lumen size (Minimal Lumen Diameter) in mm from the time of the stent procedure to the follow-up procedure. $LLL = MLD_{Procedure} - MLD_{FollowUp}$
MLD	Minimal Lumen Diameter of the target coronary vessel
PCI	Percutaneous Coronary Intervention is a catch-all revascularization procedure that may include balloon dilatation of narrowed coronary arteries (PTCA – coronary angioplasty) and/or intra-coronary stent placement
RCT	Randomized Controlled Trial is a clinical research study that randomly allocates the interventions of interest to subjects so as to minimize selection and study biases.
SCAI	Society of Cardiovascular Angiography and Interventions is a professional society of interventional cardiologists and vascular specialists.
TLR	Target Lesion Revascularization is defined as the need for a repeat intervention (PTCA or CABG) due to a specified lesion
TVR	Target Vessel Revascularization is defined as the need for a repeat intervention (PTCA or CABG) due to the original target lesion and/or a new lesion within the same coronary vessel.

[1] OHTAC Recommendation - Based on the Final Report of the Programs for Assessment of Technology in Health (PATH) Research Institute Field Evaluation of Drug Eluting Stents (DES). Available at: http://www.health.gov.on.ca/english/providers/program/ohtac/tech/recommend/rec_des_20070330.pdf. Accessed on June 1, 2009.

[2] TA152 Coronary artery disease - drug-eluting stents: guidance. Available at: http://guidance.nice.org.uk/TA152/Guidance/pdf/English. Accessed on June 1, 2009.

[3] Chen MS, John JM, Chew DP, Lee DS, Ellis SG. Bare metal stent restenosis is not a benign clinical entity. *Am Heart J.* June, 2006; 2006:151(6):1260-4.

[4] Douglas P, Brennan MJ, Anstrom KJ, Sedrakyan A, Eisenstein EL, Haque G, Dai D, Kong DF, Hammill B, Curtis, L, Matchar, D, Brindis R, Peterson ED. Clinical effectiveness of coronary stents in elderly persons: Results from 262,700 Medicare patients in the American College of Cardiology-National Cardiovascular Data Registry. *J. Am. Coll. Cardiology.* May 5, 2009 2009;53(18).

Health Technology Clinical Committee Findings and Coverage Decision

Topic: Cardiac Stent
Meeting Date: May 8, 2009
Final Adoption:

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

❖ Limitations of Coverage

1) Bare Metal Stents are covered without conditions.
2) Drug eluting stents are conditionally covered, for patients with high risk of revascularization only, defined as:
    a. Vessel diameter of less than 3 mm,
    b. Lesions longer than 15 mm, or
    c. Patients with diabetes mellitus.

❖ 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

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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.

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 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

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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.

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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

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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.

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Health Technology Assessment

HTA Draft Findings & Decision Public Comments on Cardiac Stents

Date: Monday, August 10th, 2009

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August 10, 2009

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Re: Proposed Cardiac Stent Conditions and Reimbursement Determination

Dear program staff and Committee:

On behalf of our eight hospitals operating in Washington State, Providence Health & Services is writing to provide comments on the Health Technology Clinical Committee's (HTCC) proposed conditions and reimbursement determination for Drug Eluting Stents (DES). In our prior public comment letter, submitted May 1, 2009, Providence asked HTCC to consider situations that are operationally unfeasible to implement. We are disappointed to learn that our comments were not addressed.

HTCC has preliminarily determined the following three conditions where DES will be authorized for State-sponsored patients:

a) Vessel diameter of less than or equal to 3 mm, or
b) Lesions equal to or greater than 15 mm in length, or
c) Patient with diabetes mellitus.

Operationally Unfeasible – Provider

A patient's payer source information typically will not be known prior to an ***emergent or urgent***, life-saving stenting procedure. Your conditions will create situations where the interventionalist may insert a stent only later to find out the patient was a State-sponsored patient – requiring the stent to meet the aforementioned conditions. In these situations, the claim will be either denied outright, or paid at the bare metal stent rate. Either way, the hospital will be forced to realize a financial loss through no fault or control of its own.

According to the Clinical Outcomes Assessment Program, primary (emergent) Percutaneous Coronary Interventions (PCI, stenting procedure) accounted for nearly 38%, or 5,456, of all PCI procedures performed in 2008 – the remainder being elective procedures. For patients needing emergent PCI, industry standard calls for a "door-to-balloon" time of 90 minutes or less. This is the time it takes to get the patient from the hospital's emergency department (door) to the cardiac lab and insert a catheter (balloon). When the patient's artery is blocked, the heart begins to die in the areas

where the blood is not reaching. This phenomenon has been dubbed, "time is muscle", meaning the more time that passes, the more heart muscle is lost. Industry standard is to have this door to balloon time be 90 minutes or less. High quality hospitals will aim for the shortest time possible.

Typically a patient's payer source is not usually known at the time of emergent stenting. A hospital can not be expected to wait to determine if the patient is eligible for Medicaid or on a public employee benefit plan prior to the clinician performing the life-saving procedure. In these emergent and urgent situations, the physician's clinical discretion should continue to take precedent so that no time is wasted combining clinical decisions with coverage determinations.

During a phone call on Wednesday, August 5, 2009, the Department of Social and Health Services' Chief Medical Officer and Director of Division of Medical Management, Dr. Jeff Thompson, stated that it is his aim to see all other payers follow these same conditions. That way a provider will not have to consider a patient's payer source prior to choosing the stent type. This is not a practical solution to Providence's concern because it is unclear how many commercial and indemnity payers will restrict DES use and what methods will be used in doing so. ***Too, it is not likely that Medicare will limit coverage based on these conditions***. These conditions may not be appropriate for Medicare beneficiaries – the HTCC chose the three conditions based on clinical data that was not specific to, and may not be appropriate for Medicare beneficiaries. Therefore, the hospital will continue to have to monitor a patient's payer status prior to choosing the stent type. This decision sequence is illogical and therefore operationally unfeasible – further making it dire that the HTCC exempt emergent and urgent PCI procedures from the conditions.

Just to make clear, Providence will comply with the Committee's decision, but profoundly request that the Committee make an exemption for emergent and urgent cases. In fact, Dr. Jeff Thompson even had recommended that any restrictions be placed on non-emergent (***elective***) stenting, yet the Committee didn't place that clarification in the recommendations they will be voting on.

> "***Non-emergent*** PCI should be subject to some form of prior authorization or quality controls to ensure effective "on label" and evidence based "off label" use. [Emphasis added] Coverage limitations for DES should be limited to high risk clients (e.g., diabetes). Quality controls should ensure the client has adequate informed consent of safety, revascularization, risks, benefits and options." (Agency recommendations as provided by Dr. Jeff Thompson, Friday, May 8, 2009.) [1]

[1] Source: Draft minutes from May 8, 2009 HTCC meeting. http://www.hta.hca.wa.gov/documents/draft_minutes_htcc_050809.pdf

If the decision is made to conditionally cover DES, Providence again respectfully requests an exception be made for emergent and urgent cases where the procedure is not scheduled in advance. Providence also respectfully requests Dr. Jeff Thompson to reaffirm his position to the Committee that these conditions apply to "non-emergent" procedures as he previously stated.

Operationally Unfeasible - Administration

It should also be noted that Dr. Jeff Thompson stated on Wednesday, August 5, 2009, that he does not know if or even how these conditions can be implemented. For example, it is not yet known how the new ProviderOne payment system would be able to determine if the conditions are present. Dr. Thompson suggests solutions such as calling to obtain an expedited approval. Calls for prior authorization would be required 24 hours per day, 7 days per week. Providence would like assurance by Dr. Thompson that the Department of Social and Health Services (DSHS) will be able to provide authorizations during the hours needed.

Further, DSHS has historically applied extrapolation techniques to their financial recovery audits. (See WAC 388-502A-900) Under this method, during a retrospective payment review, if the chart does not contain the required documentation, the auditor may extrapolate the error over the total number of cases to determine the over or under payment. Providence is concerned that this extrapolation technique will not be appropriate given the fact that the distribution of patients with the three conditions may not be statistically valid. ***Providence respectfully requests the HTCC suggest a special analysis be performed during the next statistical study commissioned by DSHS. This analysis would be designed to determine the population of patients who contain these three conditions relative to the entire population of Medicaid patients receiving stent(s).*** Doing so will assure providers that extrapolation techniques performed during recovery audits will appropriately identify over or under payments that may have been made by the State.

Typo

Providence believes the minutes and subsequent recommendations contain a typographical error. When the conditions were discussed at the May 8 meeting, the agreement was for a vessel diameter of less than ***or equal to*** 3 mm, or a lesion length of greater than ***or equal to*** 15 mm in length, or diabetes mellitus. However, in the draft findings document, the "or equal to" language is not present. Providence respectfully requests Health Technology Assessment staff review the audio recordings of the meeting to confirm the conditions that were agreed to and voted on towards the end of the meeting.

If you have any questions, please contact me at William.Callicoat@Providence.org or by phone at (360) 486-6651.

Sincerely,

William Callicoat
Director of Health Care Policy
Washington/Montana Region
Providence Health & Services

Cc: Dr. Michael E. Ring, MD, FACC, FSCAI
Mike Marsh
Chuck Hawley
Tom Brennan
Kurt Miller

VIA ELECTRONINC TRANSMISSION TO: shtap@hca.wa.gov

August 10, 2009

Leah Hole-Curry, JD
Program Director
Health Technology Assessment Program
P.O. Box 42712
Olympia, Washington 98504

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

Dear Ms. Hole-Curry

The undersigned organizations are writing to express our disappointment with the draft findings and decision "20090508A – Cardiac Stent: Drug Eluting Stents (DES) and Bare Metal Stents (BMS) for the treatment of coronary artery disease."

The Society for Cardiovascular Angiography and Interventions (SCAI) is a professional association representing over 4,000 invasive and interventional cardiologists. SCAI promotes excellence in cardiac catheterization, angiography, and interventional cardiology through physician education and representation, and quality initiatives to enhance patient care.

The Washington State Chapter of the ACC provides ongoing education and advocacy for more than 530 physicians, Nurse Practitioners, Registered Nurses, Physicians' Assistants in the State of Washington. The majority of these practice Adult Cardiology and Interventional Cardiology.

We continue to be mystified that your organization will not fully consider data that was published online on March 28, 2009 on over 262,000 stenting patients of all types. It found significantly better outcomes in patients with DES versus BMS. That study and others were reviewed in our earlier 14 page letter and in the brief 5 minutes sessions when we were allowed to address the committee which made this decision.

Your draft decision is not consistent with the clinical evidence; it will deny necessary and appropriate access to DES, place patients at increased risk of restenosis and the increase their chance of death because repeat revascularizations are not benign procedures. Additionally, we question whether limiting access to DES will save the State any money. Some of the patients denied access to a DES, may instead opt for a more expensive coronary artery bypass graft (CABG) procedure, additionally there will be an increasing number of repeat revascularizations.

This decision sets up two tiered access to this technology with those people whose health care is covered by the State of Washington receiving significantly inferior care.

As is pointed out in the HTA document, no insurer including the Centers for Medicare and Medicaid Services currently denies coverage for DES. The abundant literature supports their use despite your findings. See for example the most recent meta analysis published in Circulation this June and attached for your convenience. If there is an adverse outcome due to the use of BMS instead of DES will the State or HTA accept responsibility or will physicians and hospitals bear that risk. We urge the HTA to request a legal opinion from the Attorney General regarding this question.

DES do significantly decrease the need for repeat procedures but you have chosen, for reason that are not clear, to use as your primary outcome mortality. As we have pointed out these devices were not designed, in the elective patient population, to decrease mortality. However because they do treat angina there is an important impact of these devices on the quality of life. If you are going to use mortality as a primary outcome measure to determine coverage then much of the care that physicians deliver (e.g. hip replacement and cataract surgery) should be removed from coverage.

Implementation of this decision will create significant difficulties for hospitals and physicians. When treating acute myocardial infarction every effort is made to treat them as rapidly as possible. To implement this policy physicians and hospitals will now need to slow down the process of care to inquire about insurance coverage before treating them. Doing that is however banned (we believe) by EMTALA law, so this is probably a coverage policy that can't be implemented for emergency patients – and hospitals will simply have to eat the cost of a DES.

The State's economic analysis of this proposed change is rudimentary at best. Why aren't the following factors considered?

- The cost of implementing this policy on hospitals and on the administrators of the insurance program.
- The percentage of patients who denied a DES will opt for CABG procedures and at what additional cost
- The lost time and effort of employees that will now be more likely undergo repeat revascularizations.

How can you be certain that this policy will even save the State money?

If for whatever reason access to DES is going to be limited in Washington State we urge you to at least make the following changes:

- To be consistent with most research, FDA labeling and actual product sizes, the criteria for the diameter should be 3 mm or less not less than 3mm.
- Patients who have already had one BMS or DES re-stenosis, should be eligible for a DES.[1] (Some of the factors leading to re-stenosis are based on the individual characteristics of the patient.)
- Patients with left main coronary stenosis[2,3]
- Bifurcation lesions[4]
- Chronic Total Occlusion[5]

We also request that the COAP database be modified to specifically track the outcomes that result from the final decision and that this information be reviewed to inform subsequent decisions regarding modification or abandonment of the coverage decision.

Finally we would like to again strongly state that we are the patients' advocates in this decision. We have nothing to gain financially from our recommendations on this coverage policy; our fees are independent of what type of stent we implant. While we understand the significant financial burden that the State faces this is not an appropriate coverage decision.

Sincerely,

Steven R. Bailey, M.D., FSCAI,
President
Society for Cardiovascular Angiography and Interventions

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[1] Dibra A, Kastrai A, Alfonso, F, et al. Effectiveness of Drug-Eluting Stents in Patients With Bare-Metal In-Stent Restenosis: Meta-Analysis of Randomized Trials. JACC 2007;49:616-623

[2] Chieffo A, Park S, Valgimigli M, et al. Favorable Long-Term Outcome After Drug-Eluting Stent Implantation in Nonbifurcation Lesions That Involve Unprotected Left Main Coronary Artery. A Multicenter Registry. Circulation 2007;116:1424-32

[3] Park SJ, Kim YH, et. al. Sirolimus-Eluting Stent Implantation for Unprotected Left Main Coronary Artery Stenosis Comparison With Bare Metal Stent Implantation 2007; J Am Coll Cardiol 2005;45:351– 6

[4] Colombo A, Moses JW, Morice MC, et al. Randomized study to evaluate sirolimus-eluting stents implanted at coronary bifurcation lesions. Circulation 2004:109:1244-9.

[5] Werner GS, Krack A, et. al. Prevention of Lesion Recurrence in Chronic Total Coronary Occlusions by Paclitaxel-Eluting Stents; J Am Coll Cardiol 2004;44:2301– 6

Daniel P. Fishbein, M.D., F.A.C.C.
President
Washington State Chapter of the American College of Cardiology

cc: Steve Hill, Administrator - Washington State Health Care Authority at lken107@hca.wa.gov

TRANSMITTED VIA EMAIL

Washington State Hospital Association

August 10, 2009

Denise C. Santoyo
Program Coordinator
Health Technology Assessment Program
Washington State Health Care Authority
PO Box 42712
Olympia, WA 98504-2712

Re: Cardiac Stent Decision

Dear Ms. Santoyo:

On behalf of the hospitals of Washington State, the Washington State Hospital Association (WSHA) wishes to thank you for the opportunity to comment on the Health Care Authority's recent decision regarding cardiac stents. WSHA is supportive of evidence based medicine and efforts to encourage clinical practice based on research. We appreciate the purpose of and the work done by the committee.

WSHA's hospital members have deep concerns about the committee's decision to restrict coverage of drug eluting stents (DES) to very narrow clinical circumstances including: (a) vessel diameter of less than 3 mm; (b) lesions longer than 15 mm; or (c) patients with diabetes mellitus. A number of clinicians believe evidence does not solidly support the decision made by the committee.

WSHA requests the committee re-consider its decision and take clinician concerns into account. If the committee would like more information from the clinicians who provided comments, WSHA welcomes the opportunity to help make the connection.

Among the concerns expressed are:

- Clinical evidence does not support such limited coverage for DES. There are many other circumstances where DES may be appropriate. Examples include restenosis and left main stenting. WSHA received lists of clinical circumstances not accounted for by the committee's decision. Questions were also raised about current "off label" use of DES. The stents may be helpful and safe to use in a number of clinical scenarios not addressed by the guidance.

- If the goal of the committee's decision is to help save the state money, it has probably not accomplished the goal. According to clinicians, DES are associated with significant declines in patients returning for a second procedure related to in-

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stent restenosis. While bare metal stents (BMS) may be less costly initially, many clinicians predicted the state will lose money in the long term due to restenosis of BMS.

- Cardiac vessels larger than 3 mm may experience restenosis. DES may be appropriate for those vessels in some circumstances.

- Lesion size determination can be very subjective and is often inaccurate. Clinicians question using lesion size as a parameter for coverage decisionsp.

- If a cardiologist determines a DES is clinically appropriate, hospitals face either nonpayment for the procedure or potential liability associated with inappropriate care.

- The guidance does not take into account emergent situations where decisions must be made very quickly. Will there be exceptions to reimbursement in these situations given that there will be no opportunity to discuss the restrictions on payment?

- One physician raised this important issue: From a clinical perspective most clinicians feel the most important issue is whether to perform re-vascularization rather than which type of stent should be used. The physician felt it would make more sense to regulate the procedure rather than the technical means of performing the procedure.

- A number of clinicians think the decision by the Health Care Authority may increase the number of repeat procedures. A request was made for the Clinical Outcomes Assessment Program to track use and outcomes that occur as a consequence of the Health Care Authority's decision.

Again, thank you for the opportunity to comment. We understand the committee's work involved research into the clinical evidence on stent use. We believe the interventional cardiologists and other clinicians we heard from may be able to lend additional perspective to this research and to the committee's work. We hope the strong feedback we received from hospitals and clinicians is taken into consideration by the committee.

If you have any questions, I can be reached at (206) 216-2554 or tayab@wsha.org.

Best regards,

Taya Briley, RN, MN, JD
General Legal Counsel

August 6, 2009

Denise C. Santoyo

Washington State Health Care Authority

Health Technology Assessment

Program Coordinator

denise.santoyo@hca.wa.gov

Dear Ms. Santoyo:

We have been asked to provide a response to the proposed recommendations by the Washington State Health Care Authority regarding coverage for Drug Eluting Stent (DES) implantation. As several well formulated responses have been submitted to the initial analysis commissioned by HCA, the details of these responses will not be reiterated however, the consensus among our practicing interventional cardiologists is that we concur with the detailed response submitted by the American College of Cardiology (ACC) and the Society for Catheterization and Intervention. We agree that while the methods to assemble the data are valid, we wish to note that the aims of the analyses have significant limitations and do not address key aspects of data or the clinical scenarios that support DES use compared with bare metal stent use. Importantly, the aims of DES development were not to reduce death or myocardial infarction but rather to reduce the risk of restenosis compared with Bare Metal Stents (BMS). The effect in reducing restenosis has been established by large randomized controlled trials and is generally accepted as clinically relevant by the vast majority of interventional cardiologists. As a result, it is unclear to many practitioners as to why the HCA criterion for effectiveness was defined as reduction in death or myocardial infarction, as studies of DES were not been designed to address this endpoint and were not expected to reduce these events compared with BMS. The decision to adopt DES was based largely on the desire to reduce restenosis and avoid clinical consequences and additional PCI procedures. While there is some controversy from the public health perspective regarding the long term safety of DES based on large epidemiological studies, the consensus is that the current level of concern is not significant enough to abandon DES as a useful component of therapy in performing percutaneous coronary interventions.

In viewing the critical issues from a clinical perspective, most clinicians feel the important issue is whether revascularization should be performed, rather than whether DES or BMS should be used. This distinction is important because the factors that lead to stent selection is complex, including angiographic and clinical considerations which are not easily captured in a clinical study and are not easily facilitated with an algorithmic approach. As a result, many clinicians are unclear how global oversight of this process

will lead to better outcomes for patients. In contrast, most interventional and non-invasive cardiologists agree that it is quite reasonable to request valid reasons for pursuing revascularization, and appropriateness criteria and guideline recommendations have been formulated by the ACC/American Heart Association (AHA) to guide this decision making. As a result, if regulation of the process of revascularization is required, it seems more reasonable to regulate the procedure rather than the technical means of accomplishing the procedure.

Another significant concern is that the current criteria are far too vague to provide meaningful guidance on the numerous scenarios encountered in planning revascularization. As a consequence, there is concern that cases will occur in which DES implantation makes implicit sense to the practicing community, but reimbursement for appropriate treatment will be denied by authorities with little clinical or technical knowledge of the clinical scenario. Moreover, there is concern that will lead to inefficient or substandard care, which will cost more and cause considerable frustration on the part of providers and patients.

In particular, there are several scenarios that have not been addressed by the criteria. Specifically, is there an intention to provide guidance on saphenous vein graft interventions, in stent restenosis, bifurcation stenting, bailout stenting, or chronic total occlusions? These scenarios are considered off label use of DES but most practitioners consider DES to be a major benefit in conducting these procedures. Second, will there be a mechanism to appeal to HCA if situations arise in which the clinical community feels that DES would be appropriate despite the reimbursement mandate? Third, the nature of coronary disease is that emergent situations arise in which decisions must be made in an expedited manner, and frequently this includes intra-operative decisions regarding stent selection. Will there be exceptions to reimbursement in these situations given that a discussion will likely be impractical?

Finally, will there be an effort to track the impact of the HCA decision through the state COAP registry? Given the implications for potential repeat procedures, it would seem reasonable to request that an effort be made to follow the use and outcomes that occur as a consequence of the decision. The most immediate concern would be a net increase in repeat procedures due to resteonsis. On the other hand, if the criteria lead to more cost efficient care without leading to repeat procedures, the recommendations may serve as a potential useful guide for stent selection.

We hope there is an opportunity for further dialogue on this topic. The decision to limit DES use based on the current criteria seems somewhat arbitrary and unfortunately may be counterproductive to the intentions of the HCA. We would be happy to participate in further work to help assist with this project.

Sincerely,

John L. Petersen, II, MD, MHS

Medical Director, CV Research

For The

Swedish Heart and Vascular Institute

Swedish Medical Center

August 8, 2009

Leah Hole-Curry, JD
Program Director
Health Technology Assessment Program
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Olympia, Washington 98504

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

Dear Ms Hole-Curry,

I would like to respond to the draft findings and decision "20090508A – Cardiac Stent: Drug Eluting Stents (DES) and Bare Metal Stents (BMS) for the treatment of coronary artery disease."

I have been in an academic teaching practice for greater than 20 years and it that role I have taught countless medical students, residents and fellows the role of interventional techniques in the treatment of coronary artery disease. In addition I have taught my colleagues, both in this country and throughout the word, the rightful place of interventional cardiology in the treatment of this chronic disease. I have served and continue to serve on editorial boards of major cardiovascular journals and review abstracts and manuscripts dealing with interventional cardiology before their publication including national guidelines. I also teach the appropriate use of these techniques in courses that other cardiologist attend in preparation for taking the American Board of Internal Medicine's Interventional Cardiology Board certification. I tell you this because I believe I am well versed on the evidence base on which drug eluting stent use is based.

Simply put I remain mystified by the approach that the committee has taken on the coverage decision restricting the use of DES. I believe that one must clearly understand the history, particularly the recent history, of these devices in order to make sense of the evidence base. In the fall of 2006 reports surfaced in abstract form at the European Society of Cardiology meeting in Barcelona that suggested that DES use was associated with excess mortality. Soon thereafter began the period of increased scrutiny of these devices vs. BMS. As you know in late 2006 the FDA convened a panel of experts to review the evidence and it is important to remember that no restrictions of use or box warnings resulted from this review.

Then followed an intense period where meta-analyses of previous RTCs occurred to determine if the concern over excess mortality could be confirmed. I would remind the committee that this data by its very nature is old since all the subsequent meta-analyses reviewed in the HTA were based on studies beginning in early 2000. As detailed in the HTA, countless assessments have found no mortality signal. It is critical to understand that these studies were not undertaken to prove that DES had a mortality benefit since that has never been their purpose in patients with chronic coronary disease. Because the HTA and committee have used this as a primary endpoint for superiority, the HTA and the committee have simply misinterpreted the purpose of these studies and have therefore reached erroneous conclusions. In addition since registries have been discounted as a source of evidence the HTA and committee are reinforcing the misunderstanding of the meta-analyses. While I understand that in most cases registries should be hypothesis generating in this case the signal from recently published registries is that DES may in fact be associated with less mortality than BMS. This is also true for more recent meta-analyses.

Although the HTA relegated repeat revascularization to a secondary endpoint this is the superiority endpoint for which DES was developed. As the HTA points out there is no doubt that this endpoint is significantly impacted by the use of DES. This impacts quality of life for patients who receive these devices but it is unfair to hold a device that treats angina to a long-term impact on a chronic disease such as coronary artery disease. Long-term impact on outcomes would only logically be impacted by chronic therapy which is clearly the role of medical treatment. There is no doubt that the aggressive management of this chronic disease has resulted in the remarkable decline in mortality from heart disease in this country, an impact that far exceeds the impact of cancer therapy on cancer's long term outcome. However, followed long enough chronic diseases such as heart disease do result in additional events including death. I ask the committee to think of this as they review studies that show mitigation of some endpoints over time when using DES.

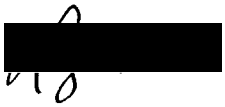
It is clear that the impetus for this HTA was based on early concerns regarding DES outcomes which in some cases have been completely refuted with the analysis of additional data. Since the committee has been unwilling to give significant credence to newer studies because they are not yet "mature" the only logical conclusion one can draw is that it is premature to make a coverage decision based on data that is in some cases more than 5 years old even though publication dates suggest that it is more contemporary. This HTA simply rehashes older HTAs and meta-analyses. Newer studies have a clear and consistent signal of DES benefit.

Much has been written and debated about so called unlabeled uses of devices including stents. While there should always be concern about this when there is a lack of evidence of safety and efficacy that is not the case with stents, particularly DES. Most of the information in this area is from registries but there is no signal suggesting that DES is inferior to BMS and in fact the signal in recent publications is that DES use results in superior outcomes with respect to BMS. Taken it totality DES is superior to BMS when used on and off label.

With respect to the cost effectiveness analysis some of the limitations of that body of evidence have been pointed out by the HTA. It is clear that the differences are driven by the cost differential between BMS and DES but it seems very short sighted to me to use static historical State cost data to make decisions. Two DES have been approved by the FDA in recent months which will make these devices a commodity. Based on market forces, cost should decline which will impact this type of analysis. At the very least the committee should request a sensitivity analysis using current stent cost.

I hope at this late hour that the committee is still open to reflection on their draft decision which I believe is misguided. To quote George Santayana: "Those who cannot learn from history are doomed to repeat it". I hope we are not back with this topic a few years from now in a process to undo the committee's draft proposal if it is approved as written. I have purposely not included references for my comments but would be happy to provide them to the committee if requested.

Sincerely,



Larry S. Dean, MD FACC, FAHA, FSCAI
Professor of Medicine and Surgery
University of Washington School of Medicine and
Director, UW Medicine Regional Heart Center

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

Dear Ms. Hole-Curry:

I was asked to consult for Spectrum as they prepared their report for the Washington Health Technology Assessment Program, and therefore have been following this with keen interest. Of note, I am the Director of the Cardiac Catheterization Laboratory at the University of Washington and an active interventional cardiologist. Because this is a salaried position, the coverage decision is unlikely to have much impact on my personal economic circumstances. However, I am concerned that this decision will have a greater impact on the well-being of our patients, and create significant confusion for health-care workers. I continue to feel that the report from Spectrum, and the subsequent agency document chose to present data in such a manner which limited the proper assessment of the value of drug-eluting stents, with the apparent agenda of finding some degree of cost-savings at some level. Thus, for example, recent data suggesting that off-label use of drug-eluting stents appeared to have even greater value of on-label use of stents was not taken into account, nor were recent randomized studies documenting the role of drug-eluting stents in acute myocardial infarctions. These are only a couple of points in which the presentation of data was consistently weighed, I believe inappropriately, against the value of this technology.

In addition, this will add yet another layer of bureaucratic confusion. There are now FDA labeled indications, CMS coverage considerations, and now Washington state considerations for a select population. This will be very difficult to monitor, and it is likely that most of the cost-savings will be by denying coverage to a hospital whose personnel is confused by the multiple layers of bureaucracy and interpretations which need to be taken into consideration. Therefore, this will add a financial burden upon hospitals to absorb these costs.

Finally, it seems that the choices made by the agency were fairly arbitrary, based primarily upon older assessments from England and Canada, thereby deviating from the stated goal of reliance upon scientific data.

I would urge the Agency to reconsider these decisions, as being harmful to the citizens of the state of Washington, as well as being economically and scientifically unsound.

Thank you very much.

Sincerely yours,

Steven L. Goldberg, MD.
Clinical Associate Professor of Medicine
Director, Cardiac Catheterization Laboratory
University of Washington Medical Center
Seattle, Washington

Washington State Health Care Authority

Health Technology Clinical Committee
Date: May 8, 2009
Time: 8:00 am – 5:00 pm
Location: Marriott Hotel – 3201 South 176th Street, Seattle, WA 98188
Teleconference Bridge: 1-360-923-2997 Access Code: 360-946-1464
Adopted: March 20, 2009

HTCC MINUTES

Members Present: Brian Budenholzer; Michael Myint; Carson Odegard; Richard Phillips; Michelle Simon; C. Craige Blackmore; Michael Souter; Louise Kaplan; Megan Morris and Christopher Standaert.

HTCC FORMAL ACTION

1. **Call to Order**: Dr. Budenholzer, Chair, called the meeting to order at 8:00 a.m. Sufficient members were present to constitute a quorum.
2. **Cardiac Computed Tomographic Angiography (CCTA) Decision & Findings:** Dr. Budenholzer referred members to the draft findings and decision and called for further discussion or objection. The CCTA findings & decision was unanimously approved by the committee on March 20th, 2009 with a condition. Final approval was subject to a review by the Chair of any additional comments received through the close of the public comment period.
   - *Action: Eight committee members unanimously approved the Computed Tomographic Angiography findings and decision document. The two newly appointed committee members abstained from voting since they were not present at the previous clinical committee public meeting.*
3. **March 20th, 2009 Meeting Minutes:** Chair referred members to the draft minutes and called for a motion and discussion.
   - *Action: Six committee members unanimously approved the March 20th, 2009 meeting minutes. Four committee members abstained from voting due to not being present at the meeting.*
4. **Cardiac Stents – Comparison of Drug Eluting Stents (DES) and Bare Metal Stents (BMS):** The HTCC reviewed and considered the Drug Eluting Stent (DES) compared to Bare Metal Stent (BMS) for the treatment of coronary artery disease technology assessment report; information provided by the Administrator; state agencies; public members; and heard comments from the evidence reviewer, HTA program, agency medical directors, a clinical expert, and several public members. 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.

Washington State Health Care Authority

HTCC COMMITTEE COVERAGE DETERMINATION VOTE			
	Not covered	Covered Unconditionally	Covered Under Certain Conditions
Cardiac Stents	**0**	**2**	**8**

- Conditions for coverage: The committee decided to continue coverage for bare metal stents and conditionally cover drug eluting stents. Conditions for DES are patients with highest risk of revascularization: vessels of less than 3 mm, lesions longer than 15 mm, diabetics.

- *Action:* The committee chair directed HTA staff to prepare a Findings and Decision document on Cardiac Stents reflective of the majority vote for final approval at the next pubic meeting.

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Washington State Health Care Authority

SUMMARY OF HTCC MEETING TOPICS, PRESENTATION, AND DISCUSSION

Agenda Item: Welcome & Introductions

- ✓ The Health Technology Clinical Committee (HTCC) met on May 8, 2009.

Agenda Item: Meeting Open and HTA Program Update

Dr. Brian Budenholzer, HTCC Chair opened the public meeting. Leah Hole-Curry, HTA Program Director, provided an overview of the agenda, meeting guide and purpose, room logistics, and introductions.

Leah Hole-Curry, HTA Program Director, provided an update on HTA program activities and outcomes.

- ✓ New Committee Member Appointments: Leah Hole-Curry introduced the new committee member appointments of Megan Morris and Dr. Christopher Standaert due to the resignation of two previous committee members.
- ✓ Evidence Reports Underway: Bone Growth Stimulators, Calcium Scoring, Vagus Nerve Stimulator and Hip Resurfacing are currently underway with the vendor and the HTA program. Evidence Reports not yet started are Glucose Monitoring and Sleep Apnea Diagnosis and Treatment.
- ✓ Program Operations: The Governor, Chris Gregoire, has featured the Health Technology Clinical Committee (HTCC) and Health Technology Assessment (HTA) program in several presentations, including at the White House Regional Health Reform. Current HTCC member has been included to participate in a new legislatively created committee workgroup for evidence based radiology guidelines. Lastly, bill for proposed program changes did not pass the legislative committee.
- ✓ Program presented HTCC members with a letter of thanks from Governor Chris Gregoire.

Agenda Item: Previous Meeting Business

- ✓ March 20th, 2009 Meeting Minutes: Chair referred members to the draft minutes and called for a motion and discussion.
  - ➢ *Action: Six committee members unanimously approved the March 20th, 2009 meeting minutes. Two committee members abstained from voting.*
- ✓ Cardiac Computed Tomographic Angiography (CCTA) Findings and Decision: Chair referred members to the draft findings and decision and called for further discussion or objection. The CCTA findings & decision was unanimously approved by the committee on March 20th, 2009 with a condition. Final approval was subject to a review by the Chair of any additional comments received through the close of the public comment period.
  - ➢ *Action:* Eight committee members unanimously approved the Cardiac Computed Tomographic Angiography (CCTA) findings and decision document. The two newly appointed committee members abstained from voting since they were not present at the previous clinical committee public meeting.

Washington State Health Care Authority

Agenda Item: Cardiac Stents Topic Review

Leah Hole-Curry, HTA Program Director, introduced the primary technology topic to up for discussion:

- ✓ Drug Eluting Stents (DES) with Bare Metal Stents (BMS) for the treatment of coronary artery disease: review of the evidence of the safety, efficacy and cost-effectiveness of Cardiac Stents.

Cardiac Stents

- ✓ 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.
    - o CAD may be asymptomatic or lead to chest pain (angina), heart attack, myocardial infarction (MI) or death.
- ✓ Treatments include:
    - o Manage and reduce risk factors, such as: smoking, obesity, high blood pressure and cholesterol.
    - o Medication therapy – beta blockers, nitrates, statins, antiplatelet agents and calcium channel blockers.
    - o 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 Advantages: physically opening the artery and being less invasive than bypass surgery.
- ✓ Cardiac Stent Disadvantage: targeted solution to widespread disease, unclear protocols, clotting and re-operation.
- ✓ Important, unanswered questions remain about whether and when stent placement is appropriate versus other medical management or surgery.
- ✓ Current FDA approval for cardiac stents is for the placement of a single stent in a new lesion occurring in arteries of a specific size. In acute situations, stenting is also performed outside FDA indications.
- ✓ In general, for non-acute situations, clinical guidelines indicate stent placement is appropriate after a trial of optimal medical therapy and where documented evidence of ischemia exists, but do not limit use to single stent or certain disease severity of location. In practice, stenting is now routinely performed in patients with varying disease levels, locations and symptoms.
- ✓ Cardiac Stent Research Issues – Stent studies vary in population and disease level and do not specifically focus on efficacy of non-FDA approved uses, and may not categorize multiple stent placements separately or use same definitions.

- ✓ Medicare Coverage and Clinical Guidelines:
  - o Centers for Medicare and Medicaid Services (2008) -- no national coverage decision (NCD). Overall PTA coverage memo: 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. Coverage for all other indications is at local Medicare contractor discretion
  - o Guidelines -- No guidelines for clinical care or appropriateness have been published regarding the use of BMS versus DES. Most comprehensive joint ACC/AHA guidelines address broader perspective on setting and issues involved in the decisions leading to coronary stent placement.

Agenda Item: Public Comments

- ✓ Scheduled Public Comments: Four scheduled public comments–
  - o Robert Bersin, MD, representing SCAI presented concerns with the technology assessment and recommends DES be used based on physician decision.
  - o Mary Greg, MD, representing COAP; provided additional information on COAP (WA state) data, the ACC guidelines, and urged collaboration with data collection and quality organizations.
  - o Wayne Powell, representing SCAI presented information on issues and concerns with cost information and analysis.
  - o Will Callicoat representing Providence Health & Services presented concerns with limits on DES and recommends DES maintained as covered.

- ✓ Open Public Comments: Four individuals provided comments during the open portion (limited to three minute comments):
  - o Oren Sreebny, patient, provided a statement about his positive personal experience with DES.
  - o John Capps, individual and potential consumer, provided a statement approving the use of DES based on quality of life years measured.
  - o Dan Fishbein, University of Washington, provided a statement about using real world patients, particularly with the Douglas trial, regarding DES.
  - o Richard Page, head of Cardiology at the University of Washington, provided a statement approving the use of DES.

Agenda Item: Cardiac Stent Topic – Agency Data

Dr. Jeff Thompson, Department of Social & Health Services (DSHS) Medical Director, presented to the committee the agency utilization and outcomes for Cardiac Stents.

- ✓ Key agency concerns for prioritization:

- Efficacy concerns – High: efficacy of stenting to prevent death or major cardiac event and high stent diffusion with low or mixed evidence on appropriateness. Concerns about high use variation, especially 70% non-FDA approved uses in generally sicker or more complicated patients; drug eluting stent use; use instead of optimized medical therapy in lower risk patients and instead of CABG in high risk patients.
- Safety concerns – High: long term risks, procedure risks, frequency, FDA panel findings on thrombosis for DES off label.
- Cost concerns – Medium: reflect mainly concern about over or mis-utilization, and wide cost differences between treatment choices.
- 70% of stent use is "off label" – increasingly common are stent use in multiple vessels, multiple stents in a single vessel, or in vessels outside FDA diameters and lengths.
- The majority of patients with PCI have no assessment of MI risk.

✓ State Agency Utilization Criteria for Cardiac Stents:

Procedure	UM/UR
PTCA (HCA, LNI, DSHS)	No PA or restrictions
Stents (HCA, LNI, DSHS)	No PA or restrictions
On Label vs. Off Label (DSHS)	Some risk for an audit

✓ Cardiac Stent Procedure Utilization: 2004 thru 2007 – Clinical Outcomes Assessment Program (COAP)*

Year	2004	2005	2006	2007
Total PCI Procedures**	**15,158**	**15,330**	**15,686**	**14,164**
No Prior PCI	10,022	10,146	10,265	9,135
Repeat Procedures	5,136	5,184	5,421	5,029
% Repeat Procedures	34%	34%	35%	36%
PCI Procedures with Stents	**13,348**	**14,104**	**14,542**	**13,032**
% stented PCIs	88%	92%	93%	92%
Count of All Stents	18,860	19,931	21,048	19,688
Count of Bare Metal Stents	3,224	1,408	2,122	5,214
Count of Drug-Eluting Stents	15,636	18,523	18,926	14,474
% Bare Metal Stents	17%	7%	10%	26%

** A program of the Foundation for Healthcare Quality in WA State*
*** Inpatient and outpatient procedure*

- ✓ Cardiac Stent Procedure Utilization: 2004 thru 2007

	2004	2005	2006	2007
Total Costs*	**$14,263,103**	**$15,505,519**	**$17,218,988**	**$16,544,589**
Total Procedures**	**988**	**1,010**	**1,040**	**954**
Bare Metal***	175	80	117	283
Drug-Eluting***	781	919	904	650

** Inpatient, outpatient, Medicaid and Uniform Medical Plan as primary and secondary payers*
*** Procedure codes 36.06, 36.07, 92980, 92981, G0290 and G0291 performed as primary or secondary procedures*
**** Excludes patients who received both types in same procedure*

- ✓ Cardiac Stent Procedure Costs and BMS/DES Cost Differential

2009 Procedure Costs †	**Costs**	**Differential**
Medicaid		
Inpatient		
Bare Metal	$13,024	
Drug-Eluting	$16,670	$3,646
Outpatient		
Bare Metal	$4,863	
Drug-Eluting	$6,615	$1,752
Uniform Medical Plan		
Inpatient		
Bare Metal	$22,360	
Drug-Eluting	$26,497	$4,137
Outpatient		
Bare Metal	$13,038	
Drug-Eluting	$17,345	$4,307

† Inpatient costs based on APDRGs 852 and 854. Outpatient costs based on weighted facility fees for CPT code 92980 and HCPCS code G0290

- ✓ Other Health Technology Assessments
  - Aetna: Members with angina and >50% stenosis
  - Cigna: DES for symptomatic disease; however, DES for E&I including acute MI, unprotected LMCA and SVG – not covered.
  - VA: Covers PCI for one or more arteries for FDA and conditions may be considered for cost sharing.
  - Ontario HTA: Two of following (1) long lesions *(>20mm)*, (2) narrow lesions *(<2.75mm)* and (3) diabetes, to target higher risk clients.

- ✓ Agency Recommendations: Non-emergent PCI should be subject to some form of prior authorization or quality controls to ensure effective "on label" and evidence based "off label" use. Coverage limitations for DES should be limited to high risk clients (e.g., diabetes). Quality controls should ensure the client has adequate informed consent of safety, revascularization, risks, benefits and options.

Washington State Health Care Authority

Agenda Item: Evidence Review Presentation

Spectrum Research, Inc. presented an overview of their evidence report.

- ✓ Scope: Research comparing drug-eluting stents (DES) with bare metal stents (BMS) for the treatment of coronary artery disease.
- ✓ Stent placements in coronary artery disease were designed to address narrowing of coronary vessels caused by plaque. A catheter is inserted across the lesion. Balloon inflation expands the stent and compresses plaque. The stent remains to act as a scaffold to keep the lumen open allowing increased blood flow. New endothelial lining forms over the stent.
- ✓ Cardiac Stent Background: PTCA (balloon angioplasty) initially decreased lumen narrowing, injury to the vessel walls led to acute closures (6% - 8%) and restenosis (30% - 50%). Bare Metal Stents (BMS), approved by the FDA in 1993, was introduced as a way to overcome the limitations of PTCA. BMS created a more uniform vessel opening, leaving in place a metal scaffolding to prevent closure. Inflammatory reaction and exaggerated cell proliferation resulted in re-stenosis in 20% - 25% of patients within 6 months. Drug-eluting stents (DES) were designed to prevent neointimal hyperplasia and subsequent restenosis. A polymer coating applied to the metal stent releases anti-proliferative drugs into the local environment. Anti-platelet therapy is used with BMS and DES.
- ✓ FDA: Indications – treatment of symptomatic ischemic disease in patients with de novo lesions in native coronary arteries. Contraindications – hypersensitivity to stent components (including drugs used in DES, polymers and metals used); patients in whom anti-platelet or anti-coagulation therapy is contraindicated; and lesions that don't allow for complete balloon inflation. FDA approval granted for 9 BMS and 4 DES designs.
- ✓ Literature Search: 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.
- ✓ Primary Date Source Overview:
    - o HTA's or similar reports – 2 (Hill, ECRI) did own meta-analysis of RCTs; 1 (KCE) used results from previous meta-analyses; 1 (Ontario) did meta-analysis on registry studies; 4 (Hill, KCE, Ontario, FinOHTA) did full economic analyses
    - o Meta-analyses published after HTA's - 1 meta-analysis in general populations included 38 RCTs, N = 18,023 (Stettler 2007). 1 meta-analysis with outcomes for diabetic patients separated and length of anti-platelet therapy evaluated from 35 RCTs, N = 14, 799 (Stettler 2008).
- ✓ Revascularization: refers to repeat revascularization with PCI or CABG to address narrowing (restenosis) of the vessel from scar tissue growing beneath the new endothelial layer.
- ✓ Efficacy Summary: Neither DES or BMS are favored with respect to mortality, cardiac mortality or myocardial infarction based on conventional MA and follow-up to 4 years. DES are favored with regard to TLR.
- ✓ Efficacy Summary (non randomized): There are mixed results; it is unclear whether DES or BMS are favored with regard to mortality, cardiac mortality and myocardial infarction in studies with > 1 year follow-up. DES are favored with regard to TLR.

- ✓ Special Populations -- Diabetic Patients Summary:
  - o Efficacy – no difference in mortality, cardiac death or MI in those with ≥ 6 months DAT (0 to 4 years). 2-fold increase in mortality and cardiac death in those with < 6 months (0 to 4 years). Significant reduction in TLR with DES.
  - o Effectiveness – Mixed results for death/cardiac death, no difference in MI. TLR less frequent with DES.
  - o Safety – Although no differences between DES and BMS for stent thrombosis or late stent thrombosis were found, there may be insufficient power to detect a difference.
- ✓ Safety Summary: Most previous HTAs and meta-analysis indicate no statistically significant different between DES and BMS with regard to risk of stent thrombosis.
  - o 1 review focused on safety concluded that the majority of evidence suggested an increased risk with DES. 2 reports concluded there was significantly higher risk after 1 year with DES. Stent thrombosis is a rare event; studies may have been underpowered to detect a difference.
  - o FDA conclusions: DES for off-label indications was related to increased incidence of stent thrombosis, MI and death. Discontinuation of anti-platelet therapy was an independent risk factor. Risk of thrombosis does not outweigh advantage of DES over BMS in reducing repeated revascularization when used for approved indications.
- ✓ Economic Analysis Summary: HTA reviews of 43 economic studies + 5 additional analysis suggested DES is not cost effective across populations vs. BMV but may be in special populations. Broad range of outcomes and ICERs. Significant variability in modeling, quality and consistency of findings.
- ✓ Conclusions: Evidence review - interpretation for what is known
  - ➢ There is no statistically significant different between DES and BMS with regard to death, cardiac death or myocardial infarction up to 4 years.
  - ➢ DES are consistently associated with lower rates of TLR.
  - ➢ While no statistically significant differences in stent thrombosis or late stent thrombosis were seen, analyses may be underpowered; no comparative studies for bleeding.
  - ➢ Among diabetic patients, < 6 months of dual anti-platelet therapy was associated with a 2-fold increase in death and cardiac death with DES but there was no difference in MI regardless of therapy duration.
  - ➢ Nonrandomized studies show mixed results for death and MI.
  - ➢ Most extensive CEAs concluded DES were not cost-effective in general populations; ICERs driven by DES cost, #, TLR.
  - ➢ Professional guidelines do not address use of DES vs. BMS.
- ✓ Conclusions: What we don't know from the evidence
  - ➢ Are statistically significant findings also clinically significant? Are the risk differences of public health importance?
  - ➢ How should the relative importance of the various outcomes be weighed, over the short-term and over the long-term?

- Is TLR/TVR correlated with decreased rats of death, cardiac death and MI over the long term? Why or why not?
- How might newer DES designs or drugs compare with BMS for various outcomes in the short term and long term?
- What is the long term safety of prolonged anti-platelet use?
- What are the specific indications for DES vs. BMS in general and special populations? What are the indications for TLR?
- Will methodologically rigorous US-based CEAs draw different conclusions from HTA CEAs as ICERs are driven by DES cost, number of stents and TLR?
- How does comparison of DES vs. BMS fit within the bigger context of comparative effectiveness with medical therapy, CABG and other treatments?

Agenda Item: HTCC Cardiac Stents Discussion and Findings

Brian Budenholzer, Committee Chair, led a discussion of the evidence related to the safety, efficacy, and cost effectiveness of Cardiac Stents beginning with identification of key factors and health outcomes, and then a discussion of what evidence existed on those factors.

1. Evidence availability and technology features

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. Patients with CAD range from no symptoms, to chest pain (angina), to myocardial infarction (MI), to death. Prediction of risk and symptoms 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). The main difference between the stents is that DES are treated with a drug coating intended to prevent restenosis that occurred with PCI using BMS.

1.3 The evidence based technology assessment report identified a large amount of literature, including previously done technology assessments. Due to the large amount of already produced material, this evidence report summarizes previous technology assessments and then updates the summary with information from subsequently published studies. Recently conducted technology assessments had a high degree of overlap in the included studies. The evidence base consisted of 304 potentially relevant citations. There were 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. The evidence basis also included trials or separately reported sub-analysis amenable to evidence review on several subpopulations: diabetic patients, and patients with acute MI. Registry study on the elderly discussed in section 1.5.

1.4 Given the high overlap in studies, the evidence review focused on summarizing five recent health technology assessments, most conducted with their own meta-analysis, and one focusing on registry studies. The evidence review included one meta-analysis of 38 trials that

was published after the technology assessments, *Stettler* 2007. The Stettler study meta-analyzed 38 randomized trials with 18,023 patients; and a separate analysis of diabetics in 35 of the trials with 14,799 patients. Additionally, 26 recently published non-randomized studies were included to update the information. The evidence review presents study results related to key questions in each of the three categories (HTA, Meta-analysis, and Non-randomized studies) if the studies contained applicable information. The technology assessment also includes a color coded summary table of the overall evidence for each key question and important health outcome *(see pg 159*).

1.5 Additional evidence: some additional studies were 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 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. The technology assessment vendor urged caution in relying on these studies as none are critically appraised. The technology assessment vendor also noted that the study results, if valid, did not significantly alter conclusions already in the report related to mixed findings of non-randomized studies and results in myocardial infarction patients.

1.6 The committee commented on the large amount of randomized and observational studies available comparing DES and BMS on many of the important health outcomes they identified for stents. Committee discussed the nature of the evidence and the role of registries and observational studies in the face of robust randomized trial evidence. Some committee members advocated that the evidence hierarchy is well established and randomized trials provide the highest level of confidence in reported outcomes, so if relevant and well conducted RCT's, or as here, meta-analysis of multiple RCT's are available for important outcomes, observational studies should not be used to contradict findings. For these members, the appropriate role of observational studies is to shed light on rare complications and potential additional sub-population information. Other committee members advocated that these observational studies were on a significantly larger population, are better powered to detect rare events and are more valid or relevant because of the inclusion of "real world" patients. The committee discussed the inclusion of the recently published articles and whether an additional appraisal was necessary, but chose to move forward with the outcomes discussion bearing in mind that the newer studies had not yet been critically appraised and noting that if the majority of committee members felt further review was necessary because their final vote might change based on the un-appraised studies, additional specific information could be obtained from the evidence vendor and presented at a later meeting.

2. Evidence about the technology's safety

The committee discussed multiple key factors and health outcomes that were important for consideration in their overall decision on whether the technology is safe. Summary of committee considerations follows.

1.1 Overall Mortality and Cardiac Mortality: this topic was discussed in the context of efficacy (see below).

1.2 Stent Thrombosis: The evidence based technology assessment report indicated that this 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.

- 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 may be underpowered, three reported there was a higher risk of stent thrombosis with DES.
- 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.
- The evidence based technology assessment also included information from ten recent nonrandomized studies, with most showing no difference, and 1 reporting significantly higher rate of very late stent thrombosis for DES.

1.3 Stent Thrombosis in diabetics: The evidence based technology assessment report included several analysis and studies reporting on this rare, but serious complication in the diabetic subpopulation. 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. The later Stettler meta-analysis specific to diabetic patients indicate no statistically significant difference up to four years, but wide confidence intervals suggest variability perhaps related to sample size. This finding is consistent with two other, later published meta-analysis and several randomized trials. One HTA of registry data indicated higher in-stent thrombosis with DES (2.4 to 4.4%) versus BMS (0.8%).

1.4 Stent Thrombosis in patients with acute MI: The evidence based technology assessment report included several analysis and studies reporting on this rare, but serious complication in the subpopulation of patients treated with a stent after acute MI. One HTA, two meta-analyses, and three recent RCT's report no statistically significant difference in rates of stent thrombosis between DES and BMS groups.

1.5 Bleeding: the evidence based technology assessment report reviewed this safety issue, 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.

1.6 Stent Fracture: The evidence based technology assessment did not identify any HTA or randomized trials with evidence about comparison between DES and BMS of this complication. Small case series in DES patients indicated that fracture ranged from 1.9% to 7.7%.

3. Evidence about the technology's efficacy and effectiveness

The committee discussed multiple key factors and health outcomes that were important for consideration in their overall decision on whether the technology is effective. Summary of committee considerations follows.

1.1 Freedom from Overall and Cardiac Mortality: The evidence based technology report includes death, and specifically cardiac-related death, as a key health outcome in treatments for cardiac artery disease. 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.

- 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.
- 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.
- 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.
- Overall committee discussion centered on agreement that majority of reliable evidence finds no difference between DES and BMS in mortality or cardiac mortality.
- 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.
- 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.

1.2 Freedom from MI: 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.

- 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%).
- Mixed results in non-randomized studies reporting on MI – with 7 studies showing no significant different in MI, while 3 studies showed a lower rate in DES patients.
- 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.
- 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.
- 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.

1.3 Freedom or reduction of Target vessel revascularization/target lesion revascularization (TVR): 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.
- The committee discussed the implication of dual anti-platelet therapy and whether that impacts revascularization rates.
- 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.
- The results of the reviewed non-randomized studies also suggested lower revascularization rates for DES (5.2% - 14.2%) and for BMS (8.1% to 24.4%).
- 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%).
- 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%).
- 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.

1.4 Quality of Life: 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. 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. Evidence about the technology's value and cost-effectiveness

The committee discussed multiple key factors that were important for consideration in their overall decision on whether the technology has value and is cost-effective. Summary of committee considerations follows.

1.1 Overall context from the evidence based technology report and discussed by the committee: there remains uncertainty regarding efficacy, effectiveness, and safety of DES versus BMS and differing assumptions contribute to variability in analysis. The incremental cost effectiveness ratios (ICER) were most influenced by the price premium of DES.

1.2 The evidence included 43 cost effectiveness, 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.

1.3 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.

1.4 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%.

1.5 State agency cost data: Utilization at the three agencies over the same time period is 15% BMS and 83% DES.

Medicare Decision and Expert guidelines

Committee reviewed and discussed the Medicare coverage decision and expert guidelines as identified and reported in the technology assessment report.

- 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.
- 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.
- 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 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:

1. Evidence availability and technology features

The committee concludes that the best available evidence on cardiac stents has been collected and summarized. The evidence is comprehensive and robust:

1.1. Where evidence from meta-analysis of multiple, well designed randomized or well designed controlled trials, with adequate participants, assessment of all patient centered health outcomes, and for sufficient duration exists for efficacy, that evidence should have highest weight. A large body of high quality evidence on over 30,000 patients studying use of BMS and DES stents exists.

1.2. Additionally, complications and adverse events, especially rare events, can be identified by case-review studies and other sources such as the FDA database.

2. Is it safe?

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

2.1. *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.

2.2. *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.

2.3. *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.

3. 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:

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

3.2. *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.

3.3. *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.

3.4. *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.

3.5. *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.

4. 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.

4.1. 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).

4.2. 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 he cost per QALYs.

4.3. For certain subpopulations of high risk patients, some HTAs reported, and five committee members agreed that DES is cost-effective.

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 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).

Cardiac Stent Vote

The clinical committee utilized their decision tool to first gauge committee judgment on the status of the evidence in the three primary areas of safety, efficacy, and cost.

Cardiac Stent Evidentiary Votes:

Is there sufficient evidence under some or all situations that the Drug Eluting Stents, as compared with Bare Metal Stents are:

	Unproven (no)	**Equivalent** (yes)	**Less** (yes)	**More** (yes)
Effective	1	9	0	0
Effectiveness (Revascularization)	0	0	0	10
Safe	1	9	0	0
Cost-effective Overall	0	0	10	0
Cost-effective Some Situations	4	0	1	5

Cardiac Stent Coverage vote: Based on the evidence provided and the information and comments presented, the committee moved to a vote on coverage.

HTCC COMMITTEE COVERAGE DETERMINATION			
	Not covered	**Covered Unconditionally**	**Covered Under Certain Conditions**
Cardiac Stent - DES	**0**	**2**	**8**

- Outcome: The committee chair directed HTA staff to prepare a Findings and Decision document on Cardiac Stents reflective of the majority vote for final approval at the next public meeting.
  - Bare metal stents continue to be covered. Drug Eluting stents are conditionally covered. Conditions for DES coverage are limited to patients with a vessel diameter of less than 3 millimeters; or a lesion longer than 15 millimeters; or diabetic patients.

Washington State Health Care Authority

Health Technology Assessment Program

Health Technology Clinical Committee

August 2009 Meeting

Washington's Health Technology Assessment Program Background

- **Part of Governor's 2006 Five point health strategy for state to lead by example**
  - **Emphasize evidence-based health care**

http://www.hca.wa.gov/contf/doc/GovGregoireHealthBrief.pdf

- **Program Purpose: Achieve better health by paying for technologies that work**
  - Better health with better information: investigate what works and maintain a centralized website.
  - Open and transparent process: publish process, criteria, reports, and committee decisions in public meeting.
  - Eliminate Bias: contract for independent evidence report and independent clinical committee.
  - Promote consistency: state agencies rely on a single, scientifically based source.
  - Flexible: review evidence regularly to ensure update information is included.

Washington State Health Care Authority

- Overall Issue: WA citizens pay high cost for health care and receive poorer outcomes
- Government Issue: Public Programs have limited and/or shrinking resources and rising costs and needs.
- Common reaction: Reduce Eligibility, Rates or Benefits
  - "Thin the soup or cut the line"

Vision: Transform WA state from a passive payer to an active purchaser of higher quality, more efficient health care

- Action: Ensure WA pays for technologies that are proven safe, effective and cost-effective

"Better ingredients in the soup make it go farther"

Outcome: Pay for What Works

- Coverage decisions:
  - scientifically based
  - use transparent process, and
  - consistent across state health care purchasing agencies

- Formal, systematic process to identify, review, and cover appropriate health care technologies.
  - Is it safe?
  - Is it effective?
  - Does it provide value (improve health outcome)?

HTA Program – Ongoing Operations

Pay for What Works: Better Information is Better health

- Topic Selection
  - No updates 2009 selections underway
- Coverage Decisions
  - Cardiac Stents Finalization
- Evidence Reports - Underway
  - Calcium Scoring (CACS)
  - Hip Resurfacing
  - Electrical Neural Stimulation (ENS)
- Evidence Reports - Not Yet Started
  - Sleep Apnea Diagnosis and Treatment
  - Glucose Monitoring

Washington State Health Care Authority

Topic Selection & Decision Process

Washington State Health Care Authority

Process Overview

1. HCA Administrator Selects Technology

Nominate, Review, Public Input, Prioritize

↓ *Semi-annual*

2. Vendor Produce Technology Assessment Report

Key Questions and Work Plan, Draft, Comments, Finalize

2-8 Months ↓

3. Clinical Committee Makes Coverage Determination

Review Report, Public Hearing

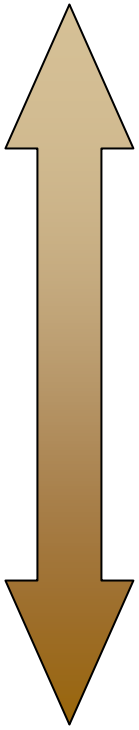
↓ *Meet Quarterly*

4. Agencies Implement Decision

Implements within current process unless statutory conflict

Hierarchy of Evidence

Best: Meta-analysis of large randomized head-to-head trials.



Large, well-designed head-to head randomized controlled clinical trials (RCT):

- Long-term studies, real clinical endpoints
- Well accepted intermediates
- Poorly accepted intermediates

Smaller RCTs, or separate, placebo-controlled trials

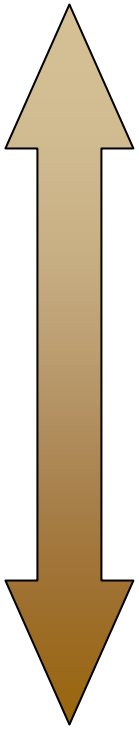
Well-designed observational studies, e.g., cohort studies, case-control studies

Safety data without efficacy studies

Case series, anecdotes

Least: Expert opinion, non-evidence-based expert panel reports, and other documents with no direct clinical evidence

Evidence in Health Care Decision Making



- **Level 3:** *"What would I recommend to the state or nation?"*
  - **Must be based on rigorous assessment of the scientific evidence.**
  - **Affects hundreds of thousands, even millions of people.**
- **Level 2:** "*What would I recommend to my patient/client?"*
  - Influenced by prior experience, but the scientific evidence may play a greater role.
  - Affects possibly hundreds of people.
- **Level 1:** *"Would you have this done for yourself or for someone else in your immediate family?"*
  - Influenced by one's personal experience with the disease and capacity to deal with risk.
  - Affects few people.

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Washington State Health Care Authority

Evidence for use in Policy Decisions

Different Data Sources

- Efficacy
  - How technology functions in “best environments”
    - Randomized trials-distinguish technology from other variables
    - Meta-analysis
- Effectiveness
  - How technology functions in “real world”
    - Population level analyses
    - Large, multicenter, rigorous observational cohorts (consecutive pts/objective observers)
- Safety
  - Variant of effectiveness
    - Population level analyses
    - Case reports/series, FDA reports
- Cost
  - Direct and modeled analysis
    - Administrative/billing data (charge vs cost)
- Context
  - Mix of historic trend, utilization data, beneficiary status, expert opinion