



Health Technology Clinical Committee

Date: August 20th, 2010

Time: 8:00 am – 5:00 pm

Location: Marriott Hotel – 3201 South 176th Street, Seattle, WA 98188

Teleconference Bridge: 1-218-936-4700 **Access Code:** 9461464

Adopted: October 22nd, 2010

HTCC MINUTES

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

Absent: Kevin Walsh and Megan Morris

HTCC FORMAL ACTION

1. **Call to Order:** Dr. Budenholzer, Chair, called the meeting to order. Sufficient members were present to constitute a quorum.
2. **May 14th, 2010 Meeting Minutes:** Chair referred members to the draft minutes; motion to approve and second, and adopted by the committee.
 - *Action: Eight committee members approved the May 14th, 2010 meeting minutes. One committee member abstained from voting.*
3. **Hyaluronic Acid / Viscosupplementation (HA) draft Findings & Decision:** Chair referred members to the draft findings and decision and called for further discussion or objection. The Hyaluronic Acid / Viscosupplementation findings & decision was approved and adopted by the committee.
 - *Action: Eight committee members approved the Hyaluronic Acid / Viscosupplementation findings & decision document. One committee member abstained from voting.*
4. **Breast MRI (BMRI):** The HTCC reviewed and considered the Breast MRI technology assessment report; information provided by the Administrator; state agencies; public members; and heard comments from the evidence reviewer, HTA program, an invited clinical expert, the public and agency medical directors. 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.

HTCC COMMITTEE COVERAGE DETERMINATION VOTE			
	Not covered	Covered Unconditionally	Covered Under Certain Conditions
Breast MRI	2	0	7

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- *Action:* The committee chair directed HTA staff to prepare a Findings and Decision document on Breast MRI reflective of the majority vote.

5. Spinal Cord Stimulation (SCS): The HTCC reviewed and considered the Spinal Cord Stimulation technology assessment report; information provided by the Administrator; state agencies; public members; and heard comments from the evidence reviewer, HTA program, an invited clinical expert, the public and agency medical directors. 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.

HTCC COMMITTEE COVERAGE DETERMINATION VOTE			
	Not covered	Covered Unconditionally	Covered Under Certain Conditions
Spinal Cord Stimulation	8	0	1

- *Action:* The committee chair directed HTA staff to prepare a Findings and Decision document on Spinal Cord Stimulation reflective of the majority vote.



SUMMARY OF HTCC MEETING TOPICS, PRESENTATION, AND DISCUSSION

Agenda Item: Welcome & Introductions

- ✓ The Health Technology Clinical Committee (HTCC) met on August 20th, 2010.

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.

Agenda Item: Previous Meeting Business

May 14th, 2010 Meeting Minutes: Chair referred members to the draft minutes and called for a motion and discussion. Minutes were circulated prior to the meeting and posted.

- *Action: Eight committee members approved the May 14th, 2010 meeting minutes. One committee member abstained from voting.*

Hyaluronic Acid / Viscosupplementation (HA) Findings and Decision: Chair referred members to the draft findings and decision and called for further discussion. The draft findings and decision document was circulated prior to the meeting and posted to the website for a two week comment period. One public comment was received by the program during the publication of the HA draft findings and decision and was included in the committee meeting packets.

- *Action: Eight committee members approved the Hyaluronic Acid / Viscosupplementation findings & decision document. One committee member abstained from voting.*

Agenda Item: HTA Program Review

- Leah Hole-Curry, HTA Program Director, provided the HTA context for the meeting and an update on program activities including:
 - State purchasing context and budget reductions and reform efforts, medical technology is driver of increased medical costs and has quality gaps
 - HTA is designed to use reliable science and independent committee to get best information on what works, what is safe and what provides value
 - HTA Outcomes include transparency; reports and articles reviewed; and coverage decisions made
 - Comparison with private industry and Medicare decisions completed
 - Program has received recent recognition from public media, clinical press, and various medical and health policy groups with either story highlights or invited presentations



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- Transparency improvement based on stakeholder meetings resulted in enhanced process documentation

Agenda Item: Breast MRI (BMRI) Topic Review

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

- ✓ Staff provided an overview of the timeline and referred HTCC members to the included key questions and population of interest for Breast MRI review.
- ✓ Staff welcomed, per HTCC request, an invited clinical expert, Dr. Edgar Clark a radiologist from Portland and consultant to evidence based programs such as MED. Dr. Clark prepared a COI with no conflicts listed.

Agenda Item: Public Comments

The Chair called for public comments.

- ✓ Scheduled Public Comments: No stakeholders scheduled time for public comments.
- ✓ Open Public Comments: one individual provided comments during the open portion.
 - Dr. Constance Lehman, UW urged committee members to approve coverage for women at high risk; acknowledged overuse and training issues in some areas but stressed recent quality guidelines would improve.

Agenda Item: Breast MRI Topic – Agency Comments

Dr. Nancy Fisher, Health Care Authority, Medical Director, presented the agency utilization and outcomes for Breast MRI to the committee, full presentation published with meeting materials.

- ✓ AMDG Perspective: Technology is not new, but the application is changing;
 - Screening of high risk (BRCA1 and 2) and high risk is changing (post cancer treatment surveillance);
 - Screening the contralateral breast prior to mastectomy; and
 - Screening breast when dense tissue or implants are present.
- ✓ Coverage Overview: No current formal coverage / non coverage, no current restrictions.
 - DSHS allows MRI of the breast in: high risk clients and Hayes recommendation
 - UMP allows MRI: Hayes recommendation
- ✓ Agency Questions:
 - Safety: Do less expensive screenings (mammography and ultrasound) have less risk for false positives, and therefore fewer women moving onto chemo and radiation therapies? Does the identification of non-specific findings lead to unnecessary interventions?



- Effectiveness: Is the evidence of sensitivity, specificity and reliability enough to make a benefit decision? Can we define when screening mammogram vs. MRI is needed in a “high risk” population?
- Cost: Higher cost, proposed additional test. Do added tests in cases of suspicious lesions, equivocal results or poor study add to inappropriate costs? What is the impact of differential activity in the community?
- ✓ State Agency Utilization (SFYs 2005 and 2009) – While average costs per MRI remain fairly constant over the past five years, usage has doubled from 2005 to 2009.

Figure 1. Washington State Agency Annual Reimbursement Costs for Breast MRI, 2005-2009

Year/Agency	2005	2006	2007	2008	2009	5 Year Total
UMP/PEP						
Annual Total Cost	\$388,836	\$434,526	\$707,429	\$787,489	\$793,663	\$3,111,943
BMRI Count ¹	352	391	676	761	756	2936
Average cost ¹	\$1,105	\$1,111	\$1,046	\$1,035	\$1,050	\$1,060
DSHS						
Annual Total Cost	\$95,210	\$112,996	\$46,520	\$93,869	\$117,854	\$466,449
BMRI Count ²	160	180	90	156	248	834
Average cost ²	\$595	\$628	\$517	\$602	\$475	\$559
Totals						
Annual Total Cost	\$484,046	\$547,522	\$753,949	\$881,358	\$911,517	\$3,578,392
BMRI Count	512	571	766	917	1004	3770
Average cost	\$945	\$959	\$984	\$961	\$908	\$949

- ✓ There is differential use across populations and reasons: Do we know why?
- ✓ Are reimbursements causing differential?
- ✓ Screening Mammogram before an MRI?
- ✓ State Agencies Summary View:
 - MRI in Breast Cancer Screening - improved Sensitivity(SN)/Specificity(SP) but no outcome data; data is best in BRCA1 and 2; and no evidence that increase screenings improves health outcomes.
 - Safety Issues not resolved - increased incidence of biopsies stemming from false positive is not known.
 - Costs Issues - added test adds cost; cost-effectiveness studies are limited; and tests performance has wide variability in the community.
 - Consistent with Medicare and three evidence-based guidelines - Breast MRI is of unknown benefit or no benefit in screening; average risk women (not within scope here); dense breasts and breasts with implants; and high risk.



- If coverage for high risk, limited to only the highest risk women due to high false-positives, unknown health outcome benefit and very high test cost; and BRCA1 and 2 and other high risk mutations for breast cancer with mammogram screening first.
- Pre-operative staging - current evidence shows that Breast MRI changes treatment but no evidence on outcome, at least limit to contralateral mastectomy decision making.

Agenda Item: Evidence Review Presentation

Delfini presented an overview of their evidence report on Breast MRI, full presentation in meeting materials.

- ✓ Definitions: *High risk* – high risk for developing breast cancer is variously defined in clinical trials but frequently refers to women: with a calculated lifetime risk of 20% or greater; with a calculated risk of greater than 1% per year; with genetic BRCA1 or BRCA2 mutation; with a history of breast cancer; and with a family history consistent with a hereditary breast cancer syndrome. Other risk factors such as age, ethnicity, age at menarche, previous breast biopsy, parity, age at first birth are included in some risk calculation models.
- ✓ Background: In 2002, the United States Preventive Services Task Force found adequate evidence of film mammography's sensitivity and specificity and evidence of mammography's effectiveness in decreasing breast cancer mortality in women at average risk based on randomized controlled trials (RCTs) and concluded that film mammography was the standard for detecting breast cancer in women at average risk of developing breast cancer (USPSTF 2002).
 - USPSTF concludes (Grade I) that the current evidence is insufficient to assess the additional benefits and harms of magnetic resonance imaging (MRI) instead of film mammography. Noted evidence related to higher detection rate in women at high risk, but did not separately recommend.
 - American Cancer Society (ACS) 2007 recommends women at high risk of breast cancer be also screened with MRI -no evidence cited in recommendation. High risk defined as MRI screening for women starting at age 30 if their lifetime risk is approximately 20% to 25% - no evidence cited.
 - National Cancer Institute recommends mammography and clinical breast exams and self breast exams citing fair evidence of benefit; no recommendation for MRI
- ✓ Aim of Evidence Review: To systematically review, critically appraise and analyze research evidence regarding the accuracy, efficacy, effectiveness and safety of MRI in the detection of breast cancer in women at high risk for developing breast cancer.
- ✓ Evidence Review Key Questions: For women at risk of breast cancer based on presentation of with an abnormal mammogram; palpable breast abnormality; or relevant demographic and clinical risk factors:
 - What is the evidence that Breast MRI has the ability to diagnose or exclude breast cancer compared to current tests including mammography?
 - What is the evidence that breast MRI improves health outcomes for patients with suspected or diagnosed breast cancer
 - What is the evidence of the safety of breast MRI?

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- What is the evidence that breast MRI has differential efficacy or safety issues in sub populations?
- What is the evidence about the cost implications and cost effectiveness of breast MRI?
- ✓ Key Points: Adding MRI to annual screening with mammography (MX) in women at high risk - will increase sensitivity over MX alone in screening for breast cancer in women at high risk and will detect approximately **2 to 5 additional breast cancers per 100 breast screenings**; will increase detection of breast cancer in women with increased breast density; will increase incidence of false positives (benign biopsies) – **up to 11 false positives (benign biopsies) per 100 MRI exams**; will change treatment plans including wider excisions and conversion to mastectomy for some women undergoing surgical planning for recently diagnosed breast cancer; and may or may not change re-excision rates, cancer recurrence rates or mortality rates.
- ✓ Key Points – Safety: No reliable evidence for harm from increased radiation exposure; no reliable evidence to suggest that gadolinium-based contrast agents are associated with adverse outcomes in the fetus, infants or children; no reliable evidence for meaningful adverse psychological outcomes from false-positive MRI test results in women at high risk for breast cancer; and no reliable evidence for increased cancer in women with breast implants.
- ✓ Key Points – Cost and Cost Effectiveness: Adding MRI to mammographic breast cancer screening in women at high risk of breast cancer will increase diagnostic and therapeutic costs; accurately predicting mortality reduction and other health outcomes in high-risk women may not be possible unless results from valid RCTs become available; cost per QALYs gained range from approximately \$25,000 to \$311,000 depending upon assumptions about various costs, yearly risk, mortality reduction with the addition of MRI, frequency of screening, etc.
- ✓ Key Question 1: Diagnostic Accuracy – Findings: Adding yearly screening with MRI to mammographic screening will increase detection of breast cancer; and adding yearly screening with MRI to mammographic screening will result in a higher rate of false positive tests, benign breast biopsies and more extensive surgeries.
 - Sensitivity (SN): Lifetime risk of 20% or greater -- Lord 07 Systematic Review (best evidence for accuracy); 5/91 relevant studies included in review based on acceptable quality criteria; sensitivity with addition of MRI to mammography (3 studies) women high risk 94% (95% CI, 86% to 98%); incremental sensitivity (over MX) was 58% (95% CI, 47% to 70%). Level of Evidence (LOE): Borderline. Detection of breast cancer in contralateral breast in women with breast cancer by adding MRI to mammography; Brennan 09: meta-analysis 22 studies; detection of suspicious findings (true positives plus false positives): 9.3% (95% CI, 5.8% to 14.7%); and incremental cancer detection rate (ICDR): 4.1%.
 - Specificity (SP): Lifetime risk 20% or greater -- Lord 07 Systematic Review. Specificity: Study results were inconsistent, but suggested a 3-5-fold higher risk of patient recall for investigation of false positive results with the addition of MRI; false positive recall rates (two studies) ranged from 6 to 106 per 1000 MRI exams. LOE: inconclusive.
 - SN / SP: Recent Diagnosis of Breast Cancer - Lehman 07 prospective observational study (N=969), recent diagnosis of breast cancer, negative mammogram and clinical exam of contralateral breast within 90 days before enrollment. MRI detected clinically and mammographically occult breast cancer in the contralateral breast in 30 of 969



- women (3.1%). Sensitivity of MRI in the contralateral breast was 91%. Specificity of MRI in contralateral breast was 88%.
- Adding MRI to MX for yearly screening in high risk women will result in: an increased detection of approximately 2 to 5 breast cancers per 100 breast screenings; and an increased incidence of false positives (benign biopsies)—up to 11 false positives (benign biopsies) per 100 MRI exams.
- ✓ Key Question 2: Improved Outcomes – what is the evidence that breast MRI improves health outcomes for patients with suspected or diagnosed breast cancer?
- Reduced Need for Other Tests: Breast cancers may be missed if MRI or mammography is omitted from screening high risk women (Lord 07, Berg 08, Weinstein 09, Kuhl 10). Reducing the need for other tests becomes a judgment call based on evidence and other factors such as patient preference, breast density, contraindications to MRI contrast and cost. LOE: Inconclusive.

Diagnostic Test	Sensitivity	Specificity
MX Alone	25% to 59%	NR
MX+MRI	94% (95% CI, 86% to 98%)	True value not calculated in meta-analysis but studies reported from 77% to 96% for MRI+conventional testing
MX+US	49% to 67%	NR
MRI+Mammography + US	86% to 100%;	NR

- ✓ Change in Treatment Plans: preoperative MRI testing in women with recently diagnosed breast cancer will change treatment plans for some women (LOE: Borderline). The evidence is insufficient to determine whether changes in treatment plans based on the results of preoperative MRI testing are beneficial (LOE: Insufficient).
- Houssami 08: meta-analysis of 19 retrospective observational studies of 2,610 women with breast cancer; 16% increase in detected ipsilateral breast cancer with MRI compared to conventional testing; 11.3% underwent more extensive resections; and conversion from wide local excision (WLE) to mastectomy was 8.1% (95% CI, 5.9 to 11.3).
 - Lim 10: Retrospective cohort study of patients with newly diagnosed breast cancer (N=535) with planned breast conservation surgery; 18.3% had additional suspicious lesions on breast MRI, but not detected with conventional methods; 8.8% had additional malignancies; 6.9% had benign lesions; 15.7% had a change in surgical treatment plans based on the MRI results; and mastectomy rate did not change significantly (OR 0.98; 95% CI, 0.95 to 1.00; P = 0.059).
 - Pengel 09: Retrospective cohort study of women with invasive breast cancer (N=349); and treatment changes in MRI group: mastectomy (8.7%) or wider excision (2.3%).
- ✓ Change in Re-excision Rates: LOE for effect of preoperative MRI testing on re-excision rates following surgical treatment = inconclusive.
- Mann 10: Retrospective study using pathological and oncological databases; invasive lobular carcinoma (N=267); significant difference in re-excision rate; 27% re-excision

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- rate in patients not receiving preoperative MRI compared to 9% re-excision rate in the MRI group, OR 3.64 (95% CI, 1.30 to 10.20, P = 0.010).
- Pengel 09: Retrospective cohort study (N=349); and no significant difference in incomplete excision rates between the MRI group, 13.8%, and the non-MRI groups, 19.4% (P = 0.17).
 - Turnbull 10: The first randomized controlled trial (RCT) to assess whether preoperative breast MRI in early-stage breast cancer can decrease reoperation rates (6 months) for incompletely excised breast cancer included 1,623 women with early breast cancer. No significant difference in re-excision rates with MRI 10.4% vs. 11.2% (no MRI).
- ✓ Recurrence Rates: There is insufficient evidence to determine if preoperative MRI testing in women with early invasive breast cancer reduces recurrence rates or mortality rates and adequately powered prospective trials are lacking. LOE: Inconclusive.
- Fischer 04: Retrospective study of 346 patients. Local recurrence rate after breast conservation treatment was 6.8% (9/133) in patients without a breast MRI and 1.2% (1/86) in patients with a breast MRI (P < .001).
 - Recurrence and Mortality -- Solin 08: Retrospective cohort study of 756 women with early stage invasive breast carcinoma or ductal carcinoma in situ who underwent breast conserving surgery (BCS) + irradiation. There were no statistically significant differences between the two groups for — 8-year local failure rate (3% vs. 4%, P=.32); 8-year rates of overall survival (86% v 87%, P=.51); freedom from distant metastases (89% v 92%, P=.16); and contralateral breast cancer (6% v 6%, P=.39).
 - Health Outcomes -- adding preoperative MRI testing for surgical planning in women with diagnosed breast cancer -- will change treatment plans for some women and result in wider local excisions and conversion from wide local excision to mastectomy; may or may not change; rates of re-excision; rates of breast cancer recurrence; and mortality rates.
- ✓ Key Question 3: Safety – Radiation Exposure: There is no reliable evidence to suggest that that MRI radiation exposure from screening or testing results in adverse outcomes for women at high risk of breast cancer (LOE: Inconclusive). *MRI uses non-ionizing radiation.* Pregnancy: There is no reliable evidence to suggest that gadolinium-based contrast agents are associated with adverse outcomes in the fetus, infants, and children (Chen 08). *Classified as category C drug: Either studies in animals have revealed adverse effects on the fetus (teratogenic or embryocidal or other) and there are no controlled studies in women, or studies in women and animals are not available.*
- Chronic Kidney Disease -- Sherlock 06: 79 observational studies of gadolinium chelates in conjunction with MRI imaging; data totaled more than 1.5 million applications of gadolinium agents; and adverse event rates were similar in the contrast agent group (13%) and placebo group (17%).
 - Adverse Psychological Outcomes -- The evidence is insufficient to conclude that false-positive MRI test results in women at high risk for breast cancer lead to meaningful adverse psychological outcomes (LOE: Borderline). *Indirect evidence from MX studies in average risk women.* Brewer 07: narrative review of 313,967 women at average risk for breast cancer reported no long-term symptoms of depression in women with false positive mammograms
- ✓ Key Question 4: Subpopulations –



- Breast Implants: No clinical trials designed to evaluate differential risk of breast cancer in women with breast implants. Howshaw 01: Meta-analysis of 10 cohort and case-control studies totaling more than 152,000 women with implants followed from 10 to 20 years found no increased risk in breast cancer in women with implants. LOE: Inconclusive.
- Breast Density: The evidence is suggestive that adding MRI to mammography increases sensitivity for detecting breast cancer in women with increased breast density or fibroglandular breast tissue. Sardanelli 04: Patients with planned mastectomy (N=90); and breasts with fibroglandular dense pattern sensitivity for mammography was 60% vs. 81% for MRI, P<0.001.
- Technical and Provider Issues: The evidence is insufficient for establishing optimal technical specifications for MRI testing. Warren 09: post-hoc assessment of the effect of technical aspects of MRI on diagnostic performance based on the Houssami 08 meta-analysis. None of the technical parameters (year of study, slice thickness or repetitions after contrast-medium injection) were associated with True Positive:False Positive (TP:FP) ratio or significant performance differences. LOE: Inconclusive.
- ✓ Key Question 5: Cost Outcomes -- The evidence is suggestive that adding MRI to mammographic breast cancer screening in women at high risk of breast cancer will increase diagnostic and therapeutic costs.
 - Cost Effectiveness: Accurately estimating cost-effectiveness may not be possible because RCTs evaluating the mortality reduction with screening or testing women at high-risk for breast cancer have not been conducted. LOE for Cost-Effectiveness: Inconclusive. QALYs gained by adding MRI to mammographic breast cancer screening in women at high risk for breast cancer vary greatly depending upon assumptions, e.g., sensitivity of MRI; number and frequency of diagnostic tests; type and costs of therapeutic interventions; risk of recurrence; and mortality assumptions

Population At High Risk For Breast Cancer	Breast Cancer Prevalence Rate*	Cost Per QALYs Gained With Addition of Annual MRI Screening to MX Screening
Women With BRCA 1/2	4%	\$25,277
High Risk Without BRCA 1/2: Seconario 1	3%	\$45,000
High Risk Without BRCA 1/2: Seconario 2	2%	\$72,360
High Risk Without BRCA 1/2: Seconario 3	1%	\$151,642
High Risk Without BRCA 1/2: Seconario 4	0.5%	\$310,616

Data from Taneja 09

- *5 Year Risk of Developing Breast Cancer Based based on Gail model available From NCI Breast Cancer Assessment Tool (available at <http://www.cancer.gov/bcrisktool/Default.aspx>).
- Plevritis 06 : Cost-effectiveness study assumed 14% breast cancer mortality reduction for yearly mammography alone (based on RCT data average risk women) and **38% mortality reduction** for mammography plus MRI ages 25 to 69 with BRCA 1 (based on modeling).
- LOE Cost-effectiveness: Inconclusive

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Agenda Item: HTCC Breast MRI Discussion and Findings

Brian Budenholzer, Committee Chair, led a discussion of the evidence related to the safety, efficacy, and cost-effectiveness of Breast MRI 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 in 2009, an estimated 192,370 cases and 40,170 deaths occurred in women with breast cancer (National Cancer Institute, 2010) in the US.
- 1.2 The evidence based technology assessment report summarized the evidence on accuracy and efficacy of MRI compared with conventional techniques for detecting breast cancer and its role in reducing breast cancer mortality and other meaningful health outcomes in women at increased risk for breast cancer based on abnormal mammogram, palpable breast anomaly or relevant demographic and clinical risk factors. Current practice as reflected through clinical guidelines does not support routine use of MRI in screening average risk women.
- 1.3 Evidence included in the technology assessment review was obtained through systematic searches of the medical literature for relevant systematic reviews including meta-analyses, other diagnostic studies, randomized controlled trials and economic studies. Selected national guidelines and previous technology assessment were also summarized in the technology assessment report.
- 1.4 The evidence based technology assessment report focused on two recent large systematic reviews (Lord, 2007 and Warner, 2008) found to be of acceptable quality.
 - Lord 07: 5 adequate studies involving a total of 2059 patients were included in the review of MRI accuracy in screening women at high risk. No studies addressed mortality or recurrence or earlier stage disease.
 - Warner 08: 11 included studies involving xx patients were included in the review of MRI accuracy in screening women at high risk. No studies addressed mortality, recurrence, or earlier stage disease.
 - Two additional studies were included in the review: Brennan 09 involved 22 studies of 3,253 women with breast cancer and Lehman 07 involving 969 women comparing detection in the contralateral breast with MRI compared to conventional screening.
 - Definition of high risk women varied among studies from gene mutation BRCA 1 and/or BRCA 2; previous history of breast cancer; family history of breast cancer; other gene mutations; lifetime risk of breast cancer over 20% or 25%
 - Trials assessed efficacy of MRI in screening of women at high risk when added to (not substitute) conventional screening usually mammography +/- ultrasound, +/- clinical breast exam
- 1.5 The evidence based technology assessment report identified 7 expert treatment guidelines and a CMS policy.
- 1.6 The committee also reviewed information provided by the state agencies, and public members; and heard comments from the evidence reviewer, HTA program, the public and agency medical directors.

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.

- 2.1 The evidence based technology assessment report reported several key outcomes related to safety of MRI in screening women at high risk of breast cancer, including: harms of test itself (no radiation, but contrast agents); psychological harms from screening, false positives and false negatives; harms by and from change in treatment, including unnecessary treatment (biopsy) with false positives; harms related to over diagnosis.
- 2.2 The evidence based technology assessment report concluded that no evidence was found to suggest that MRI radiation exposure results in adverse outcomes for women at high risk of breast cancer being screened with MRI. The evidence from observation studies suggests that gadolinium-based agents (with the possible exception of gadodiamide) may be safely used as MRI contrast agents in non-pregnant adults without chronic kidney disease (CKD).
- 2.3 The report concludes that insufficient evidence exists to conclude that false-positive breast cancer screening tests or recalling patients for false positive tests leads to clinically meaningful negative psychological outcomes.
 - One narrative review of 313,967 women at average risk for breast cancer reported no long-term symptoms of depression in women with false positive mammograms (Brewer, 2007).
- 2.4 No other evidence was reported on the harms of unnecessary treatment and over diagnosis. Evidence about change in treatment discussed in efficacy.

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.

- 3.1 The evidence about the efficacy and effectiveness included outcomes of: diagnostic accuracy (sensitivity and specificity); reduction in mortality; reduced need for other tests; changes in treatment plan; excision and re-excision rates; and cancer recurrence rates.
- 3.2 Overall: The evidence based technology assessment report concluded that adding yearly screening with MRI to mammographic screening will increase detection of breast cancer. The increase in cancer detection is offset by a higher rate of false positive tests, benign breast biopsies, and more extensive surgeries, including an increase in more unnecessary mastectomies; no reliable evidence exists on reduction in mortality, recurrence, or re-excision rates.
- 3.3 Diagnostic accuracy: The evidence based technology assessment report concluded that adding yearly screening with MRI to mammographic screening will increase detection of breast cancer. Based on higher quality evidence about sensitivity, the addition of MRI to annual breast cancer screening with mammography will
 - Detect an estimated additional 2 to 5 breast cancer per 100 screenings.
 - Add more false positives, resulting in 11 additional benign biopsies per 100 screening rounds.
- 3.4 Diagnostic accuracy in contralateral breast: The evidence based technology assessment report concluded that MRI detects contralateral breast lesions in 9% more women than mammography alone, but does not reliably distinguish benign from malignant findings with a positive predictive value of 47%.
- 3.5 Reduction of need for other tests: The evidence based technology assessment report concluded that insufficient evidence exists to conclude that, in high risk women, the addition of MRI to mammographic screening reduces the need for mammography or ultrasound. Current trials and convention focus on addition of MRI, not replacement test.

- 3.6 Change in treatment: The evidence is borderline quality, but sufficient to conclude that adding MRI screening in high risk women and preoperative MRI testing in women with recently diagnosed breast cancer will change treatment plans for some women, however evidence is inconclusive as to whether the treatment change is beneficial.
- 15.7% of women will have change in treatment
 - Wide local excision to more extensive surgery occurs in 11%
 - Wide excision to mastectomy occurs in 8%
 - Women with dense breasts may experience change (44% based on one retrospective study).
 - 7% of women with changes in treatment based on MRI had benign lesions
- 3.7 Health Outcomes: The evidence is insufficient to conclude whether adding MRI screening in high risk women impacts health outcomes of mortality, recurrence, or re-excision.
- Evidence on re-excision rates exists but is conflicting and low level, ranging from no difference to 18% decrease in re-excision in women who pre-operatively underwent MRI
 - Evidence on recurrence also conflicts with one study reporting a 5% reduction in recurrence rates while another larger study (both observational) showing no difference over 8 years.
 - No evidence assessed effect of adding MRI on mortality rates.

4. Special Populations

- 4.1 *Breast Implants*: the evidence based technology assessment report stated that insufficient evidence exists to conclude that breast implants increase the risk of developing breast cancer. Adding MRI to mammography appears to increase the detection rate for breast cancer in women with increased breast density.
- 4.2 *Technical specifications and provider issues in MRI Testing*: the evidence is insufficient for establishing technical MRI specifications or establishing provider qualifications.

5. 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.

- 5.1 The evidence based technology report concluded that adding MRI to mammography breast cancer screening in women at high risk of breast cancer will increase diagnostic and therapeutic costs.
- Accurately estimating cost-effectiveness may not be possible because RCTs evaluating the mortality reduction with screening or testing women at high-risk for breast cancer have not been conducted.
- 5.3 Washington state agency utilization and cost information indicated 5 year Breast MRI costs of \$3,111,943 for UMP/PEP and \$466,449 for DSHS.

6. Evidence on Medicare Decision and Expert guidelines

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

- 6.1 Centers for Medicare and Medicaid Services (CMS), 2007 – annual breast cancer screening with clinical examination and mammography is covered by Medicare. Breast cancer

- screening with MRI is not covered as a routine preventive measure (preventive services must be specifically covered). However, breast MRI may be covered as a diagnostic procedure.
- 6.2 Guidelines – 7 recent guidelines were identified providing specific recommendations for women at increased risk of breast cancer. Recommendations for this population were also found in the National Institute for Health and Clinical Excellence (NICE) database.
 - 6.3 Two guidelines were rated as high quality and are summarized:
 - 6.3.1 (1) USPSTF, 2009 – if a woman has an abnormal mammographic finding on screening or a concerning finding on a physical examination, additional imaging and biopsy may be recommended. Additional imaging may help classify the lesion as a benign or suspicious finding to determine the need for biopsy.
 - 6.3.1.1 The focus of the guideline was on women at average risk of breast cancer. Relevant evidence mentioned by the USPSTF is retrospective observational data and from expert opinion and is rated as medium risk or high risk of bias.
 - 6.3.1.2 Breast MRI improved local staging in almost 20% of patients and that preoperative breast MRI studies may be particularly useful in surgical planning for, and managing of, patients with lobular carcinoma.
 - 6.3.2 (2) National Cancer Institute, 2010 (last updated) – based on fair evidence, screening mammography in women aged 40 to 70 years decreases breast cancer mortality. The benefit is higher for older women, in part because their breast cancer risk is higher.
 - 6.4 One guideline was rated as fair quality and are summarized below:
 - 6.4.1 (1) NICE, 2006 – adding MRI to mammography increases sensitivity over mammography alone in screening for breast cancer in women at high risk; mammography may be useful adjunct to MRI in the high risk group; MRI is more sensitive than mammography in BRCA1 carriers; MRI combined with mammography is a cost-effective intervention in women with BRCA1 mutation aged 30-49; annual MRI combined with mammography is a cost-effective intervention in non-BRCA1 women aged 30-39 with an 8% or greater 10-year risk; and MRI combined with mammography is a cost-effective intervention in non-BRCA1 women aged 40-49 with a 20% or greater 10-year risk.
 - 6.5 Four guidelines were rated as low quality, those included: American College of Radiologists (ACR), 2010; European Society of Breast Cancer Specialists (EUSOMA) working group, 2010; National Comprehensive Cancer Network (NCCN), 2009 and American Cancer Society, 2007.

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 Breast MRI has been collected and summarized.

- 1.1. This evidence review summarized the evidence on the accuracy and efficacy of MRI compared with conventional techniques (mammography, sometimes with ultrasound and sometimes with clinical breast exam) for detecting breast cancer and its role in reducing breast cancer mortality and other meaningful health outcomes in women at increased risk for breast cancer.



2. Is it safe?

The committee concludes that the comprehensive evidence indicates that Breast MRI is equally safe to alternative tests. Key factors to the committee's conclusion included:

- 2.1. The committee agreed that MRI screening in addition to mammography and/or other tests does not create additional radiation risk from the test itself, though there may be rare harms associated with the gadolinium-based MRI contrast agents.
- 2.2. The addition of Breast MRI as a screening tool will result in additional false positives and treatment, including biopsy and potential harms from biopsy.
- 2.3. The committee agreed that the psychological harms related to the testing may be present but were well tolerated.

3. Is it effective?

The majority of the committee concludes that the comprehensive evidence shows that Breast MRI is more effective treatment than other conventional medical treatments.

- 3.1. The committee agreed that sufficient evidence exists to conclude that for women at high risk, adding yearly screening with MRI to mammographic screening increases detection of breast cancer, likely between 2 to 5 cancers per 100.
- 3.2. The committee agreed that the increase in cancer detection is offset by a higher rate of false positive tests, about 10 in 100, which will lead to additional benign breast biopsies.
- 3.3. The committee also agreed that Breast MRI changed treatment, including an increase in more extensive surgeries, including an increase in mastectomies, some of which may be unnecessary; and that evidence about the ultimate health impact of the changed treatment is inconclusive. For instance, re-excision rates varied widely from 5% to 50%.
- 3.4. The committee agreed that there is no evidence about the effect of Breast MRI on mortality rates, but that mammography screening (early detection) does reduce mortality, and the evidence reviewed indicates more cancers are found through Breast MRI in high risk women.

4. Evidence about the technology's special populations, patient characteristics and adjunct treatment

The committee agreed that no compelling evidence exists to differentiate sub groups or special populations.

- 4.1. The committee agreed with the evidence based report that there is inadequate evidence to conclude that patients with breast implants, increased breast density, or fibroglandular breast tissue benefit from Breast MRI or are at increased risk of breast cancer.

5. Is it cost-effective?

The committee concludes that the Breast MRI is unproven to be cost effective; agreeing with the comprehensive evidence review that no evidence based conclusions about cost effectiveness can be drawn.

- 5.1. The evidence report adequately summarized the moderate quality evidence that because Breast MRI is a more expensive and additional test, adding Breast MRI will increase diagnostic and therapeutic costs.
- 5.2. The evidence report also adequately summarized the poor cost-effectiveness evidence about whether Breast MRI screening in addition to mammography is cost effective largely



because cost-effectiveness is highly dependent on mortality reduction and no evidence is available about mortality reduction.

- 5.3. Committee acknowledged the state agency costs of breast cancer. Costs were nearly 3.6M and averaged \$950 per treatment over the 5 years beginning in 2005.

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, and agency and state utilization information. The committee concluded that the current evidence on Breast MRI demonstrates that there is sufficient evidence to cover with conditions the use of Breast MRI in diagnosis and treatment of cancer in women at high risk. 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. Based on these findings, the committee voted 7 to 2 to cover with conditions Breast MRI.

Breast MRI Coverage 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.

Breast MRI Evidentiary Votes:

Is there sufficient evidence under some or all situations that Breast MRI in diagnosis and treatment of cancer in women at high risk is:

	Unproven (no)	Equivalent (yes)	Less (yes)	More (yes)
Effective	2	0	0	7
Safe	3	5	0	1
Cost-effective Overall	6	1	1	1

Breast MRI 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
Breast MRI	2	0	7

Outcome: The committee chair directed HTA staff to prepare a Findings and Decision document on Breast MRI reflective of the majority vote for final approval at the next public meeting.

- MRI is covered for screening for breast cancer with a minimum of 11 months between screenings in women at high risk of breast cancer. Women at high risk is defined as:
 1. A personal history or strong family history of breast cancer;

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2. A genetic mutation of BRCA 1, BRCA2, TP53 or PTEN genes (Li-Fraumeni syndrome and Cowden and Bannayan-Riley-Ruvalcaba syndromes);
 3. GAIL model lifetime cancer risk of 20% or higher; or
 4. History of radiation treatment to the chest between ages 10 and 30, such as for Hodgkin's disease.



Agenda Item: Spinal Cord Stimulation (SCS) Topic Review

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

- ✓ Staff provided an overview of the timeline and referred HTCC members to the included key questions and population of interest for spinal cord stimulator review.
- ✓ Staff welcomed, per HTCC request, an invited clinical expert Hugh Allen, MD. Dr. Allen prepared a COI with no conflicts listed.

Agenda Item: Public Comments

The Chair called for public comments.

- ✓ Scheduled Public Comments: Nine stakeholder groups requested scheduled time for public comments. Six of the nine stakeholder groups were available at the public meeting to provide public comment.
 - Gordon Irving, MD, Medical Director, Swedish Pain & Headache Center, commented on how spinal cord stimulators will not cure pain; however, some patients may respond to the device which could reduce narcotic usage for patients.
 - Robert Levy, MD, Ph.D., Board Member, North American Neuromodulation Society (NANS), commented that class I level evidence on SCS demonstrates that with the correct population SCS works better than medical management. Believes that studies have good long-term data, and SCS treatment is significantly less expensive than other treatments and medical management. LNI study at the University of Washington was only on workers comp patients.
 - Robert Lang, MD, Chair, Industrial Insurance Medical Advisory Committee, commented that his experience with SCS has demonstrated that they do not work. SCS does not minimize pain or usage of opioids among patients. A device such as SCS should eliminate these conditions, but they have proven to not minimize any of them. Believes that the Turner study was performed well, and that the state agencies should continue their non-coverage policy.
 - Daniel Kwon, MD, Yakima Valley Medical Hospital, commented that SCS can be helpful for some populations, but believes that the problem is with patient selection. Poor selection will lead to poor outcomes.
 - Kathy Wang, DO, South Sound Neurosurgery, commented that SCS should only be used as a last resort for chronic pain patients. Physical and psychological tests should be administered prior to SCS implantation. Pointed out that the LNI study didn't compare their workers comp population against the general population. SCS should not be used as a first step for primary treatment.
 - Judith Turner, Ph.D, University of Washington School of Medicine, (included presentation in meeting materials) commented that the SCS group did not have significantly better pain, function, or opioid use outcomes at 24 months. No evidence SCS was cost-effective for workers' compensation recipients with FBSS in Turner study. Medical care and productivity loss costs over 24 months for a patient who received trial SCS were on average \$20,300 higher than for a patient who received a pain clinic evaluation and \$29,970 higher than for a patient who received usual care.

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- ✓ Open Public Comments: no individuals provided comments during the open portion.

Agenda Item: Spinal Cord Stimulation (SCS) – Agency Data

Dr. Lee Glass, Department of Labor & Industries, Medical Director, presented to the committee the agency utilization and outcomes for Spinal Cord Stimulation.

- ✓ SCS Treatment: Background: Involves insertion of electrodes into the epidural space. Electrodes are connected to a surgically implanted pulse generator. Electrical impulses generated are thought to inhibit the conduction of pain signals to the brain. Intended to treat pain for many years; not a short-term treatment.
- ✓ Agency Concerns:
 - Safety Concerns (Medium) -- Implanted device with risk of infection, morbidity, and death. High risk for further interventions (revision, removal, re-implantation).
 - Efficacy Concerns (High) -- Short term, modest pain relief, no clear improvement in function; no evidence of longer term improvement in pain or function; real world-outcomes worse than RCTs.
 - Cost Concerns (Medium) -- Usage and costs escalating rapidly; very high per patient cost.
- ✓ Coverage Overview:
 - Currently paid by DSHS, PEBB, and DOC.
 - Labor and Industries (L&I): long-standing non-coverage policy based on no evidence of substantially improved pain AND function (required under WAC); non-coverage decision upheld after cohort study completed Sept, 2008. Continuing non-coverage policy based on formal review and advice of statutory Industrial Insurance Medical Advisory Committee (IIMAC).
- ✓ L&I invested in identifying whether SCS works, over 15 years of working with evidence and researchers, including evidence Development for Spinal Stimulation:
 - 1995: commissioned systematic review of SCS literature addressing long-term risks and benefits. *Turner et al, Neurosurgery 1995; Dec 37(6): 1088-95.*
 - 2003: commissioned systematic review of SCS literature addressing effectiveness and complications. *Turner et al, Pain 2004; 108: 137-47.*
 - 2004: contracted cohort study of Failed Back Surgery Syndrome (FBSS).
 - 2004-2008: injured workers with FBSS were eligible for treatment with SCS
 - Effectiveness data published, included in report: *Turner et al, Pain 2010; 148: 14-25.*
 - Complete cost study submitted: *Hollingworth et al.*
- ✓ Short-Term SCS Implantation Costs: Costs per patient receiving trial + implant +/- revision and removal: UMP: N=118; \$54,353 (22 months); L&I: N=27; \$38,373 (24 months) and DSHS: N=30; \$9706 (2.6 months). *Duration observed in administrative data.*



- ✓ Agency SCS costs-total reimbursed* (*costs included only SCS related charges), 2006–2009: UMP = \$4,686,442; L&I = \$3,553,608** + \$575,861 (study administration); and DSHS = \$254,000. (**Total n=161 injured workers with at least trial stimulation).
- ✓ Agency Data: Adverse Events, 2005-2009: UMP- 23% revision/removal; 28% other adverse events; adverse events account for 17.4% of all costs, and averaged \$24,646/patient (\$13-\$248,000). L&I (Turner cohort study) -- 1 trial patient with severe, life-threatening event; permanent implant-3 superficial, 1 deep infection (14%); 19% revision; 19% removal.
- ✓ Mortality: Coffeey et al, Anesthesiology 2009; 111: 881-91 -- One year unadjusted mortality rates: Intrathecal infusion pump-3.89%; Spinal cord stimulator-1.36%; and Medicare lumbosacral spine surgery-3.52%.
- ✓ Efficacy vs. Effectiveness: **Efficacy studies** - “Can it work under ideal conditions”? attempt to tightly control potential confounding factors and bias; and may not be applicable to many patients seen in everyday practice.
- ✓ **Effectiveness studies** - “Does it work in real-world setting”? Use less stringent eligibility criteria, more often assess health outcomes, and have longer follow-up periods than most efficacy studies. The results of effectiveness studies are more applicable to the average patient than results from the highly selected populations in efficacy studies.

Study	Condition Longest F/U	Outcomes		Comparator	Sponsor
		Pain	Function		
Kemler 2000, 2004, 2006	CRPS 5 years	-	-	PT	Dutch Health Insurance Council
Kumar 2007, 2008	FBSS 1 year	+	+	CMM	Medtronic
North 2005	FBSS 2.9 +/- 1.1 years	+	-	Re-operation	Medtronic
Turner 2010	FBSS 2 years	-	-	Pain clinic, usual care	L&I

- ✓ Scientific Evidence: Considerations -- Current evidence is conflicting and limited to relatively short-term. Modest pain relief only in short term. 3/4 studies with no improvement in function. Positive studies of efficacy and cost-effectiveness are industry funded and managed. Invasive technology with high rates of complications (i.e., revision, removal).
- ✓ Impact of Industry Sponsorship on Studies – “Industry funded studies demonstrated a statistically greater likelihood to report positive results than studies with other funding sources.” Shah et al, Spine, 2005. Results: 16% had industry support, 13% foundation support, 10% government support, 3% institution support, 58% “not funded”. Odds ratio of industry funded reporting positive results 3.3 times (P<0.001) that of other funding sources.
- ✓ Cost-Effectiveness (C/E) Evidence Concerns: No long-term efficacy / effectiveness showing SCS reduces pain and improves function; all studies asserting C/E assume effectiveness over very long-term; assumptions are not adequate / reflective of all available evidence. Example: Taylor & Taylor 2005 -- assumes 80% trial success; one-way sensitivity analyses- not reflective

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of real-world or RCT experience; multi-way analysis presented only for 'best case' and assumptions based on efficacy data from 1 Level II RCT (North et al.) with 2.5 yrs follow-up.

- ✓ AMDG Recommendations – Non Coverage Due to:
 - Safety concerns: repeat interventions for clinical / technical failure are common. Severe infections, death potential.
 - Very limited efficacy: only for modest pain relief only in short term; 2/3 RCTs with no effect on function; no evidence that patient selection (trial results, psychological screening) improves outcomes.
 - No clear effectiveness in workers' comp: limited benefit with increased opioid use at 6 months, no effect beyond that.
 - Huge cost per implanted patient
 - SCS currently lacks compelling evidence of appropriate benefit (length/type); and has high device complication and removals, and very high cost - not ready yet.

Agenda Item: Evidence Review Presentation

Spectrum Research presented an overview of their evidence report on Spinal Cord Stimulation for neurological pain.

- ✓ Background – Indications for SCS (FDA): Chronic intractable pain in the trunk and/or limbs including unilateral or bilateral pain associated with FBSS and intractable low back and leg pain, and for some devices: *CRPS, radicular pain syndrome or radiculopathies resulting in pain, post-laminectomy pain, unsuccessful disc surgery, degenerative disc disease or herniated disc pain refractory to conservative or surgical interventions, peripheral causalgia, epidural fibrosis, arachnoiditis or lumbar adhesive arachnoiditis, and multiple back surgeries.* Potential patients should undergo a period of trial stimulation prior to permanent SCS implantation.
- ✓ Background -- Contraindications for SCS (FDA): Failed trial stimulation due to ineffective pain relief; poor surgical risks; pregnancy; active general infections or multiple illnesses; inability to operate the SCS system; and cardiac pacemakers (with specific exceptions and precautions) or cardioverter defibrillators.
- ✓ Literature Search:



✓ Comparative Clinical Studies:

Study	Study Type	Preop diagnosis	Follow-up	Treatment	Patient characteristics	Permanent implant	Study Sponsor
Kemler (2000, 2004, 2008) The Netherlands	RCT	Chronic CRPSI	6 months (100%) 24 months (94%) 60 months (81%)	<ul style="list-style-type: none"> • SCS + PT (n = 36) • PT alone (n = 18) 	N = 56 Mean age: 38 years Sex: 31% male	24/36 (67%)	Dutch Health Insurance Council
Kumar (2007, 2008) Europe, Canada, Australia, Israel	RCT	FBSS with leg pain > back pain	6 months (94%) 12 months (88%)	<ul style="list-style-type: none"> • SCS + CMM (n = 52) • CMM alone (n = 48) 	N = 100 Mean age: 50 years Sex: 51% male	43/52 (83%)	Managed, analyzed (with external direction), & funded by Medtronic
North (2005) Johns Hopkins University	RCT	FBSS with leg pain > back pain	2.9 ± 1.1 years (range: 1.8–5.7) (75%)	<ul style="list-style-type: none"> • SCS (n = 30) • Reoperation (n = 30) 	N = 60 Mean age: 50 years Sex: 50% male	17/24 (71%)	Funded by Medtronic; Johns Hopkins received profit from related sale
Turner (2010) University of Washington	Prospective cohort study	FBSS with leg pain > back pain	6 months (97%) 12 months (93%) 24 months (87%)	<ul style="list-style-type: none"> • SCS (n = 51) • Pain Clinic (n = 39) • Usual Care (n = 68) 	N = 159 Mean age: 44 years Sex: 77% male Open workers' comp claims	27/51 (52%)	Funded by WA State Department of Labor & Industries

✓ Internal Validity:

Methodological principle	Kemler 2000, 2004, 2008	Kumar 2007, 2008	North 2005	Turner 2010
Study design				
Randomized controlled trial	✓	✓	✓	
Cohort study				✓
Statement of concealed allocation*	✓	✓	✓	
Intention to treat*	✓	✓	✓	
Independent or blind assessment	✓	✓	✓	✓
Co-interventions applied equally	✓	✓	✓	✓
Complete follow-up of ≥ 80%	✓	✓		✓
Adequate sample size	✓	✓	✓	✓
Controlling for possible confounding	✓	✓		✓
Evidence class	I	I	II	II

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- ✓ Key Question 1: Efficacy – studies that met our inclusion criteria: 3 RCTS – CRPS: 1 RCT (Kemler) and FBSS: 2 RCTs (Kumar, North)
 - Efficacy: “Success” – 1 RCT (FBSS) with 19 SCS patients and 26 reoperation patients: “Success” = composite of pain relief \geq 50% and patient satisfaction. 47% SCS relief vs 12% reoperation relief
 - Efficacy: Pain Relief – 2 RCTs (FBSS, CRPS) – Kumar: FBSS (6 months) leg pain
- ✓ Efficacy – Kemler: CRPS I (6, 24 & 60 months)
- ✓ Efficacy – Function:

Author	Diagnosis	Treatments	Outcome measure	F/U period	Results
Kumar (2007)	FBSS	SCS + CMM vs. CMM	ODI	6 months	SCS: better scores
Kemler (2000, 2004)	CRPS	SCS +PT vs. PT alone	Jebesen hand scores; Kemler foot scores	6 & 24 months	No statistical differences
North (2005)	FBSS	SCS vs. reoperation	Neurological status; Daily activities	2.9 years (mean)	No statistical differences

- ✓ Efficacy – Quality of Life:

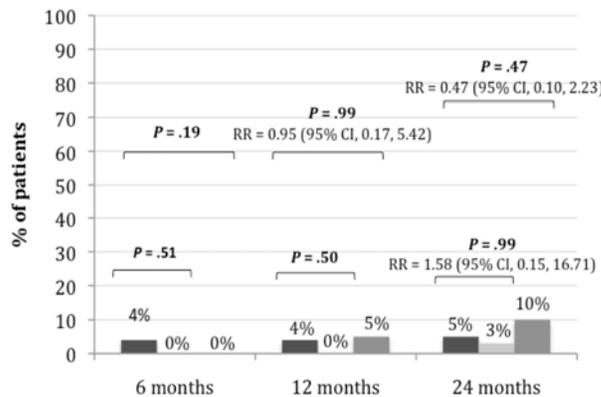
Author	Diagnosis	Treatments	Outcome measure	F/U period	Results
Kumar (2007)	FBSS	SCS + CMM vs. CMM	SF-36; EQ-5D utility scores	6 months	SCS: better scores (except role-physical subscale of SF-36: no difference)
Kemler (2000, 2004, 2008)	FBSS	SCS + PT vs. PT	% change in QoL; Nottingham Health Profile, EQ-5D, Self-Rating Depression Scale	6 & 24 months; 60 months	No differences

- ✓ Efficacy – Patient Satisfaction & Perceived Effect – 2 RCTs (FBSS, CRPS):
- ✓ Efficacy – Medication Usage: 2 RCTs (FBSS)
- ✓ Efficacy – Summary Strength of Evidence:



- Pain, perceived effect of treatment and patient satisfaction – *SCS is superior* to conventional therapies (CMM, physical therapy, or reoperation) in the first 2–3 years. This benefit in reducing pain tends to decrease after 2 to 3 years. Strength of evidence = High
- Function and quality of life -- It is unclear whether SCS is better than conventional therapies in improving function and QoL. One trial reports substantial improvement in both function and QoL after 6 months. A second trial reports no difference in function at 6 or 24 months or QoL at 6, 24 or 60 months. A third trial reports no difference in function at a mean of 2.9 years. Strength of evidence = Low
- ✓ Key Question 1: Effectiveness – Studies that met our inclusion criteria: 1 prospective cohort study (Turner 2010) – FBSS patients receiving workers’ compensation payments in the state of Washington.
- ✓ Effectiveness “Success” = leg pain relief ≥ 50%, RDQ improvement of ≥ 2 points, and less than daily opioid usage. **Alternate definition of “success”** = leg pain relief ≥ 30%; RDQ improvement of ≥ 5 points, and less than daily opioid usage. At 6 months, significantly more SCS patients achieved this outcome compared with PC (22% versus 5%; $P = .03$) and UC (22% versus 5%; $P = .01$); the differences were no longer significant by 12 or 24 months.

Turner: FBSS (6, 12 & 24 months)



- ✓ Effectiveness – Pain Relief: *Clinical meaningful difference may be pain relief ≥ 30%: SIMILAR RESULTS.* Mean VAS leg pain and back pain scores were similar in all three groups at all follow-ups.
- ✓ Effectiveness – Other Outcomes:
 - Function: There were no differences in function between treatment groups as measured by the Roland-Morris Disability Questionnaire, ability to perform tasks, work/disability status, and mean time lost from work.
 - HR-QoL: There were no differences in mean SF-36 mental health scores between treatment groups.
 - Medication Usage: There were no differences between groups in the usage of most medications (except anticonvulsants, which was higher in the SCS versus PC group).
- ✓ Effectiveness – Summary of Strength of Evidence: In FBSS patients receiving workers’ compensation payments, *SCS is similar* to conventional therapies (Pain Clinic, Usual Care) with respect to the composite score “success” in the first 2 years; *SCS may result in better leg pain*

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relief compared with conventional therapies (Pain Clinic, Usual Care) in the first 6 months; and no other outcome measure (pain, function, daily opioid usage, and quality of life) were significantly different between SCS and conventional therapies in the first 2 years. Strength of Evidence = Low

- ✓ Key Question 2: Safety – studies that met our inclusion criteria:
 - 3 RCTs, 1 cohort study (from Key Question 1) – FBSS, CRPS
 - 6 case series (follow-up ≥ 5 years) – Neuropathic pain in ≥ 75% patients. N= 36 – 338 patients per study (mean N = 158).

Revision / Replacement: SoE = High that revision is not uncommon following SCS

Revision/ replacement:	2 – 3 year f/u <small>(from 3 RCTs, 1 cohort study)</small>	≥ 5 year f/u <small>(from 1 RCT, 6 case series)</small>
Electrode	4 – 21% patients	3 – 34% patients 7.4% electrodes
Generator	1 – 11% patients	1 – 54% patients 5.4% generators
Entire system (replacement)	3 – 4% patients	1.2 – 6% patients
Entire system (removal)	8 – 22% patients	(% patients: NR)
Overall rate	25 – 38% patients	42 – 60% patients

Other Complications & Side Effects

	2 – 3 year f/u <small>(from 3 RCTs, 1 cohort)</small>	≥ 5 year f/u <small>(from 1 RCT, 6 case series)</small>
SCS-related	8 – 100% patients	0 – 6.5% patients
Related to trial stimulation	16% patients	NR

Mortality – SoE = High that the rate of mortality due to SCS is low

No deaths were attributed to the SCS device, procedure or implantation.

In the cohort study one patient nearly died due to complications that resulted from the trial stimulation.

	2 – 3 year f/u <small>(3 RCTs, 1 cohort)</small>	≥ 5 year f/u <small>(1 RCT, 6 case series (CS))</small>
Death (any cause)	SCS group: 1.4% patients (2 deaths; 4 studies) Control groups: 0% patients (4 studies)	SCS group: 0% patients (1 RCT) 1.0% patients (3 CS) Control groups: 0% patients (1 RCT)

- ✓ Key Question 3: studies that met our inclusion criteria included 6 prognostic studies: neuropathic pain in ≥ 75% patients, permanent SCS devices implanted in 32 – 53 patients per study.
- ✓ Subpopulations (reported by ≥ 2 studies) – no strong evidence of differential efficacy or safety in subpopulations based on the following characteristics: age; sex; workers’ compensation or other disability payments; pain intensity, duration or location; MMPI scores and number of prior surgeries.
- ✓ Economic Conclusions: 2 published studies, 1 HTA that included two independent models –

	Population	Conclusions
Taylor & Taylor	FBSS: SCS versus CMM	<u>2 years:</u> SCS cost-effective, but more data needed <u>Lifetime model:</u> SCS is more effective and less costly than CMM
North*	FBSS: SCS versus reoperation	<u>3 years:</u> SCS is more effective and less costly than reoperation
Simpson HTA (ABHI & ScHARR models)	FBSS: SCS versus reoperation or CMM CRPS: SCS versus CMM	<u>15-year model:</u> SCS is more effective and less costly than CMM

- ✓ Economic Conclusions: At moderate (< \$20,000) ICER levels, SCS is associated with improved outcomes and increased costs compared with CMM and/or reoperation in the shorter term. In the longer term, SCS dominance over control treatments is less certain due to lack of efficacy evidence past 2 – 3 years. Strength of evidence = Moderate.

Agenda Item: HTCC Spinal Cord Stimulation Discussion and Findings

Brian Budenholzer, Committee Chair, led a discussion of the evidence related to the safety, efficacy, and cost-effectiveness of Spinal Cord Stimulation 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 *Condition:* The evidence based technology assessment report indicates that neuropathic pain is pain resulting from a primary lesion or dysfunction in the central or peripheral nervous system. Chronic neuropathic pain is likely underdiagnosed and undertreated; its estimated prevalence has been reported to range from 1.5 to 8%. Stimulation before having the device permanently implanted. The evidence based technology assessment report indicates the aim of treatment for chronic pain is to improve function and quality of life while relieving pain. Treating chronic neuropathic pain is challenging, as the pain is often refractory to conservative therapies.
- The two of the most common types of chronic neurogenic pain treated with spinal cord stimulation include failed back surgery syndrome (FBSS) and complex regional pain syndrome (CRPS).
 - FBSS has been estimated to affect approximately 30% of patients following lumbar spine surgery, though reported estimates range from 10 to 40%.
 - Complex regional pain syndrome (CRPS) is a neuropathic pain disorder of unknown pathophysiology that affects one or more limbs.
- 1.2 *Technology and alternatives:* The evidence based technology assessment report indicates spinal cord stimulation (SCS) is an alternative treatment proposed for patients with chronic

neuropathic pain who have not responded to conventional therapies such as medication, physical and/or psychological therapy, and in some cases, reoperation.

- Potential benefits include pain relief, improved quality of life and functionality, reduction in pain medication usage. Implantation of SCS components is minimally invasive (compared to back surgery) and is reversible. Patients typically undergo a trial period.
- 1.3 *Outcomes:* Patient oriented outcomes of interest include measures of pain relief, improved function, reduction of medication, quality of life, and patient satisfaction. The evidence based technology assessment report indicates many pain related outcomes are subjective, and considerable debate remains about clinically meaningful differences.
- Reduction in pain is the most commonly reported outcome, and a greater than 50% reduction on a VAS pain intensity is commonly used to determine success, though more studies are needed to determine significance.
- 1.4 *Evidence Base:* The evidence based technology assessment report focuses on three RCTs and one prospective cohort study, and includes additional case series and cost studies, as well as guidelines.
- One RCT included patients with CRPS; two RCTs included patients with FBSS. The prospective cohort study included patients with chronic pain and an open Washington state workers' compensation claims. 375 total patients in the primary four studies.
 - For safety considerations, six additional case series, all with mid-term follow-up were identified and three cost-effectiveness analyses were also included.
 - The evidence based technology assessment report identified 9 expert treatment guidelines and a national Medicare policy relating to spinal cord stimulation.
- 1.5 *Other Information:* The committee also reviewed information provided by the state agencies, and public members; and heard comments from the evidence reviewer, HTA program, the public and agency medical directors.

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.

- 2.1 The evidence based technology assessment report includes evidence on several safety outcomes including device complications, revisions, other complications and side effects and mortality for SCS and in several time frames. Short-term (< 5 years) safety data were reported by three RCTs and one prospective cohort study; mid-term (5 – 10 years) safety data were reported by one RCT and six case series. No long-term safety data were available.
- 2.2 *Revision:* the evidence based technology assessment report found three RCTs and one cohort study which reported short-term revision rates of SCS devices; one RCT and all six case series reported mid-term revision rates. Overall, short term revision rates ranged from 25% to 38% of patients; and mid-term revision rates ranged from 42% to 60% (not including 54% of patients undergoing pulse generator replacements due to battery life). No long term revision rates available.
- *Total Removal:* short term total removal, reported as a subset of revisions occurred in 3% to 22% of patients due to infection, rejection, discomfort, or ineffective pain relief. Mid term total removal rates ranged from 4% to 17% of patients.

- 2.3 *Other SCS-related complications or side effects:* the evidence based technology assessment report found that complications or side effects ascribed to the SCS device were reported by two RCTs, one cohort study, and six case series and included dural punctures, amplitude by bodily movements; paresthesia in other body parts, pain, disturbed urination, lead fracture, loss of effect, infection.
- Overall short-term complication rates ranged from 8-100% of patients. At two years follow-up, one RCT reported that side effects had occurred in 100% of available SCS patients; another RCT reported device-related complications not requiring revision in 14% of patients.
- 2.4 *Mortality:* the evidence based technology assessment report found short-term mortality data from three RCTs and one prospective cohort study. Two deaths occurred in the SCS groups (2/139) though these were not directly attributed to SCS. No deaths occurred in the control groups (0/179). Mid-term mortality data were obtained from one RCT and three case-series and identified 2 deaths in SCS patients, though not directly attributed to SCS; one patient nearly died from complication following trial stimulation.

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.

- 3.1 The evidence based technology assessment report included three RCT's and one prospective cohort study for evidence about efficacy and effectiveness of SCS for treatment of neurological pain.
- Efficacy studies included: one RCT *Kemler* (level 1) comparing SCS with physical therapy in 54 CRPS patients funded by Dutch Gov; and two RCTs (*Kumar* Level 1 and *North* Level 2) reported on 160 patients with FBSS comparing SCS and conventional medical management (CMM) to CMM alone, or compared to lumbar reoperation (both funded by Medtronic).
 - Effectiveness studies included one prospective cohort study, *Turner* (Level 2) on effectiveness of SCS compared with Pain Clinic and Usual Care treatments in 159 FBSS patients with open workers' compensation claims (funded by State of Washington).
 - In general, the efficacy studies reported improvements in the SCS patients over the control groups whereas the effectiveness study did not find improvements in the SCS patients over control groups.
- 3.2 *Trial Design:* Overall, the internal validity of included studies was high; however, several limitations were noted, including the overall small patient sample of 375. Appropriate comparators are not a criterion used by the evidence based technology report to score the quality of the study, but were noted in the study limitations of several studies. Additionally, blinding is a criterion included in scoring the studies, but was not met by any of the studies.
- *Comparators:* In *Kemler*, SCS plus PT was compared to PT, although the inclusion criteria required that patients be unresponsive to PT for six months to be eligible so SCS was compared to a treatment known to be ineffective. Similarly, in *North* SCS was compared to re-operation in patients diagnosed with failed back surgery syndrome. Finally, the SCS groups received SCS plus other treatments (e.g. PT, Medications, Chiropractic) which confounds the effect of SCS alone.

- *Blinding*: Neither patients nor treatment providers were blinded, none of the trials included sham stimulation or surgery to address potential placebo effect.
- 3.3 *Outcomes*: Patient oriented outcomes of interest include measures of pain relief, improved function, reduction of medication, quality of life, and patient satisfaction. The evidence based technology assessment report indicates many pain related outcomes are subjective, and considerable debate remains about clinically meaningful differences.
- Reduction in pain is the most commonly reported outcome, and a greater than 50% reduction on a VAS pain intensity is commonly used to determine success, though more studies are needed to determine significance.
 - No information on determining clinically significant differences for QOL, patient satisfaction, functional improvement, or reduction of medication was included in the evidence report.
 - Most improvement is reported as a change from baseline
- 3.4 *Composite Success score*: Two studies used a composite score of success:
- *North* used a composite of pain relief of greater than 50% and patient satisfaction, the pain measure was not disclosed, patient satisfaction was measured by whether patients would go through treatment again. Of 19 SCS patients, 47% achieved success versus 12% of 26 reoperation patients over a mean of 2.9 years.
 - *Turner* used a composite of leg pain relief of greater than 50%, greater than 2 point improvement on Roland disability index, and less than daily opioid use. Less than 10% in any group, and no significant difference between SCS, pain clinic (PC), or usual care (UC) groups at any follow-up up to 24 months achieved success.
- 3.5 *Pain Relief*: Studies reported on pain relief, usually using VAS scores (0-10pt pain scale) at baseline and follow up and looking for a greater than 50% improvement. Patients in the randomized SCS trials reported significant improved pain relief compared with those randomized to undergo control treatments in two RCTs with ≤ 2 year follow-up.
- *Kemler* reported significantly improved VAS scores at 6 months (4.2 vs. 6.6) and 24 months (4.3 vs. 6.6) for SCS compared to PT alone, but no difference at 60 months (5.0 vs. 5.9).
 - *Kumar* reported more SCS patients 48% at 6 months and 47% at 24 months reported greater than 50% improvement of VAS compared to CMM patients of 9% at 6 months and 7% at 24 months achieving 50% improvement. Mean VAS scores for SCS were 3.99 compared to 6.66 for CMM.
 - *Turner* reported that more patients in the SCS group achieved $\geq 50\%$ leg pain relief by six months (18% vs. 3%) than those in the UC group; but no difference between the SCS and PC group (15% vs. 5%). No differences were identified between any groups in the percentage of patients achieving leg pain relief of $\geq 50\%$ or at the 12- and 24-month follow-ups (range 0% to 10%).
- 3.6 *Function*: The Oswestry Disability Index and Roland-Morris Disability Questionnaire were used to assess improvement in function in two studies.
- *Kumar* found SCS group had significantly lower Oswestry scores than those in the CMM group (Mean score of 57.4 vs. 55.2 at baseline and 44.9 vs. 56.1 at six months).
 - *North* reported no significant differences between the SCS and reoperation groups in the neurological status or ability to perform daily activities a mean of 2.9 years follow-up, however, raw data were not provided.
 - *Turner* reported no significant differences in either the Roland-Morris Disability Questionnaire (RDQ) score improvement of greater than 2 points or ability to perform

daily tasks between treatment groups SCS 51%; PC 41%; UC 44% with mean scores of 18.1, 17.9, and 17.5).

- 3.7 *Health-related quality of Life (HR-QoL)*: Two trials reported no differences, while on trial reported better quality of life scores for SCS.
- Kemler reported no difference in several QoL outcome measures between the SCS and physical therapy groups, including the mean percent change in quality of life at the 6- and 24- month follow-ups as well as the Nottingham Health Profile, EQ-5D (EuroQol-5D), and Self-Rating Depression Scale scores at five years.
 - Kumar reported that patients randomized to receive SCS had significantly better scores in seven of the eight SF-36 (Short-Form 36) outcome scales compared with those randomized to receive CMM at six months.
 - Turner reported no significant differences between treatment groups in SF-36 scores and work/disability status.
- 3.8 *Additional Patient Satisfaction and Perceived Effect*: Several RCTs also reported patient satisfaction, generally using questions (non-validated instruments) to patients. One RCT reported that significantly more patients in the SCS group were satisfied with both their level of pain relief and with their treatment in general than those in the CMM group at six months follow-up. Another RCT incorporated patient satisfaction with pain relief into a composite outcome, “success”, which was reported above. Another RCT reported global perceived effect (GPE) scores. Significantly more patients in the SCS group reported GPE of “much improved” or “best ever” at both the 6- and 24- month follow-ups compared with the physical therapy group; however the differences between groups were no longer statistically significant by five years.
- 3.9 *Medication Usage*: Several trials reported on pain medication changes.
- *Kumar* reported no differences at six months between the SCS and CMM groups in the percentage of patients using opioids, non-steroidal anti-inflammatory medications, or antidepressants; however, significantly fewer SCS patients were taking anticonvulsants than those in the CMM group.
 - i. Other treatments: no differences between the SCS and CMM groups in the percentage of patients using all reported non-drug therapies (e.g., physical or psychological rehabilitation, acupuncture, or massage) except for TENS (transcutaneous electrical nerve stimulation), for which the rate of use was lower in SCS compared with CMM patients.
 - North reported significantly more patients in the SCS group were taking a stable or decreased dosage of opioids (versus baseline) than those in the reoperation group at a mean of 2.9 years follow-up.
 - Turner reported no significant differences for less than daily opioid usage between SCS, PC, and UC groups 21%, 32%, 34%.

4. Special Populations

- 4.1 The evidence based technology reported rated six small prognostic studies (four prospective and two retrospective studies). In general, very little evidence was found that suggests that any of the factors evaluated were associated with differential outcome following SCS. Prognostic factors included: age, sex, workers’ compensation or other disability payments, duration of pain, pain intensity, time since first lumbar surgery, number of prior operations for pain, pain location, laterality of pain, allodnia or hyposthesia at baseline, McGill Pain Questionnaire, Minnesota Multiphasic Personality Inventory (MMPI) and mental health component.

- 4.2 *Duration of Pain:* Two studies evaluated and found no relationship between duration of chronic pain and pain relief in the first year following SCS implantation. One study reported that CRPS patients with a longer duration of chronic pain had significant improvements in quality of life at nine months as measured by two (of eight) domains of the SF-36 outcome measure by multivariate analysis; however, no association was found between pain duration and GPE scores.
- 4.3 *Workers' compensation or other disability payments:* One study found no difference in the percentage of patients who achieved at least 50% pain relief at three months between those receiving workers' compensation or other disability payments than those not under such programs.
- 4.4 *Pain Intensity:* One study evaluated and found no association between the pain intensity at baseline and pain relief at one year.
- 4.5 *Pain Location:* Four studies evaluated and found no association between pain location and pain relief at follow-up, though each study compared different locations. One study reported no association between hand versus foot pain with nine-month SF-36 or GPE scores; another study found no difference in a combination of everyday activities, neurological function, and medication use between patients with axial versus radicular pain.

5. 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.

- 5.1 The evidence based technology report included three economic evaluations; two were published economic evaluations of SCS compared with other interventions for pain and one was included as part of the recent HTA conducted by NICE in the UK.
- The UK report found that there is some evidence that SCS is cost-effective at moderate (<\$20,000) incremental cost effectiveness ratio (ICER) levels compared with CMM or reoperation, and that SCS cost-effectiveness increases and may be dominant over time compared with control treatments (i.e., CMM or reoperation) assuming device longevity of 4 years and at least a 30% pain threshold criteria. However, the evidence based technology assessment report indicated that overall efficacy data is moderate and a key assumption of continued efficacy past 3 years is questionable, given the only RCT reporting pain 5-10 years after implantation. A further limitation is that only one study was conducted in a US setting.
- 5.2 Washington State Agency utilization and cost information indicated rising utilization (except in L&I due to current non-coverage); costs of SCS of \$9.6M over 4 years (average of \$2.4 million per year and per treatment cost of \$29,000).

6. Evidence on Medicare Decision and Expert guidelines

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

- 6.1 Centers for Medicare and Medicaid Services currently covers SCS under certain conditions based on a 1995 policy, with no evidence evaluation cited. Conditions include: SCS implantation is only used as a late or last resort for patients with chronic intractable pain; patients have undergone careful physical and psychological screening by a team of physicians; there has been a previous demonstration of pain relief with temporarily implanted electrodes; everything needed for the proper treatment and follow-up of the patient is available (i.e., facilities, equipment, professional and support personnel, etc); and SCS implantation employs percutaneous insertion of electrodes into the epidural space.

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- 6.2 Guidelines – a search of the core sources and relevant specialty groups identified nine guidelines for SCS (American Society of Anesthesiologist Task Force and the American Society of Regional Anesthesia and Pain Medicine, 2010; American Pain Society, 2009; Comprehensive evidence-based guidelines for interventional techniques in the management of chronic spinal pain, 2009; Institute for Clinical Systems Improvement, 2008; National Institute for Health and Clinical Excellence, 2008; American College of Occupational and Environmental Medicine, 2007; European Federation of Neurological Societies, 2007; Reflex Sympathetic Dystrophy Syndrome Association, 2006; and Evidence-based clinical practice guidelines, 2005
- Five guidelines recommend use for various pain treatments citing evidence; two guidelines indicate SCS may be considered citing weak or equivocal evidence; and two guidelines do not recommend use based on insufficient quality evidence.

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 Spinal Cord Stimulation has been collected and summarized.

- 1.1. Spinal Cord Stimulation (SCS) is an alternative treatment proposed for patients with chronic neuropathic pain who have not responded to conventional therapies such as medication, physical and/or psychological therapy, and in some case, reoperation.
- 1.2. Current best evidence is available primarily from four trials on 375 patients; which are rated at a Level 1 or 2 (good quality), which is a better level of evidence than some interventions. However, total patient sample size is small, comparators were weak or inappropriate, reported outcomes are mostly subjective and not consistently reported, industry funding and management may have an impact, and no trial included a sham stimulation/procedure arm. The overall body of evidence was inconsistent, with several trials showing benefits on some outcomes at generally shorter follow up periods and others showing no difference.
- 1.3. SCS is an implanted, long term treatment, but no evidence exists on either long term efficacy or safety.

2. Is it safe?

The committee concludes that the comprehensive evidence indicates that Spinal Cord Stimulation is less safe than alternative treatments. Key factors to the committee's conclusion included:

- 2.1. The committee agreed that SCS is less safe than alternatives, is an invasive procedure, and has many adverse events. While conventional medical management is not invasive, so would generally have a lower risk profile, reoperation is also a comparator and had less complications. SCS device related complications can be serious and include dural punctures, amplitude by bodily movements; paresthesia in other body parts, pain, disturbed urination, lead fracture, loss of effect, infection.
- 2.2. The committee agreed that safety was a significant factor: the number of trial reported complications ranged from 8 to 100%. Device related complication requiring revision ranged from 25% to 38% of patients in short term and 42% to 60% in up to 5 years (not including 54% of patients undergoing pulse generator replacements due to battery life).



- 2.3. The committee agreed that there were currently no reported mortality rates, but that the FDA data was not available and the small sample size is likely underpowered to detect.
- 2.4. The committee agreed that the removal rate could be considered an efficacy or safety issue, but the rates ranging from 4% to 17% were concerning, especially considering that trial stimulation is done first on all patients.

3. Is it effective?

The majority of the committee concludes that the comprehensive evidence about Spinal Cord Stimulation effectiveness is unproven.

- 3.1. The committee agreed that the studies had serious limitations in design, low patient sample sizes, and weak or inadequate comparators. Additionally, placebo effects of a new intervention for patients with chronic pain who have already failed multiple therapies is a serious concern and no study involved sham stimulation or procedures and outcome measures were generally subjective.
- 3.2. The committee found that evidence overall on important patient outcomes was limited. For all outcomes, there is no evidence of longer term improvement, particularly important when there are significant risks (including 1/3 revision and high removal rate) and the device is intended for permanent implant.
- 3.3. Given the serious limitations of the studies, the committee agreed that, at best, weak evidence exists that SCS may provide temporary improvement of pain in some patients, but there is no evidence of mid or long term pain improvement.
- 3.4. While pain is a critical patient outcome, evidence about other important patient outcomes was either not available or not consistent with the pain findings.
 - For instance, for reduction in pain medication in short term: Kumar and Turner found no difference, while North found SCS patients did have reduction.
 - For functional improvements, 1 trial found short term functional improvement, but 2 others did not; and there was no reliable evidence of functional improvement at mid (or long) term.
- 3.5. For all other outcomes, including improvement in quality of life, there is no reliable evidence of effect.

4. Evidence about the technology's special populations, patient characteristics and adjunct treatment

The committee agreed that no compelling evidence exists to differentiate sub groups or special populations.

- 4.1. The committee agreed with the evidence based report that there is inadequate evidence to identify characteristics that either enhance or reduce the efficacy of SCS such as age, sex, workers' compensation or other disability payments, duration of pain, pain intensity, time since first lumbar surgery, number of prior operations for pain, pain location, laterality of pain, allodynia or hyposthesia at baseline, McGill Pain Questionnaire or the Minnesota Multiphasic Personality Inventory (MMPI).

5. Is it cost-effective?

The committee concludes that SCS is unproven to be cost effective.

- 5.1. The committee agreed that the cost of SCS is substantial, averaging \$27,000 per patient.



- 5.2. The committee agreed that overall value cannot be ascertained without evidence of net benefit of effectiveness and reduced harm. Reliable cost-effectiveness analysis cannot be performed.

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, and agency and state utilization information. The committee concluded that the current evidence on Spinal Cord Stimulation demonstrates that there isn't sufficient evidence to cover the use of Spinal Cord Stimulation for chronic neuropathic pain. 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. Based on these findings, the committee voted 8 to 1 to not cover with Spinal Cord Stimulation.

Spinal Cord Stimulation Coverage 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.

Spinal Cord Stimulation Evidentiary Votes:

Is there sufficient evidence under some or all situations that Spinal Cord Stimulation for chronic neuropathic pain:

	Unproven (no)	Equivalent (yes)	Less (yes)	More (yes)
Effective	8	0	0	1
Safe	2	0	7	0
Cost-effective Overall	7	0	2	0

Spinal Cord Stimulation 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
Spinal Cord Stimulation	8	0	1

- Action: The committee chair directed HTA staff to prepare a Findings and Decision document on Spinal Cord Stimulation reflective of the majority vote for final approval at the next public meeting.

The committee reviewed the Clinical guidelines and Medicare decision. The Medicare decision was did not cite evidence and was decided prior to any of the studies reviewed by the committee. The guidelines recommendations conflict and not all have reviewed the latest trials included in this report.

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