

Health Technology Assessment Clinical Committee Meeting Program Update

Leah Hole-Curry, JD
Health Technology Assessment
October 22, 2010



Presentation Overview

- **WA State Government Context**
- **Health Care Access, Quality, and Cost efforts**
- **HTA Program Introduction**

- **HTA Program Updates**
 - HTA Program Outcomes / Measures
 - Recognition
 - Program Transparency Improvement
 - 2010 Topics

- **Today's Topics - Breast MRI and Spinal Cord Stimulators**

Governor Gregoire's strategy : Improve quality in health care

- **Governor Gregoire's five point plan to improve health care (2005)**
 - Emphasize evidence based health care
 - Create more transparency in the health care system
 - Promote prevention, healthy lifestyles, and healthy choices
 - Better managed chronic care
 - Make better use of information technology
- **Blue Ribbon Commission (2006)**
 - Goals set for 2012 including use of evidence based medicine
- **Collaboration of Programs across State purchasing –**
 - Total of about 450,000 beneficiaries and 3.5 billion purchased
 - Health Care Authority – Public Employees and subsidized low income (Basic Health, **Uniform Medical Plan**, PEBB)
 - **Medicaid** Purchasing Agency – federal/state low income health care program with **fee for service** and managed care plans
 - Labor and Industries – **Worker's compensation** program
 - Department of Corrections – Correctional health care

2

Why Health Technology Assessment?

- **Part of an overall strategy**
- **Medical technology is a primary driver of cost**
 - The development and diffusion of medical technology are primary factors in explaining the persistent difference between health spending and overall economic growth.
 - Some health experts arguing that new medical technology may account for about one-half or more of real long-term spending growth.
[Kaiser Family Foundation](#), March 2007: [How Changes in Medical Technology Affect Health Care Costs](#)
- **Medical Technology has quality gaps**
 - Medical technology diffusing without evidence of improving quality Highly correlated with misuses, overutilization, underutilization.
Cathy Schoen, Karen Davis, Sabrina K.H. How, and Stephen C. Schoenbaum, "U.S. Health System Performance: A National Scorecard," *Health Affairs*, Web Exclusive (September 20, 2006): w459

3

KEY HTA Products

Pay for What Works: Better Information is Better health

- **Transparency:** Publish topics, criteria, reports, open meeting
- **Technology Assessment Report:** Formal, systematic process to review appropriate healthcare technologies.
- **Independent Coverage decision:** Committee of practicing clinicians make decisions that are scientifically based, transparent, and consistent across state health care purchasing agencies.

Key focus questions:

- Is it safe?
- Is it effective?
- Does it provide value (improve health outcomes)?

4

HTA Program Elements

- 1. HCA Administrator Selects Technology**
Nominate, Review, Public Input, Prioritize
- 2. Vendor Produce Technology Assessment Report**
Key Questions and Work Plan, Draft, Comments, Finalize
2-8 Months
- 3. Clinical Committee makes Coverage Determination**
Review report, Public hearing
Meet Quarterly
- 4. Agencies Implement Decision**
Implements within current process unless statutory conflict

5

Evidence for use in Policy Decisions

Different Data Sources

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

6



HTCC Decision Basis

- **Clinical Committee Decision must give greatest weight to most valid and reliable evidence**
 - Objective Factors for evidence consideration
 - Nature and Source of evidence
 - Empirical characteristics of the studies or trials upon which evidence is based
 - Consistency of outcomes with comparable studies
 - Additional evaluation factors
 - Recency (date of information)
 - Relevance (applicability of the information to the key questions presented or participating agency programs and clients)
 - Bias (presence of conflict of interest or political considerations)

WAC 182-55-030: Committee coverage determination process

7

HTA Program Recognition

- **Council of State Governments (CSG), Western Region**
 - Winner of the 2010 CSG Innovations Award
- **Program Director Appointment to National Board**
 - HTA Program Director appointed to serve as a founding board member of Patient Centered Outcomes Research Institute (PCORI), a new organization charged with developing national standards and priorities for Comparative Effectiveness Research

8



2010 Technologies

- **Hyaluronic Acid**
- **Spinal Cord Stimulators**
- **Breast MRI**
- **Knee Replacement Surgery**
- Vertebroplasty, Kyphoplasty, Sacroplasty
- Glucose Monitoring
- Sleep Apnea Diagnosis and Treatment
- **Routine Ultrasound in Pregnancy**
- CT/MR for Pelvic and Abdomen
- ABA Therapy for Autism
- Spinal Injections

9



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:

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

Draft Version Not Officially adopted – 10-5-2010



- *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.

DRAFT



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



- 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?

Draft Version Not Officially adopted – 10-5-2010

- 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

- 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



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;

-
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.

DRAFT



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.

Draft Version Not Officially adopted – 10-5-2010



- ✓ 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

Draft Version Not Officially adopted – 10-5-2010



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%)	• 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%)	• 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%)	• 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%)	• 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

Draft Version Not Officially adopted – 10-5-2010



- ✓ 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 ≥ 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	Jebsen 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:

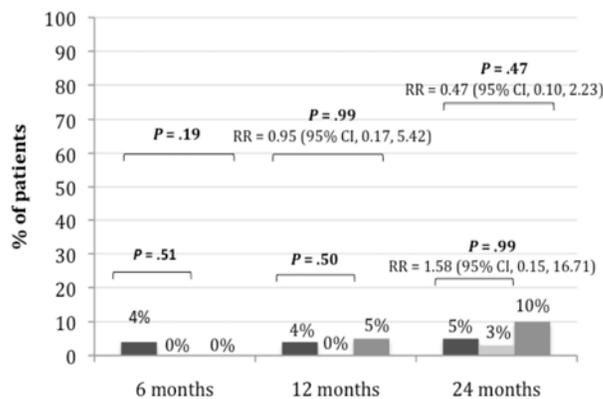
Author	Diagnosis	Treatments	Outcome measure	F/U period	Results
Kumar (2007)	FBSS	SCS + CMM vs. CMM	SF-36; EQ-5D utility scores	6 months	SCS: better scores (except role-physical subscale of SF-36: no difference)
Kemler (2000, 2004, 2008)	FBSS	SCS + PT vs. PT	% change in QoL; Nottingham Health Profile,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

Draft Version Not Officially adopted – 10-5-2010



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	<u>FBSS:</u> 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*	<u>FBSS:</u> SCS versus reoperation	<u>3 years:</u> SCS is more effective and less costly than reoperation
Simpson HTA (ABHI & ScHARR models)	<u>FBSS:</u> SCS versus reoperation or CMM <u>CRPS:</u> 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.

Draft Version Not Officially adopted – 10-5-2010

- 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.

**Health Technology Clinical Committee
Findings and Coverage Decision**

Topic: Breast MRI
Meeting Date: August 20th, 2010
Final Adoption:

Number and Coverage Topic

20100820A – Breast MRI

HTCC Coverage Determination

Breast MRI is a **covered benefit with conditions** consistent with the criteria identified in the reimbursement determination.

HTCC Reimbursement Determination

❖ **Limitations of Coverage**

Breast MRI is a covered benefit 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 are defined as:

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

❖ **Non-Covered Indicators**

- N/A

❖ **Agency Contact Information**

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

Health Technology Background

The Breast MRI topic was selected and published in December 2009 to undergo an evidence review process. 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. 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). 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. *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.

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. The evidence based technology assessment report focused on two recent large systematic reviews (Lord, 2007 and Warner, 2008) found to be of acceptable quality. The evidence based technology assessment report identified 7 expert treatment guidelines and a CMS policy.

In June 2010, the HTA posted a draft and then followed with a final report from a contracted research organization that reviewed publicly submitted information; searched, summarized, and evaluated trials, articles, and other evidence about the topic. The comprehensive, public and peer reviewed Breast MRI report is 83 pages, and identified a relatively large amount of literature.

An independent group of eleven clinicians who practice medicine locally meet in public to decide whether state agencies should pay for the health technology based on whether the evidence report and other presented information shows it is safe, effective and has value. The committee met on August 20, reviewed the report, including peer and public feedback, and heard public and agency comments. Meeting minutes detailing the discussion are available through the HTA program or online at <http://www.hta.hca.wa.gov> under the committee section.

Committee Findings

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

1. Evidence availability and technology features

The committee concludes that the best available evidence on breast MRI has been collected and summarized. The evidence is presented below:

- 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.
- 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.
- 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.
- 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
- The evidence based technology assessment report identified 7 expert treatment guidelines and a CMS policy.
- The committee also reviewed information provided by the state agencies; public members; and heard comments from the evidence reviewer, HTA program, agency medical directors and the public.

2. Is the technology safe?

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.

- 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.
- 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).
- 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).
- No other evidence was reported on the harms of unnecessary treatment and over diagnosis. Evidence about change in treatment discussed in efficacy.

3. **Is the technology effective?**

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.

- 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.
- 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.
- 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.
- 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%.
- 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.
- 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
- 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?

- *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.
- *Technical specifications and provider issues in MRI Testing:* the evidence is insufficient for establishing technical MRI specifications or establishing provider qualifications.

5. Is the technology cost-effective?

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.

- 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.
- 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. Medicare Decision and Expert Treatment Guidelines

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

- 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.
- 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.

- Two guidelines were rated as high quality and are summarized:
 - (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.
 - 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.
 - 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.
 - (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.
- One guideline was rated as fair quality and are summarized below:
 - (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.
- 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.

- 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:

- 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.
- The addition of Breast MRI as a screening tool will result in additional false positives and treatment, including biopsy and potential harms from biopsy.

- 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.

- 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.
- 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.
- 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%.
- 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.

- 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.

- 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.
- 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.
- 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 considered all the evidence and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

The committee 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 is a covered benefit 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 are defined as:

1. A personal history or strong family history of breast cancer;
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.

Health Technology Clinical Committee Authority

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

Breast MRI

Draft Findings & Decision Timeline and Overview of Comments

The Health Technology Assessment (HTA) program received comments in response to the posted Health Technology Clinical Committee (HTCC) draft findings and decision on Breast MRI.

Commenter	Comment Period Oct. 6–Oct. 15	Cited Evidence
Patient, relative, and citizen	1	0
Legislator and public official	0	
Physician and health care professional	2	0
Industry and Manufacturer	0	
Professional Society and Advocacy Organization	1	0

All Total = 4

Comments without Evidence:

Physician and Health Care Professional Comments

Bruce Porter, Medical Director, First Hill Diagnostic Imaging

- Submitted an article on BMRI for review by the Health Technology Clinical Committee

Connie Lehman, MD

- Submitted comments on a few patient populations that she feels will be questioned and requested an adjustment in the draft findings and decision language.

Professional Society and Advocacy Organization Comments

Dave Fisher, Executive Director, Medical Imaging and Technology Alliance (MITA)

- MITA agrees that the findings of the Health Technology Clinical Committee on the coverage for breast MRI are in accordance with the state of science and practice as we know it. We appreciate the work that the WA State HTA has put forth in this analysis.

Citizen, Patient and Relatives Comments

Diane Priebe, Medical Policy Supervisor, Regence

- Concurs with the draft findings and decision concerning Breast MRI.

Actual Timeline		Total Public Comment Days
Preliminary recommendations published	<i>October 27, 2009</i>	
Public comments due:	<i>November 10, 2009</i>	15 days
Selected set of topics published:	<i>December 8, 2009</i>	
Public comments due:	<i>January 11, 2010</i>	35 days
Draft Key Questions Published:	<i>April 23, 2010</i>	
Public comments due:	<i>May 7, 2010</i>	
Key Questions Finalized:	<i>June 21, 2010</i>	
Draft report due:	<i>June 21, 2010</i>	
Draft report published:	<i>June 24, 2010</i>	
Public Comments due:	<i>July 16, 2010</i>	23 days
Final report due:	<i>July 19, 2010</i>	
Final report published:	<i>July 23, 2010</i>	
Public meeting Date:	<i>August 20, 2010</i>	
Findings & Decision Published	<i>October 6, 2010</i>	
Public Comments due:	<i>October 15, 2010</i>	10 days



Breast MRI Screening of Women With a Personal History of Breast Cancer

Sandra Brennan¹
 Laura Liberman
 D. David Dershaw
 Elizabeth Morris

OBJECTIVE. The purpose of this article is to determine the cancer detection and biopsy rate among women who have breast MRI screening solely on the basis of a personal history of breast cancer.

MATERIALS AND METHODS. This retrospective review of 1,699 breast MRI examinations performed from 1999 to 2001 yielded 144 women with prior breast cancer but no family history who commenced breast MRI screening during that time. Minimal breast cancer was defined as ductal carcinoma in situ (DCIS) or node-negative invasive breast cancer < 1 cm in size.

RESULTS. Of 144 women, 44 (31% [95% CI, 15–29%]) underwent biopsies prompted by MRI examination. Biopsies revealed malignancies in 17 women (12% [95% CI, 7–18%]) and benign findings only in 27 women (19% [95% CI, 13–26%]). Of the 17 women in whom cancer was detected, seven also had benign biopsy results. In total, 18 malignancies were found. One woman had two metachronous cancers. MRI screening resulted in a total of 61 biopsies, with a positive predictive value (PPV) of 39% (95% CI, 27–53%). The malignancies found included 17 carcinomas and one myxoid liposarcoma. Of the 17 cancers, 12 (71%) were invasive, five (29%) were DCIS, and 10 (59%) were minimal breast cancers. Of 17 cancers, 10 were detected by MRI only. The 10 cancers detected by MRI only, versus seven cancers later found by other means, were more likely to be DCIS (4/10 [40%] vs 1/7 [14%]; $p = 0.25$) or minimal breast cancers (7/10 [70%] vs 3/7 [43%]; $p = 0.26$).

CONCLUSION. We found that breast MRI screening of women with only a personal history of breast cancer was clinically valuable finding malignancies in 12%, with a reasonable biopsy rate (PPV, 39%).

The American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography now recommend screening of women with a 20–25% or greater lifetime risk of breast cancer. Included in this group are women with a strong family history of breast or ovarian cancer, including those with BRCA mutation and women who received mantle radiation for Hodgkin disease between the ages of 10 and 30 years [1]. The guidelines also state that there are several risk subgroups for which the available data are insufficient to recommend for or against screening, including women with a personal history of breast cancer. Among these women, tumor recurrence rates after breast conservation therapy (BCT) have historically been estimated at 1–2% per year [2]. With recent improvements in chemotherapy and the use of tamoxifen, recurrence rates at 10 years are now less than 10%, and

lifetime risk for these women depends on their age at diagnosis.

In addition to the absolute risk of recurrence, it is important to note that, as with the original breast cancer, the long-term survival of patients with new malignancy after BCT improves with early detection [3]. Detection of treatment failure in these women while it is still subclinical improves relative survival by 27–47% [3]. Conversely, large or node-positive recurrent tumors are poor prognostic indicators [4].

Recurrence in the adequately treated breast rarely is discovered sooner than 18–24 months after treatment. Recurrences at the lumpectomy site usually occur within a few years of treatment of the original cancer and likely represent failure to eradicate the entire original tumor. Cancer developing elsewhere in the treated breast is thought to be the result of a new carcinoma and usually is a later event [5]. Mammography's ability to detect recur-

Keywords: breast, breast MRI, cancer, mammography, screening

DOI:10.2214/AJR.09.3573

Received August 31, 2009; accepted after revision January 22, 2010.

¹All authors: Department of Radiology, Breast Imaging Section, Memorial Sloan-Kettering Cancer Center, 300 E 66th St, New York, NY 10065. Address correspondence to S. Brennan (brennans@mskcc.org).

AJR 2010; 195:510–516

0361–803X/10/1952–510

© American Roentgen Ray Society

Breast MRI of Women With History of Breast Cancer

rence has been calculated as one third less than its ability to discover the original cancer [6]. The detection of recurrence with mammography is compromised by increased density, architectural distortion, and other post-therapy changes, but it does play a role and is able to detect 25–45% of recurrences. In particular, mammography is better able to detect recurrent tumors that have associated calcifications, because distortion at the surgical site limits evaluation for underlying masses.

Breast MRI has a high sensitivity in the detection of breast cancer. Its sensitivity is reported to be as high as 94–100%. Several studies have already shown the benefit of breast MRI in the detection of tumor recurrence in patients treated with BCT [7–10]. Breast MRI has a high sensitivity, specificity, and accuracy in differentiating scar from recurrent tumor [11–13]. To the best of our knowledge, no data are available on the use of breast MRI in screening women with a personal history of breast cancer and no other risk factors. This study was undertaken to determine whether women without indications for MRI screening under current American Cancer Society guidelines and with a personal history of breast cancer would benefit from screening.

Materials and Methods

Patient Population

An institutional review board–approved retrospective review of the records of 1,699 breast MRI scans acquired from 1999 to 2001 was performed. Women with prior breast cancer and without a history that, under current American Cancer Society guidelines, would include them in MRI screening and who met the following criteria were included: no family history of breast cancer, commenced screening during 1999–2001, and had at least 1 year of follow-up with MRI. This yielded 144 women with a history of a prior breast cancer who commenced screening MRI during 1999–2001. These women had a median age of 48 years and a mean age of 49 years (range, 22–73 years). We chose to start reviewing patients from 1999 because this was the first year that we had the capabilities to perform MRI-guided interventions. Choosing this earlier time period allowed us to then follow this cohort of patients for a number of years, from 1999–2001 until 2008. The electronic medical record, including radiology reports and clinical notes, was reviewed to determine which patients developed recurrence. We also reviewed the records of the 1,699 breast MRI examinations performed from 1999 to 2001 to identify women with both a personal and family history of breast cancer who commenced screening MRI examination during

that time, so that they could be compared with the group of women with a personal history only.

Breast MRI Technique

MRI was performed on a 1.5-T commercially available system (Sigma, GE Healthcare) using a dedicated surface breast coil. The imaging sequence included a localizing sequence followed by a sagittal fat-suppressed T2-weighted sequence (TR/TE, 4,000/85). A T1-weighted 3D fat-suppressed fast spoiled gradient-echo sequence (17/2.4; flip angle, 35°; bandwidth, 31–25 Hz) was then performed before and three times after a rapid bolus injection of gadopentate dimeglumine (Magnevist, Berlex; 0.1 mmol/L/kg of body weight), delivered through an IV catheter. Image acquisition started after contrast material injection and saline bolus. Images were obtained sagittally for an acquisition time

per volumetric acquisition of less than 3 minutes each. Total imaging time per breast, including three contrast-enhanced acquisitions, was approximately 20 minutes. Section thickness was 2–3 mm with no gap using a matrix of 256 × 192 and a field of view of 18–22 cm. Frequency was in the anteroposterior direction. After the examination, the unenhanced images were subtracted from the first contrast-enhanced images on a pixel-by-pixel basis.

Breast MRI Interpretation

Breast MRI examinations were interpreted by breast imaging specialists in conjunction with clinical history and other breast imaging studies, including mammography and ultrasound, when available. The individual radiologist classified the lesion detected on MRI on a scale of 1 to 5 adapted from the mammographic BI-RADS classification:

TABLE I: Findings in 144 Women With a Personal History of Breast Cancer Who Underwent Breast MRI Screening

Patient Characteristics	Women Who Had an MRI-Detected Cancer (n = 17)	Women Who Had No Cancer Detected (n = 127)
Age (y)		
Median	47	48
Mean	46	49
Range	31–71	22–73
Menopausal status, no. (%) of subjects		
Premenopausal	9 (53)	67 (53)
Postmenopausal	8 (47)	60 (47)
Breast density, no. (%) of subjects		
Fatty	1 (5)	7 (5)
Mild	2 (12)	33 (26)
Moderate	11 (65)	53 (42)
Dense	3 (18)	34 (27)
Background enhancement, no. (%) of subjects		
Marked or moderate	7 (41)	29 (23)
Minimal or mild	10 (59)	98 (77)
Prior radiation, no. (%) of subjects	13 (76)	91 (72)
Prior tamoxifen, no. (%) of subjects	5 (29)	88 (69)
Histology of prior cancer, no. of subjects		
Invasive ductal carcinoma	12	83
Invasive lobular carcinoma	2	24
Mixed	0	4
Ductal carcinoma in situ	3	15
Unknown	0	1
No. of MRI examinations, median (range)	2 (1–7)	5 (2–11)
No. (range) of subjects who had short-term follow-up	7 (0–3)	51 (0–6)
Biopsy recommended, no (%) of subjects	17 (100)	27 (21)
No. (%) of subjects who had baseline preoperative MRI	4 (24)	51 (40)

BI-RADS I, negative finding; BI-RADS II, benign finding; BI-RADS III, probably benign finding; BI-RADS IV, suspicious finding; and BI-RADS V, highly suggestive of malignancy. Classification was based primarily on lesion morphology. Kinetic features were visually assessed on the three contrast-enhanced image acquisitions, with quantitative kinetic curves generated in specific cases at the discretion of the interpreting radiologist. MRI-detected lesions referred for biopsy included masslike and non-masslike enhancement (linear, clumped, or segmental).

Correlative ultrasound was recommended at the discretion of the interpreting radiologist if it was thought that the lesion might be sonographically evident and amenable to ultrasound-guided biopsy. If it was not seen on ultrasound, then MRI-guided needle localization for surgical excision or MRI-guided core needle biopsy was performed.

Data Collection and Analysis

The electronic medical records of these 144 women were reviewed to determine their age, menopausal status, and breast parenchymal density. Family history was determined from the medical records, including radiology reports and patient questionnaires. Prior surgery, radiation, chemotherapy, and tamoxifen use were recorded.

Findings on mammography, ultrasound, and physical examination were reviewed to assess for a correlate to the MRI-detected cancers. Biopsy results were reviewed, including pathology records, to determine the size and stage of breast cancers found and prior breast cancer histology. The MRI screening year in which the cancer was detected was recorded. The number of MRI examinations performed and the number of women who underwent short-term follow-up were also noted. We also determined which patients had preoperative staging with breast MRI for their original cancers.

Data were collected and recorded in spreadsheets (Access and Excel, Microsoft). Statistical analysis was performed with Fisher's exact test using statistical software (Epi Info, Centers for Disease Control and Prevention), with a *p* value less than 0.05 considered significant. Exact 95% CIs were calculated in accordance with the Geigy scientific tables based on the binomial approximation or exact method. Fisher's exact test was used to compare the distribution of categorical variables between women who had an MRI-detected cancer and those who did not.

Results

These 144 women underwent MRI screening (range, 1–11 MRI examinations) at 1–13 years after their original diagnosis of breast

cancer (Table 1). For those patients who had a cancer detected by MRI, the range of follow-up with MRI was 1–9 years (mean, 2.7 years; median, 2 years). For those patients who did not have a cancer detected, the range of follow-up was 1–8 years (mean, 4.2 years; median, 4 years). On the basis of these studies, a total of 61 biopsies were performed, and 18 malignancies were found. One woman had two metachronous cancers. The median number of MRI examinations performed before the cancers were detected was two (range, 1–7), versus five (range, 2–11) in the group who did not develop a cancer. Histologic findings were 17 cancers and one myxoid liposarcoma (Table 2). Of the 17 cancers, 12 (71%) were invasive (11 ductal and one lobular cancer) and five (29%) were ductal carcinoma in situ (DCIS); 10 (59%) were minimal breast cancers defined as DCIS or node-negative breast cancer < 1 cm. The median histologic size of the invasive cancer was 0.8 cm (range, 0.2–4.3 cm). Three (18%) of 17 cancers, representing three (25%) of 12 invasive cancers, had axillary metastases. Prior breast cancer histology had no significant impact on cancer detection rate (Table 3). There was no significant difference between patients with cancer detected and those with

TABLE 2: BI-RADS Categories, MRI Features, and Pathology Finding of the 18 MRI-Detected Malignancies

Lesion	BI-RADS Category			MRI Features		Pathology Findings		
	Mammography	MRI	Ultrasound	Enhancement	Margin or Shape	Size (cm)	Histology	No. of Positive Nodes
1	3	4	1	Mass, heterogeneous	Irregular	NA	DCIS	NA
2	2	4	4	Mass, heterogeneous	Oval	0.8	Myxoid liposarcoma	NA
3	2	5	1	Nonmass, clumped	NA	0.15 (IDC)	IDC and DCIS	0
4	4	4	1	Mass, heterogeneous	Spiculated	1.0	IDC and DCIS	0
5	4	4	NA	Mass, heterogeneous	Irregular	NA	DCIS	0
6	6	4	4	Mass, rim	Irregular	2.2	IDC and DCIS	0
7	2	4	2	Nonmass, clumped	NA	Multifocal, largest 1.0	ILC	26
8	NA	5	5	Mass, heterogeneous	Irregular	1.7	IDC	0
9	2	4	2	Nonmass, clumped	NA	NA	DCIS	NA
10	2	4	2	Mass, heterogeneous	Irregular	0.4 and 0.2	IDC and DCIS	0
11	5	5	5	Mass, heterogeneous	Spiculated	Multifocal	IDC	1
12	2	4	NA	Nonmass, linear	NA	NA	DCIS	NA
13	3	5	2	Nonmass, linear	NA	1.1	IDC and DCIS	0
14	NA	4	NA	Nonmass, linear	NA	1.2	IDC	0
15	4	5	4	Mass, heterogeneous	Irregular	4.3	IDC and DCIS	7
16	2	4	2	Mass, heterogeneous	Lobulated	NA	DCIS	NA
17	NA	4	NA	Mass, heterogeneous	Spiculated	0.6	IDC and DCIS	0
18	2	4	4	Mass, heterogeneous	Irregular	0.4	IDC	0

Note—DCIS = ductal carcinoma in situ, IDC = invasive ductal carcinoma, ILC = invasive lobular carcinoma, NA = not applicable.

Breast MRI of Women With History of Breast Cancer

no cancer detected with regard to menopausal status ($p = 0.80$), breast density ($p = 0.31$), and histology of prior cancer ($p = 0.80$). Of 17 cancers, 10 were nonpalpable and were detected by MRI only; seven had correlates on post-MRI mammography ($n = 2$), ultrasound ($n = 2$), or ultrasound, mammography, and physical examination ($n = 3$). The 10 cancers detected by MRI only, versus seven cancers later found to have correlates, were more likely to be DCIS (4/10 [40%] vs 1/7 [14%]; $p = 0.25$) or minimal breast cancers (7/10 [70%] vs 3/7 [43%]; $p = 0.26$).

The MRI-detected carcinomas were in the treated breast in seven cases (four in or near the lumpectomy bed) and in the contralateral breast in 10 cases. The myxoid liposarcoma developed in the contralateral breast. In total, 13 (76% [95% CI, 50–93%]) of 17 women with an MRI-detected cancer received prior radiation. Of the seven women who developed cancer in the treated breast, four had received prior radiation. Of the 127 women screened who did not have an MRI-detected cancer, 91 (72% [95% CI, 63–79%]) received prior radiation versus 36 (28% [95% CI, 21–37%]) who did not. Five (29% [95% CI, 10–56%]) of the 17 women who had an MRI-detected cancer had taken hormonal therapy versus 88 (69% [95% CI, 60–77%]) of the 127 women in the other group.

Cancers were most likely to be found in early screening rounds and within the first 3 years after conservation. Twelve (67% [95% CI, 41–87%]) of the 18 malignancies were detected during the first 1–2 years after initiation of MRI screening. Ten (56% [95% CI, 31–78%]) of the 18 malignancies were found

TABLE 3: Histology of Prior Cancer

Histology	No. (%) of Women Who Had an MRI-Detected Cancer ($n = 17$)	No. (%) of Women Who Had No Cancer Detected ($n = 127$)
Ductal carcinoma in situ	3 (18)	13 (10)
Invasive ductal carcinoma	12 (70)	79 (62)
Invasive lobular carcinoma	2 (12)	24 (19)
Mixed ductal and lobular invasive carcinoma	0 (0)	5 (4)
Tubular	0 (0)	1 (0.8)
Mucinous	0 (0)	1 (0.8)
Papillary	0 (0)	1 (0.8)
Paget	0 (0)	2 (1.6)
Adenocarcinoma	0 (0)	1 (0.8)

during the first 1–3 years from the original cancer diagnosis, and 13 (72% [95% CI, 46–90%]) of the 18 malignancies were found during the first 1–5 years.

The use of preoperative MRI for staging the original cancer at the time of initial treatment appeared to have some impact on results. Four (24% [95% CI, 7–50%]) of 17 patients with recurrence had a preoperative MRI at the time of treatment of their original cancer, and 51 (40% [95% CI, 31–48%]) of the 127 women who did not have a recurrence had a preoperative MRI. In addition, of those 12 women diagnosed with recurrence shortly after their initial conservation, only two had a preoperative MRI to evaluate extent of disease at the time of the original cancer.

The median age at diagnosis of the original cancer was 47 years (range, 31–71 years) in the group who had an MRI-detected cancer, versus 48 years (range, 22–73 years) in the oth-

er group. Eighty-three percent of the women who had an MRI-detected cancer had moderately dense or dense breasts, versus 69% in the other group. The findings were not influenced by menopausal status. Nine (53%) of 17 women in the group who had an MRI-detected cancer were premenopausal, versus 67 (53%) of 127 women in the other group. Forty-one percent of the women who developed a cancer had marked or moderate background enhancement, versus 23% in the other group.

Biopsies were prompted by MRI findings in 44 (31%) of 144 of the women screened, revealing malignancy in 39% of the 44 women who had biopsies. Benign biopsies were performed for 34 (24%) of 144 women screened, with a range of one to five biopsies being performed. MRI screening resulted in a total of 61 biopsies being performed. Biopsy revealed high-risk lesions (including atypical ductal hyperplasia, atypical lobular hyperplasia, lob-

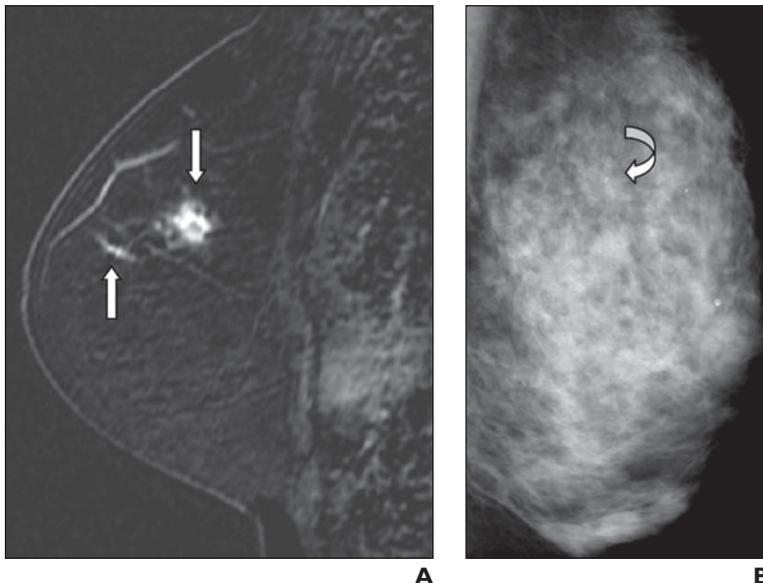


Fig. 1—60-year-old woman with history of right lumpectomy for invasive ductal carcinoma and ductal carcinoma in situ 13 years before this screening MRI examination. Pathologic analysis revealed invasive ductal carcinoma and ductal carcinoma in situ. **A**, Sagittal subtraction image of left breast shows enhancing spiculated mass in upper outer quadrant of left breast (downward-pointing arrow) with linear enhancement anteriorly (upward-pointing arrow). **B**, Mediolateral oblique view from mammogram, which was prompted by MRI findings, shows some faint pleomorphic calcifications in upper outer left breast (arrow).

TABLE 4: Pathologic Findings on Positive Screening MRI Examinations in 17 Women With a Personal History Only Versus 20 Women With an Additional Risk Factor of a Family History

Personal History Only (<i>n</i> = 17 Women; <i>n</i> = 18 Pathologic Findings)		
Size of Lesion (cm)	Histologic Finding	No. of Positive Nodes
NA	DCIS	NA
0.8	Myxoid liposarcoma	NA
0.15 (IDC)	IDC and DCIS	0
1.0	IDC and DCIS	0
NA	DCIS	0
2.2	IDC and DCIS	0
Multifocal, largest 1.0	ILC	26
1.7	IDC	0
NA	DCIS	NA
0.4 and 0.2	IDC and DCIS	0
Multifocal	IDC	1
NA	DCIS	NA
1.1	IDC and DCIS	0
1.2	IDC	0
4.3	IDC and DCIS	7
NA	DCIS	NA
0.6	IDC and DCIS	0
0.4	IDC	0
Personal and Family History (<i>n</i> = 20 Women; <i>n</i> = 22 Pathologic Findings)		
Size of Lesion (cm)	Histologic Finding	No. of Positive Nodes
Multifocal	IDC, ILC, and DCIS	0
1.0	IDC and ILC	0
1.4	IDC and DCIS	0
NA	DCIS	NA
0.5	ILC	0
0.3	IDC and DCIS	0
NA	DCIS	NA
0.5	IDC and DCIS	0
NA	DCIS	NA
NA	DCIS	NA
NA	DCIS	NA
Multicentric	ILC	13/15
NA	DCIS (microinvasive)	1/3 microinvasive
0.7	IDC and DCIS	0
0.5	IDC and DCIS	1/2
Multifocal	IDC and DCIS	0
1.5	IDC and DCIS	0
0.5	IDC and DCIS	2/3
No data	IDC	No data
0.5	IDC and DCIS	0
NA	DCIS	NA
NA	DCIS	NA

ular carcinoma in situ, and papilloma) in six women. In addition to biopsies, short-term follow-up MRI examination was recommended for 58 of the 144 women screened. The biopsy method used for the 18 malignancies was MRI-guided core biopsy in three cases, MRI-guided needle localization in 10 cases, surgical biopsy in three cases, and ultrasound-guided core biopsy in two cases.

We then compared the results of the women with only a personal history of breast cancer (*n* = 144) with those of the women who also had a family history of breast cancer (*n* = 136). We found 136 women with both a personal and family history of breast cancer (Table 4). Screening MRI found 22 cancers in 20 women. Screening MRI resulted in a total of 49 biopsies performed in 40 women, including benign and malignant results. MRI detected cancer in 15% (20/136 [95% CI, 9–22%]) of these women and in 50% (20/40 [95% CI, 34–66%]) of women who had biopsies prompted by the MRI findings. The positive predictive value (PPV) of a biopsy recommendation in this group was 50%, versus 39% in the women with a personal history of breast cancer only (*p* = 0.4) (Table 5). Benign biopsies were performed in 22 (16% [95% CI, 10–23%]) of 136 women screened (range, one to three biopsies per patient) versus 34 (24%) of 144 women with a personal history only (*p* = 0.1). Similar to patients with a personal history only, cancers were more likely to be found in the early screening rounds; 65% of the cancers were found during the first two screening years. Of the 22 cancers, 14 (64%) were invasive (ductal in 11 cases, lobular in two cases, and mixed in one case), and 8 (36%) were DCIS; 13 (59%) of the 22 breast cancers found were minimal breast cancers.

Discussion

Although the standard of care for screening women with a personal history of breast cancer is mammography, evaluation of the conserved breast is limited. Mammography is better able to detect recurrent tumors that have associated calcifications (Fig. 1) but is less successful in the evaluation of underlying masses in areas of postoperative distortion. Screening mammography is also limited in women with dense breasts (Fig. 2) [14–16]. Breast MRI has a high sensitivity in the detection of breast cancer and, in particular, a high sensitivity and specificity in differentiating scar from recurrent tumor [11–13].

We present the first study, to our knowledge, evaluating the use of breast MRI in screening women with a personal history only of breast cancer. Prior breast cancer histology (*p* = 0.80), menopausal status (*p* = 0.80), and breast density (*p* = 0.31) had no significant im-

Note—DCIS = ductal carcinoma in situ, IDC = invasive ductal carcinoma, ILC = invasive lobular carcinoma, NA = not applicable.

Breast MRI of Women With History of Breast Cancer

fact on cancer detection rate. A meta-analysis has shown that hormonal therapy reduces local recurrence by 50% [17], but only 29% of the women who developed cancer in our group had taken hormonal therapy, versus 69% in the other group. Screening with breast MRI detected cancer in 12% (17/144) of women with a history of prior breast cancer and in 39% (17/44) of women who had biopsies prompted by MRI findings. Seventy-two percent (13/18) of malignancies were detected in the first 3 years after initiation of screening, and only 15% of these patients (2/13) had a baseline preoperative MRI. More than half (59%) of the cancers found were minimal breast cancers. DCIS accounted for 29% of the cancers found. In prior reports, DCIS has accounted for 0–57% of cancers detected by MRI screening in high-risk women [15, 16, 18–20]. The advantage of MRI screening was apparent earlier in the women who did not have a baseline preoperative MRI at the time of original cancer treatment. Thus, although the initial results may have been due to the absence of preoperative MRI, cancers did start to develop further out, and these cancers are difficult to detect with mammography or clinical examination alone. Even if we exclude the three women who devel-

TABLE 5: Positive Predictive Value of Biopsy and Other Results in Women With a Personal History Versus Women With an Additional Risk Factor of a Family History

Factor	Personal History Only (n=17)	Personal and Family History (n=20)
MRI examinations, median no. (range)	2 (1–7)	2 (1–8)
Subjects who had short-term follow-up, no. (range)	7 (0–3)	6 (0–3)
Biopsy recommended, no (%) of subjects	17 (100)	20 (100)
Benign biopsy performed, no (%) of subjects	7 (41)	2 (10)
Total no. of biopsies	27	24
Malignant	18	22
Benign	9	2
Minimal breast cancers, no. of subjects/total (%)	10/17 (59)	13/22 (59)
Positive predictive value of biopsy, no. of subjects/total (%)	17/44 (39)	20/40 (50)

oped cancer in the treated breast and did not receive radiation at the time of their initial treatment, on the basis of the fact that this is not standard care, we have a total of 14 women with 15 malignancies. The PPV of a biopsy recommendation in this group is still acceptable at 34% (14/41).

The importance of a personal history of breast cancer as an indication for MRI screening has been suggested by other data. Morris et al. [21] studied MRI screening in a high-

risk population and found that the PPV of a biopsy recommendation based on MRI findings in women with a family history of breast cancer (PPV, 32%), was further increased to 50% in women who also had a personal history of breast cancer. Thus, it may not be surprising that the addition of breast MRI in screening women with a personal history of breast cancer, with or without a family history, enables the detection of unsuspected breast cancer and does so with a high PPV (39%).

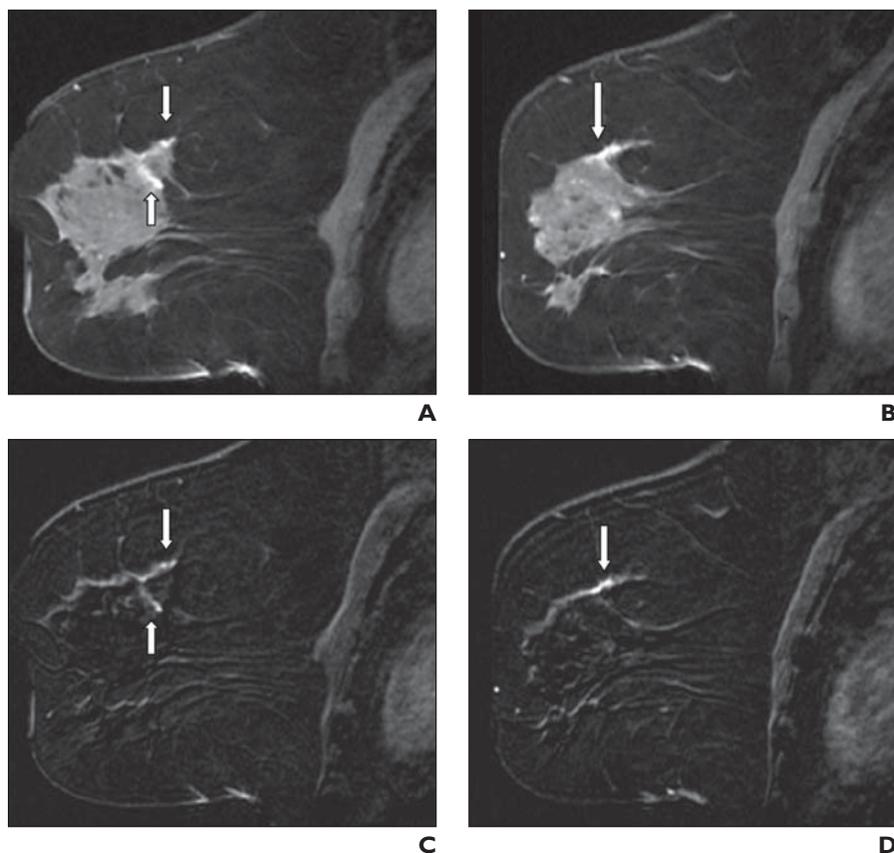


Fig. 2—57-year-old woman with history of right mastectomy for invasive lobular carcinoma 4 years before this screening MRI study. There was no mammographic correlate. MRI biopsy revealed invasive lobular carcinoma and lobular carcinoma in situ. **A and B,** Sagittal T1-weighted contrast-enhanced images of left breast show branching linear enhancement in upper left breast (arrows). **C and D,** Sagittal subtraction images of left breast again show branching linear enhancement (arrows).

Although Gorechlad et al. [22] argue that the addition of screening MRI in patients after breast-conserving surgery would incur significant cost and would be unlikely to improve overall survival rates, we think that our results show a potential benefit. Gorechlad et al. had an overall recurrence rate of 4%. Ipsilateral recurrences developed in eight patients (1.7%) with a mean diameter of 1.6 cm. Contralateral cancers developed in 11 patients (2.3%) with a mean diameter of 1.5 cm. All of the recurrences were invasive. In contrast, in the present study, we had a cancer detection rate of 12% (17/144). The mean histologic size of the invasive cancers in our group was smaller at 0.8 cm. In addition, 5 (29%) of the cases were DCIS. Earlier detection may therefore be beneficial in allowing the use of less-toxic therapies. Thus, although Gorechlad et al. argue that the cost of screening MRI in terms of patient stress, physician effort, and dollars is high, we see the potential benefit of earlier detection. It is beyond the scope of this study to look at the cost-effectiveness of screening MRI or its impact on survival, but other studies have looked at screening with MRI in women with BRCA1/2 mutations [23–25]. A study by Taneja et al. [26] found that screening women with MRI was cost effective not only in patients with BRCA1/2 mutations but also among other high-risk women.

In conclusion, this is the largest series to date, to the best of our knowledge on the use of screening with breast MRI in women with a personal history of breast cancer. This screening resulted in the discovery of cancer in 12% of women, with a reasonable biopsy rate and a PPV of 39%. Cancers discovered were those benefiting from early detection, with more than half of the MRI-detected cancers being minimal breast cancers. Although we recognize that screening MRI is costly and does generate many benign biopsies and short-term follow-ups, we think that it may benefit certain subsets of patients with a personal history of breast cancer. In particular, those who have not had a preoperative MRI at the time of initial cancer diagnosis and those who have not taken hormonal therapy may benefit. We realize that a randomized prospective trial would best determine the effectiveness of MRI screening in women with a personal history of breast cancer and that data from other institutions should be assessed to determine whether our conclusions are supported.

References

1. Saslow D, Boetes C, Burke W, et al. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA Cancer J Clin* 2007; 57:75–89
2. Fisher B, Redmond C, Poisson R, et al. Eight-year results of a randomized clinical trial comparing total mastectomy and lumpectomy with or without irradiation in the treatment of breast cancer. *N Engl J Med* 1989; 320:822–828
3. Houssami N, Ciatto S, Martinelli F, Bonardi R, Duffy SW. Early detection of second breast cancers improves prognosis in breast cancer survivors. *Ann Oncol* 2009; 20:1505–1510
4. Ciatto S, Houssami N, Martinelli F, Bonardi R, Cafferty FH, Duffy SW. Second breast cancers in a Tuscan case series: characteristics, prognosis, and predictors of survival. *Br J Cancer* 2008; 99:539–544
5. Dershaw DD. Mammography in patients with breast cancer treated by breast conservation (lumpectomy with or without radiation). *AJR* 1995; 164:309–316
6. Dershaw DD, McCormick B, Osborne MP. Detection of local recurrence after conservative therapy for breast carcinoma. *Cancer* 1992; 70:493–496
7. Kramer S, Schulz-Wendtland R, Hagedorn K, Bautz W, Lang N. Magnetic resonance imaging in the diagnosis of local recurrences in breast cancer. *Anticancer Res* 1998; 18:2159–2161
8. Murray AD, Redpath TW, Needham G, Gilbert FJ, Brookes JA, Eremin O. Dynamic magnetic resonance mammography of both breasts following local excision and radiotherapy for breast carcinoma. *Br J Radiol* 1996; 69:594–600
9. Heywang-Kobrunner SH, Schlegel A, Beck R, et al. Contrast-enhanced MRI of the breast after limited surgery and radiation therapy. *J Comput Assist Tomogr* 1993; 17:891–900
10. Mumtaz H, Davidson T, Hall-Craggs MA, et al. Comparison of magnetic resonance imaging and conventional triple assessment in locally recurrent breast cancer. *Br J Surg* 1997; 84:1147–1151
11. Belli P, Costantini M, Romani M, Marano P, Pastore G. Magnetic resonance imaging in breast cancer recurrence. *Breast Cancer Res Treat* 2002; 73:223–235
12. Davis PL, McCarty KS Jr. Sensitivity of enhanced MRI for the detection of breast cancer: new, multicentric, residual, and recurrent. *Eur Radiol* 1997; 7[suppl 5]:S289–S298
13. Soderstrom CE, Harms SE, Farrell RS Jr, Prunedda JM, Flamig DP. Detection with MR imaging of residual tumor in the breast soon after surgery. *AJR* 1997; 168:485–488
14. Mandelson MT, Oestreicher N, Porter PL, et al. Breast density as a predictor of mammographic detection: comparison of interval- and screen-detected cancers. *J Natl Cancer Inst* 2000; 92:1081–1087
15. Ciatto S, Visioli C, Paci E, Zappa M. Breast density as a determinant of interval cancer at mammographic screening. *Br J Cancer* 2004; 90:393–396
16. Olsen AH, Bihmann K, Jensen MB, Vejborg I, Lyng E. Breast density and outcome of mammography screening: a cohort study. *Br J Cancer* 2009; 100:1205–1208
17. Early Breast Cancer Trialists' Collaborative Group. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomized trials. *Lancet* 2005; 365:1687–1717
18. Kuhl CK, Schmutzler RK, Leutner CC, et al. Breast MR imaging screening in 192 women proved or suspected to be carriers of a breast cancer susceptibility gene: preliminary results. *Radiology* 2000; 215:267–279
19. Warner E, Plewes DB, Shumak RS, et al. Comparison of breast magnetic resonance imaging, mammography, and ultrasound for surveillance of women at high risk for hereditary breast cancer. *J Clin Oncol* 2001; 19:3524–3531
20. Sardanelli F, Podo F, D'Agnolo G, et al. Multi-center comparative multimodality surveillance of women at genetic-familial high risk for breast cancer (HIBCRIIT study): interim results. *Radiology* 2007 242:698–715
21. Morris EA, Liberman L, Ballon D, et al. MRI of occult breast carcinoma in a high-risk population. *AJR* 2003; 181:619–626
22. Gorechlad J, McCabe E, Higgins J, et al. Screening for recurrences in patients treated with breast conserving surgery: is there a role for MRI? *Ann Surg Oncol* 2008; 15:1703–1709
23. Norman RPA, Evans DG, Easton DF, et al. The cost-utility of magnetic resonance imaging for breast cancer in BRCA1 mutation carriers aged 30–49. *Eur J Health Econ* 2007; 8:137–144
24. Griebisch I, Brown J, Boggis C, et al. Cost-effectiveness of screening with contrast enhanced magnetic resonance imaging vs x-ray mammography of women at a high risk of breast cancer. *Br J Cancer* 2006; 95:801–810
25. Plevritis SK, Kurian AW, Sigal BM, et al. Cost-effectiveness of screening BRCA1/2 mutation carriers with breast magnetic resonance imaging. *JAMA* 2006; 295:2374–2384
26. Taneja C, Edelsberg J, Weycker D, et al. Cost effectiveness of breast cancer screening with contrast-enhanced MRI in high-risk women. *J Am Coll Radiol* 2009; 6:171–179

From: Lehman, Constance
Sent: Tuesday, August 31, 2010 12:36 AM

Hello,

A few interested parties have asked me my opinion on the list of "approved indications" drafted to date and I had sent an email with some of my thoughts. I'll attach below. Overall, I think this makes sense and does follow the published research.

There are a few patient populations that will be questioned and I don't recall these populations being reviewed or the respective literature in detail at the meeting (but I may have missed it as I was not there for the full discussion):

1. Axillary adenopathy, unknown primary. The data are supportive of this very rare but important clinical indication for breast MRI. This specific clinical indication occurs in less than 1% of all women diagnosed with breast cancer, but when it does occur, MRI will identify the location of the breast cancer in 60% of women, allowing appropriate treatment of the otherwise "unknown primary"

2. Implants. I do not recall this being discussed in detail...or a review of this literature (use of MRI in women with implants to assess integrity of implant---not necessarily to assess cancer in the breasts of a woman with implants). I think the data are sparse in this area and this should ONLY be used after a full clinical, mammographic and US evaluation first and ONLY if the MRI findings will change management. This is a really tricky topic, though, as the package inserts on silicone implants now require annual MRIs.....frankly this area is a bit of a mess. Neither our imaging team nor our plastic surgery team support routine screening of implants with MRIs and it is the rare case we have (but not never) that needs an MRI for implants. The percentage of our patients who have MRI for implant evaluation is about 3% of all breast MRIs we do.....so not "never" but very rarely.

3. Patients undergoing MRI for assessing response to chemotherapy. This literature is mixed and I don't recall this being reviewed at the meeting. I am not sure how the committee would view this (patient undergoing chemotherapy, and the CBE, mammography and US are inconclusive regarding whether the patient is responding or not...MRI has been shown to assess more accurately whether the patient is responding and to define more accurately the extent of disease prior to the final surgery). Still, this is not a "routine" exam for these patients but is used in an important subgroup where mammography, US and CBE are inconclusive.

4. extent of disease evaluation for patients with a current diagnosis of breast cancer. I appreciated the wisdom of the group of including women with a personal history in the "high risk" group. That makes sense and our data (accepted for presentation at RSNA this fall, to be published this year) support that for continued (but not more than annually) screening after diagnosis. At the time of diagnosis, the cancer yield of the contralateral cancer is very high in an otherwise asymptomatic, negative mammogram breast.

I would adjust "personal history of breast cancer" to perhaps "personal current or past diagnosis of breast cancer" to clarify that the breast cancer need not be "historical". That just may help clarify...and with the 11 month freq it will avoid multiple MRIs being used during the treatment. This allows women the opportunity to have the 30-40 contralateral cancers out of 1000 women identified at the time of their intitial diagnosis of cancer. (good discussion by the group to try to clarify if the contralateral exam was a 'screening' or a 'diagnostic').

My biggest question is how as a community can we grapple with exams that are indicated IN A MINORITY of patients...but sometimes are important. For example, a minority of women need a 6 month follow up MRI but that small minority do need the follow up. Those are not covered below. We could consider waiting a year rather than 6 months, and frankly I do think the short interval follow up is grossly over-used in many practices. However, I hate to have the 6 month follow up MRI NEVER allowed. Same for the neoadjuvant patient. What are your thoughts on how to manage the judicious use of some clinical applications vs. the "over use" of a certain indication for all patients. (an example.....two women undergoing chemotherapy prior to surgery. In woman A, her CBE, mammogram and US all clearly show she is responding well to the therapy. No need for an MRI. In woman B, the CBE, mammogram and US are equivocal and the surgeon and med onc are uncertain whether or not to proceed with the current therapy or change. That woman (B) can benefit from an MRI. However, if the clinical indication of "assess response to chemotherapy" is approved, how can its overuse in this population (centers using it in both woman A and woman B) be managed?

I also am very interested in how to link quality of imaging into this overall work. The current ACR accreditation program requires cites perform audits and I am curious if the audits will be used to help identify cites that are not performing within recommended guidelines.

I'll send a few items that might be of interest....and I appreciate the opportunity to participate in the discussions.

Dr. Connie Lehman



MITA

MEDICAL IMAGING
& TECHNOLOGY ALLIANCE

A DIVISION OF 

1300 North 17th Street • Suite 1752
Arlington, Virginia 22209
Tel: 703.841.3200
Fax: 703.841.3392
www.medicalimaging.org

October 14, 2010

Leah Hole-Curry, JD
Program Director
Health Technology Assessment Program
Washington State Health Care Authority
P.O. Box 42712
Olympia, WA 98504-2712

Re: Comments Regarding Final Committee Decision on the Use of Breast MRI

Dear Ms. Hole-Curry:

The Medical Imaging and Technology Alliance (MITA) appreciates this opportunity to comment on the final Committee decision regarding the use of breast MRI. As the leading trade association representing medical imaging and radiotherapy technology manufacturers, we have an in-depth understanding of the significant benefits to the health of women that breast MRI provides, particularly those at high risk. MITA looks forward to working with you to continue exploring the effectiveness of this technology as this area continues to be evaluated and researched as means to better diagnose and treat Washingtonians.

Medical imaging encompasses X-ray imaging, computed tomography (CT) scans, radiation therapy, related image acquisitions, diagnostic ultrasound, and nuclear medical imaging (including positron emission tomography (PET)), and magnetic resonance imaging (MRI). Medical imaging is used to diagnose patients with disease, often reducing the need for costly medical services and invasive surgical procedures.

MITA appreciates the work that the HTA has put into studying the importance of MRI for evaluation of the breast. In the August 20, 2010 document, “Health Technology Clinical Committee Findings and Coverage Decision” the Committee found that:

“Based on these findings, the committee voted 7 to 2 to cover with conditions Breast MRI. Breast MRI is a covered benefit 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 are defined as:

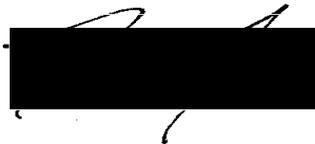
- 1. A personal history or strong family history of breast cancer;**

- 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.”**

MITA agrees that the findings of the Committee in outlining the above coverage for breast MRI are in accordance with the state of science and practice as we know it. We appreciate the work that the WA State HTA has put forth in this analysis. We look forward to continuing to work with the Committee should new evidence present itself which would amend the above outlined uses of this technology.

MITA appreciates this opportunity to comment on the draft report. We would be pleased to answer any questions you might have about these comments. Please contact me at (703) 841-3279 if MITA can be of any assistance.

Respectfully submitted,

A black rectangular redaction box covers the signature of Dave Fisher. The box is positioned below the text "Respectfully submitted," and above the typed name and title.

Dave Fisher
Executive Director, MITA
Vice President, NEMA

Regence concurs with the draft findings and decisions concerning spinal cord stimulation and breast MRI.

Diane Priebe RN, BSN, CPC
Supervisor, Medical Policy
Pharmacy Services
Regence - Portland
Phone: 503.220.4766
Fax: 503.276.1894
dwprieb@regence.com

Health Technology Clinical Committee
Findings and Coverage Decision
Topic: Spinal Cord Stimulation
Meeting Date: August 20th, 2010
Final Adoption:

Number and Coverage Topic

20100820B – Spinal Cord Stimulation

HTCC Coverage Determination

Spinal Cord Stimulation for chronic neuropathic pain is **not a covered benefit**.

HTCC Reimbursement Determination

- **Limitations of Coverage**
 - N/A
- **Non-Covered Indicators**
 - N/A
- **Agency Contact Information**

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

Health Technology Background

The Spinal Cord Stimulation topic was selected and published in December 2009 to undergo an evidence review process. 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. 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. SCS is an implanted, long term treatment, but no evidence exists on either long term efficacy or safety.

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. 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. 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.

In June 2010, the HTA posted a draft and then followed with a final report from a contracted research organization that reviewed publicly submitted information; searched, summarized, and evaluated trials, articles, and other evidence about the topic. The comprehensive, public and peer reviewed Spinal Cord Stimulation report is 164 pages, and identified a relatively large amount of literature.

An independent group of eleven clinicians who practice medicine locally meet in public to decide whether state agencies should pay for the health technology based on whether the evidence report and other presented information shows it is safe, effective and has value. The committee met on August 20, reviewed the report, including peer and public feedback, and heard public and agency comments. Meeting minutes detailing the discussion are available through the HTA program or online at <http://www.hta.hca.wa.gov> under the committee section.

Committee Findings

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

1. Evidence availability and technology features

The committee concludes that the best available evidence on Spinal Cord Stimulation has been collected and summarized. The evidence is presented below:

- *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.
- *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.
- *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.
- *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.
- *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. Is the technology safe?

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.

- 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.
- *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.
- *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.
- *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. Is the technology effective?

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.

- 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.
- *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.
- *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
- *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.
- *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%).
- *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 r 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 s 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).
- *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.
- *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.
- *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.
 - 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?

- 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.
- *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.
- *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.
- *Pain Intensity:* One study evaluated and found no association between the pain intensity at baseline and pain relief at one year.
- *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. Is the technology cost-effective?

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.

- 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.
- 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. Medicare Decision and Expert Treatment Guidelines

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

- 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.
- 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.

- 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.
- 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.
- 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:

- 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.
- 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).
- 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.
- 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.

- 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.
- 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.
- 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.
- 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.
- 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.

- 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.

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

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.

Health Technology Clinical Committee Authority

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

Spinal Cord Stimulators

Draft Findings & Decision Timeline and Overview of Comments

The Health Technology Assessment (HTA) program received comments in response to the posted Health Technology Clinical Committee (HTCC) draft findings and decision for no coverage on Spinal Cord Stimulators.

Commenter	Comment Period Oct. 6–Oct. 15	Cited Evidence
Patient, relative, and citizen	26	
Legislator and public official	0	
Physician and health care professional	7	1
Industry and Manufacturer	1	1
Professional Society and Advocacy Organization	3	1

All Total = 37

Comments with Evidence:

Professional Society and Advocacy Organization Comments

Eric Hauth, Executive Director, NTAC

- Opposes the decision and requests the committee convene an ad-hoc committee for Spinal Cord Stimulation; cites evidence of RCTs and requests committee review previous correspondence between NTAC and LNI which detail concerns with Turner study which were not previously made available to HTCC.

Michael Gofeld, Center for Pain Relief at the University of Washington

- Opposes the decision citing issues with the Turner study; question of effectiveness of SCS in a worker compensation population; attached OHTAC's recommendation; proponent of Ontario's recommendation; and the dismissal of studies based on funding (Medtronic).

Industry and Manufacturer Comments

William Fehrenbach, State Government Affairs Reimbursement Director, MedTronic

- Opposes the lack of full and interactive expert involvement; abbreviated timelines for submissions and testimony; devaluation of appropriate evidence in favor of lower level evidence; little consideration given to Medicare and professional guidelines; and transparency and openness regarding process expectation and execution.

Comments without Evidence:

29 total identical (or nearly identical) comments were submitted via E-mail which opposed the decision or expressed concern with the decision. These comments appear to be generated from a public comment template and include concerns with several decisions within Washington State related to pain care. Template letters came from individuals and providers, some wrote additional notes. A representative sample is included in the comments packet.

- 19 of the 29 commented only on their opposition to a chronic pain management bill (SL 2876).
- 10 of the 29 commented on their opposition to the lack of treatment options available due to previous HTCC decisions (referenced SCS, Intrathecal pump and TENS), as well as their opposition to the chronic pain management bill (SL 2876).

Physician and Health Care Professional Comments

Charles Chabal, MD, President, Washington Academy of Pain Management

- Commented on his opposition to the SCS decision due to a lack of public comment time allotted to experts; several level 1 SCS studies dismissed and the blanket denial of coverage.

John A. Hatheway, MD, Inland Neurosurgery & Spine

- Commented on his opposition to the SCS decision due to the Turner study; dismissal of other studies and proponents for spinal cord stimulation were severely limited in time to for public comment.

Citizen, Patient and Relatives Comments

Diane Priebe, Medical Policy Supervisor, Regence

- Concurs with the draft findings and decision concerning Spinal Cord Stimulation.

One individual patient opposed the decision based on her personal experience using SCS for chronic pain relief.

Professional Society and Advocacy Organization Comments

Matthew Gunderman, Director of Health Economics and Reimbursement, Boston Scientific Neuromodulation

- Concerned with the weight given to the Turner study and the inaccurate morbidity data related to SCS discussed during the Health Technology Clinical Committee review. Requests for an ad hoc committee to be convened in order to review deficiencies in the study by Turner et al, before a final coverage decision on spinal cord stimulation is rendered.

Actual Timeline		Total Public Comment Days
Preliminary recommendations published	<i>October 27, 2009</i>	
Public comments due:	<i>November 10, 2009</i>	15 days
Selected set of topics published:	<i>December 8, 2009</i>	
Public comments due:	<i>January 11, 2010</i>	35 days
Draft Key Questions Published:	<i>February 4, 2010</i>	
Public comments due:	<i>February 18, 2010</i>	15 days
Key Questions Finalized:	<i>March 16, 2010</i>	
Draft report due:	<i>June 21, 2010</i>	
Draft report published:	<i>June 24, 2010</i>	
Public Comments due:	<i>July 16, 2010</i>	23 days
Final report due:	<i>July 21, 2010</i>	
Final report published:	<i>July 23, 2010</i>	
Public meeting Date:	<i>August 20, 2010</i>	
Findings & Decision Published	<i>October 6, 2010</i>	
Public Comments due:	<i>October 15, 2010</i>	10 days
Findings & Decision Adopted		



neuromodulationaccess.org

Ensuring Patient Access. Promoting Quality Care.

October 12, 2010

Leah Hole-Curry, JD – Program Director
Washington State Health Technology Assessment
676 Woodland Square Loop SE
Lacey, WA 98503

Dear Ms. Hole-Curry:

We are writing on behalf of the Neuromodulation Therapy Access Coalition (NTAC) to formally request that the Health Technology Clinical Committee (HTCC) form an ad hoc advisory committee, as provided by WAC 182-55-045, to review significant and highly relevant stakeholder input that was inappropriately omitted from the material provided to the HTCC, before rendering a final decision on spinal cord stimulation (SCS).

As you know, Medicare has covered SCS for more than a decade for the treatment of certain forms of chronic pain. This therapy is widely available as a late or last resort option for the treatment of chronic pain by every major private health plan and, apart from Washington State, every state workers' compensation program in the country. It is also covered by the federal Veteran's Administration and the Department of Defense.

Nevertheless, despite its demonstrated success in treating appropriately selected patients with chronic neuropathic pain and the existence of substantial, high-level evidence in support of this therapy, the HTCC voted against coverage. We have several, specific concerns with the process that led to this decision and that warrant the formation of an ad hoc committee to further review the evidence on SCS.

1. Omission of Relevant Stakeholder Information from the HTCC's Review:

We strongly object to the contention made in the draft Findings and Coverage Decision, posted on October 6, that *"the committee decided that it had the most complete information: a comprehensive and current evidence report, public comments, and agency and state utilization information."*

In fact, the HTCC reached its conclusion without having seen – as confirmed by email correspondence between you and NTAC's Executive Director, Eric Hauth – significant and highly relevant information concerning evidence that the HTCC relied upon to make its non-coverage determination. Specifically, our coalition made clear on several occasions our concern that this process may give undue weight to a single, non-randomized study by Turner et al. commissioned by a Washington State agency with a long track record of denying access to this therapy.¹

¹ Turner JA et al. Spinal cord stimulation for failed back surgery syndrome: Outcomes in a workers' compensation setting. PAIN (2009), doi: 10.1016/j.pain.2009.08.014

Our extensive correspondence with L&I, which took place well in advance of this therapy appearing on the docket for the HTA, clearly details a number of significant evidence-based limitations in the study by Turner et al. that call into question its utility in forming any meaningful judgments about SCS. This information was omitted from the stakeholder comments submitted to the HTCC, despite several formal requests and follow-up correspondence with you to confirm that this information would be submitted to the HTCC.

It was clear from the August 20 hearing that the HTCC relied extensively on the study by Turner et al. in voting to oppose coverage of this therapy under state funded healthcare programs. They did so without the benefit of our critical analysis concerning the validity, relevancy, and limitations of that study.

NTAC made multiple requests that our correspondence be forwarded to the HTCC as part of this process. Specifically, we submitted our entire series of letters to you on January 8, 2010 and again on July 16, 2010 as attachments to our formal comments on the draft evidence report.

Also, on July 19, in response to a subsequent clarifying e-mail from Mr. Hauth asking if the comments would be submitted to the HTCC, you replied:

Evidence based comments and the responses are included in the report (appendix), which the committee receives.

NTAC representatives arrived at the August 20 public hearing on SCS assuming that all members of the HTCC had received this correspondence in advance of the meeting. However, Mr. Hauth learned at that time from an HTA staff member that it had not been forwarded as requested. Your e-mails to him on August 31 and on September 30 further confirm that this correspondence was not, in fact, submitted to the HTCC.

Moreover, these e-mails contain significant inconsistencies – suggesting on one hand that our correspondence with L&I was somehow not relevant to the process and, on the other hand, that this omission was a simple oversight. The posting of these letters on the HTA website last week (more 6 weeks after the public hearing) is confusing, to say the least, and calls into question the transparency, consistency and completeness of the review of SCS.

2. Undue Weighting of Lower Quality Evidence

In addition to the omission of relevant, evidence-based information on the limitations of the study by Turner et al., we are extremely concerned about the undue weight this process placed on a single, non-randomized study – to the exclusion of other, higher quality evidence, including two significant randomized controlled trials that support appropriate access to SCS.

It is critical to note that WAC 182-55-030 requires the following:

The committee shall give the greatest weight to the evidence determined, based on objective factors, to be the most valid and reliable, considering the nature and source of the evidence, the empirical characteristic of the studies or trials upon which the evidence is based, and the consistency of the outcome with comparable studies.

As part of its justification for minimizing the relevancy of the randomized controlled trials that support the role of SCS in treating certain forms of neuropathic pain, the draft Findings and Coverage Decision states:

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.

These are not “evidence-based” statements but rather, unsubstantiated assertions. The reference to a “sham stimulation” arm, for example, neglects the obvious fact that complete blinding of SCS is impossible, due to the sensation of paresthesia or tingling experienced by the patient. If this process relied upon meaningful input from an expert on SCS (e.g., an ad hoc voting member with the ability to directly discuss these issues with other members of the HTCC), it is very likely that these assertions would have been properly and accurately addressed. Unfortunately, that did not occur.

3. Interjection of Substantial Bias by the Agency Medical Directors Group (AMDG)

Dr. Lee Glass of L&I was chosen to represent the AMDG group, which was afforded approximately thirty minutes to make its presentation on August 20. This presentation was distributed to the HTCC in advance of the hearing. Labor and Industries is the agency that contracted the study by Turner et al. and with whom NTAC had exchanged extensive correspondence delineating the study’s shortcomings. Without the benefit of our correspondence, the committee members were not in a position to engage Dr. Glass in an exchange about the concerns we raised.

Instead, his presentation overwhelmingly focused on discounting other, higher quality evidence, while simultaneously advancing the view that Turner et al. is a more legitimate reference point for the HTCC. Dr. Glass made no reference to the significant methodological limitations in that study, which undermine its ability to properly inform a decision on SCS – a view echoed by the study authors themselves in the article that appeared in PAIN. Among other comments, Dr. Glass also made a remarkable and specious comparison of combat-related deaths in Afghanistan to deaths (inaccurately) attributed to SCS – a statement that should have no place in an objective, evidence-based review process. The process, as currently structured, offered no opportunity for expert stakeholders in the room to rebut these statements.

Because NTAC's extensive critique of the Turner et al. and the presentation of the study's significant limitations were omitted from this process, we strongly question the completeness and objectivity of the deliberations that followed. By not forwarding our correspondence, the process lacked transparency and resulted in a one-sided and biased review of the evidence, despite the existence of higher quality studies that support appropriate access to SCS.

Based on these significant process errors, we respectfully but strongly request that the HTCC form an ad hoc advisory committee, as provided by WAC 182-55-045, to fully evaluate the substance of our correspondence with L&I prior to making a final determination on this important therapy for those in Washington State living with chronic pain.

Sincerely,



Joshua Prager, MD, MS
NTAC Chair



David Kloth, MD
NTAC Vice Chair

cc:

The Hon. Christine Gregoire
Governor, State of Washington
Legislative Building
PO Box 40002
Olympia, WA 98504-0002

Melissa Burke-Cain
Assistant Attorney General
Social and Health Services, Olympia Division
7141 Cleanwater Drive SW
PO Box 40124
Olympia, WA 98504-0124

Brian Budenholzer, MD
Chair, Health Technology Clinical Committee
4013 S Regal St. Ste. 101
Spokane, WA 99223-5083

Doug Porter, Administrator
Health Care Authority
PO Box 42700
Olympia, WA 98504



neuromodulationaccess.org

Ensuring Patient Access. Promoting Quality Care.

July 15, 2010

Brian R. Budenholzer, MD – Chair, Health Technology Clinical Committee
Washington State Health Technology Assessment Program
P.O. Box 42712
Olympia, WA 98504-2712

Via email: shtap@hca.wa.gov

Dear Dr. Budenholzer and Members of the Health Technology Clinical Committee:

On behalf of the Neuromodulation Therapy Access Coalition (NTAC), I wish to provide the following comments on the Washington State Health Technology Assessment (HTA) program's draft evidence report on spinal cord stimulation (SCS). By way of background, NTAC is a national coalition of physician societies representing pain physicians, consumer advocates, and manufacturers of neuromodulation therapies.

Spinal cord stimulation has been used for the treatment of chronic pain since 1967; in particular for failed back surgery syndrome (FBSS) (chronic lumbar pain and lower leg pain after lumbar spine surgery) and complex regional pain syndrome type 1 (CRPS-I; burning pain radiating from the lower back through legs). Randomized controlled trials (RCTs) in FBSS and CRPS patients have demonstrated that SCS can provide statistically significant and clinically meaningful improvement in pain compared to conventional medical management, reoperation, and physical therapy (Kumar K, et al. Pain 2007; Kumar K, et al. Neurosurgery 2008; North RB, et al. Neurosurgery 2005, Kemler MA, et al. NEJM 2000; Kemler MA, et al. Ann Neurol 2004).

We commend the evidence vendor, Spectrum, for developing an extensive overview of the literature on SCS. However, the report contains some significant errors that skew the evidence on SCS and could lead to an inaccurate assessment of SCS and its clinical role in treating patients with certain chronic pain conditions.

We offer the following specific comments concerning the draft evidence report.

1. Despite the lack of any reported incidents in the literature of mortality directly attributable to SCS, it is unclear why the evidence vendor rates the quality of evidence on mortality as "high," based on two deaths – neither of which was attributable to SCS. **We strongly recommend that the evidence vendor and the HTCC amend the presentation of mortality in the summary of evidence addressing question 2 (page 16) and Table 11 (page 125) to emphasize the absence of SCS-related mortality and ensure that this limited evidence is not inappropriately interpreted to indicate a significant mortality risk from SCS.**

2. As previously stated in our January 11, 2010 comments to the HTA, the 2010 study by Turner et al. ("U of W study") contains a number of methodological limitations that substantially undermine its utility in assessing the clinical role of SCS. Further, its inclusion in your draft report as a source of evidence on key questions 1, 2 and portions of question 3 (with the exception of its reference to sub-populations at question 3.3) is inappropriate. The draft evidence report nevertheless gives substantial and undue weight to this prospective cohort (Level of Evidence III) study well beyond its limited focus on the workers' compensation sub-population. **We recommend that the evidence vendor limit its application of this evidence to its assessment of question 3.3 only and amend the summary evidence charts at pages 16, 17, 18 and elsewhere in the report (e.g., Table 11 at pages 124-127) to reflect this limited application of the U of W study.**
3. The draft evidence report does not include the technology assessment by researchers at Sheffield University in the United Kingdom, which was independently commissioned by the National Institute of Health & Clinical Excellence (NICE) in its evaluation of SCS for coverage by the National Health Service. **We recommend that the evidence vendor amend the report to include the entire Sheffield University technology assessment, noting its applicability to the key questions.**
4. The report presents an imbalanced and partial view of sponsorship of clinical studies. **We recommend that the HTCC evaluate the evidence based first and foremost on clinical design and relevant findings of the evidence.**
5. The report mischaracterizes the clinical role of SCS in treating chronic pain conditions, which further skews the analysis of the therapy. **We recommend that the evidence vendor amend the report at pages 7 and 22 to emphasize that the first goal of treatment for chronic pain conditions is to reduce the pain suffered by the patient.**
6. The evidence vendor inappropriately included clinical treatment guidelines that fall outside the scope of this assessment and did not include a relevant guideline by the American Society of Anesthesiologists (ASA). **We recommend that the evidence vendor include the ASA guidelines in its assessment of SCS and remove its reference to the North American Spine Society guidelines *Diagnosis and Treatment of Degenerative Lumbar Spinal Stenosis (2007)*, which refers to an off-label (not FDA approved) indication.**

We address each of these concerns in greater detail, below.

Inaccurate/Misleading Presentation of Mortality Data

Despite the absence of deaths attributable to SCS, it is troubling to note that extremely limited data are reported as having a "high" level of evidence in the summary chart of key question 2.3: "*What is the evidence of the safety of spinal cord stimulation – Mortality.*" We

understand that this summary is intended to convey the strength of evidence, rather than an indication of the relative safety of SCS. However, this presentation could certainly lead some observers to conclude that SCS has a high incidence of mortality – a conclusion that is completely at odds with clinical practice and the long history of successful SCS implantations and long-term use by patients. At a minimum, this section implies that there is high-level evidence that clearly demonstrates a link between SCS and mortality, which is simply not accurate.

We urge the evidence vendor to amend the draft report, as noted above, and we urge the HTCC to properly evaluate SCS as a therapy with no therapy-induced deaths reported in the literature. By this measure alone, SCS has proven to be a remarkably safe therapeutic intervention when implanted by appropriately trained and experienced physicians.

Inappropriate Application of the University of Washington Study

As noted in the draft evidence report, the U of W study “received the LoE grade of III.” (page 47). Enrollees in this prospective cohort study were limited to workers compensation claimants in the State of Washington. In our January 11, 2010 comments to the HTA, we noted several significant methodological limitations with this study and provided the HTA with extensive prior correspondence between NTAC and the study sponsor – the Washington State Department of Labor and Industries (L&I) – detailing our concerns. With this letter, we again provide copies of this correspondence and formally request that this information be included in the Health Technology Clinical Committee’s review of evidence. These limitations clearly indicate that the generalizability of the U of W study is limited at best.

In summary, our concerns with the U of W study include the following:

- Non-randomized cohort groups: Absent randomization, there are no *a priori* selection criteria for each cohort group. As a result, essentially non-comparable groups of patients were nonetheless compared.

This concern is reinforced by the draft evidence report: “*This (the U of W study) was a well conducted cohort study. However, the potential for selection bias is a threat to validity in any cohort study and is a limitation.*” (page 74)

- The significant length of time that patients enrolled in the study were injured and receiving workers’ compensation benefits (approximately 4 years in the case of SCS cohort participants) undermines the efficacy of any intervention. (Waddell, 1998; Waddell and Burton, 2001). It is well documented that this is an extremely difficult to treat population and any clinical study of a generally efficacious therapy could anticipate challenges meeting its primary endpoint in this patient group.

This concern is echoed in the draft evidence report: *"The mean duration of chronic pain was 38 months, and was significantly longer in the SCS group than in the PC group (P < .02)." (page 73).*

The study's composite outcomes measure is unprecedented in the literature on SCS and creates an inappropriate success threshold for SCS. On behalf of NTAC, Professor Rod Taylor (University of Exeter) analyzed the study's composite measure and concluded that, in addition to appearing nowhere in the published literature, it confounds the statistical assessment of the study's outcomes: *"Because of the way the authors have constructed the primary [outcome measure] (composite that requires that 3 separate outcomes be reached) means that it is a very rarely achieved outcome (e.g. 4% of SCS patients, 0% of PC and UC patients at 6 months). This rarity is particularly challenging. Take for example that 10% SCS vs. 5% of UC or PC patients achieved the primary outcome (i.e. a doubling of effectiveness), the study would require 474 per group to prove statistical significance. 0% vs. 4% (the actual results at 6 months) would require 239 per group."* (unpublished correspondence)

- A majority of patients treated with SCS in this study did not undergo a psychiatric evaluation to determine their eligibility for treatment as recommended by clinical practice guidelines and payer criteria such as the Medicare National Coverage Determination for SCS.

Again, we urge you and the HTCC to review our correspondence with L&I for a fuller discussion of these concerns.

Apart from the specific limitations in the study itself, however, we agree with the conclusion by the study authors in cautioning against its applicability beyond the workers' compensation program and in their acknowledgement that their reported outcomes may well be the result of confounding factors in the workers compensation population and system of care:

*The lack of long-term effectiveness of SCS in this study does not necessarily imply ineffectiveness in other settings. **The issues associated with involvement in the workers' compensation system may be a stronger influence than pain therapy on patient outcomes.** It is possible that no treatment has a substantial impact on average in this patient group. An argument could be made for heightened scrutiny of all therapies applied in this population, especially those that involve substantial costs or risks, and for efforts to provide the most cost-effective care with the least possibility of harm. (Turner, et al., 2010)¹ [emphasis added]*

Given the clear methodological limitations of this study and the caution about its wider applicability by the authors themselves, we strongly question why this study has been

¹ Spinal cord stimulation for failed back surgery syndrome: outcomes in a workers' compensation setting. Turner Judith A; Hollingworth William; Comstock Bryan A; Deyo Richard A Pain 2010;148(1):14-25.

given significant prominence in the draft evidence report, not only with respect to questions regarding sub-population effects, but also in questions 1 and 2 (Efficacy/Effectiveness and Safety).

For example, in addressing key question 1, “*What is the evidence of efficacy and effectiveness of spinal cord stimulation,*” the evidence vendor included only the U of W study in its assessment of effectiveness (see summary of evidence table at page 15). Clearly, the evidence vendor has applied limited evidence from a small cohort of workers’ compensation claims – to the exclusion of all other sources of evidence on clinical effectiveness – in assessing clinical effectiveness generally. It is concerning that a LoE III study enrolling a small number of workers compensation claimants in the State of Washington is presented as the exclusive source of evidence to address clinical effectiveness.

As noted above, even the study authors would seem to strongly caution against this application of their findings.

Therefore, we urge the evidence vendor and the HTCC to limit the applicability of this study to its evaluation of key question 3.3: “*What is the evidence that spinal cord stimulation has differential efficacy or safety issues in sub populations – 3rd party coverage?*” (see, for example, summary of evidence on question 3.3 at page 17).

In addressing clinical effectiveness for the workers compensation sub-population, we note that, despite a relatively modest outcome for all interventions in this study (i.e., SCS, CMM and Pain Clinic) – outcomes which are likely attributable to the overall poor outcomes within this population – there were notable secondary benefits reported by Turner et al. “*According to per-protocol analysis, patients who received SCS had significantly lower rates of surgery (other than SCS) at two years than those who underwent at least some Pain Clinic therapy (0% (0/27) versus 19% (4/21), P = .03).*” (page 76).

Based on this evidence of clinical effectiveness, SCS may well obviate the need for some costly surgical interventions and other pain care interventions within the workers compensation population.

Omission of Tech Assessment by Sheffield University

In the context of addressing key question 4 (*What is the evidence of cost effectiveness of spinal cord stimulation?*), the draft report refers to the unpublished technology produced by the School of Health and Related Research (SchARR) at the University of Sheffield for the United Kingdom’s National Institute of Health and Clinical Excellence (NICE) review of SCS (Simpson, 2009).

However, the authors of the evidence report neglect to include the full technology assessment in its review of SCS. In our January 11, 2010 comments to the HTA, we specifically requested that the full Sheffield technology assessment be included in the

vendor's review of evidence. If it was excluded because it is an unpublished document, the evidence vendor nevertheless included other unpublished documents in its review, including the 2008 NICE Final Appraisal Determination (FAD) on SCS. The Sheffield technology assessment is among the most comprehensive and independent assessments on the SCS available. Therefore, its absence in the draft evidence report is a significant omission that does not adequately account for a substantial body of work on this therapy.

We recommend that the evidence vendor amend the report to include the entire Sheffield University technology assessment, noting its applicability to each of the key questions.

Imbalanced Presentation of Potential Bias

The draft report states that industry-sponsored studies are more likely than others to produce results favorable to the sponsor. Such results, however, might simply be the result of a well-designed and well-executed study protocols. Further, sponsorship bias can influence study results in both directions, including sponsorship by payers – such as the Washington State Department of Labor and Industries – which may or may not have incentives that influence results. Bias can exist in any trial, regardless of the specific source of sponsorship. The ultimate goal is to acknowledge the potential and minimize its influence.

The authors of the evidence report appear to nominally acknowledge this two-way potential for bias in its description of the U of W study: *"While the study was not funded by a device manufacturer, it was commissioned by Washington State Department of Labor and Industries, which administers the workers' compensation program."* (page 74). **We urge the HTCC to evaluate the evidence based on the quality of study design and not to pre-judge the evidence based on any *a priori* assertion of bias.**

Inaccurate Characterization of Pain Care

As a coalition of stakeholders focused on patient access to appropriate pain care, we are troubled by the characterization of pain care in the draft evidence report. Specifically, the report states that *"(t)he aim of treatment for chronic pain is to improve function and quality of life while relieving pain."* (page 7 and 22).

In fact, the first aim of pain care is to relieve the pain experienced by the individual living with this debilitating condition. Once the pain is appropriately controlled or alleviated to the greatest extent possible, it is clearly the goal of treatment to improve overall function and quality of life. This distinction is critical. If we lose sight of the immediate goal of controlling pain, it is often an easy step to assert that the goal of pain care is, for example, to return individuals to work. While improvements in function and quality of life are clearly important, placing the primary emphasis on these goals often introduces factors beyond the control of the clinician and the even the individual living with pain as the measure of clinical success.

Whether the intervention is aspirin or SCS, the first objective is to alleviate the pain and suffering of the individual living with this condition. **Therefore, we recommend that the evidence vendor amend the report at pages 7 and 22 to emphasize that the first goal of treatment for chronic pain conditions is to reduce the pain suffered by the patient.**

Inaccuracies in Section 2.5

The evidence vendor included in its compilation of guidelines the following: *North American Spine Society (NASS): Diagnosis and treatment of degenerative lumbar spinal stenosis (2007)*. We note that these guidelines refer to off-label (not FDA approved) indications for SCS, which we believe fall outside the scope of this review. **Therefore, we urge the evidence vendor to strike these guidelines from consideration and we urge the HTCC to not weight these guidelines in its assessment of SCS for FBSS and CRPS.**

This section also omits an important updated set of guidelines on chronic pain, recently published by the American Society of Anesthesiologists (ASA).² These guidelines contain specific language on SCS as a therapeutic option. We understand that the evidence vendor may have missed these guidelines due to the timing of publication. **Nevertheless, given the recent publication of the guidelines from one of the leading national societies in the field of pain medicine, we recommend that the evidence vendor include the ASA guidelines in its assessment of SCS.**

Thank you for the opportunity to provide these comments and for your full consideration in this process. Please do not hesitate to contact me with any questions.

Sincerely,



Eric Hauth, Executive Director
eric@neuromodulationaccess.org

cc: Leah Hole-Curry, Program Director
Spectrum Research
Joshua Prager, MD - NTAC Chair
David Kloth, MD - NTAC Vice Chair

² **Practice Guidelines for Chronic Pain Management** - An Updated Report by the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine**Anesthesiology* 2010; 112:1-1.



STATE OF WASHINGTON
DEPARTMENT OF LABOR AND INDUSTRIES
PO Box 44000 • Olympia, Washington 98504-4000

July 24, 2009

Eric Hauth, Executive Director
Neuromodulation Therapy Access Coalition
1313 Karth Lake Circle
Arden Hills, MN 55112

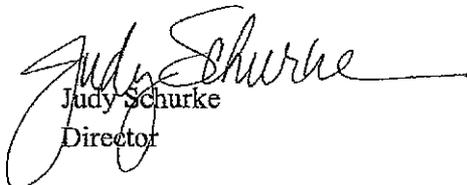
Dear Mr. Hauth:

I am writing in reply to your April 10, 2009, letter regarding the non-coverage policy for spinal cord stimulation (SCS) for injured workers in Washington State. I reviewed your letter with department clinical, research, and legal staff in order to fully understand your concerns about the University of Washington study of SCS (UW Study).

This research measured and reported the outcomes of injured workers in Washington State after at least 12 months of treatment. All treatment decisions were made by the injured workers and their physicians. The UW Study provides information on the comparative effectiveness of SCS, usual care and pain clinics as they were requested in our state during the time period of the study. The observational design and the conduct of the study are recognized as an important way to compare different medical treatments in the US as we face ever increasing healthcare costs. Dr. Turner was recently an invited speaker on this work at the Agency for Healthcare Research and Quality's *Comparative Effectiveness Research Methods Symposium* in June 2009.

As you know, the authors have reported the key outcomes and the methods used to conduct the study. Based on this information from the UW Study, the Industrial Insurance Medical Advisory Committee was not compelled to advise L&I to change its original position of non-coverage for this treatment. We submitted this technology to the State Health Technology Assessment (HTA) program for consideration. I anticipate the HTA program will ultimately review this technology allowing the Health Technology Clinical Committee (HTCC) to make a determination based on the UW Study and all other existing research.

Sincerely,


Judy Schurke
Director

cc: Bob Malooly, Assistant Director
for Insurance Services
Gary Franklin, Medical Director





neuromodulationaccess.org

Ensuring Patient Access. Promoting Quality Care.

April 10, 2009

Judy Schurke, Director
Department of Labor and Industries
Post Office Box 44100
Olympia, Washington 98504

Dear Director Schurke:

Thank you for your March 4, 2009 letter in response to our February 6, 2009 letter regarding the Department of Labor and Industries' (L&I) non-coverage policy for spinal cord stimulation (SCS) for injured workers with chronic, neuropathic pain.

For the record, we continue to have significant concerns with the department's interpretation of the University of Washington study and continuation of the SCS non-coverage policy; the discounting of other, published evidence, contrary to the stated requirements of the Washington Administrative Code (WAC); and several statements made in the department's latest response, which are not supported by facts.

Further, we are concerned that your March 4, 2009 letter did not address a number of specific concerns that we raised in our meeting with you and your staff and re-stated in our follow-up correspondence.

In response to your latest letter, we note the following:

First, your response states that the University of Washington study was "well powered." In an analysis of the results, Professor Rod Taylor (University of Exeter), whom you met at our January 23, 2009 meeting, states the following:

"Because of the way the authors have constructed the primary [outcome measure] (composite that requires that 3 separate outcomes be reached) means that it is a very rarely achieved outcome (e.g. 4% of SCS patients, 0% of PC and UC patients at 6 months). This rarity is particularly challenging. Take for example that 10% SCS vs. 5% of UC or PC patients achieved the primary outcome (i.e. a doubling of effectiveness), the study would require 474 per group to prove statistical significance. 0% vs. 4% (the actual results at 6 months) would require 239 per group."

Therefore, the study design simply does not support the statement that it was statistically "well powered." Rather, the study was substantially underpowered to detect a statistically and clinically significant difference in the primary outcome measure.

Second, your response states that the University of Washington study provides "real world outcomes." However, Professor Taylor and previously Dr. Richard North – both of whom are

world-renowned experts on SCS – have confirmed that the composite outcomes measure appears nowhere else in the literature on SCS.

Further, it is extremely important to note again that SCS significantly outperformed both the pain clinic and usual care despite the various limitations in the study that we have described, including the length of time that participants were injured – a factor that greatly limits the potential effectiveness of any treatment intervention. It is unclear why the department continues to maintain that SCS did not achieve positive real-world outcomes when it clearly outperformed both the pain clinic and usual care groups.

Again, we present these results in the chart, below:

UW Study Patient Outcomes (assuming “As Treated” Measure)

	SCS	Pain clinic	Usual care	P-value
ITT	9/51 (18%)	2/39 (5%)	2/68 (3%)	0.09 ¹ 0.02 ²
Per Rx	9/27 (33%)	2/23 (9%)	2/68 (3%)	0.04 ^{1,3} 0.0001 ^{2,3}

1 – SCS vs. Pain Clinic

2 – SCS vs. Usual Care

3 – Calculated by Professor Taylor - Fisher’s Exact Test

Third, your response letter states that the results of the University of Washington study “are in contrast to the efficacy data” found in other, published studies on SCS. We completely agree that this contrast exists, but note again that this discrepancy is due to the limitations in the University of Washington study, which is a non-randomized study involving substantially different cohorts.

Further, as we noted in our previous letter, we question why the department continues to discount the relevant peer-reviewed, published evidence on SCS – such as the PROCESS randomized controlled trial – which provides a much higher level of evidence from an evidence-based medicine perspective than the University of Washington study.

Under WAC 296-20-02704 (2)(b), the department is required to give “the greatest weight ... to the most rigorously designed studies and ... those well-designed studies that are reproducible.” (Emphasis added). The reference studies in contrast to the University of Washington study are more rigorously designed and far more reproducible. Nonetheless, the department continues to ignore this important regulatory requirement.

Fourth, the department states that the University of Washington study resulted in “remarkably consistent adverse events.” This statement is actually refuted by the authors of the University of Washington study. According to the study authors, *“a systematic review of the studies evaluating adverse events associated with SCS implantation...found a median superficial infection of 4%, lower than the 11% rate in our study. Among the studies reviewed, the mean rate of persistent pain in our region of the stimulator components was 5.8% (median 0), also lower than in our study.”*

The relatively high-rate of complications in the University of Washington study is, in fact, inconsistent with rates of complications found in the most rigorous published evidence on SCS, suggesting a further limitation in the University of Washington study.

Fifth, the department states that one of the “key features” of the University of Washington study is that “all participants are from the workers’ compensation population.” As we noted in our previous letter, we can find nothing in the administrative rules governing L&I’s review of evidence that provides for this sub-population ranking of evidence. We therefore question the legal and regulatory basis for this highly unusual approach to evidence review.

Finally, the department states “SCS for injured workers with FBSS (failed back surgery syndrome) is not an effective treatment measured by improvement in pain and function, using the criteria and methods currently in practice among community doctors.”

The department asserts this viewpoint even though it is contradicted by the clinical experience of relevant professional societies and thousands of physicians and patients throughout the country, multiple positive randomized controlled trials, a longstanding positive National Coverage Decision by Medicare, a positive determination by the UK’s National Institute of Health and Clinical Excellence, coverage by the DOD/VA and TriCare, coverage of SCS by all other state workers’ compensation programs in the United States and coverage of SCS by virtually every major private payer.

Although the department offers to “review and give strong consideration to any new, high-quality, peer-reviewed literature that becomes available,” we again question why the department has substantially disregarded recent randomized trials contrary to the rules governing L&I’s decisions.

Again, we stand ready to assist the department in developing an appropriate coverage policy that is fully reflective of the published evidence; consistent with Medicare, private payers and other state workers’ compensation programs; and based on clinically relevant patient selection and outcomes criteria.

Sincerely,


Eric Hauth, Executive Director
eric@neuromodulationaccess.org / (651) 278-4238



STATE OF WASHINGTON
DEPARTMENT OF LABOR AND INDUSTRIES
PO Box 44000 • Olympia, Washington 98504-4000

March 4, 2009

Eric Hauth, Executive Director
Neuromodulation Therapy Access Coalition
1313 Karth Lake Circle
Arden Hills, MN 55112

Dear Mr. Hauth:

Thank you for your February 6, 2009, letter regarding the department's Spinal Cord Stimulator policy and for our meeting on January 23, 2009.

As you know, the University of Washington (UW) study of SCS was carried out to develop workers' compensation specific evidence on this treatment among a Washington State sample of injured workers. The study was designed and completed by independent researchers who are highly experienced in many areas of clinical research, including those related to chronic pain. I have great confidence in and respect for the integrity of these researchers and for the quality of their work. The pragmatic design allowed for a well-powered study of the real-world outcomes of SCS treatment when prescribed, trialed, and permanently implanted by community physicians.

The UW study findings, with regard to effectiveness, are in contrast to the efficacy data from the small number of previously published studies addressing failed back surgery syndrome. Remarkably consistent adverse event rate findings emerged compared with available studies. However, the unique attributes of the UW study provide much needed and scientifically valid information to address the public policy question of whether SCS should be a covered benefit for injured workers in Washington. Key features of the study making it most relevant to this question include:

- All participants are from a workers' compensation population
- All care was directed by the patients' community doctors
- SCS devices were not brand specific
- All cost data, for SCS and comparative treatment, were captured in real-time

Eric Hauth, Executive Director

March 4, 2009

Page 2

We have concluded, with advice from the Industrial Insurance Medical Advisory Committee, that SCS for injured workers with FBSS is not an effective treatment as measured by improvement in pain and function, using the criteria and methods currently in practice among community doctors. The study confirmed high rates of adverse events, sometimes serious and life threatening. The study also showed a high rate of removal for permanently implanted stimulators, though all workers were screened using trial stimulation.

As you know, the assessment of the strengths and weaknesses of scientific studies in other populations will proceed when the State Health Technology Program prioritizes this technology for review. Before then, we will be happy to review and give strong consideration to any new, high-quality peer-reviewed literature that becomes available and adds to our understanding of when to use this treatment for chronic pain in this population.

Sincerely,



Judy Schurke
Director

cc: Bob Malooly, Assistant Director
for Insurance Services
Gary Franklin, Medical Director



neuromodulationaccess.org

Ensuring Patient Access. Promoting Quality Care.

February 6, 2009

Judy Schurke, Director
Department of Labor and Industries
Post Office Box 44100
Olympia, Washington 98504
Via email: scju235@lni.wa.gov

Dear Judy:

Thank you for taking the time on January 23 to again discuss the extremely important issue of access by injured workers in Washington State to spinal cord stimulation (SCS) for the treatment of chronic, neuropathic pain. We appreciate the open dialogue and continue to strongly encourage your re-consideration of Labor and Industries' (L&I) non-coverage policy.

To that end, it is important to re-cap several facts about spinal cord stimulation (SCS) and conclusions concerning the University of Washington study (Hollingworth, Turner, et al.)

1. Multiple randomized controlled trials have demonstrated that SCS is a clinically effective treatment option for chronic neuropathic pain. Therefore, L&I's evidence ranking criteria should incorporate results of these well-designed clinical studies.
2. Washington L&I's non-coverage policy of SCS for Workers' Compensation patients is inconsistent with coverage policies of Medicare and every other Workers' Compensation program in the United States. SCS is widely covered in the general population, both in the United States and in many countries throughout the world – as well as all other state workers' compensation programs in the United States.
3. Contrary to the assertion that SCS proved ineffective in the University of Washington study, it actually showed good results, when the denominator reflects those patients actually receiving the therapy.

Despite these facts, they appear to have had little bearing on the decision by L&I to affirm its existing non-coverage policy.

In our meeting on January 23, for example, Dr. Franklin stated that the sub-population study by the University of Washington (Hollingworth, Turner, et al.) carries a higher weight than, for example, randomized controlled trial evidence for SCS^{1 2 3} and the positive evidence-based

¹ Kumar K, Taylor RS, Jacques L, et al. The effects of spinal cord stimulation in neuropathic pain are sustained: a 24-month follow-up of the prospective randomized controlled multicenter trial of the effectiveness of spinal cord stimulation. *Neurosurgery*. 2008 Oct;63(4):762-70.

technology appraisal for SCS for chronic neuropathic pain that was conducted by the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom.⁴

However, we see nothing in L&I's own evidence ranking criteria that would justify disregarding well-designed, high-quality studies from the general population. This approach is unsupported by L&I's governing regulations concerning evidence reviews.

Second, in our meetings with you and your staff and the Industrial Insurance Medical Advisory Committee (IIMAC), we heard on several occasions that "workers' compensation patients are different," i.e., outcomes for various treatments are generally lower among this population than outcomes for similarly injured, non-workers' compensation patients.

If one assumes that "workers' compensation patients are different" -- a sentiment that is beyond the scope of the UW study or the agency's coverage policies -- one must conclude that this difference is due to (a) the incentive structure in workers compensation programs that would lead to under-reporting of therapeutic results in order to maintain disability benefits; or (b) the presumption that workers' compensation patients fare worse clinically than similarly injured patients in the general population.

Therefore, either patients in the UW study experienced *better* results from SCS than reported or there exist other, confounding variables in their care that limit the effectiveness of treatment. Neither explanation supports the conclusion that SCS failed to work.

As Professor Taylor noted, for example, patients enrolled in the UW study were out of work and injured far longer than is typical in studies evaluating this therapy for the general population. We note that these explanations demonstrate that SCS is either *more* -- not less -- effective than reported or that the level of disability sustained by the patients in the study makes it unlikely that *any* therapeutic intervention would overwhelmingly prove effective.

Third, L&I has concluded that the results of the UW Study demonstrate that SCS is not rehabilitative -- a conclusion with which we strongly disagree and one that fails to account for improvements in quality of life for patients with neuropathic pain. We also note that this conclusion was communicated in a December 2, 2008 letter to physicians throughout the state in advance of IIMAC's vote on the narrow question posed by L&I: "Does the Turner et al. study from the University of Washington provide evidence to change the Department's existing non-coverage policy for Spinal Cord Stimulator Devices?"

² Kumar K, Taylor RS, Jacques L, et al. Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicentre randomised controlled trial in patients with failed back surgery syndrome. *Pain*. 2007 Nov;132(1-2):179-88.

³ North RB, Kidd DH, Farrokhi F, Piantadosi SA. Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: a randomized, controlled trial. *Neurosurgery*. 2005;56(1):98-106.

⁴ Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin. NICE Technology Assessment Appraisal 159. Online: www.nice.org.uk/Guidance/TA159/Guidance/pdf/English.

However, when properly analyzed, the outcomes from the UW study (i.e., patients reporting statistically significant reduction in baseline pain) are actually comparable to results found in other, peer-reviewed studies for the general population. Contrary to the assertion that SCS proved ineffective, it showed good results when the denominator reflects those patients actually receiving the therapy. As the chart, below, indicates:

- Even if one uses the more conservative intention to treat analysis (ITT), in which the denominator reflects the entire study arm whether or not someone actually received a stimulator implant, SCS is more than three times as effective as treatment in the pain clinic (18 percent vs. 5 percent of patients achieving benchmark outcomes).
- Applying the more appropriate per RX or “as treated” analysis, in which the denominator reflects those patients actually receiving the implant, the results are even more pronounced (33 percent vs. 9 percent achieving benchmark outcomes). This approach reflects real-world practice, in which patients are first given trial stimulation to determine whether or not they are appropriate candidates for this therapy.
- The pain clinic and usual care groups showed far less improvement in pain reduction or function, clearly indicating just how unresponsive this group of study participants was to treatment. Despite this fact, those receiving SCS did remarkably well.

UW Study Patient Outcomes (assuming “As Treated” Measure)

	SCS	Pain clinic	Usual care	P-value
ITT	9/51 (18%)	2/39 (5%)	2/68 (3%)	0.09 0.02
Per Rx	9/27 (33%)	2/23 (9%)	2/68 (3%)	0.04* 0.0001*

* Calculated by Professor Taylor - Fisher's Exact p

We believe a fair review consistent with the agency's evidence ranking criteria would likely rank the referenced RCTs and the NICE determination “A” or “B” level evidence and the UW study “C” level evidence. Such a review would appropriately support a positive coverage determination for this therapy. In addition, were the reference studies “C” level evidence, it seems likely that L&I would discount their relevancy based on this evidence ranking. We fail to understand how a lower-rated study used to deny coverage trumps higher-level RCTs in favor of a therapy. Regardless, nothing in L&I's criteria provides for this two-tier evidence ranking based on sub-population weighting.

Based on these important considerations, we again strongly recommend that L&I re-consider its determination and implement a coverage policy comparable to the UK's NICE recommendation, pending possible future evaluation of this therapy by the state's Health Technology Assessment (HTA) program. The NICE recommendation states clearly:

“Spinal cord stimulation is recommended as a treatment option for adults with chronic pain of neuropathic origin who:

- ***continue to experience chronic pain (measuring at least 50 mm on a 0-100 mm visual analogue scale) for at least 6 months despite appropriate conventional medical management, and***
- ***who have had a successful trial of stimulation as part of the assessment specified in recommendation.***

Spinal cord stimulation should be provided only after an assessment by a multidisciplinary team experienced in chronic pain assessment and management of people with spinal cord stimulation devices, including experience in the provision of ongoing monitoring and support of the person assessed.”

We stand ready to assist your agency to fully assess the current peer-reviewed evidence on SCS and implement an appropriate coverage decision for this important therapy, pending possible future review by HTA. However, we also strongly believe that L&I's current non-coverage of SCS as a treatment option fails to meet the needs of injured workers with neuropathic pain and is not supported by the agency's evidence-ranking criteria.

Sincerely,



Eric Hauth, Executive Director
eric@neuromodulationaccess.org
(651) 278-4238
cc: Joshua Prager, MD – NTAC Chair

NTAC Membership:

American Academy of Pain Medicine
American Pain Foundation
American Society of Interventional Pain Physicians
Boston Scientific Neuromodulation
International Spine Intervention Society
Johnson & Johnson/DePuy
Medtronic Neuromodulation
National Pain Foundation
North American Neuromodulation Society
St. Jude Medical Neuromodulation



neuromodulationaccess.org

Ensuring Patient Access. Promoting Quality Care.

October 14, 2008

Judy Schurke, Director
Department of Labor and Industries
Post Office Box 44100
Olympia, Washington 98504

Re: Washington State DLI Study *Spinal cord stimulators (SCS) for injured workers with chronic low back and leg pain after lumbar surgery – A prospective study to describe costs, complications, and patient outcomes.* Hollingworth W, Turner J, Comstock BA, Deyo R. September, 2008.

Dear Director Schurke:

On behalf of the Neuromodulation Therapy Access Coalition (NTAC), I want to thank you for the continued, open dialogue concerning the above-referenced study. As this study has now been completed, and one of the authors is scheduled to present the findings this week at the October 16, 2008 meeting of the Industrial Insurance Medical Advisory Committee (IIMAC) meeting, we want to again note some significant concerns with the study and its conclusions. We stress that this study and its results stand in stark contrast to the vast body of published literature on SCS, as well as a recent technology review completed by the United Kingdom's National Institute for Clinical Effectiveness (NICE), the widely respected European health technology assessment program.

We also request that this letter be shared with the IIMAC chair and committee members prior to the October 16 meeting in order to provide a fuller context for the discussion. Finally, while we understand that the meeting on October 16 does not provide an opportunity for public comment, we would like to formally request time at any subsequent discussion of this study by the IIMAC, allowing for direct input to the committee by experts in this important therapy. Please note NTAC has recently contracted with the Delfini Group, based in Washington State, to conduct an independent evidence-based review of the study, and we look forward to including the results of that review in our subsequent discussions.

We have reviewed the final study report and, while there are some changes from the draft report, the final report is largely unchanged. As noted in our May 30 letter, there are a number of methodological concerns with this study, which significantly limit its ability to meaningfully inform the discussion on the efficacy of SCS for properly selected patients. These concerns include problems with the overall study design, patient selection, screening trials for SCS, data collection, and definition of success, the vast majority of which were unfortunately not addressed in the final report. Overall, we wish to emphasize the following issues for your agency's further consideration:

1. **Study design results in poor quality evidence**
 - Validity concerns due to non-randomization.
2. **Workers' Compensation patients**
 - Participants sustained injury on average 4 years prior to enrollment;
 - Regardless of intervention, such participants are very unlikely to return to work; and
 - Participants may have a disincentive (loss of benefits) to report successful treatment.
3. **Selection bias likely**
 - It is unclear how patients were funneled to any of the three treatment groups; and
 - Most SCS patients agreed to participate, whereas less than 50% of the patients in other two groups could be contacted and agreed to participate.
4. **Analyses: None presented are ideal**
 - Intention-to-treat (ITT) analysis is not appropriate, whereas as-treated analysis was not done;
 - Over 50% of SCS group did not receive intervention; and
 - Permanently implanted patients showed both an improvement in pain and disability.
5. **Several studies demonstrate that SCS is cost-effective**
 - Actuarial analysis from the United HealthCare (UHC) claims data noted in our previous discussion on this study, modeled data based on published literature, and data collected from prospective uncontrolled studies as well as a randomized control trial support the cost argument for SCS over other treatments (e.g. CMM, PT, reoperation); and
 - The UK's National Institute for Clinical Effectiveness (NICE) just released a new Final Appraisal Determination (FAD) recommending coverage for SCS throughout the entire UK National Health Service for failed back surgery syndrome (FBSS) and chronic regional pain syndrome.

Importantly, NICE issued its finding subsequent to our meeting in May. They state (and we agree) that "SCS is not suitable for everyone with chronic pain, and that it should be used only as part of a multidisciplinary team approach with other therapies and a strategy for rehabilitation."

With this appropriate caveat, however, NICE definitively concluded in its review of the literature that SCS for failed back surgery syndrome and CRPS is both clinically and cost effective. They state further "that, for FBSS and CRPS, the evidence suggested that SCS was more effective reducing pain than CMM," and they found that "SCS for the treatment of FBSS and CRPS would be a cost-effective use of NHS resources."

Contrary to the conclusions in the study by Hollingworth, et al., the NICE committee evaluating SCS "was persuaded that, on balance, if people with severe pain of neuropathic origin were appropriately identified, that is, undergo an assessment by a specialist multidisciplinary team which included a successful trial of stimulation, then the evidence of benefit could be generalized. The Committee therefore concluded that the use of SCS should be recommended as a treatment option for all chronic pain conditions of neuropathic origin."

Unfortunately, it would appear that these conditions were not met in the Hollingworth et al. study, which – by design – not surprisingly resulted in minimal impact of SCS in the treatment of the study participants' neuropathic pain.

We strongly urge your department and the IIMAC to view the University of Washington in the broader context of literature on SCS and, in particular, the conclusions reached by NICE in its evaluations of this therapy for individuals with chronic, neuropathic pain.

We look forward to continued dialogue on this important issue and addressing any questions you and the IIMAC may have.

Sincerely,

A black rectangular redaction box covering the signature of Eric Hauth.

Eric Hauth, Executive Director
eric@neuromodulationaccess.org
(651) 278-4238



neuromodulationaccess.org

Ensuring Patient Access. Promoting Quality Care.

January 08, 2010

Leah Hole-Curry, JD - Program Director
Washington State Health Technology Assessment
676 Woodland Square Loop SE
Lacey, WA 98503

Dear Ms. Hole-Curry:

On behalf of the Neuromodulation Therapy Access Coalition (NTAC), I wish to submit the following comments, supporting information and recommendations regarding the Washington State Health Technology Assessment's (HTA) upcoming review of spinal cord stimulation (SCS). Also, thank you for taking the time to meet earlier this week and discussing how NTAC can most effectively participate in the review process of this critically important therapy.

By way of background, NTAC is a national coalition of physician societies, patient advocates and manufacturers of neuromodulation therapies – including SCS for the treatment of chronic, intractable pain.

Spinal cord stimulation (SCS) has been used for the treatment of chronic pain since 1967; in particular for failed back surgery syndrome (FBSS) (chronic lumbar pain and lower leg pain after lumbar spine surgery) and complex regional pain syndrome.

Randomized controlled trials (RCTs) in FBSS and CRPS patients have demonstrated that SCS can provide statistically significant and clinically meaningful improvement in pain compared to conventional medical management, reoperation, and physical therapy (Kumar K, et al. *Pain* 2007; Kumar K, et al. *Neurosurgery* 2008; North RB, et al. *Neurosurgery* 2005, Kemler MA, et al. *NEJM* 2000; Kemler MA, et al. *Ann Neurol* 2004). These studies are among the most comprehensive studies undertaken for SCS and we urge the Health Technology Clinical Committee (HTCC) to include them in their review and appropriately weigh them in the determination on SCS (See key literature citations in Attachment A).

One RCT^{1 2} in FBSS patients also has shown the ability of SCS to significantly improve function and quality of life versus conventional medical management. A substantial body of non-

¹ Kumar K, Taylor RS, Jacques L, Eldabe S, Meglio M, Molet J, Thomson S, O'Callaghan J, Eisenberg E, Milbouw G, Buchser E, Fortini G, Richardson J, North RB. Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicentre randomised controlled trial in patients with failed back surgery syndrome. *Pain*. 2007 Nov;132(1-2):179-88.

² Kumar K, Taylor RS, Jacques L, Eldabe S, Meglio M, Molet J, Thomson S, O'Callaghan J, Eisenberg E, Milbouw G, Buchser E, Fortini G, Richardson J, North RB. The effects of spinal cord stimulation in neuropathic pain are sustained: a 24-month follow-up of the prospective randomized controlled multicenter trial of the effectiveness of spinal cord stimulation. *Neurosurgery*. 2008 Oct;63(4):762-70.

randomized data, including some large, longitudinal case series, complements the findings of the more rigorous RCTs. In short, SCS has received widespread acceptance throughout the U.S. and in countries throughout the world for over two decades. It is covered by:

- Every major commercial healthcare plan in U.S.;
- Medicare, through a long-standing National Coverage Determination (NCD);
- The U.S. Department of Veteran's Administration and the U.S. Department of Defense;
- Virtually every state workers' compensation program in the U.S., with the exception of Washington State; and
- The United Kingdom's National Health Service.

While SCS has relatively high upfront costs associated with its implantation, the therapy can lead to long-term reduction in health care resource utilization associated with chronic, intractable pain. Further, SCS is economically favorable in comparison to other therapies for patients with FBSS and CRPS-I. Studies have indicated that, as compared to conventional medical management of patients with FBSS and CRPS, SCS should become cost-effective after about 2 years of its use. Supporting literature on the cost-effectiveness of SCS includes:

- Kumar K, et al. Neurosurgery 2002;
- Bell GK, et al. JPSM 1997;
- North RB, et al. Neurosurgery 1997;
- Taylor RJ, et al. Int J Tech Assess Health Care 2005; and
- Kemler MA, et al. Neurology 2002.

We urge the HTA to include each of these studies as part of its review.

Significantly, in 2008, the United Kingdom's national health technology assessment body – the National Institute of Health & Clinical Excellence (NICE) – issued its findings and recommendations to the National Health Service that SCS is *both* clinically and significantly cost effective for properly selected patients with neuropathic pain. This guidance, which contains complete summaries and citations for all the evidence reviewed during the comprehensive evidence-based NICE assessment of SCS can be found at the following link:
<http://hta.nhs.uk/fullmono/mon1317.pdf>

In particular, NICE relied on the RCT described by Kumar et al., an extensive and highly rigorous multi-center, randomized controlled trial (see footnotes 1 and 2). Subsequent to the NICE assessment, other relevant literature and one major treatment guideline have been published supportive of SCS. These include:

- Kumar et al. The Effects of Spinal Cord Stimulation in Neuropathic Pain are Sustained.

Neurosurgery 63:762–770, 2008.

- Frey et al. Spinal Cord Stimulation for Patients with Failed Back Surgery Syndrome: A Systematic Review. *Pain Physician* 2009; 12:379-397.
- Bala et al. Systematic Review of the (Cost-)effectiveness of Spinal Cord Stimulation for People With Failed Back Surgery Syndrome. *Clin J Pain* 2008;24:741–756.
- American Society of Anesthesiologists. Practice Guidelines for Chronic Pain Management (2009 Update). <http://www.asahq.org/clinical/chronicpain.htm>

While there is substantial evidence on SCS that the HTA should review in arriving at its determination on this therapy, we are concerned that undue weight may be given to a recent non-randomized study that focused solely on a small number of patients enrolled through the Washington State Department of Labor and Industries' (L&I) workers' compensation population.

The study was commissioned by L&I and conducted by researchers at the University of Washington, led by Professor Judith Turner.³ We, and others⁴, have identified significant limitations in this study and in its applicability to both the workers' compensation population and the general population.

Nearly two years ago, our coalition began a series of discussions and correspondence with L&I concerning the UW study, based on a preliminary, unpublished report issued by the research team (see attached correspondence). We initiated this outreach to assist L&I in its assessment of the study results. That report has since been finalized and can be found on the Department of Labor & Industries' website at:

<http://www.lni.wa.gov/ClaimsIns/Files/OMD/FinalReportSCS.pdf>

As the attached correspondence demonstrates, NTAC representatives, including two of the world's foremost experts on SCS – one of whom is based in the United Kingdom and participated in the NICE process – met with senior L&I staff on two, separate occasions to highlight a number of limitations in the UW study. These limitations include:

- Non-randomized cohort groups: Absent randomization, there are no *a priori* selection criteria for each cohort group. As a result, essentially non-comparable groups of patients were nonetheless compared.
- The significant length of time that patients enrolled in the study were injured and receiving workers' compensation benefits (approximately 4 years in the case of SCS

³ Turner JA et al. Spinal cord stimulation for failed back surgery syndrome: Outcomes in a workers' compensation setting. *PAIN* (2009), doi: 10.1016/j.pain.2009.08.014

⁴ Wasan AD. Spinal cord stimulation in a workers' compensation population: How difficult it can be to interpret a clinical trial. *PAIN* (2009).

cohort participants) undermines the efficacy of any intervention. (Waddell, 1998; Waddell and Burton, 2001). It is well documented that this is an extremely difficult to treat population and any clinical study of a generally efficacious therapy could anticipate challenges meeting its primary endpoint in this patient group.

- The study's composite outcomes measure appears in no other SCS study and creates an inappropriate success threshold for SCS.
- A majority of patients treated with SCS in this study did not undergo a psychiatric evaluation to determine their eligibility for treatment as recommended by clinical practice guidelines and payer criteria such as the Medicare National Coverage Determination for SCS.

These limitations alone call into question the utility of this study in determining the efficacy of SCS as a therapeutic option for patients with chronic, refractory pain. Importantly, the authors themselves included in the recently published version of this study – in contrast to the earlier report provided to L&I – significant caveats concerning the applicability of their study. We commend the study authors for broadly acknowledging these limitations in the conclusion included in the published version of this study, appearing in the journal *Pain* (see footnote 3).

The following text illustrates some crucial differences between the text in the unpublished report and the language contained in the published version, which should strongly caution against its utility in guiding coverage of SCS. Please note that the text in black font is common to both printed conclusions. The text in green appears in the published version in the journal *Pain*, but not in the initial report online. The text in red appears in the initial report but does not appear in the published version in *Pain*.

In summary, we found little evidence for the superiority of SCS over alternative treatments among Washington State workers' compensation claimants with FBSS. A small advantage of SCS in improving leg pain and function at 6 months, albeit accompanied by greater daily use of opioids, disappeared by later follow-ups. We also found no evidence that SCS reduced medical or productivity costs. Differences in study population, study design, and delivery of care may explain why these results are more disappointing than those of RCTs. The lack of long-term effectiveness of SCS in this study does not necessarily imply ineffectiveness in other settings. The issues associated with involvement in the workers' compensation system may be a stronger influence than pain therapy on patient outcomes. It is possible that no treatment has a substantial impact on average in this patient group. An argument could be made for heightened scrutiny of all therapies applied in this population, especially those that involve substantial costs or risks, and for efforts to provide the most cost-effective care with the least possibility of harm.

The authors concluded that the results of this study likely say more about the complexities of the workers' compensation patient population – and the specific participants in the UW study – than about SCS as a therapeutic intervention. They also caution against extrapolating from the workers' compensation population to other patient populations.

The caveats provided by the authors themselves strongly suggest that this study cannot provide a reasonable measure of the impact of SCS on the workers' compensation population, much less on the general population. Further, as the attached correspondence demonstrates, L&I did not directly refute any of our substantive concerns; nonetheless, the agency continues to rely on the study as the basis for non-coverage of SCS and presumably as a significant factor in referring SCS for review by the HTA.

Based on the foregoing comments, we strongly urge HTA to consider the following recommendations:

RECOMMENDATIONS

1. In addition to the literature we cite in this letter and in Attachment A, we request that copies of the full NICE technology assessment report for SCS be conveyed in its entirety to members of the HTCC as part of its evidence review and evaluation (Simpson EL et al. Health Technology Assessment 2009, <http://www.hta.nhs.uk/fullmono/mon1317.pdf>)
2. We respectfully request that the HTA include the attached correspondence between NTAC and the Department of Labor & Industries, when considering the UW study. Should the HTA's third-party evidence vendor include the UW study as part of this process, we further request that this information be conveyed in entirety to the HTCC as part of its evidence review and evaluation.
3. Given the complexities of specific implantable therapies and the literature assessing patient outcomes, we also request that the HTA formally include an ad hoc clinical expert with experience implanting SCS and managing SCS patients with chronic pain as part of the HTCC's review process. Our physician society members would be pleased to provide a list of such physicians with the appropriate expertise practicing in Washington State.

As an important precedent, we commend the HTA for including an ad hoc physician representative in its recent review of drug eluting cardiac stents. A physician expert in the SCS process is also essential to ensure a complete review, understanding and applicability of the evidence on this therapy.

Thank you for the opportunity to provide these important comments in advance of HTA's review of SCS. We look forward to working with your agency to ensure the most objective, balanced and rigorous evaluation of SCS possible.

Sincerely,



Eric Hauth, Executive Director

Cc: Joshua Prager, MD – NTAC Chair
David Kloth, MD – NTAC Vice Chair

Attachment A:

Partial Literature Citations for SCS in the Treatment of FBSS and CRPS

- Bala MM, Riemsma RP, Nixon J, Kleijnen J. Systematic review of the (cost-)effectiveness of spinal cord stimulation for people with failed back surgery syndrome. *Clin J Pain*. 2008 Nov-Dec;24(9):741-56.
- Bell G, Kidd D, North RB. Cost-effectiveness analysis of spinal cord stimulation in treatment of failed back surgery syndrome. *Journal of Pain and Symptom Management*, Volume 13, Issue 5, Pages 286-295.
- Frey ME, Manchikanti L, Benyamin RM, Schultz DM, Smith HS, Cohen SP. Spinal cord stimulation for patients with failed back surgery syndrome: a systematic review. *Pain Physician*. 2009 Mar-Apr;12(2):379-97.
- Kemler MA, Furnée CA. Economic evaluation of spinal cord stimulation for chronic reflex sympathetic dystrophy. *Neurology*. 2002 Oct 22;59(8):1203-9.
- Kemler MA, De Vet HC, Barendse GA, Van Den Wildenberg FA, Van Kleef M. The effect of spinal cord stimulation in patients with chronic reflex sympathetic dystrophy: two years' follow-up of the randomized controlled trial. *Ann Neurol*. 2004 Jan;55(1):13-8.
- Kemler MA, Reulen JP, Barendse GA, van Kleef M, de Vet HC, van den Wildenberg FA. Impact of spinal cord stimulation on sensory characteristics in complex regional pain syndrome type I: a randomized trial. *Anesthesiology*. 2001 Jul;95(1):72-80.
- Kemler MA, Barendse GA, van Kleef M, de Vet HC, Rijks CP, Furnée CA, van den Wildenberg FA. Spinal cord stimulation in patients with chronic reflex sympathetic dystrophy. *N Engl J Med*. 2000 Aug 31;343(9):618-24.
- Kumar K, Malik S, Demeria D. Treatment of chronic pain with spinal cord stimulation versus alternative therapies: cost-effectiveness analysis. *Neurosurgery*. 2002 Jul;51(1):106-15; discussion 115-6.
- Kumar K, Taylor RS, Jacques L, Eldabe S, Meglio M, Molet J, Thomson S, O'Callaghan J, Eisenberg E, Milbouw G, Buchser E, Fortini G, Richardson J, North RB. Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicentre randomised controlled trial in patients with failed back surgery syndrome. *Pain*. 2007 Nov;132(1-2):179-88.
- Kumar K, Taylor RS, Jacques L, Eldabe S, Meglio M, Molet J, Thomson S, O'Callaghan J, Eisenberg E, Milbouw G, Buchser E, Fortini G, Richardson J, North RB. The effects of spinal cord stimulation in neuropathic pain are sustained: a 24-month follow-up of the prospective randomized controlled multicenter trial of the effectiveness of spinal cord stimulation. *Neurosurgery*. 2008 Oct;63(4):762-70.
- North RB, Kidd DH, Farrokhi F, Piantadosi SA. Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: a randomized, controlled trial. *Neurosurgery*. 2005;56(1):98-107.
- North RB, Kidd DH, Olin JC, Sieracki JM. Spinal cord stimulation electrode design: prospective, randomized, controlled trial comparing percutaneous and laminectomy electrodes-part I: technical outcomes. *Neurosurgery*. 2002 Aug;51(2):381-90.

Ohnmeiss DD, Rashbaum RF. Patient satisfaction with spinal cord stimulation for predominant complaints of chronic, intractable low back pain. *Spine J*. 2001 Sep-Oct;1(5):358-63.

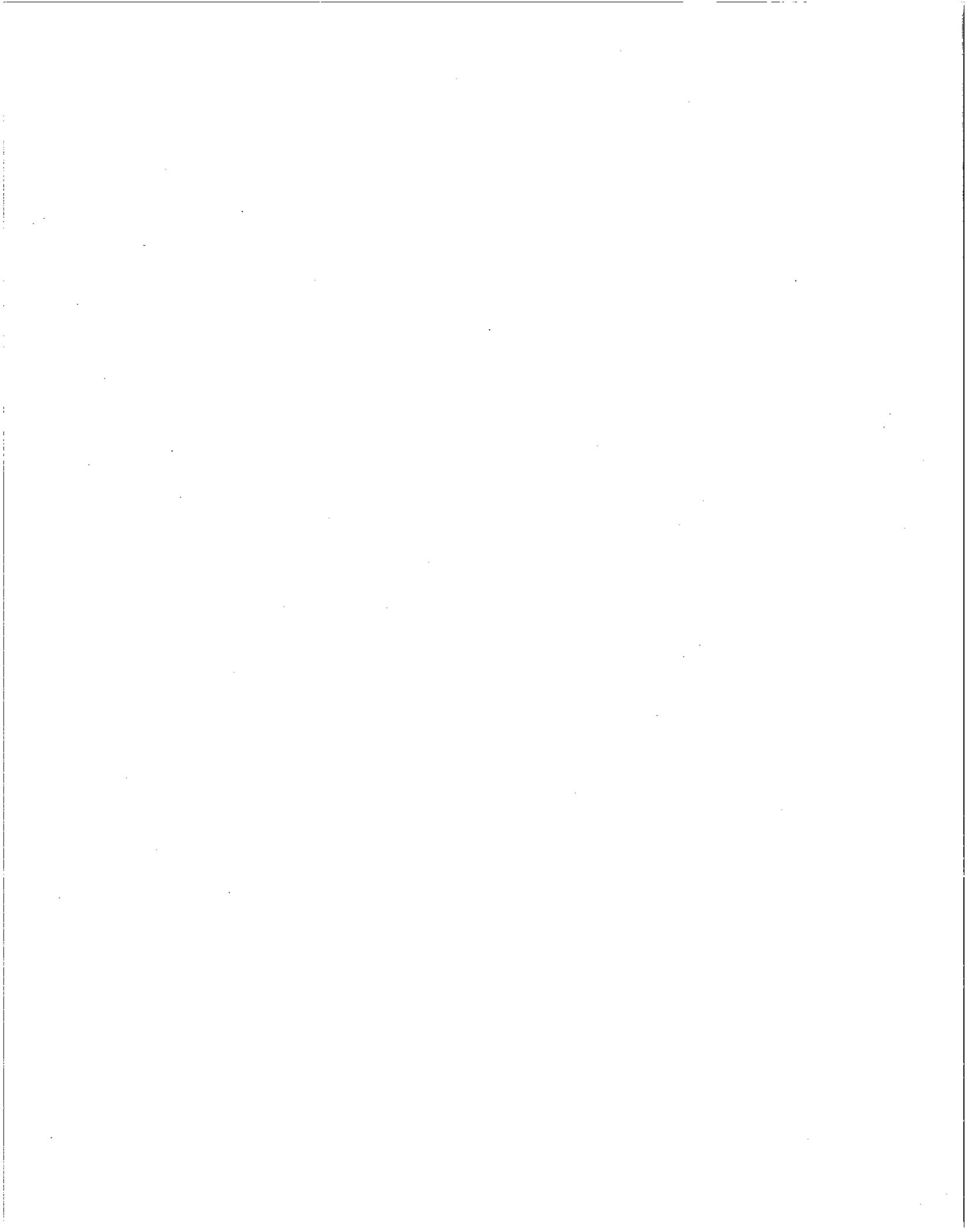
Taylor RS. Spinal cord stimulation in complex regional pain syndrome and refractory neuropathic back and leg pain/failed back surgery syndrome: results of a systematic review and meta-analysis. *J Pain Symptom Manage*. 2006 Apr;31(4Suppl):S13-9.

Taylor RS, Van Buyten JP, Buchser E. Spinal cord stimulation for chronic back and leg pain and failed back surgery syndrome: a systematic review and analysis of prognostic factors. *Spine (Phila Pa 1976)*. 2005 Jan 1;30(1):152-60.

North RB, Kidd D, Shipley J, Taylor RS. Spinal cord stimulation versus reoperation for failed back surgery syndrome: a cost effectiveness and cost utility analysis based on a randomized, controlled trial. *Neurosurgery*. 2007 Aug;61(2):361-8; discussion 368-9. Erratum in: *Neurosurgery*. 2009 Apr;64(4):601.

Taylor RJ, Taylor RS. Spinal cord stimulation for failed back surgery syndrome: a decision-analytic model and cost-effectiveness analysis. *Int J Technol Assess Health Care*. 2005 Summer;21(3):351-8.

Taylor RS, Taylor RJ, Van Buyten JP, Buchser E, North R, Bayliss S. The cost effectiveness of spinal cord stimulation in the treatment of pain: a systematic review of the literature. *J Pain Symptom Manage*. 2004 Apr;27(4):370-8.



We are committed to Predict, Diagnose and Prevent Pain from becoming a disabling disease

October 14, 2010

RE: Health Technology Clinical Committee Findings and Coverage Decision
Topic: Spinal Cord Stimulation Meeting Date: August 20th, 2010

Dear Members of Health Technology Clinical Committee,

I read the report with proposed non-coverage decision with great interest. I have also received and reviewed the transcription of the August 20th.

I did not submit my comments before the meeting hoping that the committee is able to see the overwhelming evidence of SCS efficacy and effectiveness. Unfortunately, it did not happen. The committee has recommended the non-coverage policy.

I will not attempt to bring again overview and analysis of evidence. I will challenge a number of missing or misinterpreted findings, and back it up by HTA assessment on the same topic which was performed in Canada. I believe there is a right way to practice neuromodulation techniques based on certain standards of modern outcome-based medicine.

Since the major weapon HTA used against SCS was the infamous study of Turner et al, I would like to address it first.

This study in worker's compensation setting challenged previous studies and suggested ineffectiveness of the SCS to achieve pain relief, improve functional status and decrease opioids (1). Notwithstanding impressive biostatistical methods, there are multiple questions that have remained unanswered and several concerns should be addressed.

1. Authors correctly commented regarding the generalizability of the North's et al study (2), however, this work suffered the same issue of a skewed sampling. 111 subjects declined to participate and 170 could not be contacted. Did the injured workers who participated in the study adequately represent general injured workers population? Moreover, clearly those subjects often have significant psycho-social confounding factors and by no means can represent general population.
2. Dismissing previous studies on the basis of funding (Medtronic), HTA ignored the fact that the Turner et al study was funded by Washington State L&I. Whereas industry including Medtronic Inc is continuously under FDA and other government authorities surveillance, no such control was implemented on implanters who performed SCS surgeries on L&I patients. I am personally aware of at least several accounts when SCS was done with incorrect indications or improper technique was exercised.

We are committed to Predict, Diagnose and Prevent Pain from becoming a disabling disease

3. Criticizing the PROCESS (3) study, authors pointed out that no new therapies were offered for the conservative management group. If to conclude that in L&I study Pain Clinic group represents such “new opportunity”, no difference was found between the Pain Clinic and the Usual Care group. Generally speaking, there are no such “new options” that can be offered in milieu of a chronic condition such as FBSS. Otherwise, SCS would not be considered as a salvage procedure. Though the primary outcome did not reach statistical significance in 24 months, there was interesting trend showing that the patients in the Usual Care group did better than in both the SCS and Pain Clinic group. Does it mean that the “new treatments” in the pain clinic setting were even less efficient than primary care approaches?
4. Only 53% of trialed patients proceeded to the permanent phase. This fact *per se* suggests poor selection process. Normally, about 80% of patients will pass the trial phase successfully (4).
5. Only 23% of patients had psychological evaluation. No data of those assessments were presented. The quality of evaluations remained unknown. It is true that no differences were found in a research setting whether or not mental health and social issues were assessed prior to SCS intervention. However, in the pragmatic clinical setting and by requirement of majority of insurance carriers, a clinical psychologist is seen as a watch-dog of overenthusiastic surgeons. Dr Turner and her colleagues perform psychological evaluation of all candidates for SCS at the UW Center for Pain Relief and some cases were turned down solely based on those assessments. Psychologist’s role is perhaps even more important for L&I population, where issues of attitude, expectations, functional recovery and secondary gain must be explored.
6. No onsite review of the health status (including other pain complains), imaging findings was conducted prior to enrollment into SCS group.
7. Only 18% of SCS trials and permanent implantation procedures were reviewed. Theoretically, the rest (72%) could have been performed technically wrong.
8. Asking patients about “average pain and medication use in the past month” may introduce “recall bias” and should not be used in properly designed prospective cohort studies. For instance, if the pain was severe enough on a particular day when the telephone interview was administered, a person would likely respond that “average” pain was higher on the scale.
9. Patients in the SCS group had a longer history of pain than in other two groups (48 vs. 31 vs. 36) p 0.02. Long-term observational study (4) suggested that success of SCS has reverse correlation with pain chronicity.
10. The result of only 18% patients in the SCS group reaching > 50% pain reduction is definitely unexpectedly low in comparison with both North’s and PROCESS studies (2,3) and may reflect selection or observer biases. Selection bias was previously outlined. Observer bias may lay in the fact that the subjects were observed and results were recorded. Despite the investigators’ promise to keep the information confidential and not divulge it to L&I case managers, patients might

We are committed to Predict, Diagnose and Prevent Pain from becoming a disabling disease

have had significant secondary gain issues to remain disabled and did not want to share real perception with the investigators.

11. All group got worse in the functional status at 12 months, substantiating common belief that L&I patients will get worse as time goes by while staying off work.
12. Statistical analysis of sub-groups suffered the usual problem of underpowered study. For instance, 33 SCS patients had > 50% pain improvement at 6 month in comparison to 10 patients in Pain Clinic group (p 0.06) which reached almost statistical significance. At 12 month with the numbers 25 vs. 10 subjects this trend disappeared (p 0.81). Same situation was traceable with the opioid use.
13. Even with those overall mediocre results, SCS-permanent patients had statistically significantly difference in the health care utilization in comparison to PC group: no surgeries, less physical/occupational therapy and psychological sessions.
14. Reported complication rate was also higher than expected: combined superficial and deep infection rate was 14% (4.5% in the Turner et al (5)), one case of the epidural abscess (2% vs. 0.01%). This may suggest non-adherence to aseptic-antiseptic principles and may reflect other procedural imperfections.

Some of these questions can be answered by reevaluating and reanalyzing data of Turner at all work. Biopsychosocial factors that might have contributed to such low success rate as well as competence of surgeons who performed the procedures should be addressed.

In a broader concept, the fundamental question of effectiveness of SCS in a workman's compensation population should be addressed. Multiple studies reported that disability compensation is associated with worse outcomes (6,7,8). Surgical treatment of patients on workman's compensation with lumbar disc herniation showed only short-term (3 months) beneficial results and there was no advantage for surgery at 2 years (9). In the study of Turner et al (1) similar short-term benefit of the SCS was found. Patients on workers' compensation benefit less from surgical treatment and initial success tends to decrease over time. Multiple clinical, socioeconomic and personal factors were suggested that might explain this phenomenon (10-15). Moreover, a meta-analysis published in JAMA (6) showed an association on compensation status with poor outcome after surgery. This effect was significant, clinically important, and consistent. SCS is a surgical technique and therefore patients on L&I claim did not get better.

I completely agree with the committee that, intuitively, interventional procedures should be discouraged in a workman's compensation setting. Likewise, other complex and costly health interventions, such as multidisciplinary pain clinic, might not be indicated because of a non-favorable outcome. However, in general and in the context of the SCS in patients with failed back surgery syndrome, there may be a small fraction of workman's compensation patients who will respond with long-term good result. In the study of Turner et al 5 out of 51 patients (10%) met all three primary outcome criteria at 24 months follow up.

We are committed to Predict, Diagnose and Prevent Pain from becoming a disabling disease

In 2005 Health Technology Assessment in Ontario resulted in completely opposite recommendation. **“As a result of its review, OHTAC recommends: Increased access to this technology for the management of chronic intractable neuropathic pain within the context of a multi-disciplinary comprehensive pain management program”**

Since 2006 only 3 centers perform SCS in Ontario keeping with “multidisciplinary concept” and wise allocation of the resources. I attached the THA assessment and the evidence report.

I understand the State budget is overstretched by increasing health care expenditures. However, punishment of medical technology must stop. Otherwise we will quickly get back to cheap medieval remedies such as willow bark and therapeutic touch.

Conscientious utilization of technology and rigorous selection of appropriate patients performed at the setting of multidisciplinary pain management along with outcome based metrics are tools to successful pain medicine practice in general and neuromodulation practice in particular

Sincerely,

Michael Gofeld MD

Attending Physician
Department Anesthesiology and Pain Medicine
Assistant Professor University of Washington School of Medicine
Adjunct Professor of Medicine University of Toronto

References

1. Turner JA, Hollingworth W, Comstock BA, Deyo RA. Spinal cord stimulation for failed back surgery syndrome: outcomes in a workers' compensation setting. *Pain*. 2010 Jan;148(1):14-25.
2. North RB, Kidd DH, Farrokhi F, Piantadosi SA. Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: a randomized, controlled trial. *Neurosurgery* 2005;56:98-106.
3. Kumar K, Taylor RS, Jacques L, Eldabe S, Meglio M, Molet J, Thomson S, O'Callaghan J, Eisenberg E, Milbouw G, Buchser E, Fortini G, Richardson J, North RB. Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicentre randomised controlled trial in patients with failed back surgery syndrome. *Pain* 2007;132:179-88.

We are committed to Predict, Diagnose and Prevent Pain from becoming a disabling disease

4. Kumar K, Hunter G, Demeria D. Spinal cord stimulation in treatment of chronic benign pain: challenges in treatment planning and present status, a 22-year experience. *Neurosurgery*. 2006 Mar;58(3):481-96; discussion 481-96.
5. Turner JA, Loeser JD, Deyo RA, Sanders SB. Spinal cord stimulation for patients with failed back surgery syndrome or complex regional pain syndrome: a systematic review of effectiveness and complications. *Pain* 2004;108:137-47.
6. Harris I, Mulford J, Solomon M, et al. Association between compensation status and outcome after surgery: a meta-analysis. *JAMA* 2005;293:1644-52.
7. Rohling ML, Binder LM, Langhinrichsen-Rohling J. Money matters: a meta-analytic review of the association between financial compensation and the experience and treatment of chronic pain. *Health Psychol* 1995;14:537-47.
8. Binder LM, Rohling ML. Money matters: a meta-analytic review of the effects of financial incentives on recovery after closed-head injury. *Am J Psychiatry* 1996;153:7-10.
9. Atlas SJ, Tosteson TD, Blood EA, Skinner JS, Pransky GS, Weinstein JN. The impact of workers' compensation on outcomes of surgical and nonoperativetherapy for patients with a lumbar disc herniation: SPORT. *Spine (Phila Pa 1976)*. 2010 Jan 1;35(1):89-97.
10. Hagen KB, Tambs K, Bjerkedal T. A prospective cohort study of risk factors for disability retirement because of back pain in the general working population. *Spine* 2002;27:1790-6.
11. Krause N, Frank JW, Dasinger LK, et al. Determinants of duration of disability and return-to-work after work-related injury and illness: challenges for future research. *Am J Ind Med* 2001;40:464-84.
12. Turner JA, Franklin G, Turk DC. Predictors of chronic disability in injured workers: a systematic literature synthesis. *Am J Ind Med* 2000;38:707-22.
13. Dionne CE, Bourbonnais R, Fremont P, et al. A clinical return-to-work rule for patients with back pain. *CMAJ* 2005;172:1559-67.

UW Medicine
DIVISION OF
PAIN MEDICINE

We are committed to Predict, Diagnose and Prevent Pain from becoming a disabling disease

14. Puolakka K, Ylinen J, Neva MH, et al. Risk factors for back pain-related loss of working time aftersurgery for lumbar disc herniation: a 5-year follow-up study. *Eur Spine J* 2008;17:386–92.

15. Hadler NM, Carey TS, Garrett J. The influence of indemnification by workers' compensation insurance on recovery from acute backache. North Carolina back pain project. *Spine* 1995;20:2710–5.

OHTAC Recommendation

Spinal Cord Stimulation for the Management of Neuropathic Pain

March 2, 2005

OHTAC Ontario
Health Technology
Advisory Committee

Spinal Cord Stimulation

The Ontario Health Technology Advisory Committee (OHTAC) met on March 2, 2005 and reviewed the use of spinal cord stimulation for the management of neuropathic pain, following an application to OHTAC by the Toronto University Health Network (UNH).

Based on a health technology policy analysis of spinal cord stimulation completed by the Medical Advisory Secretariat (MAS), OHTAC offers the following recommendations to the Ministry of Health and Long-Term Care (MOLTC) for its consideration. These recommendations comply with the OHTAC terms of reference.

Neuropathic pain is described as burning, shooting or lancinating pain caused by damage or dysfunction to the nervous system (Mersky, 1994). It is pain that is difficult to manage with other treatment modalities, becoming a chronic pain condition if symptoms persist beyond 6 months or exceed the expected time for tissue healing (The Canadian Pain Society, 1997).

Chronic pain is an emotional, social and economic burden for those experiencing it. Depression, reduction in quality of life, absenteeism from work and a lower household income correlate positively with chronic pain (Meana, 2004; Moulin, 2002; Currie, 2004).

The prevalence of depression among Canadians with chronic pain is twice that compared with those without chronic pain (Meana, 2004).

Spinal Cord Stimulation

On average there are 9.3 working days missed by Canadians due to chronic pain and 16 days for those with severe pain (Moulin, 2002).

Furthermore, there is a reported significant reduction in the income of people with chronic pain compared with those without chronic pain (Moulin, 2002).

The estimated prevalence of neuropathic pain is 1.5% of the US population (Bennett, 1998) and up to 10% of all chronic pain is neuropathic pain (personal communication with Clinical Expert).

Current standard treatments for neuropathic pain fall into three categories: pharmacological, non-pharmacological and surgical. However, approximately 10% of people will develop intractable pain defined as failure to obtain pain relief from standard treatments despite reasonable efforts. . This cohort is the target population for spinal cord stimulation.

Many different medical conditions elicit neuropathic pain. However, three medical conditions including leg and back pain after back surgery (failed back surgery syndrome), limb pain after injury (complex regional pain syndrome type I) and pain after herpes zoster infection (post herpetic neuralgia) are the most common neuropathic pain conditions treated with spinal cord stimulation.

Developed in 1960, spinal cord stimulation is a form of neuromodulation, a process that alters the transmission of nerve impulses to the brain. The

Spinal Cord Stimulation

most common indication for its use is to manage chronic intractable neuropathic pain.

The spinal cord stimulator device consists of a battery, an extension cable and a thin wire with electrodes on it called a lead. The battery is implanted under the skin in the abdomen. The extension cable runs underneath the skin and connects the battery to the lead, which is inserted into the epidural space and positioned on the posterior aspect of the spinal cord. The battery generates low voltage electrical pulses, which the electrodes conduct to the spinal cord. This action blocks the transmission of pain to the brain and initiates a paresthesia or tingling feeling over the painful body part, which masks the pain. Four spinal cord stimulator devices are licensed and approved by Health Canada for the management of chronic intractable pain.

A neuropsychologist assesses potential spinal cord stimulation candidates for cognitive functioning and psychological comorbidities. If the assessment is favorable candidates then undergo a test stimulation period.

During test stimulation, the physician inserts a lead into the epidural space and connects it to an external battery. The patient lives with the device for up to 1 week during which time he/she monitors their level of pain. People experiencing at least a 50% decrease in pain are eligible for permanent implantation of the spinal cord stimulator device.

Spinal Cord Stimulation

After permanent implantation of the device, the patient requires on-going monitoring by a neurosurgeon or pain specialist. Up to 6 clinic visits may be required in the first year after implantation to monitor the patient and refine the stimulator parameter settings.

Technical failures and procedural complications can occur. Lead migration (movement of the lead off its target spot in the epidural space) is the most common technical failure and occurs at a rate of 13.2% (Cameron, 2004). Local wound infection occurs at a rate of 3.4% most often at the battery implantation site. (Cameron, 2004).

Six health technology systematic reviews have been completed since 2000. All concluded that spinal cords stimulation is an effective pain therapy. However, there is variation among these reviews regarding the quality of evidence.

The Medical Advisory Secretariat evaluated the current literature to determine the effectiveness of spinal cord stimulation to manage chronic intractable neuropathic pain. Results indicated that spinal cord stimulation significantly reduced the level of pain in people with chronic neuropathic pain conditions. Likewise, there was supportive evidence for improvement in functional status and quality of life in people treated with spinal cord stimulation.

Spinal Cord Stimulation

An estimated 5600 people per year will develop neuropathic pain from failed back surgery syndrome, complex regional pain syndrome type I and post herpetic neuralgia. Approximately 10 per cent will develop intractable pain. An estimated 70% will proceed to test stimulation after psychological testing of which on average 84% or 330 people/year will be eligible for permanent implantation. Currently Ontario does 30-50 spinal cord stimulation procedures annually.

While eight hospitals in Ontario have implanted spinal cord stimulators, one centre is currently the most active, implanting approximately 30 people/year (data from London Health Sciences Centre medical records department). An Eastern Ontario hospital stopped implanting SCS approximately 1.5 years ago reportedly due to lack of infrastructure support and funding for the program. Likewise, a major Toronto SCS referral centre closed as of January 2005, for similar reasons. Five other centres do a minimum number of implants of SCS.

A meta-analysis of 14 cost-effectiveness studies of SCS confirmed long-term cost-savings associated with this pain therapy (Taylor, 2004). A Canadian economic analysis of SCS compared with conventional pain therapy reported cost-savings of approximately \$11,000 over a five-year post-operative period with the breakeven point at 2.5 years (Kumar, 2002).

Spinal Cord Stimulation

The Medical Advisory Secretariat determined the Ontario specific costs of spinal cord stimulation. The total cost, including hospital costs, professional costs and device costs, is estimated at \$20,000 per procedure.

As a result of its review, OHTAC recommends:

Increased access to this technology for the management of chronic intractable neuropathic pain within the context of a multi-disciplinary comprehensive pain management program.

Spinal Cord Stimulation for Neuropathic Pain

An Evidence-Based Analysis

March 2005



Medical Advisory Secretariat
Ministry of Health and Long-Term Care

Suggested Citation

This report should be cited as follows:

Medical Advisory Secretariat. Spinal cord stimulation for neuropathic pain: an evidence-based analysis. *Ontario Health Technology Assessment Series* 2005;5(4).

Permission Requests

All inquiries regarding permission to reproduce any content in the *Ontario Health Technology Assessment Series* should be directed to MASinfo.moh@ontario.ca.

How to Obtain Issues in the Ontario Health Technology Assessment Series

All reports in the *Ontario Health Technology Assessment Series* are freely available in PDF format at the following URL: www.health.gov.on.ca/ohtas.

Print copies can be obtained by contacting MASinfo.moh@ontario.ca.

Conflict of Interest Statement

All analyses in the Ontario Health Technology Assessment Series are impartial and subject to a systematic evidence-based assessment process. There are no competing interests or conflicts of interest to declare.

Peer Review

All Medical Advisory Secretariat analyses are subject to external expert peer review. Additionally, the public consultation process is also available to individuals wishing to comment on an analysis prior to finalization. For more information, please visit http://www.health.gov.on.ca/english/providers/program/ohtac/public_engage_overview.html.

Contact Information

The Medical Advisory Secretariat
Ministry of Health and Long-Term Care
20 Dundas Street West, 10th floor
Toronto, Ontario
CANADA
M5G 2N6
Email: MASinfo.moh@ontario.ca
Telephone: 416-314-1092

ISSN 1915-7398 (Online)
ISBN 1-4249-0129-4 (PDF)

About the Medical Advisory Secretariat

The Medical Advisory Secretariat is part of the Ontario Ministry of Health and Long-Term Care. The mandate of the Medical Advisory Secretariat is to provide evidence-based policy advice on the coordinated uptake of health services and new health technologies in Ontario to the Ministry of Health and Long-Term Care and to the healthcare system. The aim is to ensure that residents of Ontario have access to the best available new health technologies that will improve patient outcomes.

The Medical Advisory Secretariat also provides a secretariat function and evidence-based health technology policy analysis for review by the Ontario Health Technology Advisory Committee (OHTAC).

The Medical Advisory Secretariat conducts systematic reviews of scientific evidence and consultations with experts in the health care services community to produce the *Ontario Health Technology Assessment Series*.

About the Ontario Health Technology Assessment Series

To conduct its comprehensive analyses, the Medical Advisory Secretariat systematically reviews available scientific literature, collaborates with partners across relevant government branches, and consults with clinical and other external experts and manufacturers, and solicits any necessary advice to gather information. The Medical Advisory Secretariat makes every effort to ensure that all relevant research, nationally and internationally, is included in the systematic literature reviews conducted.

The information gathered is the foundation of the evidence to determine if a technology is effective and safe for use in a particular clinical population or setting. Information is collected to understand how a new technology fits within current practice and treatment alternatives. Details of the technology's diffusion into current practice and input from practicing medical experts and industry add important information to the review of the provision and delivery of the health technology in Ontario. Information concerning the health benefits; economic and human resources; and ethical, regulatory, social and legal issues relating to the technology assist policy makers to make timely and relevant decisions to optimize patient outcomes.

If you are aware of any current additional evidence to inform an existing evidence-based analysis, please contact the Medical Advisory Secretariat: MASinfo.moh@ontario.ca. The public consultation process is also available to individuals wishing to comment on an analysis prior to publication. For more information, please visit http://www.health.gov.on.ca/english/providers/program/ohtac/public_engage_overview.html.

Disclaimer

This evidence-based analysis was prepared by the Medical Advisory Secretariat, Ontario Ministry of Health and Long-Term Care, for the Ontario Health Technology Advisory Committee and developed from analysis, interpretation, and comparison of scientific research and/or technology assessments conducted by other organizations. It also incorporates, when available, Ontario data, and information provided by experts and applicants to the Medical Advisory Secretariat to inform the analysis. While every effort has been made to reflect all scientific research available, this document may not fully do so. Additionally, other relevant scientific findings may have been reported since completion of the review. This evidence-based analysis is current to the date of publication. This analysis may be superseded by an updated publication on the same topic. Please check the Medical Advisory Secretariat Website for a list of all evidence-based analyses: <http://www.health.gov.on.ca/ohtas>.

Table of Contents

Table of Contents	4
Abbreviations	9
Executive Summary	10
Objective	10
Clinical Need	10
The Technology	10
Review Strategy	11
Summary of Findings	11
Conclusions	11
Objective	12
Background	12
Clinical Need: Target Population and Condition	12
Indications for Spinal Cord Stimulation	13
Existing Treatments Other Than Technology Being Reviewed	14
Pharmacological Therapy for Neuropathic Pain	14
Anticonvulsants and Antidepressants	15
Nonpharmacological Interventions	19
Surgical Treatments	20
Measuring Pain	20

New Technology Being Reviewed: Spinal Cord Stimulation	20
The SCS Device	20
Psychological Evaluation	22
SCS Test Stimulation Phase	22
Permanent Implantation Phase	23
Patient Follow-up	23
Efficacy of Spinal Cord Stimulation	23
Complications Associated With Spinal Cord Stimulation	24
Regulatory Status	26
Literature Review on Effectiveness	28
Objective	28
Questions Asked	28
Outcome Measures	28
Methods	28
Search Strategy	28
Inclusion Criteria	29
Exclusion Criteria	29
Intervention	29
Outcomes of Interest	29
Assessment of Methodological Quality of Randomized Controlled Trials	29

Results of Literature Review	30
Health Technology Assessments	31
Technical Failures and Procedural Complications Reported in the Health Technology Assessments: 40	
Summary of Existing Health Technology Assessments	42
Medical Advisory Secretariat Systematic Review	42
Quality of Evidence	42
Outcome Measures	45
Population Characteristics	46
Treatment Characteristics	47
Results	48
VAS Pain Scores	48
Other Pain Measurements	49
Functional Status	50
Quality of Life	51
Numbers Needed to Treat	51
Technical Failures and Procedural Complications	53
Summary of Findings of Medical Advisory Secretariat Literature Review	55
Economic Analysis	56
Ontario-Based Economic Analysis	56
Hospitalization Costs	56
Device Costs	57

Professional Costs	57
Cost-Effectiveness	59
Existing Guidelines for Use of Technology	59
European Task Force	59
American Society of Anesthesiologists	59
Consensus Statement	60
Canadian Pain Society	60
Policy Considerations	60
Demographics	60
Estimate of Target Population	61
Number of Spinal Cord Stimulation Devices Implanted in People in Ontario	61
Diffusion of Technology	61
Number of Sites Offering Spinal Cord Stimulation Therapy	61
Health System Considerations	61
Infrastructure	61
Equipment	62
Conclusions	62
Glossary	63
Appendices	65
Appendix 1: Literature Search Strategy – Spinal Cord Stimulation	65

Appendix 2: College of Physicians and Surgeons of Ontario: Interventions for the Treatment of Neuropathic Pain, 2000	67
Appendix 3: Study Characteristics	68
Appendix 4: ICD-10 and CCI Codes	72
References	73

Abbreviations

CI	Confidence interval
CPSO	College of Physicians and Surgeons of Ontario
CRPS	Complex regional pain syndrome
FBSS	Failed back surgery syndrome
IPG	Implantable pulse generator
MPQ	McGill Pain Questionnaire
NNT	Number needed to treat
PHN	Postherpetic neuralgia
QOL	Quality of Life
QALY	Quality-adjusted Life-year
RCT	Randomized controlled trial
SCS	Spinal cord stimulation
SD	Standard deviation
SSRI	Selective serotonin reuptake inhibitor
TCA	Tricyclic antidepressant
TENS	Transcutaneous electrical nerve stimulation
VAS	Visual analogue scale

Executive Summary

Objective

The objective of this health technology policy assessment was to determine the effectiveness of spinal cord stimulation (SCS) to manage chronic intractable neuropathic pain and to evaluate the adverse events and Ontario-specific economic profile of this technology.

Clinical Need

SCS is a reversible pain therapy that uses low-voltage electrical pulses to manage chronic, intractable neuropathic pain of the trunk or limbs. Neuropathic pain begins or is caused by damage or dysfunction to the nervous system and can be difficult to manage.

The prevalence of neuropathic pain has been estimated at about 1.5% of the population in the United States and 1% of the population in the United Kingdom. These prevalence rates are generalizable to Canada.

Neuropathic pain is extremely difficult to manage. People with symptoms that persist for at least 6 months or who have symptoms that last longer than expected for tissue healing or resolution of an underlying disease are considered to have chronic pain. Chronic pain is an emotional, social, and economic burden for those living with it. Depression, reduced quality of life (QOL), absenteeism from work, and a lower household income are positively correlated with chronic pain.

Although the actual number is unknown, a proportion of people with chronic neuropathic pain fail to obtain pain relief from pharmacological therapies despite adequate and reasonable efforts to use them. These people are said to have intractable neuropathic pain, and they are the target population for SCS.

The most common indication for SCS in North America is chronic intractable neuropathic pain due to failed back surgery syndrome (FBSS), a term that describes persistent leg or back and leg pain in patients who have had back or spine surgery. Neuropathic pain due to complex regional pain syndrome (CRPS), which can develop in the distal aspect of a limb a minor injury, is another common indication. To a lesser extent, chronic intractable pain of postherpetic neuralgia, which is a persistent burning pain and hyperesthesia along the distribution of a cutaneous nerve after an attack of herpes zoster, is also managed with SCS.

For each condition, SCS is considered as a pain management therapy only after conventional pain therapies, including pharmacological, nonpharmacological, and surgical treatments, if applicable, have been attempted and have failed.

The Technology

The SCS technology consists of 3 implantable components: a pulse generator, an extension cable, and a lead (a small wire). The pulse generator is the power source for the spinal cord stimulator. It generates low-voltage electrical pulses. The extension cable connects the pulse generator to the lead. The lead is a small, insulated wire that has a set of electrodes at one end. The lead is placed into the epidural space on the posterior aspect of the spinal cord, and the electrodes are positioned at the level of the nerve roots

innervating the painful area. An electrical current from the electrodes induces a paresthesia, or a tingling sensation that masks the pain.

Before SCS is initiated, candidates must have psychological testing to rule out major psychological illness, drug habituation, and issues of secondary gain that can negatively influence the success of the therapy. Successful candidates will have a SCS test stimulation period (trial period) to assess their responsiveness to SCS. The test stimulation takes about 1 week to complete, and candidates who obtain at least 50% pain relief during this period are deemed suitable to receive a permanent implantation of a spinal cord stimulator

Review Strategy

The Medical Advisory Secretariat (MAS) reviewed all published health technology assessments of spinal cord stimulation. Following this, a literature search was conducted from 2000 to January, 2005 and a systematic review of the literature was completed. The primary outcome for the systematic review was pain relief. Secondary outcomes included functional status and quality of life. After applying the predetermined inclusion and exclusion criteria, 2 randomized controlled trials (MAS level 2 evidence), and 2 prospective non-randomized controlled trials with a before-and-after-treatment study design (MAS level 3a evidence) were retrieved and reviewed.

Summary of Findings

The authors of 6 health technology assessments concluded that evidence exists to support the effectiveness of SCS to decrease pain in various neuropathic pain syndromes. However, the quality of this evidence varied among reports from weak to moderate.

The systematic review completed by MAS found high quality level 2 evidence that SCS decreases pain and level 3a evidence that it improves functional status and quality of life in some people with neuropathic pain conditions. The rate of technical failures was approximately 11%, which included electrode lead migration and/or malposition. Procedural complications included infection and dural puncture; each occurred at a rate of 1.2%.

Conclusions

SCS may be considered for patients with chronic, neuropathic pain for whom standard pain treatments have failed and when there is no indication for surgical intervention to treat the underlying condition.

Objective

The purpose of this health technology assessment was to determine the effectiveness of spinal cord stimulation (SCS) as a pain management therapy for chronic, intractable neuropathic pain and to evaluate the adverse events and Ontario-specific economic profile of this technology.

Background

Clinical Need: Target Population and Condition

SCS is a form of neuromodulation used to manage chronic, intractable neuropathic pain of the trunk and limbs. (1;2) Pain is defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.” (3) Neuropathic pain is a specific type of pain that is characterized by unique symptoms and initiated or caused by damage or dysfunction to the nervous system. (3-5) Neuropathic pain is often described as shooting, burning, or lancinating. (4;6-8). In some cases of neuropathic pain, actual nerve damage is not always apparent, despite symptoms indicating neurological dysfunction. (4;9)

The prevalence of neuropathic pain has been estimated at about 1.5% of the population in the United States and 1% of the population in the United Kingdom. (4;10) Although the actual number is unknown, a proportion of people with chronic neuropathic pain fail to obtain pain relief from pharmacological therapies despite adequate and reasonable efforts to use them. These people are said to have intractable (11) neuropathic pain, and they are the target population for SCS.

Neuropathic pain is extremely difficult to manage. People with symptoms that persist for at least 6 months or who have symptoms that last longer than expected for tissue healing or resolution of an underlying disease are considered to have chronic pain. (4;12;13) Chronic pain is an emotional, social, and economic burden for those living with it. Depression, reduced quality of life (QOL), absenteeism from work, and a lower household income are positively correlated with chronic pain. (13-16)

Meana et al. (16) reported that the prevalence of depression among Canadians with chronic pain was twice that experienced by those without chronic pain. It was twice as high among people younger than 65 years with chronic pain compared with people aged 65 years and older. Currie and Wang (15) reported a more than 6-fold (6.2; 95% confidence interval [CI], 5.2–7.6) increase in depression in Canadians with chronic back pain compared to those without. Moulin et al. (13) found that Canadians missed, on average, 9.3 working days (95% CI, 4.7–13.7) due to chronic pain; 16 days (95% CI, 5.1–26.9) if the pain was severe. Furthermore, people with chronic pain had significantly lower incomes compared with those without chronic pain. (13) Regarding QOL, Moulin et al. (13) found that 49% of Canadians reported great difficulty attending social and family events, 61% were unable to participate in their usual recreational activities, and 58% were unable to carry out their daily activities at home.

Neuropathic pain is associated with medical conditions that are etiologically heterogeneous. Some of these conditions are listed in Table 1. (4) However, each medical condition shares common symptoms associated with neuropathic pain, such as no visible injury, a paradoxical combination of sensory loss and hypersensitivity in the painful area, paroxysms of pain, and a gradual increase of pain following repetitive stimulation. (17) Because of this, it has been proposed that neuropathic pain may be explained by the same or similar mechanisms despite the medical condition. (17)

Table 1: Medical Conditions Associated With Neuropathic Pain

Medical Condition
Failed back surgery syndrome
Complex regional pain syndrome, Type I and II
Postherpetic neuralgia
Trigeminal neuralgia
HIV-associated pain
Pain after amputation
Pain after stroke
Multiple sclerosis
Cancer-related pain
Diabetic neuropathy
Spinal cord injury

Indications for Spinal Cord Stimulation

Of the medical conditions listed in Table 1, neuropathic pain from failed back surgery syndrome (FBSS) is the most common indication for SCS in North America. Neuropathic pain due to complex regional pain syndrome (CRPS) is another common indication. To a lesser extent, neuropathic pain due to postherpetic neuralgia, persistent burning pain and hyperesthesia along the distribution of a cutaneous nerve which can occur after an attack of herpes zoster, is also managed with SCS. For each condition, SCS is considered only after conventional pain therapies, including pharmacological, nonpharmacological, and surgical treatments, if applicable, have been tried and have failed.

Less commonly in North America, SCS has been used to manage ischemic pain of peripheral vascular disease and angina.

Failed Back Surgery Syndrome

FBSS is a generalized term used to describe persistent low back pain and leg pain in patients who have not had a successful result with back or spine surgery. (18;19) Those people whose leg pain is greater than their back pain are suitable candidates for SCS. About 15% to 40% of patients will have chronic back and limb pain after undergoing lumbar surgery. (20)

Complex Regional Pain Syndrome

CRPS is a neuropathic pain condition that develops in the distal aspect of a limb, usually after an injury, which may be even minor in nature. However, 6% to 10% of the cases are initiated spontaneously with no precipitating injury. (5;5;21) There are 2 types of the syndrome: I and II. Although the salient criterion differentiating them is a definable nerve injury for Type II, the symptoms of both types are the same. The pathophysiology of this pain syndrome is not well understood; therefore, treatment is focused on managing the symptoms. (22). Diagnostic criteria include these (3;22):

- An initiating injury (for example a minor fracture) or cause of immobilization (for example, a stroke) for Type I; and a known nerve injury for Type II
- Spontaneous pain or evoked pain (allodynia /hyperalgesia) that is not limited to the area of a single peripheral nerve and is disproportionate to the initiating event
- Evidence (past or present) of edema (swelling), skin blood flow abnormality, or abnormal sudomotor (sweat gland) activity in the region of the pain since the initiating event
- Exclusion of a medical condition that would explain the pain and dysfunction

Treatment for CRPS is focused on restoring functional capacity through physiotherapy and/or occupational therapy, improving QOL by fostering coping skills through psychological therapy, and managing pain to provide relief and encourage rehabilitation. It has been suggested that if a patient has failed all conservative pain management techniques and is not progressing in rehabilitation by 12 to 16 weeks, then it is reasonable to consider SCS. (5;23)

CRPS most commonly affects people aged 36 to 42 years and is diagnosed more often in women than in men. The upper extremity is involved 44% to 61% of the time, and the lower extremity is affected 39% to 61% of the time. It is estimated that it occurs at a rate of 16% after a fracture, 10% to 29% after a strain or sprain, 3% to 24% after surgery, and 8% after a crash injury. (5;23) The prevalence of CRPS Type I is estimated at 20.57 cases per 100,000 people. The incidence rate is 5.46 per 100,00 person-years at risk. (24)

Postherpetic Neuralgia

Post herpetic neuralgia is persistent pain, which can occur after an attack of the herpes zoster virus. Herpes zoster, also known as shingles, is caused by the reactivation of the varicella zoster virus that has lain latent since primary infection. Antivirals can reduce the pain if they are given early in the course of the illness. (25) Several drugs, including gabapentin, tricyclic antidepressants and opioids, are used to manage chronic pain due to postherpetic neuralgia.

The lifetime risk of herpes zoster is 10% to 30%, and the incidence increases with age. About 20% of those older than 50 years will experience pain (post herpetic neuralgia) 6 months after the onset of a herpes zoster rash. (25). More than 60% of herpes zoster cases in Canada are in adults older than 45 years, and the highest rate is in adults aged 65 years and older. Brisson et al. (26) estimated the incidence of herpes zoster in Canada using physicians' consultation rates for herpes zoster infections. In adults 45 to 64 years of age, the mean consultation rate was 423 per 100,000 population years, and for adults aged 65 years and older, the rate was 812 per 100,000 population years.

Existing Treatments Other Than Technology Being Reviewed

The goal of pain management is to make pain tolerable and to improve functionality. (27) Pain management includes multiple therapies categorized into pharmacological, nonpharmacological, and surgical. (28) Generally, a treatment progresses from therapies that are less invasive and have minor side effects to those that are more invasive. (29) Often, multiple medications for pain relief will be combined and used with nonpharmacological therapies. (27) The drug therapies for neuropathic pain recommended by the council of the College of Physicians and Surgeons of Ontario (CPSO) and common nonpharmacological therapies are examined in this review.

Pharmacological Therapy for Neuropathic Pain

The CPSO (27) ratified evidence-based recommendations for pharmacological treatment of neuropathic pain on November 3, 2000. (See Appendix 2.) These recommendations included anticonvulsants, antidepressants, oral drugs with local anesthetic type properties, opioids, topical capsaicin, and intravenous regional sympathetic blocks.

The CPSO's recommendations recognized that neuropathic pain usually requires multidrug therapy and that therapies should be started sequentially not simultaneously. The guidelines suggest that first-line pharmacotherapy may include tricyclic antidepressants and/or anticonvulsants as adjuvant medications. The recommendations also note that opioids may be used in selected patients, but not as a first-line therapy. (27)

Of the pain medications recommended in the CPSO guidelines, only the opioid analgesics and capsaicin are approved as pain treatments by the Health Protection Branch of Health Canada. Anticonvulsants, antidepressants, and oral drugs with local anesthetic properties are considered adjuvant pain therapies. Adjuvant pain therapies are those with a primary treatment indication other than pain management.

Anticonvulsants and Antidepressants

The CPSO (27) has determined that strong evidence from a least 1 systematic review of multiple well-designed randomized controlled trials (RCTs) (CPSO level 1 evidence)(See Appendix 2) exists for anticonvulsants and antidepressants in different neuropathic syndromes (Appendix 2). The mechanism by which anticonvulsants and antidepressants control pain is unknown.(30)

Anticonvulsants

Gabapentin, carbamazepine, clonazepam, sodium valproate, and phenytoin have been evaluated as treatments neuropathic pain. (8) Of these, gabapentin was ranked as a first-line treatment, and carbamazepine as a second-line treatment, by an expert panel at the fourth international conference on the mechanisms and treatment of neuropathic pain. (9) In a systematic review of anticonvulsant drugs for acute and chronic pain, Wiffen et al. (8) estimated that 66% (95% CI 61%–71%) of patients who receive either gabapentin or carbamazepine for neuropathic pain will obtain good pain relief; however, they found no clear therapeutic advantage of gabapentin over carbamazepine.

How gabapentin works to relieve pain has not been established. (31) Common adverse effects of gabapentin include dizziness and, in the elderly, balance and gait problems, and cognitive impairment. Adjusting the dose may be required. (32) Gabapentin has an excellent tolerability and safety profile and a lack of reported drug interactions. (9) It is eliminated solely by renal excretion as an unchanged drug. People with impaired renal function need a lower dose. It is not metabolized in humans; therefore, liver impairment is not an issue. (31)

It would take about 3 to 8 weeks for titration, plus 1 to 2 weeks at a maximum tolerated dose, to determine if adequate pain relief can be obtained with gabapentin.

Carbamazepine is recommended for patients who have not responded to gabapentin and is the drug of choice for trigeminal neuralgia. (9) Common adverse effects of carbamazepine are drowsiness, headache, unsteadiness, diplopia, dizziness, nausea, vomiting, and allergic skin reactions. These often dissipate after the initial phase of therapy. More serious adverse reactions include hematologic, hepatic, cardiovascular, and dermatologic reactions, which require discontinuation of therapy. (32)

Gabapentin is approved in Canada as an anticonvulsant. The United States Food and Drug Administration approved it in May 2002 to treat postherpetic neuralgia. (31) Carbamazepine is also approved in Canada

as an anticonvulsant.(32) The United States Food and Drug Administration has approved carbamazepine for the treatment of trigeminal neuralgia. (9)

Table 2 shows the number needed to treat (NNT) for gabapentin and carbamazepine to obtain 1 patient with at least 50% pain relief compared with a placebo. (8)

Table 2: Effectiveness of Anticonvulsants: Number Needed To Treat

Diagnosis	Drug	Number of Studies	N	Number Needed To Treat (95% Confidence Interval)
Neuropathic pain	Gabapentin*	2	380	3.7 (2.6–4.9)
	Carbamazepine†	5	537	2.5 (2.0–3.4)

*This includes diabetic neuropathy and postherpetic neuralgia.

†This includes diabetic neuropathy, trigeminal neuralgia, and central stroke pain.

Antidepressants

Two types of antidepressants have been used to treat neuropathic pain: tricyclic antidepressants, which include amitriptyline, clomipramine, desipramine, imipramine and maprotiline; and selective serotonin reuptake inhibitors, which include citalopram, fluoxetine, paroxetine, and tramadol. The usefulness of tricyclic antidepressants is often limited by their adverse effects, which include sedation, blurred vision, dry mouth, constipation, postural hypotension, weight gain, loss of balance, and cognitive impairment in the elderly. (9) They should be used cautiously with patients who have a history of cardiovascular disease, glaucoma, urinary retention, or autonomic neuropathy.

It takes about 6 to 8 weeks, with at least 1 to 2 weeks at the maximum tolerated dosage, to determine if adequate pain relief can be obtained with an antidepressant. (9)

Amitriptyline, clomipramine, desipramine, imipramine, citalopram, fluoxetine, and paroxetine are available in Canada, but Health Canada has not approved these to treat neuropathic pain. (32)

Table 3 shows the NNT for tricyclic antidepressants and selective serotonin reuptake inhibitors to achieve at least 50% pain relief in various neuropathic pain conditions compared with a placebo. (17)

Table 3: Effectiveness of Antidepressants: Number Needed To Treat

Diagnosis	Type of Antidepressant	Number of Studies	N	Number Needed To Treat (95% Confidence Interval)
Painful neuropathy	TCA*	12	276	2.4 (2.0–3.0)
	SSRI*	3	83	6.7 (3.4–435)
Postherpetic neuralgia	TCA	3	77	2.3 (1.7–3.3)
	SSRI	NR*	NR	NR
Peripheral nerve injury	TCA	1	15	2.5 (1.4–10.6)
	SSRI	NR	NR	NR

*TCA indicates tricyclic antidepressant; SSRI, selective serotonin reuptake inhibitor; NR, not reported.

Drugs with Local Anesthetic Type properties

The CPSO (27) has determined that strong evidence from at least 1 properly designed randomized controlled trial (RCT) of appropriate size (CPSO level 2 evidence)(See Appendix 2) exists for oral drugs with local anesthetic type properties in different neuropathic syndromes. Mexiletine is a Class I, type 1B antiarrhythmic and a drug with local anesthetic-type properties. (7) It is approved in Canada as an antiarrhythmic. (32)

Table 4 shows the NNT for mexiletine at 625 mg per day to obtain 50% pain relief in painful neuropathy compared with a placebo. (17)

Table 4: Effectiveness of Mexiletine: Number Needed To Treat

Diagnosis	Drug	Number of Studies	N	Number Needed To Treat (95 %confidence interval)
Painful neuropathy	Mexiletine	1	126	10 (3-∞)

Opioid therapy

The CPSO (27) has determined that strong evidence from at least 1 properly designed RCT of appropriate size (CPSO level 2 evidence) exists for the use of opioids for postherpetic neuralgia. Level 5 evidence, defined as the opinions of respected authorities, based on clinical evidence, descriptive studies, or on reports of an expert committee; exists for the use of opioids for trigeminal neuralgia (see Appendix 2).

The CPSO's recommendations include managing neuropathic pain with an opioid in accordance with the following guidelines:

- An attempt to identify probable pain mechanism is undertaken by the clinician.
- Caution, but not contraindication, in patients whose pain is due primarily to psychological factors.
- Awareness of risk factors for the development of dependence on prescribed opioids.
- In most cases an adequate trial of a nonopioid and adjuvant analgesics should be done first.
- Avoid short-acting opioids such as meperidine and anileridine.

The CPSO also recommends that opioid therapy for neuropathic pain should be initiated at a relatively low dose and titrated to the patient's reports of pain relief and adverse effects. The optimal dose is when the patient reports satisfactory pain relief and no adverse effects. It has been suggested that titration of sustained-release strong opioids should be introduced over 3 to 4 months. (33)

Common adverse effects of opioids are constipation, sedation, and nausea. Cognitive impairment and problems with mobility can also occur. Abruptly discontinuing opioid therapy may cause symptoms of withdrawal. It would take about 4 to 6 weeks to determine if adequate pain relief can be obtained with an opioid. (9)

Codeine, morphine, hydromorphone, oxycodone, and fentanyl are approved analgesics by Health Canada. (32)

The NNT for opioids to obtain at least a 50% reduction in neuropathic pain is about 3. (12)

Topical Capsaicin

The CPSO (27) has determined that strong evidence from at least 1 properly designed RCT of appropriate size (CPSO level 2 evidence)(see Appendix 2) exists for the use of topical capsaicin in diabetic neuropathy and postherpetic neuralgia.

Health Canada has approved capsaicin as a topical analgesic (32).

Table 5 shows the NNT for 0.075% topical capsaicin to achieve at least 50% reduction in pain after 8 weeks of use compared with a placebo. (34)

Table 5: Effectiveness of Topical Capsaicin: Number Needed to Treat

Diagnosis	Drug	Number Needed To Treat (95% confidence interval)
Neuropathic pain	Topical capsaicin (0.075%)	5.7 (4.0–10)

Intravenous Regional Sympathetic Blocks

The CPSO (27) has determined that evidence from well-designed trials without randomization, single group pre-post, cohort, time series or matched case-controlled studies (CPSO level 3) (see Appendix 2) exists for the use of intravenous regional sympathetic blocks for reflex sympathetic dystrophy (CRPS, Type I). However, the CPSO does not recommend the use of intravenous regional sympathetic blocks for reflex sympathetic dystrophy.

Nonpharmacological Interventions

Nonpharmacological interventions may include physiotherapy, transcutaneous electrical nerve stimulation (TENS), psychological counseling, or acupuncture. Each of these therapies will be briefly described; however, it is beyond the scope of this health technology assessment to complete a full review of the effectiveness of each nonpharmacological therapy.

Physiotherapy and Exercise

Physiotherapy and exercise are used to improve functional status and minimize functional disability of patients with chronic pain. A systematic review by White et al. (35) did not find evidence to support the ability of an exercise program to improve the functional ability of people with peripheral neuropathy. However, van Tulder et al. (36) concluded that there is strong evidence that exercise and conventional physiotherapy are equally effective at improving pain and functional status in people with chronic low back pain (including patients with nerve root pain and sciatica).

Psychologically Based Pain Therapies

The purpose of psychologically based pain therapies is to restore function and psychological integrity despite continuing pain. Various psychological interventions are used with the goal of improving activity level and reducing maladaptive pain behaviours and drug use. (37)

Transcutaneous Electrical Nerve Stimulation

TENS is a noninvasive therapy that is used to relieve pain by electrically stimulating peripheral nerves through electrodes placed on the skin's surface. (38) Carroll et al. (39) did a systematic review of TENS for chronic pain and concluded it was not possible to provide evidence-based recommendations for its use to manage chronic pain because of the poor quality of the studies. A meta-analysis by Brosseau et al., (40) found that TENS therapy did not significantly relieve pain in people with chronic low back pain.

Acupuncture

In 1998 to 1999, 1% to 2% of Canadians reported receiving acupuncture treatments. (38) Acupuncture involves inserting a needle into a specific site on the body to relieve symptoms of a disease or medical condition. The Alberta Heritage Foundation for Medical Research (38) determined that the evidence on the effectiveness of acupuncture to treat back or chronic pain was inconclusive. Similarly, Linde et al. (41) concluded that the evidence to support the effectiveness of acupuncture to treat chronic back pain was inconclusive.

Surgical Treatments

Reoperation for failed back surgery syndrome

FBSS refers to persistent low back pain and leg pain after lumbar spine surgery. (18;19) Spincemaille et al. (42) have suggested that the population with FBSS can be divided into those with back pain, those with leg pain, and those with back and leg pain. The last 2 groups are classified as persistent neuropathic limb pain secondary to surgery. An estimated 30% to 50% of patients benefit from a second surgical procedure. (43) It has been suggested (5) that reliable indicators for surgery may include recurrent disc herniation or disc herniation de novo with evidence of neural compression on objective imaging studies and physical examination.

Neuroablative Techniques

Many neuropathic pain syndromes are thought to be due to sympathetically maintained pain. Sympathetically maintained pain is defined as pain maintained by sympathetic efferent innervation or by circulating catecholamines. (28) This has led to using therapies that temporarily or permanently interrupt the sympathetic nervous system. Temporary interruption can be performed through injections of alcohol, phenol, or local anesthetics. Permanent interruption can be done either chemically or surgically.

Mailis and Furlan (28) reviewed the effects of chemical and surgical sympathectomies, the surgical interruption of a pathway in the sympathetic nervous system, on neuropathic pain and concluded that both interventions are based on poor-quality evidence, uncontrolled studies, and personal experience. Importantly, the complications of these procedures were considerable and included worsening pain, new pain and abnormal forms of sweating. (28)

Measuring Pain

Valid and reliable measures of pain intensity include the visual analogue scale (VAS) for pain and the McGill Pain Questionnaire (MPQ). A VAS has a 10 cm horizontal or vertical line with a label of “no pain” at one end and “worst pain ever” at the other. (44) The MPQ provides information on the quality and intensity of the pain. (45;46) Farrar et al. (47) determined that a reduction of 2 points, or about 30% on an 11-point pain intensity numeric rating scale, represents a clinically important difference. Collins et al. (48) determined that a VAS score over 3.0 cm would be comparable to moderate pain on a 4-point categorical scale; 5.4 cm would be comparable to severe pain.

New Technology Being Reviewed: Spinal Cord Stimulation

The SCS Device

SCS was first used in 1967 and is a reversible method of managing chronic intractable neuropathic pain of the trunk or limbs. (29;49;50) Pain control with SCS is achieved by the production of an electrical field over segments of the spinal cord that are presumed to be involved in initiating the pain. (29;51) SCS blocks neuropathic pain but not nociceptive pain. (29) Nociceptive pain occurs from the irritation of

specialized pain receptors in tissues such as the skin, bones, joints, and viscera and often indicates ongoing tissue damage. (12) Examples of nociceptive pain include pain from a burn and pain due to osteoarthritis.

The precise mechanism of action of SCS is not known; (1) however, it is thought that it modulates the perception of pain by electrically stimulating the large-diameter afferent nerve fibers in the dorsal (toward the back) columns of the spinal cord. (29) This action creates a tingling feeling called paresthesia and at the same time inhibits the transmission of pain to the brain. This results in the paresthesia or tingling feeling replacing or “painting over” the sensation of pain. (52;53)

The SCS technology has 3 implantable components (54):

- A pulse generator
- An extension cable
- A lead

The Pulse Generator

The pulse generator is the battery of the spinal cord stimulator, which generates the low-voltage electrical pulses for stimulation. (29;55) The amplitude, pulse width, and pulse rate are programmed by a physician using a remote-control-like device called a physician programmer. The amplitude is the strength of the stimulation measured in volts (V), and the number of volts used determines the strength of the tingling or paresthesia. The pulse width, which is measured in microseconds (μ s), determines how long the stimulation lasts and how wide an area the paresthesia covers. Finally, the pulse rate is the number of electrical pulses per second measured in Hertz (Hz). It determines the speed of the stimulation. Once the optimal stimulating parameters are found, the patient can control the amplitude or strength of the stimulation within the parameters set by the physician by using a remote-control-like device called a patient programmer.

There are 2 types of neurostimulators: an implantable pulse generator (IPG) and a radio frequency neurostimulator. (29;55) Both types are surgically implanted just under the skin in the lower abdomen or in the buttock area. The IPG must be surgically replaced once the battery is depleted. The radio frequency neurostimulator is powered by an external radio frequency power source and is no longer available in Canada.

The Extension Cable

The extension cable connects the pulse generator to the lead and is available in varying lengths. The extension cable can be detached from the lead and the pulse generator. (29;55)

The Lead

The lead is an insulated wire that connects at one end to the extension cable and has at its other end a set of 4 to 8 electrodes. (55) The electrodes deliver the electrical stimulation generated by the IPG (the battery) to the dorsal columns of the spinal cord. The anode is a positive electrode and the cathode is the negative electrode. The physician programs different anode and cathode combinations called arrays to conduct the electrical stimulation to the dorsal columns of the spine.

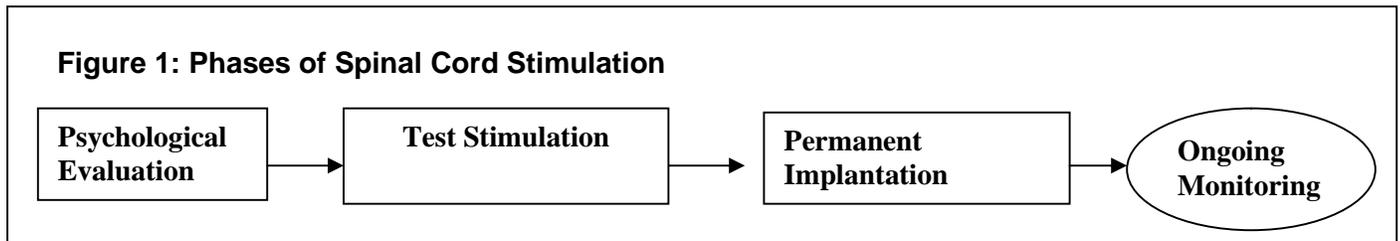
The lead is positioned within the epidural space on the posterior aspect of the spinal cord. (29) Areas of the body called dermatomes can be mapped to certain segments of the spinal cord, which are closely related to the vertebral levels of the spine. By placing the electrodes over several contiguous vertebral

segments, more than one dermatome can be covered with paresthesia when stimulation is activated. This is important because neuropathic pain often involves more than one dermatome. (50) The adequacy of the paresthesia coverage of the painful dermatomes determines successful SCS. (29)

There are 2 types of leads: percutaneous and paddle leads. (29) Both types are inserted into the epidural space. (51) The percutaneous lead is inserted percutaneously (through the skin) and the paddle lead is inserted surgically. Percutaneous insertion involves threading the lead through a hollow needle called a Tuohy needle into the epidural space. (29) Local anesthetic and radiological imaging devices such as fluoroscopy are used to make insertion easier. The advantages of using percutaneously placed leads are that less operating room time is required and it is a less-invasive procedure.(1) However, previous surgery or anatomical changes in the spine may preclude a percutaneous lead insertion.

Surgically placed leads are placed under direct vision through a small laminotomy and tend to move or migrate less often within the epidural space than percutaneously inserted leads. However, the surgical insertion is more invasive than percutaneous insertion.

Before the spinal cord stimulator is permanently implanted, the candidate must have a psychological assessment and then complete a test stimulation period. (See Figure 1.)



Psychological Evaluation

Emotional and behavioural influences can affect the perception of pain and pain relief. (1) Psychiatric disorders, poor comprehension, lack of compliance, drug or alcohol abuse, drug-seeking behaviour, or issues related to secondary gain may interfere with the patient's commitment to, and the success of, the therapy and are contraindications to SCS. (1;56) For these reasons, patient evaluation by a neuropsychologist is required.

SCS Test Stimulation Phase

If the psychological assessment is favourable, patients have test stimulations to determine if they are responsive to SCS therapy and can tolerate the paresthesia. Generally, only those who obtain at least a 50% reduction in pain intensity during the test stimulation phase and can tolerate the paresthesia should have the SCS device permanently implanted. (1)

Test stimulation starts with the physician percutaneously placing a lead and connecting it to a temporary external pulse generator. The patient is sedated but not unconscious for the lead insertion, which takes between 45 minutes and 2 hours (Personal communication with clinical expert, February 14, 2005). To correctly position the electrodes, the spinal cord stimulator is activated during this procedure and the patient helps guide the electrode placement by reporting to the physician where he or she is feeling the paresthesia.

While the nature of this procedure renders it a day surgery, many patients are admitted overnight for

monitoring and patient teaching (Personal communication with clinical expert, February 14, 2005). After discharge from the hospital and over the next 4 to 7 days, the patient with the help of a nurse (neuromodulation nurse) or pain doctor monitors his or her pain intensity. During this period the stimulation parameters may be changed to optimize pain control. A successful test stimulation period is defined as at least a 50% reduction in pain. Successful candidates can then have a permanent spinal cord stimulator implanted. On average, about 70% to 80% of candidates will have a successful SCS trial stimulation. (Personal communication with clinical expert, February 14, 2005) If the trial stimulation phase is unsuccessful, the percutaneously placed lead is removed.

Permanent Implantation Phase

During the implantation phase, a permanent lead is inserted percutaneously. The lead is then attached to the extension cable, which is tunneled under the skin to connect to the IPG. The IPG is implanted just under the skin in the abdomen or gluteal (buttock) area. The insertion of a permanent lead and implantation of a pulse generator takes about 2 to 3 hours, and the patient is admitted overnight for recovery (Personal communication with clinical expert, February 17, 2005).

Patient Follow-up

Several follow-up visits occur in the first year after implantation to adjust stimulation parameters and assess pain control. Follow-up may occur at 1, 3, and 6 weeks after the procedure and then at 3, 6, and 12 months for the first year, but may vary among practitioners. Annual visits are scheduled thereafter to assess for any needed modifications in stimulation parameters to maintain pain control and to make sure the SCS battery is not depleted. (Personal communication with clinical experts on February 17, 2005 and April 13, 2005).

Efficacy of Spinal Cord Stimulation

There have been 2 studies comparing SCS with a placebo. A summary of each study follows.

In 1991, Marchand et al. (57) published a prospective randomized placebo-controlled crossover single-blinded trial on 8 chronic back pain patients who were using SCS and reporting at least a 30% decrease in pain intensity. The patients were told the purpose of the study was to test new parameters of stimulation. Stimulation was discontinued at least 8 hours before the study started. During the study, patients were given either 30 minutes of active SCS with their normal stimulation parameters or 30 minutes of placebo stimulation. For the placebo stimulation, the investigator pretended to manipulate the SCS controls. Patients recorded their perceived pain intensity and the unpleasantness of the pain on a VAS before treatment, every 10 minutes during treatment, and after treatment.

All of the patients reported paresthesia during placebo stimulation. However, the ratings of perceived pain intensity ($P = .006$) and pain unpleasantness ($P = .007$) were significantly reduced with the active stimulation compared with the placebo.

The authors concluded that active SCS reduced perceived pain intensity and unpleasantness significantly compared with placebo stimulation.

This study was limited by its small sample size.

In 1996, Tesfaye et al. (58) published a prospective non-randomized placebo-controlled crossover trial of patients during test stimulation. Ten patients with disabling diabetic neuropathy without previous

exposure to SCS had a 7-day test stimulation in which they received placebo stimulation for 2 days and active stimulation for 2 days. During each 2-day period, the patients rated their pain level every 4 hours using a VAS of pain.

Results showed the median (interquartile range) baseline VAS score was 62.5 (28.2–71.8), and the median VAS score during placebo stimulation was 33.5 (15.5–56.3). The median VAS score during active stimulation was 15.5 (1.5–31.2). Pain was significantly lower with active stimulation than with placebo stimulation ($P = .004$).

The authors concluded that, “Spinal cord stimulation offers a new and effective treatment for chronic diabetic neuropathic pain.” (58)

It is unclear if patients in this study were blinded to their treatment allocation. If not, then this is a limitation of the study. This study also had a small sample size.

Complications Associated With Spinal Cord Stimulation

Complications can be divided into procedural complications and technical failures. (59) Procedural complications include wound infection, cerebrospinal fluid leaks, dural puncture headaches, and the inability to thread the lead percutaneously into the epidural space. Technical failures include lead migration and fracturing, unwanted stimulation, inadequate paresthesia coverage and pain over the IPG battery implantation site. Early IPG battery failure can also occur. (49) The longevity of the IPG battery depends on the amplitude use and the pulse width requirements and whether the stimulator is used continuously or intermittently (cycling mode) (personal communication with clinical expert, April 13, 2005)

Infection is the most common procedural complication, with a reported incidence ranging from 1.4% to 11%. (59) North et al. (50) reported an incidence of 5% for superficial surgical wound infections in a cohort of 205 patients followed-up between 2 years and 20 years. Superficial infections may clear with intravenous antibiotics but if it fails to resolve the spinal cord stimulator is removed. The stimulator may be reimplanted once the infection has resolved.

There has been one report of paralysis associated with a bacterial infection located at the tip of the lead with the subsequent development of an epidural and intradural abscess requiring surgical intervention. (60) Four cases of aseptic meningitis have been reported, 2 that resolved spontaneously and 2 that required removal of the spinal cord stimulator. (60)

One hundred and fourteen infections were reported to Medtronic Inc. between September 1, 2000 and July 1, 2002. (61) Bacterial growth was reported in 47% of the cases, and no bacterial growth was reported in 18% of the cases. Eighty-seven percent of cases were treated with antibiotic therapy. The IPG implantation site was the most common site of infection (54%), the electrode lead (17%) was the second most common. (Infection of the electrode lead can occur at the site where the lead and the connector cord join. Personal communication with clinical expert, April 13, 2005). In 94% of the cases, the spinal cord stimulator was removed in whole or in part, and 91% of patients had a successful resolution. There were no infection-related deaths.

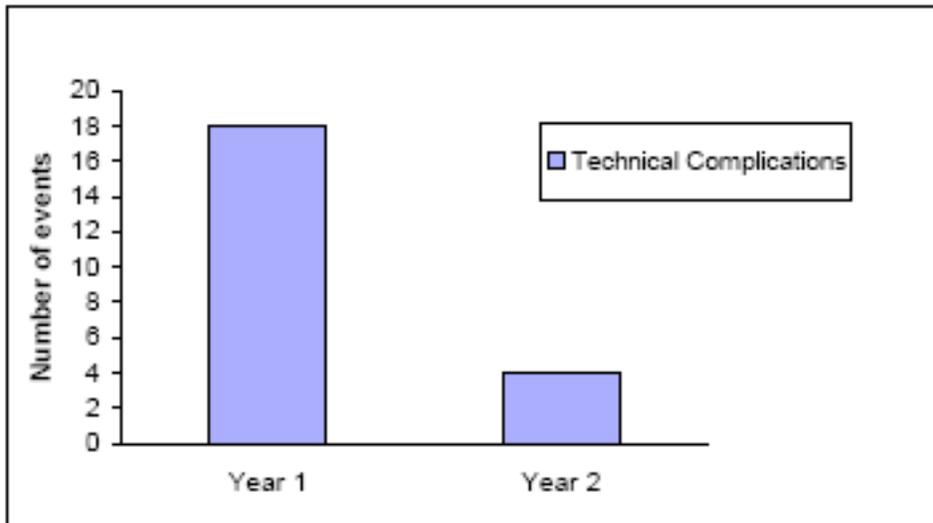
There has been one report of relapsing ulcerative colitis approximately 6 weeks after implantation of the spinal cord stimulator and continuous stimulation. Stimulation was discontinued, but the device remained implanted while the ulcerative colitis was treated. Once the ulcerative colitis was in remission, stimulation resumed. However, 2 weeks after the initiation of stimulation the ulcerative colitis symptoms

recurred. Stimulation was again stopped, and the device was explanted. Remission returned and was sustained after explantation. (62)

The most common technical failure is lead migration. (49) Lead migration occurs when the lead shifts position longitudinally (up or down) or laterally (side to side) within the epidural space. The leads may also fracture, which impedes proper transmission of the electrical pulses. The result of each of these technical failures is inadequate paresthesia coverage of the painful dermatomes and less pain relief. Often there is an attempt by the clinician to reprogram the stimulation parameters to recapture adequate paresthesia; however, if this fails, then surgical revision of the lead is needed. (29) Kemler et al. (63) reported that the incidence of technical complications is greatest in the first year after implantation and falls markedly thereafter. (See Figure 2.)

Painful antenna coupling is a technical failure unique to the radio frequency SCS device. Explanting the device often solves the problem. (64). There has been one report of accidental activation of a radio frequency spinal cord stimulator with an anti-theft device. The patient sustained neurological injury manifested as dysarthria, ataxia, tremor, and prolonged memory impairment. (65)

Figure 2: Incidences of Technical Complications of Spinal Cord Stimulation at 1 and 2 Years (63)



Cameron (49) calculated the incidence of technical failures and procedural complications in 68 studies of more than 2700 patients who were treated with SCS for neuropathic and ischemic pain. These results are shown in Table 6.

Table 6: Spinal Cord Stimulation Technical Failures and Procedural Complications

Complication	Incidence, %
Lead migration	13.2
Infection	3.4
Hematoma	0.3
Paralysis	0.03
Cerebrospinal fluid leak	0.3
Unwanted stimulation	2.4
Pain over implant	0.9
Allergic reaction	0.1
Skin erosion	0.2
Lead breakage	9.1
Hardware malfunction	2.9
Loose connection	0.4
Battery failure	1.6
Other	1.4

Contraindications to SCS include these (56):

- No partial sparing of the dorsal column fibers (e.g., total paraplegia)
- The presence of other stimulation devices with sensing capacities (e.g., pacemakers or implantable cardiac defibrillators are contraindicated to SCS)
- Severe diseases likely to interfere with neuromodulation procedures, such as coagulopathies and immunodeficiency diseases
- Existing drug habituation problem (should be treated before commencing SCS)
- Major psychiatric disorders such as active psychosis, severe depression, or hypochondria and somatization disorder; poor compliance and/or insufficient understanding of the therapy; lack of appropriate social support; and drug and alcohol abuse or drug-seeking behaviour

Regulatory Status

Health Canada (http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/index_devices_e.html, accessed January, 2005) licenses 7 spinal cord stimulator devices. However, only 4 are currently available (See Table 7). The Itrel 3 System is a single-lead device, the Synergy Neurostimulator is a dual-lead device, and the Synergy Veristrel is a smaller (with a smaller battery) dual-lead system only available from the manufacturer through special order and rarely used in Canada (Personal communication, Medtronic Inc., January 11, 2005). Health Canada recently approved the Genesis Neurostimulation System in February 2005. Radio frequency spinal cord neurostimulators (X-Trel RF and Matrix RF) are no longer available in Canada (Table 8).

Table 7: Spinal Cord Stimulation Devices Licensed and Available in Canada

Licence Number	Licence Name	Class	Device Name	Purpose
14740	Itrel System	IV	Itrel 3 System Implantable Pulse Generator	To treat chronic intractable pain and gastroparesis
645	Synergy Neurostimulator System For Spinal Cord Stimulation	IV	Synergy Neurostimulator Dual-Channel Itrel IPG For Spinal Cord Stimulation	To help manage chronic intractable pain
37764	Synergy Veristrel Implantable Pulse Generator	IV	Synergy Versitrel IPG	To help manage chronic intractable pain of the trunk or limbs
67516	Genesis Neurostimulation System	IV	Genesis IPG Neurostimulator -Power Source	Indicated as aid in the management of chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with any of the following: failed back surgery syndrome, and intractable low back and leg pain.

Table 8: Spinal Cord Stimulation Devices Licensed but Not Available in Canada

Licence Number	Licence Name	Class	Device Name
871	X-Trel RF System	IV	X-Trel Receiver
871	X-Trel RF System	IV	X-Trel RF Transmitter
11115	Matrix System	IV	Matrix Receiver
11115	Matrix System	IV	Matrix Transmitter
14740	Itrel System	IV	Itrel II IPG

Literature Review on Effectiveness

Objective

The primary objective was to evaluate the effectiveness and safety of SCS to manage chronic neuropathic pain.

Questions Asked

Does pain management with SCS:

- Decrease perceived pain intensity?
- Improve functional status?
- Improve the QOL of people with neuropathic pain?

Outcome Measures

The primary outcome was pain relief.

The secondary outcomes were as follows:

- Functional status
- QOL
- Technical failures and procedural complications

Methods

Search Strategy

The Medical Advisory Secretariat did a computer-aided search limited to human studies. Case reports, letters, editorials, non-systematic reviews, and comments were excluded. Foreign-language studies were included to determine bias in reviewing only English-language reports. (Appendix 1)

Initial Search

- 2000 to November week 3, 2004
- OVID MEDLINE
- EMBASE
- Other Non-Indexed Citations
- Cochrane Database of Systematic Reviews
- Cochrane CENTRAL
- INHATA

Updated Search

- 2000 to January week 3, 2005
- OVID MEDLINE
- Other Non-Indexed Citations
- EMBASE

Inclusion Criteria

- Systematic reviews, RCTs, prospective non-RCTs including before-and-after treatment designs
- Studies that compared SCS to alternate treatment(s) or treatment states (before-and-after studies)
- Adults with neuropathic pain conditions
- Patients with FBSS with leg pain equal to or greater than low back pain
- Subjects who have had at least one of the following: pain for at least 6 months and/or have failed conservative treatments
- Publicly available Health Technology Assessments

Exclusion Criteria

- Studies that did not include a subjective measure of pain intensity
- Studies that compared technical factors of SCS
- Studies that investigated chronic mechanical back pain, ischemic limb or cardiac pain
- Studies with a study sample of mixed pain conditions (neuropathic pain and nociceptive pain conditions in same study sample) and separate results for each type of pain were not reported
- Multiple reports that include results of same study sample (in these cases the study with the longest follow-up period reported was selected for inclusion in this review)

Intervention

SCS with any of the following techniques:

- Percutaneous or paddle electrodes
- Implantable pulse generator or radio frequency receiver
- Single or dual electrodes
- Single- or multi-channel electrodes
- Any type of stimulation parameters used
- Mono-polar or multi-polar

Controls included conventional pharmacological, nonpharmacological, or surgical therapies; or self-controlled (before-and-after study design)

Outcomes of Interest

- Subjective measurement of pain intensity with at least one of the following validated pain scales: VAS, or MPQ.
- Other measures of pain including a numerical rating scale or medication quantification scale, or the percentage of patients experiencing pain relief.
- Functional status
- QOL

Assessment of Methodological Quality of Randomized Controlled Trials

- Relevant RCTs were assessed using the instrument to measure the likelihood of bias in pain research reports developed by Jadad et al. (66)
- In addition, each study was evaluated for allocation concealment (67) where:
 - A = adequate
 - B = unclear
 - C = inadequate
 - D = not done

Description of the Scale by Jadad et al.(66)

1. Was the study described as randomized?
2. Was the study described as double blinded?
3. Was there a description of withdrawals and dropouts?

Score 1 for “Yes” and 0 for “No”

Give 1 additional point if: For question 1, the method to generate the sequence of randomization was described and was appropriate.

Deduct 1 point if: For question 1, the method to generate the sequence of randomization was described and it was inappropriate and/or for question 2, the study was described as double blinded but the method of blinding was inappropriate.

Results of Literature Review

The initial search yielded 311 citations, and the updated search yielded an additional 16 citations, for 327 citations. Twenty-six were foreign-language studies. Of the 301 English-language articles, 20 met the inclusion criteria

The full articles were retrieved for 20 of the citations (Table 9). Of these, 4 health technology assessments were excluded: 3 because they were assessed as non-systematic reviews (lack of clearly defined question, no inclusion/exclusion criteria or clear outcome measures proposed),(68-70) and 1 because it had case control studies only. (71)

Six clinical trial reports including 1 RCT and 5 non-randomized controlled trials (non-RCT) were excluded: 1 RCT was a multiple report; (72) 1 non-RCT with a sample comprised of a heterogenous pain population; (73) 2 non-RCTs that included patients with predominately low back (axial) pain; (74;75) 1 non-RCT that compared the effects of different stimulation programs among patients; (64), and 1 non-RCT study that did not report a measure of pain relief. (18). Therefore, 10 reports were excluded, leaving 10 to be reviewed fully (Table 9).

Table 9: Results of Literature Search by Medical Advisory Secretariat

Type of Trial	Initially Retrieved	Included
Existing health technology assessments	10	6
Randomized controlled trials	3	2
Non-randomized controlled trials	7	2

Health Technology Assessments

Six health technology assessments of small RCTs were reviewed. Five were published in peer-reviewed journals. (19;49;51;59;76) The sixth was completed by the Australian Safety and Efficacy Register of New Interventional Procedures-Surgical (ASERNIP-S) (Table 11). (54) Each review is discussed in turn below.

Taylor et al., 2005(77)

Spinal Cord Stimulation for Chronic Back and Leg Pain and Failed Back Surgery Syndrome: A Systematic Review and Analysis of Prognostic Factors.

Taylor and colleagues (77) used the updated methods guidelines for systematic reviews of the Cochrane Collaboration Back Review Group. They searched the Cochrane Controlled Trials Register, MEDLINE, and EMBASE up to January 2002. The search was not restricted by language and included RCTs and non-RCTs. They retrieved 1 RCT, 1 cohort study, and 72 case series. They pooled the results from the case series and estimated relative risk or risk difference for the before-and-after studies (probability of patient achieving outcome before SCS compared with after SCS).

Results: Randomized Controlled Trial

Taylor et al.(77) report results of a randomized trial by North et al.(77) that were presented at a scientific meeting in 2000. North et al.(77) randomized 50 patients with FBSS to receive either SCS or a reoperation. They found that significantly more patients treated with SCS had at least 50% pain relief compared with the patients that had reoperations (37.5% for SCS vs. 11.5% for reoperation; $P = .0475$). Taylor et al. gave the study a grade of 4/5 using the Jadad et al. (66) methodological quality scale.

Results: Cohort Study

Dario et al. (18) completed a cohort study that compared people with neuropathic pain treated successfully with medical therapy with people who were treated with SCS because medical therapy had not worked for them. In their assessment, Taylor et al. (77) suggested that a limitation of the study is the imbalance in prognostic variables between groups, because people who failed medical therapy and were treated with SCS may have had more severe disease compared with those that did not fail medical therapy. Dario et al. (18) did not complete a statistical analysis of the VAS pain scores between the spinal cord stimulation treated patients and the medical therapy treated patients because they felt the two treatment groups were not comparable (personal communication with the author, January 21, 2005). While Taylor et al. (77) state that there was no difference in functional capacity between the SCS and medically treated patients as measured by the Pain Disability Index and Oswestry scores this is inconsistent with that reported by Dario et al.(18) Dario et al. (18) report a statistically significant difference ($P < .05$) in the Oswestry scale score between the medically treated patients and those treated with spinal stimulation. The baseline average Oswestry scale score in the medically treated group before treatment was 23 (range 10-35) and the average score at 7-year follow-up was 6 (approximate range 3-11). However, the baseline average score before treatment in the spinal cord stimulation group was 12 (range 6-17) and the average score at the 7-year follow up was 9 (range 16-5). There was no adjustment in the statistical analysis to allow for the differences in baseline Oswestry scores and this may confound the statistical analysis of the parameter. Taylor et al. (77) gave this study by Dario et al. (18) a grade of 1/5 using the methodological quality scale developed by Jadad et al. (66)

Results: Case Series

The 72 case series comprised 3,427 patients with spinal cord stimulator implants. Sample sizes ranged from 1 to 304, and all patients had received SCS. Follow-up monitoring ranged from 1 to 106 months. Taylor et al.(77) rated the quality of these case series with an assessment tool developed specifically for the systematic review and that had not been validated. Higher scores indicated better-quality studies. The median score was 1 (range, 0—6). There was statistical heterogeneity in the level of pain relief with SCS across studies ($Q, 2521.90$; $df, 64$; $P < .0001$). (77) Despite this, the authors computed a pooled random-effects model for the outcome of at least 50% pain relief (Table 10).

Table 10: Pooled Random-Effects Model for at Least 50% Pain Relief

Outcome	Case Series That Reported the Outcome	Number of Cases/Total Number of Cases	Pooled Results % (95% CI)
Pain relief of at least 50%	65	1992/3313	62 (5669)

The percentage of patients that obtained at least a 50% reduction of pain intensity after SCS was 15% to 20% lower in the higher-quality studies, compared with lower-quality studies ($P = .010$). It was also higher in studies that had shorter follow-up periods ($P < .0001$), in chronic low back pain or FBSS populations ($P < .0001$), and in multicentre studies ($P = .013$).

Taylor et al (77) concluded that the level of evidence to support the effectiveness of SCS to treat patients with chronic low back pain or failed back surgical syndrome is moderate. They also concluded that poor-quality studies may exaggerate the estimate of a SCS treatment effect.

The main limitation of this systematic review by Taylor et al. (77) is that results from the case series were pooled statistically despite statistical heterogeneity between studies.

Mailis-Gagnon et al., 2004(51)

Spinal Cord Stimulation For Chronic Pain

This systematic review was published in the Cochrane Database of Systematic Reviews. Mailis-Gagnon and colleagues (51) searched MEDLINE and EMBASE, up to September 2003, and the Cochrane Central Register of Controlled Trials (CENTRAL) up to Issue 3, 2003. They also searched textbooks and reference lists in retrieved articles. They consulted experts in the field of pain and the main manufacturer of the stimulators. They did not impose a language restriction on the search and included RCTs and non-RCTS that evaluated SCS for chronic pain. Their search retrieved 2 RCTs. The heterogeneity of the participants, interventions, and outcome measures precluded statistically pooling the results.

Results: Randomized Controlled Trials

Kemler et al. (72) did an RCT of 54 patients with CRPS Type I treated either with SCS plus physiotherapy (n = 36) or physiotherapy only (n = 18). In the intention to treat analysis pain was significantly lower at 6 months in the patients who had received SCS and physiotherapy, compared with those who received only physiotherapy ($P < .001$). On health-related QOL, they found no difference between the groups at 6 months. Using the scale developed by Jadad et al. (66) Mailis-Gagnon et al. graded the methodological quality of this study as 3/5.

In the other RCT, North et al. (20) reported the preliminary results of an RCT that compared patients who received SCS with a control group that had reoperations. At 6 months after treatment, 17% (2/12) of patient receiving SCS had crossed over to the reoperation group, while 67% (10/15) of the control group had crossed over to SCS ($P = .018$). Mailis-Gagnon et al. graded the methodological quality of this study as 1/5.

Mailis-Gagnon et al (51) conclude that there is limited evidence in favour of SCS to treat FBSS and CRPS, but insufficient evidence to determine the benefits and harms of SCS. More trials are needed to assess if SCS effectively treats chronic pain conditions.

Cameron, 2004(49)

Safety and efficacy of spinal cord stimulation for the treatment of chronic pain: a 20-year literature review

Cameron (49) specified explicit inclusion and exclusion criteria for a literature review of the efficacy and safety of SCS to treat chronic pain, including pain of the trunk and limbs, ischemic pain, and angina pain. He searched MEDLINE from January 1981 to the beginning of 2003, and he hand-searched articles published in the journal *Neuromodulation*. The search was restricted to English-language articles. He included RCTs, prospective controlled and non-controlled, and retrospective studies.

Cameron retrieved 68 articles:

- 16 with back and leg articles (2 RCTs, including North 1995, Marchand 1991)
- 12 with CRPS Types I and II (1 RCT including that by Kemler, 2000)
- 13 with ischemic limb pain studies (2 RCTs)
- 11 with angina pain studies (3 RCTs)
- 16 with studies including various pain diagnoses (0 RCT)

For the data analysis, he pooled outcomes obtained with similar outcome measures and calculated means and standard deviations. The author does not describe methods used to pool data.

Results: Back and Leg Pain Studies

- North et al. (20): as reported in the review by Mailis-Gagnon et al. (51)
- Cameron (49) classified the study by North et al. (20) as a non-randomized study.
- Marchand et al.(57) reported results of a placebo-controlled crossover trial of 8 patients treated with active spinal cord stimulation and placebo spinal cord stimulation. Both the perceived pain intensity ($P = .006$) and pain unpleasantness ($P = .007$) were statistically reduced by active SCS but not by placebo stimulation.
- Also reviewed by Cameron (49) under the category of back and leg pain studies were 8 prospective studies without matched controls, in which the overall success rate of SCS was 65% ($n = 332$); and 6 retrospective studies without matched controls, in which the overall success rate of SCS was 64% ($n = 232$).

Results: Complex Regional Pain Syndrome Type I or Type II Studies

- Kemler et al. (72): as reported by Mailis-Gagnon et al. (51)
- Also included under the category of complex regional pain studies were 3 prospective studies without matched controls, in which the overall success rate of SCS was 84% ($n = 19$); and 8 retrospective studies, in which the overall success rate of SCS was 84% ($n = 192$).

Cameron (49) concludes the review by stating that there is some evidence to indicate that SCS has positive, symptomatic, long-term effects on CRPS Types I and II and pain due to FBSS. However, few large randomized controlled studies examining the efficacy of SCS have been reported for chronic pain conditions including CRPS Types I and II, FBSS, refractory angina pain, severe ischemic limb pain secondary to peripheral vascular disease and peripheral neuropathic pain.

Cameron (49) has completed an exhaustive review comprising a collection of 20 years of clinical research on SCS to manage multiple chronic pain conditions. However, the review did not describe the methods used to pool the data. Treatment effects of SCS reported for the prospective no control studies may be inflated due to the observational study design.

Turner et al., 2004(19)

Spinal cord stimulation for patients with failed back surgery syndrome or complex regional pain syndrome: a systematic review of effectiveness and complications

Turner et al. (19) used explicit inclusion, exclusion, and outcome criteria. The literature search was completed by an experienced health services librarian who searched these databases: MEDLINE, EMBASE, The Science Citation Index, Cochrane Central Register of Controlled Trials, and Current Contents bibliographic databases up to May 16, 2003. The manufacturer of spinal cord stimulators was consulted for additional references. Finally, the reviewer also searched personal files, journals, and books; and reviewed the bibliographies of relevant articles for additional studies. The search was restricted to English-language articles. Turner et al.(19) included RCTs, prospective matched-group cohort studies, non-matched cohort studies, and case series. They retrieved 7 studies: 1 RCT and 6 prospective case series. The data were analyzed qualitatively.

Results: Randomized Controlled Trial

Kemler et al. (72): as reported by Mailis-Gagnon et al. (51) and Cameron, (49). Turner et al. (19) calculated the NNT for SCS from the results reported by Kemler et al. (72). A NNT of 3 was determined, which indicate that 3 patients need to be given a trial of SCS for 1 patient to report a score of at least 6 or “much pain improvement” on a 7-point Global Perceived Effect Scale at 6 months follow up.

Results: Case Series

- 5 studies found a mild to moderate improvement in pain.
- 3 studies reported that SCS was associated with a statistically significant improvement in functional status ($P < .05$); however, in the absence of a control group, the reviewers concluded that an improvement in functional status due to other events (e.g., natural history) could not be ruled out.

Turner et al. (19) concluded that there is moderate evidence that SCS plus physiotherapy is more effective at relieving pain than physiotherapy only for patients with CRPS Type I at 6 and 12 months.

Turner et al. (19) also concluded that there was inadequate evidence to support the efficacy of SCS to reduce physical disability, work disability, and medication consumption in patients who have FBSS and CRPS Type I.

There were no limitations to this systematic review by Turner et al.

Grabow et al., 2003(59)

Spinal Cord Stimulation for Complex Regional Pain Syndrome: An Evidence-Based Medicine Review of the Literature.

Grabow et al. (59) searched MEDLINE (1966-2002), The Cochrane Library (on-line version 2002), the ISI Web of Science (1954–2002), and WebSPIRS from SilverPlatter (1966–2002), each up to April 2002. The literature search also included personal files, textbooks, bibliographies of retrieved articles, and literature from the manufacturers of spinal cord stimulators. The search was restricted to English-language articles.

They included RCTs, clinical trials, case-control studies, and case reports. They retrieved 15 studies: 1 RCT, 2 prospective studies, and 12 retrospective studies. They did a qualitative analysis of the data.

Results: Randomized Controlled Trial

- Kemler et al. (72): as reported by Mailis-Gagnon et al (51), and Cameron, (49) and Turner, (19).
- Grabow et al.(59) rated the quality of the study by Kemler et al. (72)a IB using the Oxford Center for Evidenced-Base Medicine: Levels (1a-5) Grade (A-D). (http://www.cebm.net/levels_of_evidence.asp#levels) (accessed April 26, 2005). A grade of 1B is defined as an individual RCT with narrow confidence intervals.
- Similar to Turner et al. (19) Grabow et al. (59) calculated a NNT of 3.0 (95% CI, 1.9–7.0) from the results of Kemler et al. (72) using a rating of 6 (much improved) on the Global Perceived Effect scale.

Results: Other Studies

- 7 studies reported baseline VAS scores, and 5 of these reported VAS scores after SCS. The mean baseline VAS score ranged from 6.7 to 8.3, and the range at follow-up was 1.3 to 4.5. Statistical testing on differences between baseline and follow-up was done in 4 of the 7 studies.
- 12 studies reported that SCS was a successful and effective therapy for CRPS. Success ranged from 53.7% to 100% in these studies.
- 1 study reported SCS was unsuccessful (study completed in 1974).
- 1 study's conclusions were unclear.

Grabow et al. (59) concluded SCS was effective for the management of pain for patients with CRPS who did not respond to more conservative medical management.

There were no limitations to the systematic review by Grabow et al. (59)

Middleton et al. 2003 (54)

Table 11: Middleton et al.

Spinal Cord Stimulation (Neurostimulation): An Accelerated Systematic Review	
Author	Middleton et al.
Agency	Australian Safety and Efficacy Register of New Interventional Procedures-Surgical (ASERNIP-S)
Date	June 2003
Objective	To assess the effectiveness and safety of spinal cord stimulation by an accelerated systematic review.
Search	Up to April 2003, MEDLINE, Pre-MEDLINE, The Cochrane Library, Issue 2, 2003
Inclusion criteria	Randomized controlled trials
Outcome	Pain or pain relief
Results: Effectiveness	<p>9 randomized controlled trials including:</p> <ul style="list-style-type: none"> ▪ 1 with failed back surgery syndrome (20;69;78) ▪ 1 with complex regional pain syndrome (72;79;80) ▪ 1 with painful diabetic neuropathy (58) ▪ 2 with critical limb ischemia (not applicable to MAS systematic review) ▪ 4 with angina trials (not applicable to MAS systematic review) <p>Failed back surgery syndrome:</p> <ul style="list-style-type: none"> ▪ North et al. (20;69;78) as reported in Mailis-Gagnon et al. (51) and Cameron, (49). <p>Complex regional pain syndrome:</p> <ul style="list-style-type: none"> ▪ Kemler et al. (72;79;80) as reported by Mailis-Gagnon et al., (51); Cameron, (49); Turner, (19); and Grabow, (59).

**Spinal Cord Stimulation (Neurostimulation):
An Accelerated Systematic Review**

	<p>Painful diabetic neuropathy:</p> <ul style="list-style-type: none"> ▪ Tesfaye et al. (58) reported results from a crossover design study in which 10 patients with neuropathic pain for less than 1 year were treated with active spinal cord stimulation for 2 days and then with placebo stimulation for 2 days. ▪ Results indicated significant decrease in pain as measured by the visual analogue scale with active vs. placebo stimulation ($P = .004$) <p>Critical limb ischemia and angina pain:</p> <ul style="list-style-type: none"> ▪ Not applicable to the Medical Advisory Secretariat's review
Results: Safety	<p>Failed back surgery syndrome:</p> <ul style="list-style-type: none"> ▪ North et al. (20;69;78) did not report safety data <p>Complex regional pain syndrome:</p> <ul style="list-style-type: none"> ▪ 2 patients with a dural puncture (1 developed a headache) ▪ 1 patient with an infection at the implantation site of the pulse generator (IPG) requiring ex-plantation and subsequent reimplantation. ▪ 6 patients requiring either plug wound or IPG implantation site revision. ▪ 1 patient with a defective lead requiring replacement. ▪ 6 episodes of unsatisfactory lead positioning needing correction. <p>Painful diabetic neuropathy:</p> <ul style="list-style-type: none"> ▪ 2 patients migrated leads requiring reinsertion ▪ 2 patients with superficial wound infections requiring antibiotic. ▪ 1 patient died due to unrelated causes <p>Critical limb ischemia:</p> <p>Adverse events with spinal cord stimulation:</p> <ul style="list-style-type: none"> ▪ 13 lead displacements in 2 years ▪ 6 implant failures ▪ 3 battery failures ▪ 3 cases of infection at the IPG implantation site ▪ 1 duodenal perforation ▪ 2 cases of nausea ▪ 1 case of pruritus <p>Adverse events with best medical treatment:</p> <ul style="list-style-type: none"> ▪ 3 cases of gastrointestinal bleeding ▪ 7 cases of nausea ▪ 2 cases of dizziness.

**Spinal Cord Stimulation (Neurostimulation):
An Accelerated Systematic Review**

**Conclusion reported in
the ASERNIP-S Health
Technology Assessment**

- Spinal cord stimulation is effective in relieving pain in some of the studies.
- Spinal cord stimulation appears to be relatively safe although long-term safety and effectiveness of SCS (beyond 2 years) has not been reported in the studies reviewed.

Table 12: Summary of Health Technology Assessments on Spinal Cord Stimulation Effectiveness and Quality of Evidence

Author, Year	Population	RCT Included	Comment	SCS Effective?*/Quality of Evidence
Taylor et al., 2005 (77)	Chronic back and leg pain FBSS*	North et al. (77) (full results presented at scientific meeting)	North et al. study was scored as 4/5 on a methodological quality rating scale†	Yes Moderate
Mailis-Gagnon et al., 2004 (51)	Chronic pain	Kemler et al. : 2000, 2001, 2002 (72;79;80) North et al. 1995	Kemler et al. study was rated 3/5, and the North et al. study was rated 1/5 on a methodological quality rating scale†	“Limited evidence in favour of SCS for FBSS and CRPS Type I.” “Insufficient evidence to determine benefits and harms of SCS.”
Cameron, 2004 (49)	Chronic pain FBSS CPRPS* Type I	Kemler et al. 2000(72) North et al. 1995 (20) Marchand et al.1991 (57)	North et al. study considered non-randomized	Yes Weak
Turner et al., 2004 (19)	FBSS CRPS Type I	Kemler et al. 2000 (72)	The study by North et al. in 1994 was not included in this review because an outcome measure of pain was not reported.	Yes Moderate for CRPS only
Grabow et al., 2003 (59)	CRPS Type I	Kemler et al. 2000 (72)		Yes 1B‡
ASERNIP-S, 2003 (54)	FBSS, diabetic neuropathy CRPS, angina, critical limb ischemia	Kemler et al.: 2000, 2001, 2002 (72;79;80) North: 1994, 1995, 2002 (20;69;78)		YES Not reported

*FBSS indicates failed back surgery syndrome; CRPS, complex regional pain syndrome; SCS, spinal cord stimulation.

†By Jadad et al. (66)

‡Using the Oxford Center for Evidence-Based Medicine rating scale.

Technical Failures and Procedural Complications Reported in the Health Technology Assessments:

Table 13 lists the technical failures and procedural complications reported in each of the 5 systematic reviews published in peer-reviewed journals. Complications reported by the ASERNIP-S review were shown in Table 11.

Table 13: Technical Failures and Procedural Complications Reported in 5 Health Technology Assessments

Type of Problem	Taylor et al. 2005 (77)	Mailis-Gagnon et al. 2004 (51)	Cameron 2004 (49)	Turner et al. 2004 (19)	Grabow et al. 2003 (59)
Lead problems	27%	4%	Migration: 9.7% Breakage: 13.2%	23.1%	8.3%–42.8%
Generator-related problems	6%	None reported	1.6	5.8	None reported
Extension cable problems	10%	None reported	Not reported	None reported	None reported
Reoperation	None reported	None reported	None reported	23.1%	11.1%–50%
Subcutaneous dissection of generator pocket	None reported	8.3%	None reported	None reported	None reported
Infection	6%	4%	3.4%	4.5% superficial 0.1% deep	1.4%–11.7%
CSF* leak	7%	Not reported	0.3%	Not reported	Not reported

*CSF indicates cerebrospinal fluid.

Cameron (49) reported technical failures and procedural complication rates on more than 2700 people treated with SCS. These results are shown in Figures 3 and 4 on the next page.

Figure 3: Technical Failures

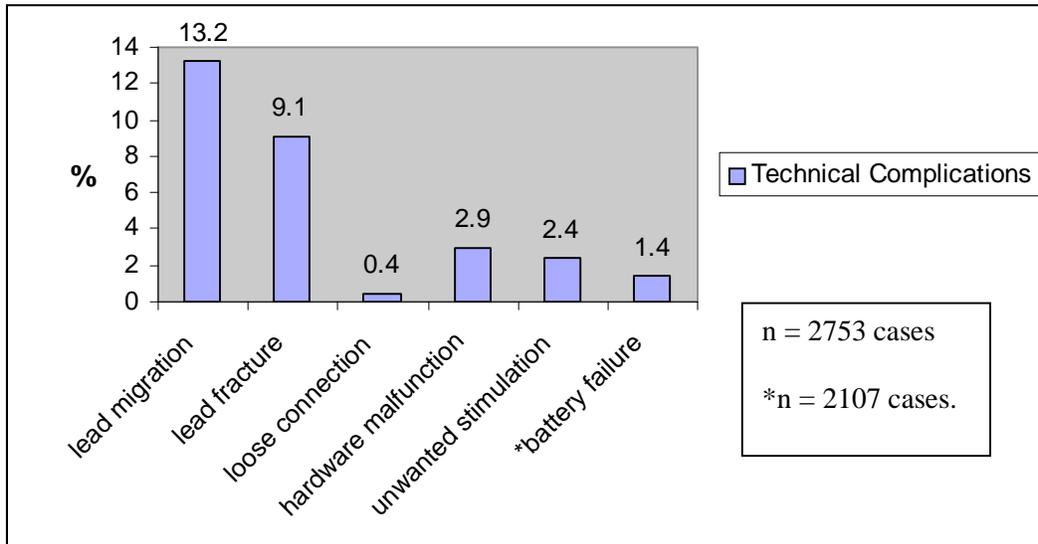
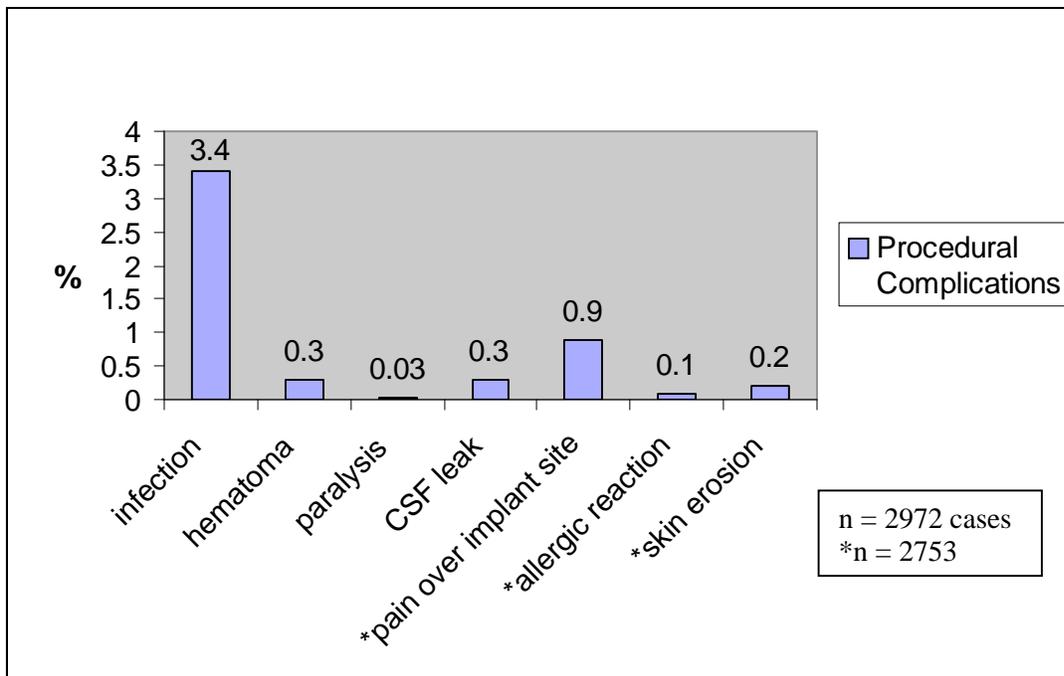


Figure 4: Procedural Complications



Summary of Existing Health Technology Assessments

The authors of all 6 health technology assessments (19;49;51;54;59;77) concluded that there is evidence to support the effectiveness of SCS to manage pain in various neuropathic pain syndromes. However, the quality of this evidence ranged from very weak to moderate.

Two reviews, including Taylor et al.'s (77) and Cameron's (49) had pooled study outcome data from non-RCTs. Taylor et al. (77) pooled results from statistically heterogeneous case series studies using a random-effects model. Cameron (49) did not describe the methods they used to pool the data. Therefore, the usefulness of these pooled estimates is questionable.

The other 4 systematic reviews gave qualitative summaries only. Turner et al. (19) and Grabow et al., (59) reported a NNT of 3 for SCS to improve pain relief using the results of the RCT by Kemler et al. (72)

Across studies included in these 6 health technology assessments the rate of technical failures ranged from 1.6% to 42.8%. The rate of infection occurred ranged from 1.4% to 11.7%.

Only 2 RCTs were identified among these 6 health technology assessments: Kemler et al. (72) and North et al. (20;78) However, a published update on 2-year outcomes for each of these studies is now available. These updated results are included and discussed in the Medical Advisory Secretariat systematic review that follows.

Medical Advisory Secretariat Systematic Review

Quality of Evidence

Table 14: Quality of Evidence of Included Studies

Study Design	Level of Evidence	Number of Eligible Studies
Systematic review(s) of large RCTs	1a	0
Large RCT	1b	0
Large RCT unpublished but reported to an international scientific meeting	1(g)†	0
Small RCT	2	2
Small RCT unpublished but reported to an international scientific meeting	2(g)	0
Non-RCT with contemporaneous controls	3a	2
Non-RCT with historical controls	3b	0
Non-RCT presented at international conference	3(g)	0
Surveillance (database or register)	4a	n/a
Case series (multisite)	4b	n/a
Case series (single site)	4c	n/a
Retrospective review, modeling	4d	n/a
Case series presented at international conference	4(g)	n/a

*RCT refers to randomized controlled trial.

†g indicates grey literature.

The Medical Advisory Secretariat included 2 RCTs and 2 prospective non-RCTs in its systematic review. One is from the United States, 2 are from The Netherlands, and 1 is from Germany. Study characteristics are detailed in Appendix 3.

Quality of Level 2 Small Randomized Controlled Trials

The 2 RCTs (63;81) were graded as 3/5 on the Jadad et al. (66) methodological quality score. Both studies were also given a Cochrane collaboration concealment grade of A, which indicates adequate concealment of the randomization schedule. (82)

In the RCT by North et al., (81) 50 patients with FBSS were randomized to receive either SCS or reoperation. The authors used a 1:1 treatment-to-control allocation ratio. In the other RCT, Kemler et al. (63) randomized 54 patients with CRPS to receive either SCS plus physiotherapy or only physiotherapy. The authors used a 2:1 treatment-to-active control allocation ratio.

North et al.'s (81) primary outcome was a composite of the number of patients that crossed over from the randomized to the active control procedure and the proportion of successes at last follow-up. Success was defined as at least 50% pain relief and patient satisfaction with treatment. North and colleagues did not adjust the level of significance to account for 2 primary outcomes. The primary outcome for Kemler et al. was the change in baseline and post-treatment VAS scores between the treatment and control groups.

North et al. (81) and Kemler et al. (63) each adequately described their sample size calculation and statistical analysis. North et al. (81) calculated their sample size based on the number of expected successes in each treatment, which was based on preliminary data. They used a statistical power of 80% (n = 50). Kemler et al. (63) based their sample size on a projected 2.3 cm difference in VAS scores between the SCS-treated group and the control group. They used a statistical power of 90% (n = 54).

Both groups of authors stated they did an intention-to-treat analysis. However, North et al. analyzed their results using the number of patients randomized and treated, not the number randomized. Kemler et al. did the intention-to-treat analysis at 6 months post-treatment; however, they excluded data from 2 patients from their 2-year analysis, including that for 1 control patient who received a spinal cord stimulator and 1 patient in the SCS treatment group who required a special SCS lead after 6 months.

Both studies accounted for dropouts and or withdrawals. North et al. (81) had 4 withdrawals and 1 death that was unrelated to treatment in the SCS group. No one withdrew from the control group. Kemler et al. (63) had 3 withdrawals at 2 years, 1 in the SCS plus physiotherapy group and 2 in the physiotherapy only group.

Quality of the Level 3a Nonrandomized Controlled Trials

The 2 prospective non-RCTs (42;83) in this review each used before-and-after-treatment study designs. Neither determined sample sizes before doing the study. Both outlined the inclusion and exclusion criteria. Harke et al. (83) stated they enrolled consecutive cases. However, they did not specify a primary outcome. Spincemaille et al. (42) prospectively enrolled eligible patients from 14 centres (personal communication with author, February 16, 2005). Eligible patients were registered with an independent research centre, which assigned the patient a unique study number. They stated that the primary outcome variable was pain reduction measured with VAS, the MPQ, and the Medication Quantification Scale. They adequately described their statistical analysis, whereas Harke and colleagues did not define the level of significance they used. Neither did an intention-to-treat analysis.

Neither the RCTs nor the non-RCTs were double-blinded. Two studies, the RCT by North et al. (81) and the non-RCT by Spincemaille et al., (42) used a disinterested third-party evaluator to collect outcome data. Neither Kemler et al. (63) nor Harke et al. (83) described how they collected outcome data. All studies used the VAS for pain to measure the effectiveness of SCS. Details on outcome are described further in this report.

Blinding is difficult in RCTs of SCS because of the paresthesia that accompanies the test stimulation.(72) Kemler et al. (72) suggest that a placebo effect is unlikely in general because of the recurrence of pain when the electrode position shifts.

Of the 2 RCTs, Kemler et al. (63) included 54 people randomly allocated in a 2:1 ratio to either SCS and physiotherapy (treatment group) or only physiotherapy (control group). They randomized 36 people to the treatment group to undergo the testing phase of SCS. Of these, 24 received a permanently implanted spinal cord stimulator. They randomized 18 people to the control group.

North et al. (81) enrolled 50 people who were randomly allocated in a 1:1 ratio to receive either a reoperation or SCS for FBSS. Of these, 24 received permanent implantation of the spinal cord stimulators and 26 had reoperations.

A total of 133 study subjects were enrolled in the 2 prospective non-RCTs.(42;83) The sample sizes were 28 in the study by Harke et al. (83) and to 105 in the study by Spincemaille et al. (42)

Pain medication was used concurrently with study treatment by people in all 4 studies. However, inclusion criteria in each study required participants to have failed pharmacological therapy before participating in the study. North et al. (81) reported that all subjects were managed with a routine physical therapy protocol. However, all study subjects had previously failed to obtain adequate pain relief with physical therapy treatment.

Table 15 shows the measures of pain intensity, functionality, and QOL in the 4 studies included in the Medical Advisory Secretariat's systematic review.

Outcome Measures

Table 15: Outcome Measures Used in the 4 Studies Included in the Medical Advisory Secretariat's Systematic Review

Study, Year	Level of Evidence	Pain	Functionality	Quality of Life
North et al. (81) 2005	2	% crossover to alternate treatment % success defined as at least 50% pain relief on VAS* and satisfaction with treatment	Ability to perform daily activities	Not assessed
Kemler et al., (63) 2004	2	VAS: 0 cm = no pain; 10 cm =very severe pain. McGill Pain Questionnaire Global Perceived effect (1, worse ever; 2, much worse; 3, worse; 4, not improved and not worse; 5, improved; 6, much improved, 7, best ever.	Test of Jebsen et al.* Kemler foot test Goniometry: Range of motion of both ankles or both wrists and all fingers Jamar dynamometer grip strength Hand held myometer strength of foot dorsi and plantar flexion	Nottingham Health Profile Euroquol-5D Sickness Impact Profile-Short Version The Self-Rating Depression Scale
Spincemaille et al., (42) 2004	3a	VAS: 0 cm = no pain; 10 cm = worse pain ever. McGill Pain Questionnaire	ROLAND disability score	Sickness Impact Profile-68 Euroquol-5D
Harke et al., (83) 2002	3a	VAS: 0 points = no pain; 10 points = unbearable pain	Pain disability index: 0, no disability; 10, total disability	Not assessed

*VAS indicates visual analogue scale of pain.

As Table 15 shows, each study used the VAS to measure perceived pain intensity. North et al. (81) reported using a VAS but did not provide details of the VAS scale itself. North et al.(81) and Kemler et al. (63) reported the proportion of study subjects obtaining at least 50% pain relief as measured by a VAS. These data were used to derive the NNT estimates, which are reported in the analysis section of this review.

Population Characteristics

The study populations, sex, average age, average duration of pain before study treatment, and previous pain therapies used are shown in Table 16.

Table 16: Study Population Characteristics

Study, Year	Level of Evidence	N Population	Average (SD) Age, Years	Sex, % Male	Average (SD) Duration of Pain, Months	Therapies Failed
North et al., (81) 2005	2	50 Failed back surgery syndrome with radiculopathy	52.0 (13.5)	48	Not reported	Non-invasive medical, physical, and behavioural therapies.
Kemler et al., (63) 2004	2	54 Complex regional pain syndrome, Type I	Treatment 40.0 (12.0) Control 35.0 (8.0)	Treatment 39 Control 17	Treatment 40 (28) Control 34 (22)	Physiotherapy, sympathetic blockade, TENS, pain medication
Spincemaille et al., (42) 2004	3a	105 Failed back surgery syndrome	52.5 (9.5)	Not reported	138 (115)	Physiotherapy, TENS, local infiltration, NSAIDS, tricyclic anti-depressants, morphine or analogues.
Harke et al., (83) 2002	3a	28 Postherpetic neuralgia Comorbid conditions: CVS; brain, lung, endocrine disorders; cancer	71.2 (8.4)	43	41.0 (35.5)	Weak and strong opioids, antidepressants, anticonvulsants, analgesics, and corticosteroids.

As Table 16 shows, the study populations comprised people diagnosed with FBSS, CRPS, and postherpetic neuralgia. North et al. (81) did not report the ages separately for the treatment and control groups. Patients with postherpetic neuralgia were older compared with patients who had other conditions in the other 3 studies. This is keeping with the incidence pattern for this disease. All patients with postherpetic neuralgia had comorbid conditions. The minimum average duration of pain was 34 months. Patients across all studies had failed to achieve pain relief with standard pharmacological or nonpharmacological therapies before enrolling in the studies.

Treatment Characteristics

Table 17 shows the type of lead used during trial stimulation, the location by vertebral level, the duration of test stimulation, the type of spinal cord stimulator permanently implanted, the stimulation parameters, and the average duration of follow-up.

Table 17: Spinal Cord Stimulation Treatment Characteristics

Study, Year	Test Stimulation Leads	Electrode Position	Duration of Test Phase/ % Success	Technology Used for Implantation: Generator/ Leads	Parameters	Average (SD) Duration of Follow-up, Months
North et al., (81) 2005	Percutaneous	Not reported	3 days/ 70%	IPG* or radio frequency receiver/ Surgically inserted leads	Not reported	34.8 (13.2)
Kemler et al., (63) 2004	Percutaneous	C4 T12	7 days/ 67%	IPG/ Percutaneous leads	85 Hz 210 µsec 0–10 volts	24
Spincemaille et al., (42) 2004	Not described	Not reported	Not reported/ 78%	Not reported/ Not reported	Not reported	12
Harke et al., (83) 2002	Percutaneous	Not reported	5–7 days/ 100%	IPG/ Percutaneous leads	50–130 Hz 90–450 µsec 1–6 volts	Median, 29 (range, 9–38.5)

*IPG indicates implantable pulse generator.

As Table 17 shows, percutaneously inserted leads were used for the test stimulation in 3 of the 4 studies. One study did not report the type of lead used. A successful test stimulation period was defined in all studies as at least 50% pain relief, which occurred in 67% to 100% of people tested. Two studies used an IPG, 1 used both an IPG and a radio frequency receiver/transmitter, and 1 did not report the type of device used. The minimum average duration of follow-up was 12 months, and the maximum was approximately 35 months (SD, 13).

Results

VAS Pain Scores

Table 18 shows the VAS pain scores either between treatment and control groups, or before and after receipt of SCS for each study.

Table 18: Visual Analogue Scale Scores for Pain

Study, Year	N	N for Analysis	Average (SD) VAS Score at Follow-up	Comment	P
North et al., (81) 2005	50	45	Score not reported Number of people achieving at least a 50% decrease in pain intensity on the VAS* Treatment: 9/19 (47.3) Control: 3/26(11.5%)		< .01
Kemler et al., (63) 2004	54	52	VAS: Treatment: -2.1 (2.8) Control: 0.0 (1.5)	Results reported as within-group mean change in VAS scores. (Negative value indicates a reduction on the VAS.) Results reported for the intention-to-treat analysis. Comparison of mean change between treatment and control groups is significant.	.001
Spincemaille et al., (42) 2004	105	96	Before: 7.3 (1.2) After: 3.0 (2.4)		< .05
Harke et al., (83)	25	23	Before: median, 9.0 (range, 7.5—10.0) After: median, 1.0 (range, 1.0—2.75)		< .001

*VAS indicates visual analogue scale of pain.

As Table 18 shows, 3 studies reported a significant decrease in pain scores with SCS compared with either a control group, or after treatment with SCS compared with baseline scores. (42;63;83) North et al. (81) found significantly more patients who had SCS experienced at least a 50% reduction in their VAS scores compared with people who had reoperations. However, 4 study subjects in the SCS group were lost to follow-up. Because of this, North et al. (81) reported a worse-case-scenario analysis. Thus, assuming that all patients lost to follow-up in the SCS group did not improve, the success rate for SCS would be 9/23 (39%) instead of 9/19 (47.4%). Comparing this to the 11.5% (3/26) success rate in the reoperation group, the difference is statistically significant at the $P < .04$ level. Harke et al. (83) did not designate pain as a primary outcome measure but completed statistical testing on 7 outcome measures. To correct for multiple comparisons a conservative approach would be to adjust the level of statistical significance using a Bonferroni correction of $.05/7$. This would yield a statistical significance level of $.007$. The level of significance for the VAS scores before and after treatment was $< .001$. Therefore, it is unlikely that this result represents a type I statistical error.

Other Pain Measurements

In addition to using the VAS of pain, all of the studies used other methods to quantify pain relief. Results of these pain measurements are shown in Table 19.

Table 19: Other Pain Measurements Used Across Studies

Study, Year	N	N for Analysis	Measurement	Result	P
North et al., (81) 2005	50	45	Opioid intake	For increase in opioid use: Treatment: 3/23 (13%) Control: 11/26 (42%)	.025
Kemler et al., (63) 2004	54	52	Global Perceived Effect of treatment score of 6: "much improved"	Treatment: 15/35 (43%) Control: 1/16 (65%)	.001
Spincemaille et al., (42) 2004	105	96	McGill Pain Questionnaire	Mean (SD) Before: 22.4 (9.4) After: 10.8 (8.0)	< .05
			Medication quantification scale	Before: 11.5 (7.9) After: 6.05 (4.8)	< .05
Harke et al., (83) 2002	25	23	Analgesic consumption	Needed pain medication during SCS Yes: 10/23 (43.5%) No: 13/23 (56.5%) Opioid used: Before: 19/23 (82.6%) After: 1/23 (4.5%)	.02 .002

As Table 19 shows, both Spincemaille et al. (42) and Harke et al. (83) reported a statistically significant decrease in pain medication consumption after SCS compared with before treatment with SCS. Harke et al. (83) noted that 14 patients in their study continued to take antidepressants for symptoms of depression after SCS; however, they denied an objective effect of antidepressants on pain because of the recurrence of pain when the SCS device was turned off. Kemler et al. (63) reported a significant decrease in pain

intensity as measured by the MPQ and also reported that more people in the SCS plus physiotherapy treatment group reported they were “much improved” (score of 6/7) on the Global Perceived Effect Scale compared with people in the control group.

Functional Status

Results of the functional status measurements for each study are reported in Table 20.

Table 20: Functional Status Outcome

Study, Year	N	N for Analysis	Measurement	Functional Status Score, Average (SD)	P
North et al., (81) 2005	50	45	Not described	Scores not reported	Not significant
Kemler et al., (63) 2004	54	31 (upper extremity) 19 (lower extremity)	Range-of-motion tests for upper and lower extremities.	All range-of-motion tests not significant except for that for the ankle, measured in degrees: SCS +*PT group (mean change from baseline at 2-year follow up): 0 (16) *PT only group (mean change from baseline at 2-year follow up): 13 (8)	< .04 (intention-to-treat analysis)
Spincemaille et al., (42) 2004	105	96	ROLAND Disability Questionnaire	Before: 16.9 (3.5) After: 12.4 (4.8)	< .05
Harke et al., (83) 2002	25	23	Disability Index: 0 = no disability 10 = total disability	Scores not reported	< .001

*PT=physiotherapy

All of the functional status outcomes were secondary outcome measures in each of the 4 studies under review. As table 20 shows, different instruments were used to quantify the effect of SCS on functional status. Spincemaille et al. (42) and Harke et al. (83) reported a statistically significant improvement in functional status measurements after SCS compared with baseline values. Spincemaille et al. (42) reported an improvement at 12 months, and Harke et al. (83) found a significant improvement at a median follow-up time of 29 months in people with postherpetic neuralgia.

However, no improvement in functional status was reported in either of the RCTS at 2-year follow-up. It is likely that because this was a secondary measure in each study, neither RCT had adequate statistical power to detect a difference in this outcome measure. While Kemler et al. (63) reported a significant improvement in the range of motion of the ankle in the control group compared with the SCS treatment group ($P < .04$), this may have been due to a type I error, because 10 statistical comparisons, excluding the primary end point, were done without statistical adjustment for multiple testing.

Quality of Life

Results of the QOL assessments for each study are shown in Table 21.

Table 21: Results of Quality of Life Assessments Across Studies

Study, Year	N	N for Analysis	Measurement	Average (SD) Quality of Life Score	P
North et al., (81) 2005	50	45		Not assessed	
Kemler et al., (63) 2004	54	52	Nottingham Health Profile	Not reported	Not significant
			Euroqol-5D	Treatment: 7 (20) Control: 12 (18)	.41
			Sickness Impact Profile-SF	Not reported	Not significant
			Self-Rating Depression Scale	Not reported	Not significant
Spincemaille et al., (42) 2004	105	96	Euroqol-5D	Before: 55.2 (14.5) After: 38.2 (19.2)	< .05
			Sickness Impact Profile-68	Before: 19.4 (10.1) After: 11.7 (9.4)	< .05
Harke et al., (83) 2002	25	23		Not assessed	

As Table 21 shows, only 2 studies assessed the effect of SCS on QOL, and QOL was a secondary outcome for both studies. Kemler et al. (63) did not find a statistically significant difference in the QOL scores at 2-year follow-up between the SCS treatment group and the physiotherapy control group. However, Spincemaille et al. (42) reported a statistically significant difference in the Euroqol-5D and Sickness Impact Profile-68 scores at 12 months compared with baseline scores.

Numbers Needed to Treat

Two RCTs reported dichotomous outcome data on the proportion of successes defined as achieving at least 50% pain relief. (63;81) The NNT are presented in Table 22.

Table 22: Success at 2-year Follow-Up

Study, Year	Group	Success Treatment Group	Success Control Group	Number Needed To Treat
North et al., (81) 2005	Test group*	9/24 (37.5%)	3/26 (11.5%)	3.8
	Implanted group*	9/17 (52.9%)	3/26 (11.5%)	2.4
Kemler et al., (63) 2004	Test group	13/36 (36.1%)	1/18 (5.6%)	3.3
	Implanted group	13/24 (54.2%)	1/18 (5.6%)	2.1

*The test group includes all candidates who underwent a test stimulation phase. The implanted group includes only those candidates that received a permanently implanted spinal cord stimulator. North et al. (81) defined success as at least 50% pain relief and patient satisfaction with treatment. Kemler et al. (63;72) defined success as 50% decrease on the VAS after SCS, compared with baseline scores.

As Table 22 shows, Kemler et al. (63) compared a group that received SCS plus physiotherapy with a control group receiving only physiotherapy for neuropathic pain. North et al. (81) compared patients who received SCS to control patients that had reoperations. The NNT for the test group for both studies is between 3 and 4. Therefore, for every 3 to 4 patients who have test stimulations, 1 will be successful, which is defined as having at least 50% pain relief 2 years after permanent implantation. For every 2 people who have a permanent implantation, 1 will be a successful 2 years after implantation.

Technical Failures and Procedural Complications

Technical failures and procedural complications are reported in Tables 23 and 24.

Table 23: Technical Failures With Spinal Cord Stimulation Across Studies

	North et al., (81) 2005	Kemler et al., (63) 2004	Spincemaille et al., (42) 2004	Harke et al., (83) 2002	Total Technical Failures	Total Technical Failures/166 Cases, %
No. of SCS* cases	19	23	96	28		
Duration of follow- up, months	34	24	12	29		
Lead problems	3	10	2	3	18	10.8
IPG* problems	0	8	0	9	17	10.2
Explant IPG	1	3	0	2	6	3.6
Re-implant IPG	1	1	0	0	2	1.2

*SCS indicates spinal cord stimulation; IPG, implantable pulse generator.

As Table 23 shows, there were lead problems in approximately 11% of 166 SCS cases. These included lead migration and malposition. The incidence of IPG problems was 10.2%. Problems with the IPG included revision of the IPG implantation site, and replacement of the IPG due to battery failure. The IPG battery was explanted due to infection, recurrent rejection, battery failure, and failed therapy. Harke et al. (83) explanted 2 spinal cord stimulator devices because of progressive dementia most likely related to comorbid illnesses.

Table 24: Procedural Complications With Spinal Cord Stimulation Across Studies

	North et al., (81) 2005	Kemler et al., (63) 2004	Spincemaille et al., (42) 2004	Harke et al. (83) 2002	Total Complications	Total Complications/ 166 cases, %
No. of SCS* cases	19	23	96	28		
Follow-up, months	34	24	12	29		
Infection	1	1	0	0	2	1.2
Dural puncture	0	2	0	0	2	1.2
Dural puncture headache	0	1	0	0	1	0.6
Recurrent device rejection	0	1	0	0	1	0.6
Relapsing ulcerative colitis	0	1	0	0	1	0.6
Death (unrelated to SCS)	1	0	1	0	2	1.2

*SCS indicates spinal cord stimulation.

Device-related infection has been reported as the most common adverse event associated with SCS. (61) As Table 24 shows, 2 studies included in this systematic review reported infections. The overall infection rate was 1.2%. Kemler et al. (63) reported clinical signs (not culture positive) of infection in 1 subject who required antibiotic treatment and removal of the SCS device. North et al. (81) reported an infection at the implantation site of a neurostimulator radio frequency receiver. The SCS device was explanted and antibiotic therapy was administered.

Two studies each reported 1 death. In the RCT by North et al. (81) one SCS-treated study subject died suddenly of a cardiac event shortly after 6 months of treatment. Spincemaille et al. (42) reported 1 death but did not provide details on the cause.

Summary of Findings of Medical Advisory Secretariat Literature Review

Table 25 summarizes the levels of evidence for the 3 neuropathic pain conditions studied in the clinical trials included in this systematic review.

Table 25: Summary: Levels of Evidence by Neuropathic Condition and Outcome of Interest

Neuropathic Pain Condition	Primary Outcome for Systematic Review	Secondary Outcomes for Systematic Review	
	Pain Relief	Functional Status	Quality of Life
Failed back surgery syndrome	Level 2 (1 study) Level 3a (1 study)	*Level 3a (1 study)	*Level 3a (1 study)
Complex regional pain syndrome Type I	Level 2 (1 study)	*Lack of evidence evidence	*Lack of evidence
Postherpetic neuralgia	†Level 3a (1 study)	†Level 3a (1 study)	Not assessed

*Secondary measure for study.

†A multiple outcome measure for study.

Pain Relief

The following summarizes the level of evidence to support the effectiveness of SCS to relieve pain by at least 50% as measured by the VAS in the 3 main neuropathic medical conditions of interest for this review.

Failed back surgery syndrome: There is level 2 evidence from 1 study of high quality and level 3a evidence from one study of high quality for the use of SCS for neuropathic limb pain secondary to failed back surgery. Pain relief was qualified as a primary outcome in both level 2 and level 3a studies.

Complex regional pain syndrome, Type I: There is level 2 evidence from 1 high-quality study for the use of SCS for neuropathic limb pain associated with this neuropathic condition. Pain relief was qualified as a primary outcome in the study.

Postherpetic neuralgia: There is Level 3a evidence from 1 study with a small sample size (n = 28). Pain relief was a multiple outcome measure in the study.

Functional Status

The following summarizes the evidence supporting the effectiveness of SCS to improve functional status as measured by the ROLAND Disability Questionnaire and the Pain Disability Questionnaire in the 3 main conditions of interest in this review.

Failed back surgery syndrome: There is level 3a evidence from one study of high quality for the use of SCS to improve functional status in people with neuropathic limb pain secondary to failed back surgery. Functional status was a secondary outcome in the study.

Complex regional pain syndrome, Type I: There is a lack of evidence for the use of SCS to improve the functional status of people with neuropathic pain associated with this condition. Functional status was a secondary outcome. A lack of evidence may reflect a type II statistical error.

Postherpetic neuralgia: There is level 3a evidence from 1 study with a small sample size, (n = 28). Functional status was a multiple outcome measure in the study.

Quality of Life

The following summarizes the level of evidence to support the effectiveness of SCS to improve QOL in the 3 main conditions of interest in this review.

Failed back surgery syndrome: There is level 3a evidence from 1 study of high quality for the use of SCS to improve the QOL in people with neuropathic limb pain secondary to failed back surgery. QOL was a secondary outcome in the study.

Complex regional pain syndrome, Type I: There is a lack of evidence for the use of SCS to improve the QOL of people with neuropathic pain associated with this condition. A lack of evidence may reflect a type II statistical error.

Postherpetic neuralgia: QOL was not evaluated in this patient population.

Technical Failures and Complications

The results of the literature review showed that the most common technical failures were lead problems (10.8%) and IPG problems (10.2%). The most common procedural complications were infection (1.2%) and dural puncture (1.2%). None of the studies reviewed reported treatment-related deaths.

Economic Analysis

Ontario-Based Economic Analysis

Disclaimer: This economic analysis represents an estimate only, based on assumptions and costing methodologies that have been explicitly stated. These estimates will change if different assumptions and costing methodologies are applied for the purpose of developing implementation plans for the technology

Hospitalization Costs

Using a combination of International Classification of Disease 10 codes (ICD-10) and Canadian Classification of Intervention (CCI) Codes (Appendix 4) the number of SCS related hospitalizations per fiscal year was estimated from the discharge abstracts database. 53 related hospitalizations were identified for fiscal year 2002 and 32 for fiscal year 2003. Therefore, a range of 32 to 53 SCS related hospitalizations annually was used to calculate hospitalization costs.

To determine the cost in Canadian dollars per SCS case, the prospectively adjusted for complexity resource intensity weights known as PAC-10 weights were used. The PAC-10 weights are based on a weight of 1.0 having a dollar value of \$4,505 during 2003 (Personal communication, Ministry of Health

and Long-Term Care, May 2005). The average PAC-10 weight for SCS related hospitalizations in fiscal year 2003 is 1.54. The 2002 average PAC-10 weight was within 0.1 of this number. Therefore 1.54 was considered to be the overall average for both fiscal years and the cost per SCS related hospitalizations was estimated at \$6,956 (1.54 x \$4,505). The associated cost for the annual range of SCS related hospitalizations (32-53) for the past 2 fiscal years is between \$223,000 and \$369,000. It is important to note that the estimated cost per SCS case of less than \$7,000 does not cover the hospital's cost of purchasing the SCS device.

Device Costs

To obtain the price of the SCS device please consult Medtronic, Inc. <http://www.medtronic.com> or Advanced Neuromodulation Systems <http://www.ans-medical.com>.

Professional Costs

This section outlines the Ontario Health Insurance Policy (OHIP) costs for SCS treatment. SCS treatment involves a psychological assessment, then surgery to insert the trial SCS lead (trial phase) which takes approximately 2 hours. 70% of the time this will lead to the insertion of a permanent SCS device (permanent phase). 6 postoperative visits with either a neurosurgeon or a neurologist are estimated after permanent implantation of the SCS device.

All possible candidates for SCS undergo a psychological assessment. However, not all will be successful and proceed to the trial phase. Therefore, more people will have a psychological assessment than will eventually receive treatment with SCS. An estimated 70% of people having a psychological assessment will proceed to the trial phase. Of the patients who undergo the trial phase, about 70% to 80% will have a successful trial course of SCS and will be candidates for permanent SCS implantation. The following fees have been adjusted upward by 2% to reflect the new OMA agreement.

Table 26: Estimated OHIP costs for SCS treatment

	Treatment Phase	Cost (Canadian Dollars)	Fee Schedule Codes (FSC) and description of code
A	Total costs for psychological Assessment	\$51	FSCCK032: Physician reimbursement for neurocognitive assessment. Ontario fee schedule code
	Trial phase	\$328.24	FSC244: Physician reimbursement for percutaneous diagnostic stimulation of brain or spinal cord or trigeminal nerve root and/or ganglion (IOP).
		\$240.11	Upper limit of expected cost for anesthesia services for the trial phase surgery The Anesthetist costs are the number of units/case and a unit cost of \$12.01 for an anesthetist. For the trial phase an upper limit of 20 units are estimated. This includes 8 base units + 1 unit for each 15 minutes in the first hour of treatment + 2 units for every 15 minutes thereafter)

	Treatment Phase	Cost (Canadian Dollars)	Fee Schedule Codes (FSC) and description of code
B	Total professional fees for trial phase	\$568	
	Permanent insertion phase	\$307.38 \$328.24 \$384.17	<p>FSCZ823: Physician payment for implantation/revision of stimulation pack leads</p> <p>FSCZ244: Physician reimbursement for percutaneous diagnostic stimulation of brain or spinal cord or trigeminal nerve root and/or ganglion (IOP)</p> <p>Total costs for anesthesia services for permanent insertion phase.</p> <p>Anesthetist costs for permanent insertion phase include 8 base units + 1 unit for each 15 minutes in first hour + 2 units for every 15 minutes thereafter. A unit fee for anesthetists is \$12.01</p> <p>Two FSC charges are used for this phase: FSCZ244 charged for 2 hours of service and FSC823 charged for 1 hour of service).</p> <p>Assumption: Base units for each FSC code of 8 units + time units of 32 units = expected number of units</p> <p>(8 base units under FSCZ823 + 8 base units under Z244 + 12 time units under FSCA823 + 4 time units under FSCZ244)</p>
C	Total Profession medical fees for Permanent insertion phase	\$1,020	
D	Follow-up assessments	\$127.50 \$25.14 \$102.00 \$26.52	Any of the following FSC codes are applicable: FSCA185: neurology consult FSCA188: neurology partial assessment FSCA045: neurosurgery consult FSCA044: neurosurgery partial assessment
	Total expected post operative physician costs	\$333	Estimated 1 consult by each of neurosurgery and neurology plus 2 partial assessments by each
	Total estimated professional medical fees per SCS case	\$2,270	Use total costs found in row A, B, C, D $\$51/(70\%*70\%) + \$568/70\% + \$1,020 + \333
	Total estimated professional medical fees based on 53 annual permanent insertion phases.	\$120,286	$53 \times \$2270$

Downstream Cost Savings

SCS procedures are known to reduce the need for medications to treat neuropathic pain. However, because these medications are prescribed for a number of ailments, and because the patterns of prescribing are not easily assessed specifically for neuropathic pain, it is difficult to quantify the potential cost offsets of SCS. Based on previous experiences the present value of a lifetime use of prescription pain medications would exceed \$10,000, which would offset a large portion of the total costs associated with SCS treatment (estimated at approximately \$20,000). It is important to note, however, that not all drug costs savings would accrue to the province, because the Ontario Drug Benefit program only covers 23.6% of the residents of Ontario.

Cost-Effectiveness

A number of studies indicate that although SCS has high up-front costs compared with conventional therapy, in the long-term, it saves costs. A study (84) at the Cleveland Clinic in the United States of 222 consecutive patients followed-up for a average of 3.1 years postoperatively found a \$17,963 (US dollars) net per-patient per-year savings compared to medical cost before SCS treatment. This was primarily due to a drop in other surgical procedures and medical imaging investigations such as magnetic resonance imaging or computed tomography scans).

Similarly, a prospective matched cohort Canadian study (85) comparing SCS with conventional pain therapy found cost-savings of approximately \$11,000 (Canadian dollars) over 5 years postoperatively and a break-even in costs at 2.5 years.

A meta-analysis of 14 cost-effectiveness studies (76) of SCS confirmed a finding of long-term cost-savings associated with this intervention.

Existing Guidelines for Use of Technology

Several professional groups have published guidelines for the use of SCS.

European Task Force

A consensus statement prepared by the Task Force of the European Federation of the International Association for the Study of Pain (IASP) (56) was published in 1998. These guidelines recommend that SCS be used “only in those patients in whom well conducted, more conservative pain treatments have failed, and there is no indication for further surgical intervention to treat the underlying pathology.” SCS was recommended in the following conditions:

- Neurogenic pain conditions
- Mixed neurogenic and nociceptive pain conditions (FBSS)
- Intractable angina pectoris
- Peripheral vascular disease

American Society of Anesthesiologists

The American Society of Anesthesiologists (86) has published guidelines for the management of chronic pain. They state: “Spinal cord stimulation should not be a first-line treatment but may be considered after failure of oral medications. Spinal cord stimulation may be effective in the management of patients with

peripheral neuropathic pain or with pain arising from the spinal cord (arachnoiditis, syringomyelia, spinal cord injury, and multiple sclerosis). It should be preceded by a trial with a percutaneous electrode system.”

Consensus Statement

Canadian Pain Society

The Canadian Pain Society does not have guidelines for the use of SCS in chronic neuropathic pain. However, a published consensus statement (12) for the use of opioid analgesics in the treatment of chronic non-cancer pain mentions SCS as a palliative surgical procedure.

Policy Considerations

Demographics

The number of people in Ontario with neuropathic pain due to FBSS, CRPS, and postherpetic neuralgia has been estimated as shown below

Failed Back Surgery Syndrome

About 15% to 40% of patients will have chronic back and limb pain after lumbar surgery. Based on fee schedule codes from provider services, about 5343 spine surgeries have been completed yearly between 2001 and 2003. Of these, it is estimated that 15% to 40%, or **801 to 2137**, will develop chronic back and limb pain.

Complex Regional Pain Syndrome

The incidence of CRPS is estimated at 5.46 cases per 100,000 people. Using the Ontario Ministry of Finance 2001 census, the number of people between the ages of 15 and 79 with CRPS is estimated at **514** (based on 9,416,627 people between the ages of 15 and 79).

Postherpetic Neuralgia

The incidence of herpes zoster in Canada has been estimated at 423 per 100,000 population-years for people aged 45 to 64, and 812 per 100,000 population-years for people aged 65 years or older. Using the Ontario Ministry of Finance 2001 census, an estimated 12,093 new cases of herpes zoster will occur per year in people aged 45 to 64 (population estimate 2,858,898), and 9373 cases will occur in people aged 65 to 79 (population estimate of 1,154,335). Twenty per cent of people older than 50 years who receive treatment will experience pain 6 months after the onset of the herpes zoster rash. (25) This yields an estimated **4293** people with postherpetic neuralgia.

It has been estimated that approximately 10% and up to 20% of people with neuropathic pain may develop intractable pain (personnel communication, December 14, 2004). Of these, about 70% will proceed to test stimulation after psychological evaluation. As this systematic review shows, 67% to 100% (average, 84%) of people undergoing test stimulation will be successful and proceed to SCS implantation. Using these estimates, and the estimates of the incidence of FBSS, CRPS and postherpetic neuralgia, the number of people in Ontario that would need SCS (target population) has been derived.

Estimate of Target Population

The lower estimate of FBSS, 15% of all spine surgeries, has been used to take into account this unknown estimate. Therefore, if we consider those with FBSS, CRPS, and postherpetic neuralgia, the estimated number of people in Ontario per year that would benefit from SCS is as follows:

- (A) People with FBSS (15% of spine surgeries) + CRPS + postherpetic neuralgia: 5608 (801 + 514 + 4293)
- (B) 10% to 20% of those in (A) will develop intractable pain: 561–1122
- (C) 70% of those in (B) will proceed to test stimulation after a psychological evaluation: 393–785
- (D) On average 84% of those in (C) will have a successful test stimulation and proceed to SCS implantation: **330–660**

Therefore it is estimated that 330-660 people per year would benefit from SCS treatment.

Number of Spinal Cord Stimulation Devices Implanted in People in Ontario

The number of SCS devices implanted in people in Ontario in the last 2 years was estimated from the number of SCS related hospitalizations extracted from the Provincial Health Planning Database using the CCI codes for the SCS procedure and the appropriate ICD-10 diagnosis codes. For the 2002 fiscal year, 53 patient separations were captured. For the 2003 fiscal year, 32 were captured. Therefore, about 30 to 50 people in Ontario are receiving SCS per year.

Diffusion of Technology

In 1998, it was estimated (56) that each year 15,000 patients world-wide (5000 in Europe alone) were using SCS.

Number of Sites Offering Spinal Cord Stimulation Therapy

Eight hospitals in Ontario implant spinal cord stimulators in people, but not all are active. One site does approximately 30 SCS implantations per year. Two sites have closed their program due to a lack of infrastructure and funding support, and 5 sites do only a few implantations (approximately fewer than 10 per year).

Health System Considerations

Infrastructure

- Neuropsychological resources are required to assess the eligibility of patients for SCS. More patients have psychological testing to determine suitability for SCS than actually receive SCS treatment.
- As more patients receive the SCS implants, the number of patients requiring long-term management will increase, which will require more downstream human resources to manage the case load. A dedicated nurse specifically trained in neuromodulation therapy (neuromodulation nurse) would facilitate patient assessment in the operating room during lead insertion and electrode placement, and during the post-operative clinic visits and long-term management. The high incidence (approximately

11% from the systematic review) of technical complications, in particular lead migration, makes patient assessment demanding in the first year.

- Need to attract interest from medical specialists, including anesthesiologists and neurosurgeons, to support the program.
- Operating room time needed to manage technical failures, which are prevalent in the first year.

Equipment

SCS supplies are required, including electrodes for test stimulation and the full device for patients that proceed to permanent implantation.

Conclusions

- Level 2 evidence from 2 studies of high quality supports the effectiveness of SCS to reduce pain in some neuropathic pain conditions.
- There is supportive evidence from secondary outcomes from level 3a evidence that treatment with SCS improves functional status and QOL.
- The need for SCS services is estimated at 330 to 660 people per year.
- Current services provide SCS to 30 to 50 people per year.

Glossary

Adjuvant therapy	A therapy that is added to a primary therapy to increase the effectiveness of the primary therapy
Afferent nerves	A nerve that carries impulses toward the central nervous system; the opposite is an efferent nerve
Analgesia	The relief of pain without loss of consciousness
Chronic pain	Persistent, long-term pain that cannot be removed
Complex regional pain syndrome	A chronic pain condition associated with intense, continuous pain that does not improve with time and that most often affects one of the arms, legs, hands, or feet; also called reflex sympathetic dystrophy syndrome and causalgia
Dermatomes	Localized areas of the body that are supplied with afferent nerves from a single spinal nerve; responsible for pain and other sensations
Epidural space	The space between the dura mater and the walls of the vertebral canal, containing venous plexuses and fibrous and alveolar tissue
Failed back surgery syndrome	A generalized term that is often used to describe the condition of patients who have not had a successful result with back surgery or spine surgery
Herpes zoster	An acute, localized infection caused by the varicella-zoster virus that produces a painful, blistering rash; also called shingles
Hyperesthesia	Extreme sensitivity to normal touch, pain, or other stimuli that can manifest as a painful sensation
Incidence	Number of new cases of a disease over time.
Interquartile range	Used to express the inner 50% of values (the range between the 75 th and 25 th percentiles)
Intractable pain	Pain that does not respond to treatment
Ischemic pain	Pain felt throughout the chest, typically as squeezing, tightness, pressure, or burning
Laminotomy	Surgery to cut the lamina also called the vertebral arch, which is a thin, flat bony layer of the vertebrae (back bone) that covers the spinal canal
Median	A distribution's midpoint at which exactly one-half of the values fall above and one-half fall below
Neuromodulation	Electrical stimulation of a peripheral nerve, the spinal cord, or the brain for relief of pain
Neuropathic pain	Pain caused by damage to the tissue of the peripheral or central nervous system (e.g., a pinched nerve); generally felt as burning or tingling and often happening in an area of sensory loss
Number needed to treat (NNT)	This is how many patients must be treated with an intervention for a certain period to prevent 1 bad outcome or result in 1 good outcome
Nociceptive pain	Pain caused by injury or disease outside the central nervous system that is often felt as a dull ache (e.g., pain due to arthritis)
Opioid	A strong drug to treat moderate to severe pain
Percutaneous	Done through the skin
Postherpetic neuralgia	Persistent burning pain and hyperesthesia along the distribution

Prevalence

Quality-adjusted Life-year

Spinal cord stimulation

Sympathectomy

Transcutaneous electrical nerve stimulations (TENS)

Type I error

of a cutaneous nerve after an attack of herpes zoster; it may last for a weeks to months

Total number of people with the disease at any one time

The number of life years adjusted by the degree of poor health

A reversible pain therapy that uses low-voltage electrical pulses to manage chronic, intractable neuropathic pain of the trunk or limbs

The transection or interruption (chemical or surgical) of any part of the sympathetic nervous system pathways

A therapy that delivers low-voltage electrical stimulation to the nerves to relieve pain

This happens when data show a statistically significant result, although no true difference or association exists; it often happens when multiple comparisons are done

Appendices

Appendix 1: Literature Search Strategy – Spinal Cord Stimulation

Search date: December 3, 2004

Databases searched: OVID Medline, OVID In Process and Other Non-Indexed Citations, Embase, Cochrane database of Systematic Reviews, Cochrane CENTRAL, INAHTA

Database: Ovid MEDLINE(R) <1996 to November Week 3 2004>

Search Strategy:

-
- 1 exp Electric Stimulation Therapy/ (5057)
 - 2 exp Electrodes, implanted/ (7923)
 - 3 exp Electric Stimulation/ (21613)
 - 4 neuromodulation.mp. (556)
 - 5 exp Spinal Cord/ or exp Spine/ (37230)
 - 6 or/1-4 (33105)
 - 7 5 and 6 (1925)
 - 8 spinal cord stimulat\$.mp. [mp=title, original title, abstract, name of substance, mesh subject heading] (423)
 - 9 dorsal column stimulat\$.mp. (21)
 - 10 7 or 8 or 9 (2059)
 - 11 exp Pain/ (68779)
 - 12 exp Complex Regional Pain Syndromes/ (961)
 - 13 exp Phantom Limb/ (327)
 - 14 neuropathic pain.mp. (2201)
 - 15 exp Peripheral Nervous System Diseases/ (24699)
 - 16 failed back surgery syndrome.mp. (69)
 - 17 exp Treatment Failure/ (8910)
 - 18 chronic pain\$.mp. (4151)
 - 19 exp Arterial Occlusive Diseases/ (36685)
 - 20 or/11-19 (135043)
 - 21 10 and 20 (558)
 - 22 limit 21 to human (375)
 - 23 limit 22 to systematic reviews (24)
 - 24 22 (375)
 - 25 limit 24 to (case reports or comment or editorial or letter or "review" or "review literature" or review, multicase or "review of reported cases") (177)
 - 26 24 not 25 (198)
 - 27 23 or 26 (213)
 - 28 limit 27 to yr=2000-2005 (123)

Similar search strategy employed for Cochrane CENTRAL

Database: EMBASE <1996 to 2004 Week 48>

Search Strategy:

-
- 1 exp electrostimulation therapy/ (33461)
 - 2 exp electrostimulation/ (11012)
 - 3 exp electrode/ (15373)
 - 4 exp neuromodulation/ (6205)
 - 5 exp electroanesthesia/ (9)
 - 6 or/1-5 (59583)
 - 7 exp spinal cord/ (13319)
 - 8 exp SPINE/ (19341)
 - 9 6 and (7 or 8) (1980)
 - 10 spinal cord stimulat\$.mp. [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name] (897)
 - 11 dorsal column stimulat\$.mp. [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name] (29)
 - 12 epidural stimulat\$.mp. [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name] (35)
 - 13 or/10-12 (935)
 - 14 9 or 13 (2707)
 - 15 exp Pain/ (144201)
 - 16 exp Agnosia/ (820)
 - 17 failed back surgery syndrome.mp. (105)
 - 18 exp Neuropathy/ (68937)
 - 19 exp Treatment Failure/ (19357)
 - 20 or/15-19 (212213)
 - 21 14 and 20 (930)
 - 22 limit 21 to (human and yr=2000-2005) (489)
 - 23 exp "Systematic Review"/ or Meta Analysis/ or systematic review\$.mp. or systematic overview\$.mp. or meta analys\$.mp. or metaanalys\$.mp. [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name] (21567)
 - 24 22 and 23 (15)
 - 25 22 (489)
 - 26 Case Report/ (333388)
 - 27 25 not 26 (408)
 - 28 limit 27 to (editorial or letter or note or "review") (174)
 - 29 27 not 28 (234)
 - 30 24 or 29 (245)

Appendix 2: College of Physicians and Surgeons of Ontario: Interventions for the Treatment of Neuropathic Pain, 2000

Reprinted with Permission from the College of Physicians and Surgeons of Ontario, Evidence-based recommendations for medical management of chronic non-malignant pain. 2000. (27)

Condition	Anti-convulsants	Anti-depressants	Oral Drugs with Local Anesthetic Type Properties	Opioids	Topical (Capsaicin)	Intravenous Regional Sympathetic Blocks
Trigeminal neuralgia	Level I	No controlled trials	Level II	Level V	No controlled trials	Not applicable
Peripheral nerve injury	No controlled trials	No controlled trials	Level II	No controlled trials	No controlled trials	No controlled trials
Postherpetic neuralgia	Level II	Level II	Level II	Level II	Level II	No controlled trials
Complex regional pain syndrome Type I	No controlled trials	No controlled trials	No controlled trials	No controlled trials	No controlled trials	Level III
Diabetic neuropathy	Level I	Level I	Level II	Refer to comments in guidelines.	Level II	No controlled trials
Pain after stroke	Level II	Level II	No controlled trials	No controlled trials	No controlled trials	No controlled trials
Spinal cord injury	No controlled trials	No controlled trials	Level II	No controlled trials	No controlled trials	Not applicable
Pain after mastectomy	No controlled trials	No controlled trials	No controlled trials	No controlled trials	Level II	Not applicable

Level legend:

- Level I: Strong evidence from at least 1 systematic review of multiple, well-designed RCTs.
 Level II: Strong evidence from at least 1 properly designed RCT of appropriate size.
 Level III: Evidence from well-designed trials without randomization, single-group pre-post, cohort, time series, or matched-case controlled studies.
 Level IV: Evidence from well-designed nonexperimental studies from more than 1 centre or research group.
 Level V: Opinions of respected authorities, based on clinical evidence, descriptive studies, or reports of expert committee.

Appendix 3: Study Characteristics

Study, Year	Methods	Participants	Interventions	Outcomes	Notes
North et al., 2005(81)	<p>RCT</p> <ul style="list-style-type: none"> - Subjects randomized to SCS or back reoperation (re-op.); - Randomization determined by opening sealed opaque envelopes that contained computer-generated random assignments from an outside biostatistician - Non-blinded study. - Withdrawals/drop-outs accounted for. - Quality 3/5 (Jadad score) 	<p>50 patients:</p> <p>Patients with failed back surgery syndrome recruited by 8 spine surgeons.</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> -Patients with surgically remediable nerve root compression with complaints of persistent or recurrent radicular pain with or without low back pain after at least 1 lumbosacral spine surgery -Pain refractory to conservative care -Imaging findings of neural compression <p>Exclusion criteria:</p> <ul style="list-style-type: none"> -Disabling neurological deficit in the distribution of a nerve root(s) caused by surgically remediable compression -Critical cauda equina compression -Gross instability needing fusion -Untreated dependency on narcotics or benzodiazepines -Major untreated psychiatric comorbidity -Unresolved issues of secondary gain -Concurrent or disabling chronic pain problem, low back pain exceeding radicular pain (hip, buttock and leg pain) 	<p>24 patients were randomized to a test period of SCS</p> <p>Test Period: 3 days with a temporary Medtronic Pisces Quad Percutaneous Leads (3487A)</p> <p>Success defined as at least 50% pain relief, stable or improved pain medication intake, improved physical activity. Successful patients proceeded to implantation phase.</p> <p>17 patients proceeded to implantation phase.</p> <p>Permanent leads were surgically inserted (Medtronic Resume Electrode 3587A or 3487 A-56) along with an Implantable Pulse Generator inserted (Medtronic X-trel or Itrel Pulse Generator)</p> <p>26 patients were randomized to a reoperation (re-op). Reoperation included laminectomy ± foraminotomy ± discectomy with or without fusion, with or without instrumentation</p> <p>All patients received standard postoperative analgesics, which were tapered as soon as possible, and routine postoperative physical therapy.</p> <p>Follow-up: 0.5, 1, and 2 years by disinterested non-blinded third party evaluator</p>	<p>Success was defined as at least 50% pain relief and patient satisfaction with treatment.</p> <p>Study end points:</p> <ul style="list-style-type: none"> -Crossover from the randomized to the alternate procedure. -Success at last follow-up. -Improvement in daily activities, neurological status and medication use. <p>Results:</p> <p>Crossover at 2 years: 5/24 (21%) crossed to re-op. vs. 14/26 (54%) crossed to SCS. ($P = .02$)</p> <p>Success at 2 years: 9/19 (47%) SCS patients vs. 3/26 (12%) re-op patients ($P < .01$)</p> <p>Opioid use at 2 years: 3/23 (13%) SCS patients vs. 11/26 (42%) re-op patients had increased opiate use ($P = .025$).</p>	<p>4 patients in the SCS group were lost to follow-up.</p> <p>1 SCS patient died suddenly of a cardiac event at 6 months follow-up.</p> <p>Intention-to-treat analysis included patients randomized and treated (N = 50).</p> <p>10 patients were randomized & not treated; in 9 patients, Workers' compensation did not authorize participation, and 1 other patient had a stroke that precluded treatment.</p>
Kemler et al., 2004(63)	<p>RCT</p> <ul style="list-style-type: none"> -Subjects randomized to SCS plus physiotherapy (PT), or standardized physical therapy in a 2:1 allocation ratio in favour of the SCS + PT group; - Table of random numbers used to make 	<p>54 Patients</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> -18–65 years old -reflex sympathetic dystrophy (RSD) diagnosed using the International Association for the Study of Pain (IASP) criteria -Patients had impaired function; symptoms beyond the area of 	<p>Study treatments: SCS + PT vs. PT only.</p> <p>36 patients were randomized to a test period of SCS</p> <p>Test period: 7 days with a temporary percutaneously inserted electrodes (model 3861; Medtronic) connected to an external simulator (Medtronic Model 3625);</p> <p>Success was defined as at</p>	<p>Outcome measures: Pain, perceived effect of treatment, functional status, quality of life.</p> <p>Results: At 2 years: mean pain intensity was reduced with SCS + PT vs. PT respectively -mean, 2.1 (SD, 2.8) vs. mean, 0 (SD, 1.5)</p>	<p>Baseline measurement taken after randomization and before treatment in all groups.</p>

Study, Year	Methods	Participants	Interventions	Outcomes	Notes
	<p>randomization schedule</p> <ul style="list-style-type: none"> - Randomization was stratified by location of pain (hand or foot); - Randomization code was concealed to investigators. <p>-Intention-to-treat analysis.</p> <p>- Non-blinded</p> <p>- Withdrawals/dropouts accounted for.</p> <p>- Quality 3/5 (Jadad score)</p>	<p>trauma; and the disease was restricted to one hand or foot</p> <ul style="list-style-type: none"> -Disease persisted for at least 6 months; there was no sustained response to standard therapy -Patient had a VAS pain score of at least 5 cm, (0 cm = no pain to 10 cm = very severe pain) <p>Exclusion Criteria:</p> <ul style="list-style-type: none"> -Raynaud's disease, current or previous neurologic issue unrelated to RSD -Concurrent condition affecting function of the diseased or contralateral extremity -Blood-clotting disorder -Anticoagulant therapy -Use of a cardiac pace maker-A serious psychiatric disorder. 	<p>least 50% pain relief on the VAS or a score of at least 6 (much improved) on a 7-point scale of global perceived effect of treatment. Successful patients would proceed to implantation</p> <p>24 patients proceeded to implantation of SCS device. Permanent leads were inserted percutaneous (model 3487A; Medtronic) along with an implantable pulse generator (Itrel III, model 7425; Medtronic).</p> <p>18 patients were randomized to receive PT only.</p> <ul style="list-style-type: none"> -Patients underwent a standardized physical therapy program of graded exercises to improve strength, mobility, and function of affected limb 30 minutes twice per week, with a minimum of 2 days between treatments for 6 months -Physical therapists were trained to provide a standardized program; coordinating physical therapist monitored standardization of treatment. -Continuation with program after 6 months was optional. -SCS trial phase failures received physical therapy. <p>Follow-up at 1, 3, and 6 months, and at 1 and 2 years.</p>	<p>($P < .001$)</p> <p>Global Perceived Effect Score:</p> <p>At 2 years: 15/35 (43%) in SCS + PT reported score of ≥ 6 (much improvement) vs. 1/16 (6%) PT patients ($P = .001$)</p> <p>% success: (defined as a 50% decrease in the VAS score at the start of treatment)</p> <p>At 2 years: 13/35 (57%) SCS + PT successfully treated vs. 1/16 (6%) PT patients.</p> <p>Functional status or quality of life was not significantly different between groups at 2 years</p>	

Study, Year	Methods	Participants	Intervention	Outcomes	Notes
Spincemaille et al., 2004(42)	<p>Prospective non-RCT with a before-and-after treatment design</p> <p>14 centres participated.</p> <p>Eligible subjects were registered with an independent centre and given a unique study number.</p>	<p>105 patients with failed back surgery syndrome, defined as persistent limb pain with or without concomitant minor back pain after prior surgery for a slipped lumbar disc or spinal.</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> -18 years of age or older -Pain for more than 12 months -Surgical therapy not an option as per surgeon-failed other non-invasive therapies -VAS pain score \geq 5. <p>Exclusion criteria:</p> <ul style="list-style-type: none"> -Previous SCS -Drug addiction -Noncompliance -Coagulopathy -Anticoagulation therapy -Immunologically compromised -Life expectancy < 1 year -Secondary nerve entrapment -Pregnant -Cardiac pacemaker -SCL-90 score \geq 225. 	<p>Study treatments:</p> <p>SCS only: patient was his/her own control before and after SCS.</p> <p>135 patients were given a test period of SCS. The type of lead used for the test period was not described. Success was defined as patients having at least 50% reduction in pain intensity. Successful patients would proceed to implantation of SCS device.</p> <p>105 patients proceeded to implantation of SCS device. Type of lead and SCS device not described.</p> <p>Follow-up: 1, 3, 6, 9, 12, 18 months.</p> <p>Data collected by an independent centre.</p>	<p>Primary outcome: pain reduction.</p> <p>Secondary outcomes: functional status and quality of life scores.</p> <p>Results: mean (S.D.)</p> <p>Pain Visual analogue scale score: Pre: 7.3 (1.3) Post: 3.0 (2.4)</p> <p>McGill Pain Questionnaire: Pre: 22.4 (9.4) Post: 10.8 (8.0)</p> <p>Functionality Roland Disability: Pre: 16.9 (3.5) Post: 12.4 (4.8)</p> <p>Quality of Life: Sickness Impact Profile-68: Pre: 19.4 (10.1) Post: 11.7 (9.4) Euroqol-5D: Pre: 55.2 (14.5) Post: 38.2 (19.2)</p> <p>For all outcomes ($P < .05$), post-SCS scores vs. pre-SCS scores.</p>	<p>9 patients were lost to follow-up at 12 months</p> <p>4 patients had insufficient stimulation.</p> <p>2 patients stated the therapy was inadequate.</p> <p>2 were waiting for lead revision.</p> <p>1 died, but the cause was not stated.</p>
Harke et al., 2002(83)	<p>Prospective non-RCT with a before-and-after treatment design.</p> <p>Consecutive enrollment between 1994 and 2000</p>	<p>28 Patients with postherpetic neuralgia (PHN);</p> <p>4 patients with acute herpes zoster pain.</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> -Postherpetic neuralgia or acute herpes zoster -Ineffective medication and increasing pain, diagnosis confirmed by neurologist <p>Exclusion Criteria:</p> <ul style="list-style-type: none"> -Responsive to selective sympathetic nerve blocks -Strong neurotic disorders 	<p>Study treatments:</p> <p>SCS only: patient was own control before and after SCS.</p> <p>28 patients with postherpetic neuralgia were given a test period of SCS for 5–7 days using a percutaneously inserted quadripolar lead. An external pulse generator 3625 Medtronic was used for all patients.</p> <p>28 patients with postherpetic neuralgia proceeded to implantation of SCS device. Patients kept same electrodes used during trial phase but received an implantable pulse generator to which the lead</p>	<p>Results:</p> <p>Of the 28 patients with postherpetic neuralgia, 23 were long-term responders.</p> <p>5/28 stopped using SCS due to progressive dementia that rendered them unable to comply with therapy.</p> <p>Results from patients with postherpetic neuralgia: Pain: Visual analogue scale scores, median (interquartile range) Pre: 9 (7.5–10.0)</p>	<p>All patients had co-morbid disorders including cardiovascular, brain, lung, and endocrine disorders; or cancer.</p> <p>Periodic SCS inactivation tests were done to test for spontaneous improvement.</p> <p>During SCS inactivation periods, there was an observed reoccurrence of pain.</p>

Study, Year	Methods	Participants	Intervention	Outcomes	Notes
			<p>was then attached. (Medtronic Itrrel II or III device)</p> <p>Follow-up: Median, 29 months (range, 9–38.5,] months)</p>	<p>Post: 1.0 (1.0–2.75) <i>P</i> < .001</p> <p>Functionality: Pain Disability Index: function improved significantly after SCS (<i>P</i> < .001)</p> <p>Pain medication: 13/23 patients did not require any pain medication during SCS</p>	<p>Antidepressants were a co-medication in 14 patients because of depressive symptoms. An analgesic effect of antidepressants could not be determined, because all patients had reappearance of pain during the inactivation period of SCS regardless of antidepressant use.</p>



N. William Fehrenbach, MSSW
Reimbursement Director

Medtronic, Inc.
Neuromodulation
7000 Central Avenue NE, RCE 395
Minneapolis, MN 55432
www.medtronic.com

tel 763-526-8193
fax 763-526-8373
william.fehrenbach@medtronic.com

October 8, 2010

Leah Hole-Curry, JD
Director, Health Technology Assessment
676 Woodland Square Loop SE
Lacey, WA 98503
Leah.hole-curry@hca.wa.gov

Brian R. Budenholzer, MD, FAAP.
Chair, Health Technology Clinical Committee
Group Health South Hill Medical Center
4102 S. Regal Street, Suite 101
Spokane, WA 99223

Re: Health Technology Assessment Process Concerns

Dear Ms. Hole-Curry and Chairman Budenholzer:

We are writing to you on behalf of Medtronic Neuromodulation. Medtronic is the world's leading medical technology company, specializing in implantable therapies that alleviate pain, restore health, and extend life. One of our technologies is the spinal cord stimulator (SCS).

Our purpose for writing is to raise concerns regarding the Washington State health technology assessment (HTA) process in general and as recently demonstrated in the discussions surrounding SCS. As we and other stakeholders have suggested in the past, we are concerned about several procedural aspects of the HTA process. These are:

- The lack of full and interactive expert involvement
- Abbreviated timelines for submissions and testimony
- Devaluation of appropriate evidence in favor of lower level evidence
- Little consideration given to Medicare and professional guidelines
- Transparency and openness regarding process expectations and execution

Our concerns related to each of these flaws are detailed below. In the SCS review specifically, we are concerned that these procedural issues resulted in a decision that is not based on appropriate evidence or expert clinical opinion, nor does it reflect the conclusions (or even significant consideration) of

Medicare or the vast majority of medical society and patient group treatment guidelines, the vast majority of which support SCS.

Full and Interactive Expert Involvement

We continue to believe that there is a critical need to have a technology expert interactively and fully participating with the Health Technology Clinical Committee (HTCC) and that it is of extreme importance. At the August 20 meeting, Dr. Hugh Allen's expert input was limited by the fact that he was only allowed to respond to questions specifically directed to him instead of being allowed to be fully and interactively engaged in the discussion. Allowing for broader expert opinion would be beneficial to the process. Specifically related to the SCS review, allowing for broader input from experts would have benefited the HTCC committee members in the following ways:

- The inaccurate mortality statistics presented by the Agency Medical Director Group presenter would have been corrected.
- The discussion of the limitations of the Turner cohort study may have been more thorough and balanced
- A more comprehensive discussion about sample size related to the three randomized controlled trials (RCTs) on SCS and the concept of "statistically powered studies," and a better understanding of why it is unreasonable to discount device RCTs due to their size may have occurred
- The discussion about the Medicare National Coverage Determination (NCD), professional society treatment guidelines and patient advocacy group treatment guidelines (the vast majority of which are supportive of SCS) may have been more complete and would have better met the intent of the law.

Timelines

During the deliberations, the presentation by the AMDG representative, Dr. Lee Glass, went far beyond the usual factual presentation about agency use and costs. More importantly, he was given as much time as all of the experts and practitioners who had come to testify on SCS, which is beyond the bounds of reasonableness. This issue was compounded by the last minute procedural change with respect to public testimony. More specifically:

- The HTA has always, including earlier during the week of August 20th, indicated that a total of 30 minutes would be allotted for total public testimony. However, at the beginning of the SCS discussion on August 20th, it was clarified that public testimony time would not be artificially limited to 30 minutes. However, it was too late for additional interested parties to be notified of this change and appear to testify.
- An advanced notification of increased time for public testimony would have allowed other physicians and patients the opportunity to attend the meeting in order to provide meaningful evidence and first-hand testimony regarding the benefits of SCS.
- The North American Neuromodulation Society, one of the relevant national professional medical societies whose members are engaged in the implantation of SCS systems, flew in a nationally known neurosurgeon familiar with SCS and its evidence base to testify, but that testimony was limited to 5 minutes. National professional societies who independently dedicate society time and resource to travel to Seattle and engage in these discussions should not be limited to only 5 minutes of testimony.

- Further, as the brief allotted time to experts came before both the AMDG comments and the evidence vendor’s review, there was no chance to comment on those presentations, even though some of the information presented was either incorrect or incomplete, highlighting the need for further process improvements.

Society panels need to be granted the same stand-alone time as the AMDG to provide opportunity for a balanced discussion. Separately, as was announced on 8/20, other public testimony needs to be unlimited, with 5 minutes for each non-society panel in advance, and 3 minutes for everyone that wants to speak that same day. This practice needs to be formalized and made public well in advance of the actual meeting to allow interested Washington citizens and others to best plan their participation. In the future, it would seemingly make sense to allow the vendor (and the AMDG) to make their comments first, followed by national society and other public testimony, and finally the interactive HTCC discussion. Clearly, establishing more of an interactive dialogue with society and external experts, and the committee would be beneficial to all involved.

Devaluation of High Level Evidence

During the SCS review, several methodologically sound and statistically powered RCT higher level studies were trumped by one lower level study, while other lower level evidence was not considered or discussed.

- Three existing RCTs demonstrating the efficacy of SCS were disregarded in favor of the Turner, et al. cohort study in the subpopulation of Workers’ Compensation patients.
- This single cohort study was the sole source of evidence used to support the evidence vendor’s conclusion about the effectiveness of SCS. Interestingly, the vendor ranked this study a level of “2” when our review, demonstrates a potential ranking of class “3” given the lack of controlling for all baseline characteristics that were unequally distributed between treatment groups as well as incongruence between the evidence vendor’s report that this was and was not done (final evidence report pg. 160, 161 and separate appendices document pg. 12).
- In addition to the three RCTs, a large body of observational data on the effectiveness of SCS could have been used to supplement the evidence vendor’s conclusions on effectiveness. In fact, the vast majority of the observational data, like RCTs, similarly show the benefits of SCS.

Medtronic has a strong commitment to evidence-based medicine. We support health technology assessments and reviews that are robust. We are concerned with the apparent devaluation of robust randomized control trials in favor of lower levels of evidence. This approach would seemingly be at odds with your own rules that require the greatest weight be given to the highest ranked evidence (WAC 182-55-030).

Appropriate and Thorough Consideration of Medicare, Professional Society and Patient Guidelines

RCW 70.14.110(3) requires that consideration be given to Medicare coverage policy decisions as well as professional society and patient advocacy group guidelines. During the review of SCS, the HTCC gave little or no consideration to either of these.

- The CMS NCD for SCS states that the implantation of central nervous system stimulators may be covered as therapies for the relief of chronic, intractable pain, subject to conditions including that the stimulator be used only as a late or last resort, that other treatment modalities have been tried and were proven unsatisfactory or unsuitable, that patients have undergone

- The HTCC's non-coverage decision stands in stark contrast to the envisioned use and corresponding positive recommendations included in most professional society treatment guidelines. More specifically, the vast majority of any relevant professional society guidelines are supportive of appropriate use of SCS including EFNS, ICSI, ASIPP, ODG, RSDSA, APS, ASA, and, to a limited extent, ACOEM.

The HTCC's decision must be revisited as the HTCC neither had a robust discussion of existing Medicare coverage policies and guidelines nor, per the RCW, was substantial evidence to support a contrary decision presented. This is highlighted by the recording and subsequent professional transcript of 8/20, which indicated that approximately 1 minute and 47 seconds was dedicated to committee discussion of Medicare (2 minutes and 17 seconds when all public testimony mentions are included) and 42 seconds to committee discussion of treatment guidelines (which actually and unfortunately contained significant misrepresentations), and as far as we are aware there was no formal presentation of these issues.

Transparency and Openness

Since the August 20 meeting, there has been significant confusion around what protocols are used by the HTA in sharing publicly submitted information with either the vendor or with the HTCC directly. Separately, questions have been raised regarding what methodology the vendor is supposed to use in determining what pieces of publicly submitted information should be included in their report as there does not seem to be a clear standard which is being applied.

In order to aid the HTA, vendor and HTCC, our two submissions provided detailed and substantive published and non-published information and critique for their consideration and inclusion.

First, the evidence-related comments submitted by Medtronic Neuromodulation in January about SCS were comprehensive (Attachment 1). In brief, the initial draft vendor report did not appear to include any reference to this document or these important components, including:

- Data from a United HealthCare Reden & Anders actuarial model based on real claims data which demonstrated cost savings for SCS.
- A summary of published clinical and economic evidence for SCS.
- A *comprehensive* review of qualifying professional society and patient advocacy guidelines based on methodologies employed, in the past, by your evidence vendors.
- A *comprehensive* and methodologically sound national and Washington State review of private payer coverage of SCS indicating that a minimum of 91% of those covered in Washington have access to this proven therapy.

Separately, in July we also submitted comments on the evidence vendor's draft report, which clearly the vendor subsequently responded to in detail.

At this time, we believe it is important that we receive verification as to whether these two submissions were respectively provided both to the evidence vendor and HTCC members for their review and consideration. Separately, we would also like to understand what pieces of these two comprehensive submissions were and were not included in the evidence report, and what methodologies were applied to determine same. Given that significant non-published data sets and information were shared directly with the vendor from the respective state agencies and incorporated appropriately, we find it important

to understand why most of the evidence and comments which we submitted were not, so we can all best understand and work within this process.

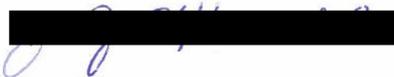
Thank you for your consideration of these comments and ensuring that we can reach a common goal of protecting patients and ensuring access to appropriate, life-changing, cost effective technologies. We look forward to your detailed response. Should you have any questions, please do not hesitate to contact William Fehrenbach at 763-607-1378 or william.fehrenbach@medtronic.com. Thank you for your consideration.

Sincerely,



N. William Fehrenbach
Reimbursement Director
*State Government Affairs
Evidence Based Medicine and
Coverage & Authorization Services*

7000 Central Avenue NE, RCE395
Minneapolis, MN 55432
Office: 763-526-8193
Cell: 763-607-1378
william.fehrenbach@medtronic.com



Jennifer Hinnenthal
Sr. Manager
Evidence Based Medicine

7000 Central Ave NE, RCE395
Minneapolis, MN 55432
Office: 763-526-6068
Cell: 763-567-1963
Jennifer.hinnenthal@medtronic.com

Cc:
shtap@hca.wa.gov (public comment period)

Doug Porter, Administrator
Washington State Health Care Authority
P.O. Box 42682
Olympia, WA 98504-2682
lken107@hca.wa.gov

Rep. Eileen Cody
Chair, House Health Care Committee
Washington State House of Representatives
PO Box 40600 Olympia, WA 98504-0600
Cody.eileen@leg.wa.gov

Senator Karen Keiser
Chair, Senate Health and Long-Term Care Committee
PO Box 40433 Olympia, WA 98504-0433
Keiser.karen@leg.wa.gov

Attachment 1: January comment letter submission



N. William Fehrenbach, MSSW
Reimbursement Director

Medtronic, Inc.
Neuromodulation
7000 Central Avenue NE
RCE 395
Minneapolis, MN 55432
www.medtronic.com

tel 763-526-8193
fax 763-526-8373
william.fehrenbach@medtronic.com

January 8, 2010

Steve Hill
Washington State Health Care Authority
676 Woodland Square Loop SE
Olympia, WA 98504
steve.hill@hca.wa.gov

Leah Hole-Curry, JD
Director, Health Technology Assessment
676 Woodland Square Loop SE
Olympia, WA 98504
leah.hole-curry@hca.wa.gov

Re: Spinal Cord Stimulation Health Technology Assessment: *Evidence for Consideration*

Dear Mr. Hill and Ms. Hole-Curry:

We are writing on behalf of Medtronic Neuromodulation. Medtronic is the world's leading medical technology company, specializing in implantable therapies that alleviate pain, restore health, and extend life. Our implantable therapies include spinal cord stimulators. Our purpose for writing is to provide comprehensive clinical and economic evidence for spinal cord stimulation for consideration as part of your 30-day public comment period. *Please note that we will be sending hardcopy sets of this submission with attachments where indicated.* Thank you in advance for your consideration. We hope you find this information useful.

I. Evidence for Spinal Cord Stimulation

Spinal cord stimulators are used in the management of chronic intractable pain of the trunk and limbs. Spinal cord stimulation (SCS) is indicated after other treatment approaches, including less invasive procedures, have failed. Over 100,000 patients in the United States have been implanted with SCS systems for the treatment of chronic pain. There are numerous studies of varying size and quality that

demonstrate the safety, efficacy, effectiveness and cost-effectiveness of SCS for the management of chronic intractable pain. Tables 1 and 2 briefly summarize the clinical and economic evidence for SCS.

Table 1. Summary of Clinical Evidence for SCS

Source Type	Source Citation	Summary
Systematic Review	<p>Simpson EL, Duenas A, Holmes MW, Papaioannou D, Chilcott J. Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin: systematic review and economic evaluation. <i>Health Technol Assess.</i> 2009 Mar;13(17):iii, ix-x, 1-154.¹</p> <p>http://www.hta.ac.uk/project/1677.asp (Due to the size of this article (190 pages), we did not include a hard copy attachment.)</p>	<p>Methods: A systematic review of the literature sought clinical and cost-effectiveness data for SCS in adults with chronic neuropathic or ischaemic pain with inadequate response to medical or surgical treatment other than SCS. Thirteen electronic databases [including MEDLINE (1950-2007), EMBASE (1980-2007) and the Cochrane Library (1991-2007)] were searched from inception; relevant journals were hand-searched; and appropriate websites for specific conditions causing chronic neuropathic/ischaemic pain were browsed.</p> <p>Results: From approximately 6000 citations identified, 11 randomized controlled trials were included in the clinical effectiveness review: three of neuropathic pain and eight of ischaemic pain. Trials were available for the neuropathic conditions failed back surgery syndrome (FBSS) and complex regional pain syndrome (CRPS) type I. The evidence suggested that SCS was more effective in reducing the pain of FBSS and CRPS type I compared to conventional medical management or reoperation.</p> <p>Conclusions: Trials were available for the neuropathic conditions failed back surgery syndrome (FBSS) and complex regional pain syndrome (CRPS) type I, CRPS type I and they suggested that SCS was more effective than conventional medical management (CMM) or reoperation in reducing pain.</p>
Systematic Review	<p>Frey ME, Manchikanti L, Benyamin RM, Schultz DM, Smith HS, Cohen SP. Spinal cord stimulation for patients with failed back surgery syndrome: a systematic review. <i>Pain Physician</i> 2009;12(2):379-97.</p>	<p>Methods: A systematic review of the literature was performed according to the Cochrane Musculoskeletal Review Group Criteria as utilized for interventional techniques for randomized trials and the Agency for Healthcare Research and Quality (AHRQ) criteria for observational studies. The 5 levels of evidence were classified as Level I, II, or III with 3 subcategories in Level II based on the quality of evidence developed by the U.S. Preventive Services Task Force (USPSTF). Data sources included relevant literature of the English language identified through searches of PubMed and EMBASE</p>

¹ Spinal cord stimulation is indicated for intractable pain of the trunk and limbs. Although some of the articles we cite in this document may mention unapproved uses, we remind you that our intent is not to promote the unapproved use. However, we could not provide comprehensive clinical and economic evidence on FDA-approved uses without inclusion of these articles.

Source Type	Source Citation	Summary
	<p data-bbox="378 268 659 443">Attachment 1 and http://www.painphysicianjournal.com/pastissue_vw.php?jcode=48</p>	<p data-bbox="675 233 1333 300">from 1966 to December 2008, and manual searches of bibliographies of known primary and review articles.</p> <p data-bbox="675 338 1321 443">Results: The indicated evidence is Level II-1 or II-2 for long-term relief in managing patients with failed back surgery syndrome.</p> <p data-bbox="675 480 1336 548">Limitations: The limitations of this review included the paucity and heterogeneity of the literature.</p> <p data-bbox="675 585 1344 869">Conclusion: The systematic review evaluating the effectiveness of SCS in relieving chronic intractable pain of failed back surgery syndrome indicated the evidence to be Level II-1 or II-2 for clinical use on a long-term basis. Based on Guyatt et al's criteria, the recommendation for SCS is 1B or 1C/strong recommendation with a caveat that this may change when higher quality evidence becomes available.</p>
Systematic Review	<p data-bbox="378 875 659 1297">Chou R, Atlas SJ, Stanos SP, Rosenquist RW. Nonsurgical interventional therapies for low back pain: a review of the evidence for an American Pain Society clinical practice guideline. <i>Spine (Phila Pa 1976)</i>. 2009 May 1;34(10):1078-93.</p> <p data-bbox="378 1335 548 1367">Attachment 2</p>	<p data-bbox="675 875 1357 1507">Methods: Electronic database searches on Ovid MEDLINE and the Cochrane databases were conducted through July 2008 to identify randomized controlled trials and systematic reviews of local injections, botulinum toxin injection, prolotherapy, epidural steroid injection, facet joint injection, therapeutic medial branch block, sacroiliac joint injection, intradiscal steroid injection, chemonucleolysis, radiofrequency denervation, intradiscal electrothermal therapy, percutaneous intradiscal radiofrequency thermocoagulation, Coblation nucleoplasty, and spinal cord stimulation. All relevant studies were methodologically assessed by 2 independent reviewers using criteria developed by the Cochrane Back Review Group (for trials) and by Oxman (for systematic reviews). A qualitative synthesis of results was performed using methods adapted from the US Preventive Services Task Force.</p> <p data-bbox="675 1545 1357 1866">Results: The authors found fair evidence from two trials that spinal cord stimulation is more effective than either repeat surgery or continued conventional medical management for failed back surgery syndrome with persistent radiculopathy. Spinal cord stimulation involves the permanent placement of a device and is associated with a high rate of post-implant complications, though these events are usually not serious.</p>
Systematic	Taylor RS, Van Buyten	Methods: A systematic review was conducted by

Source Type	Source Citation	Summary
Review	<p>JP, Buchser E. Spinal cord stimulation for complex regional pain syndrome: A systematic review of the clinical and cost-effectiveness literature and assessment of prognostic factors. <i>Eur J Pain</i> 2006;10:91-101.</p> <p>Attachment 3</p>	<p>searching electronic databases for controlled and uncontrolled studies and economic evaluations relating to the use of SCS in patients with either CRPS type I or II. Articles published up to January 1, 2002 were eligible for inclusion. Search terms were selected in order to maximize both the sensitivity and specificity of the search. There was no language restriction. The reference lists in studies and reviews meeting the inclusion criteria were hand searched for further studies. Experts in the field were contacted to identify any studies that may have been missed, or any ongoing or unpublished research.</p> <p>Results: One randomised controlled trial, 25 case series and one cost-effectiveness study were included. In the randomised controlled trial in type I CRPS patients, SCS therapy led to a reduction in pain intensity at 24 months of follow-up (mean change in VAS score -2.0), whereas pain was unchanged in the control group (mean change in VAS score 0.0) ($p < 0.001$). In the case series studies, 67% (95% CI 51%, 84%) of type I and type II CRPS patients implanted with SCS reported pain relief of at least 50% over a median follow-up period of 33 months. No statistically significant predictors of pain relief with SCS were observed in multivariate metaregression analysis across studies. SCS appears to be an effective therapy in the management of patients with CRPS type I (Level A evidence) and type II (Level D evidence).</p>
Randomized Controlled Trial	<p>Kumar K, Taylor R, Jacques L, et al. Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicentre randomized controlled trial in patients with failed back surgery syndrome. <i>Pain</i>. 2007;132(1-2):179-188, and Kumar K, et al. The effects of spinal cord stimulation in neuropathic pain are sustained: a 24-month</p>	<p>Methods: This multicenter, randomized, controlled trial of 100 failed back surgery syndrome (FBSS) patients with pain of neuropathic radicular origin, predominantly in the legs, randomized patients 1:1 to either conventional medical management (CMM) plus SCS (SCS group) or CMM alone (CMM group). Patients were followed for 24 months. The primary outcome assessed at 6 months was the proportion of patients achieving $\geq 50\%$ relief of leg pain on the VAS. The secondary outcomes included health-related quality of life and functional capacity. After 6 months, patients who did not receive adequate pain relief could cross over to the alternative treatment. Determinations of all outcomes at the 6-month follow-up were based on the intention-to-treat principle.</p> <p>Results: At 6 months, 24 of the 50 (48%) patients in the SCS group and 4 of the 43 (9%) patients in the CMM group achieved $\geq 50\%$ relief of leg pain ($P < 0.001$). Compared to the CMM group, the SCS group</p>

Source Type	Source Citation	Summary
	<p>follow-up of the prospective randomized controlled multicenter trial of the effectiveness of spinal cord stimulation. <i>Neurosurgery</i> 2008;63(4):762-770.</p> <p>Attachments 4 & 5</p>	<p>experienced significantly lower levels of back pain (P = 0.008) and leg pain (P = 0.0001), significantly greater health-related quality of life (P ≤ 0.02), functional capacity (P < 0.001), and treatment satisfaction (P < 0.001).</p> <p>At 12 months, as-treated analysis found that 34 of the 71 (48%) patients with SCS and 3 of the 17 (18%) patients receiving only CMM achieved ≥ 50% relief of leg pain (P =0.03). Intention-to-treat analysis, categorizing patients who crossed over as primary outcome failures according to their initial random allocation, found that 34% of the SCS group and 7% of the CMM group achieved the primary outcome (P= 0.005). Of the 84 patients who received an electrode during trial SCS or with SCS system implantation over the first 12-month period, 27 (32%) patients had a total of 40 device-related complications, which required surgery for their resolution in 20 of these patients. The principal complications were electrode migration (10%), infection or wound breakdown (8%), and loss of paresthesia (7%).</p> <p>At 24 months, of 46 of 52 patients randomized to SCS and 41 of 48 randomized to CMM who were available, the primary outcome was achieved by 17 (37%) randomized to SCS versus 1 (2%) to CMM (P = 0.003) and by 34 (47%) of 72 patients who received SCS as final treatment versus 1 (7%) of 15 for CMM (P = 0.02). At 24 months, there were 42 patients continuing SCS (of 52 randomized to SCS). These 42 patients reported significantly improved leg pain relief (P < 0.0001), quality of life (P ≤ 0.01), and functional capacity (P =0.0002); and 13 patients (31%) required a device-related surgical revision.</p>
Randomized Controlled Trial	<p>North RB, Kidd DH, Farrokhi F, Piantadosi SA. Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain; a randomized, controlled trial. <i>Neurosurgery</i>. 2005;56:98-107.</p> <p>Attachment 6</p>	<p>Methods: This was a prospective, randomized, controlled study of 50 FBSS patients who had been selected for repeat lumbosacral spine surgery. The mean number of prior lumbosacral spine surgeries in these patients was 2.5 ± 1.1 SD. The criteria for surgical reintervention were pain refractory to conservative care, with findings of neural compression. These patients were randomized 1:1 to receive SCS or re-operation. If the results of the randomized treatment were unsatisfactory, the patients could cross over to the alternative procedure. Effectiveness of implanted SCS and re-operation was evaluated at 6 months and annually for at least 2 years. Treatment success was</p>

Source Type	Source Citation	Summary
		<p>defined as at least 50% pain relief and patient satisfaction with treatment.</p> <p>Results: Of the 50 patients who were eligible and willing to participate in this study, 24 were randomized for SCS and 26 were randomized for re-operation. At a mean follow-up period of 2.9 ± 1.1 SD years (range, 1.8–5.7 years), 45 (90%) of the patients were available for evaluation. SCS was significantly more successful than re-operation, in that 9 of the 19 (47%) SCS patients and 3 of the 26 (12%) re-operation patients reported $\geq 50\%$ pain relief and satisfaction with treatment ($P < 0.01$). In patients randomized for SCS, opioid use was stable or decreased in 20 of the 23 (87%) SCS patients compared to 15 of the 26 (58%) re-operation patients ($P < 0.025$). Patients randomized for SCS were significantly less likely to cross over than patients randomized for re-operation, in that 5 of the 24 (21%) SCS patients and 14 of the 26 (54%) re-operation patients elected to cross over ($P = 0.02$). One SCS patient developed an infection at the receiver site, which was treated by removal of the system followed by specific antibiotic therapy. The system was replaced without further complication. Three SCS patients (9% of permanent implants) underwent hardware revisions because of technical problems (electrode migration or malposition).</p>
Randomized Controlled Trial	Kemler MA , Barendse GAM , Van Kleef M, et al. Spinal cord stimulation in patients with chronic reflex sympathetic dystrophy. <i>N Engl J Med.</i> 2000;343:618-624, and Kemler MA , et al. The effect of spinal cord stimulation in patients with chronic reflex sympathetic dystrophy: two years' follow-up of the randomized controlled trial. <i>Ann Neurol.</i> 2004;55:13-18, and Kemler MA, et al. Effect of spinal	<p>Methods: This was a prospective, randomized, controlled study of 54 type I complex regional pain syndrome (CRPS) patients who were randomized 2:1 to receive SCS plus a standardized physical therapy (PT) program or only the PT program. The CRPS had to have lasted ≥ 6 months with no sustained response to standard therapy. Thirty-three patients had CRPS in a hand and 21 had CRPS in a foot. Patients were followed up to 5 years. Outcomes included pain intensity, global perceived effect, comparative functions of the affected hand or foot, and health-related quality of life.</p> <p>Results: At six months, pain intensity in the SCS+PT group of 24 patients had decreased by a mean of 3.6 cm on the VAS , whereas in the 18 PT-only patients, it had increased by a mean of 0.2 cm ($P < 0.001$). Global perceived effect was much improved in 14 of the 24 (58%) SCS+PT patients, as compared to 1 of the 18 (6%) PT-only patients ($P < 0.001$). As compared to the PT-only patients, SCS+PT also resulted in significant improvements in a pain-rating index ($P = 0.02$) and in</p>

Source Type	Source Citation	Summary
	<p>cord stimulation for chronic complex regional pain syndrome Type I: five-year final follow-up of patients in a randomized controlled trial. <i>J Neurosurg.</i> 2008 Feb;108(2):292-8.</p> <p>Attachments 7, 8, & 9</p>	<p>health-related quality of life both for patients with an affected hand (P = 0.02) or foot (P = 0.008).</p> <p>At 24 months, pain intensity in the SCS+PT group of 24 patients had decreased by a mean of 3.0 cm on the VAS , whereas in the 11 PT-only patients, it had decreased by a mean of 0 cm (P < 0.001). Global perceived effect was much improved in 15 of the 24 (63%) SCS+PT patients, as compared to 1 of 11 (9%) PT-only patients (P < 0.001). As compared to PT-only patients, SCS+PT also resulted in significant improvements in a pain-rating index (P = 0.02), and in health-related quality of life for patients with an affected hand (P = 0.02) or foot (P = 0.008). Nine of the 24 (38%) patients had 22 complications requiring re-operation during the 2-year period after SCS system implantation. Eight patients had lead repositioning, 7 had revision of the pulse generator pocket, 2 had lead replacement, 3 had system explantation (2 permanently), 1 had system reimplantation and 1 had pulse generator replacement. The frequency of complications decreased markedly after the first year.</p> <p>At 5 years, SCS+PT produced results similar to those following PT for pain relief and all other measured variables. In a subgroup analysis, the results with regard to global perceived effect (p=0.02) and pain relief (p=0.06) in 20 patients with an implant exceeded those in 13 patients who received PT. Despite the diminishing effectiveness of SCS over time, 95% of patients with an implant would repeat the treatment for the same result.</p>
Other non-randomized studies	<p>Kumar K, et al. <i>Neurosurgery</i> 2006; Devulder J, et al. <i>JPSM</i> 1997; Dario A, et al. <i>Neuromodulation</i> 2001; Leveque J-C, et al. <i>Neuromodulation</i> 2001; Rainov NG, et al. <i>Minim Invas Neurosurg</i> 1996; Fiume D, et al. <i>Acta Neurochir</i> 1995; De La Porte C, et al. <i>Pain</i> 1993; Bennett DS, et al. <i>Neuromodulation</i> 1999; Harke H, et al.</p>	<p>In addition to the randomized controlled trials discussed above, there is a substantial body of lower level evidence with directionally similar findings in support of spinal cord stimulation.</p> <p>In a selection of studies in FBSS patients, an implanted SCS system was effective in controlling the pain at long-term follow-up. (Kumar K, et al. <i>Neurosurgery</i> 2006)(Devulder J, et al. <i>JPSM</i> 1997) (Dario A, et al. <i>Neuromodulation</i> 2001) (Leveque J-C, et al. <i>Neuromodulation</i> 2001) (Rainov NG, et al. <i>Minim Invas Neurosurg</i> 1996). These studies plus the RCT by Kumar and colleagues found that SCS provided pain relief of 50% or more in 62% of patients (range 48% to 91% of the patients in these studies). Long-term SCS for FBSS has been associated with reductions in the use of</p>

Source Type	Source Citation	Summary
	<p><i>Eur J Pain</i> 2005; Forouzanfar T, et al. <i>Br J Anaesth</i> 2004; Turner et al, <i>Pain</i> forthcoming; Wasan, <i>Pain</i> forthcoming.</p>	<p>analgesic medications, particularly opioids, (Devulder J, et al.) (Fiume D, et al. <i>Acta Neurochir</i> 1995) (De La Porte C, et al. <i>Pain</i> 1993) and significant increases in activities of daily living. (Dario A, et al.) (De La Porte C, et al.) Five studies reported that SCS enabled return to work for 53 of the 198 (27%) patients, with a range of 22% to 36% of patients in these studies reporting return to work. (Devulder J, et al.) (Dario A, et al.) (Fiume D, et al.) (De La Porte C, et al.) (North RB, et al. <i>Neurosurgery</i> 1991)</p> <p>At long-term follow-up, three studies in CRPS patients found that an implanted SCS system provided overall significant pain relief, (Bennett DS, et al. <i>Neuromodulation</i> 1999) (Harke H, et al. <i>Eur J Pain</i> 2005) (Forouzanfar T, et al. <i>Br J Anaesth</i> 2004) with one of these studies reporting that SCS also led to a reduction in the use of analgesic medications, improvements in function and activities of daily living, and enabled 70% of patients to return to work. (Harke H, et al.)</p> <p>In contrast to the bulk of the body of literature, the WA state DLI study of SCS (Turner, et al. <i>Pain</i>, forthcoming) found no statistically significant difference between SCS and Pain Clinic Care and Usual Care. We suggest referencing the editorial by Wasan in <i>Pain</i>, forthcoming, for a thoughtful discussion of the limitations of this study.</p>

Table 2. Summary of Economic Evidence for SCS

Source Type	Source Citation	Summary
Economic analysis based on data from randomized controlled trial.	<p>North RB, Kidd D, Shipley J, et al. Spinal cord stimulation versus re-operation for failed back surgery syndrome: a cost-effectiveness and cost utility analysis based on a randomized, controlled trial. <i>Neurosurgery</i>. 2007;61:361-369.</p> <p>Attachment 10</p>	<p>Methods: Hospitalization and professional charge data was obtained on 40 of the 50 patients who participated in the prospective, randomized, controlled study of the effectiveness of SCS versus re-operation for FBSS. (North RB, et al. <i>Neurosurgery</i> 2005) Three forms of analysis were conducted: 1) Intention to treat (all costs and outcomes assigned to a randomized group); 2) treated as intended (all costs and outcomes assigned to a randomized group, with crossover being considered a failure); and 3) final treatment (all costs and outcomes, including crossover outcomes, assigned to final treatment instead of a randomized group).</p> <p>Results: At a mean follow-up period of 3.1 years</p>

Source Type	Source Citation	Summary
		<p>(range, 1.6–4.7 years), 5 of the 19 (26%) patients who had been randomized for SCS had crossed over for re-operation, and 13 of the 21 (62%) patients who had been randomized to re-operation had crossed over to SCS ($P < 0.025$). The mean cost per patient for intention to treat was \$31,530 for SCS and \$38,160 for re-operation. The mean cost per patient for treated as intended was \$48,357 for 7 of the 14 patients who achieved long-term success with SCS alone, and \$105,928 for 2 of the 8 patients who achieved long-term success with re-operation alone. The mean cost per patient for final treatment was \$117,901 for 5 of the 13 patients who achieved long-term success with SCS after crossing over from re-operation, whereas none of the 5 patients who crossed over from SCS to re-operation achieved success despite a mean cost per patient of \$260,584. SCS was also more dominant (more effective and less expensive) than reoperation in incremental cost-effectiveness and cost-utility ratios.</p>
Economic analysis based on data from a randomized controlled trial	<p>Kemler MA , Furnée CA. Economic evaluation of spinal cord stimulation for chronic reflex sympathetic dystrophy. <i>Neurology</i>. 2002;59:1203-1209.</p> <p>Attachment 11</p>	<p>Methods: Health care costs for 54 CRPS patients who were randomized in a 2:1 ratio to SCS plus physical therapy (PT) (36 patients) or only PT (18 patients) (Kemler MA, et al. <i>NEJM</i> 2000) were calculated in 1998 Euros. Costs were not discounted. The factor for conversion of 1998 Euros to 1998 US dollars was 1.04. The first-year cost included the SCS system and its testing and implantation, and actual complication costs. The cost for subsequent years to death was based on a 41-year life expectancy, an annual complication rate of 28%, determined from published data, and an estimated mean battery life of 5.8 years.²</p> <p>Results: The mean first-year cost for the 36 patients who were eligible for SCS+PT was 9,805€ per patient and for the 18 patients who had only PT was 5,741€ per patient. The mean first-year cost for the 24 patients who had SCS implantation (minus the cost of PT) was 12,721€ per patient. The mean cost from the first year to death for the 36 patients who were eligible for SCS+PT was 171,153€ per patient and for the 18 patients who</p>

² This estimate was based on non-rechargeable SCS systems.

Source Type	Source Citation	Summary
		had only PT was 229,624€ per patient. The mean first-year cost from the first year to death for the 24 patients who had SCS implantation (minus the cost of PT) was 193,580€ per patient.
Actuarial analysis utilizing health care claims data.	State of Washington Worker's Compensation Financial Impact to Offer Spinal Cord Stimulation and Intrathecal Drug Delivery as a Covered Medical Service. November 1, 2006. Reden & Anders. Attachment 12	In addition to a number of cost analyses indicating that SCS becomes cost-effective within approximately two years, an actuarial analysis of health care claims data completed in 2006 by Reden & Anders, an Ingenix and United Health Group company, independently echoes this finding. The Reden & Anders analysis used the Washington Department of Labor and Industries' Medical Aid budget and demonstrated that coverage of this therapy should, on average, lead to a reduction in health care expenditures.

Finally, unlike many therapies for chronic pain, including repeat lumbosacral spine surgery, spinal cord stimulation is reversible and can be trialed prior to implant. Therefore, the empirical evidence is further enhanced when combined with the observational evidence gained through an individual trial.

II. Other Related Evidence Consideration as Required under Washington State RCW 70.14.110.

In addition to consideration of the literature review provided above, the governing Washington State Evidence-Based Medicine Law mandates that the HTA process shall result in decisions consistent with Medicare coverage and national guidelines of societies and patient advocacy organizations as listed below:

RCW 70.14.110 (3) states that EBM formal assessments and determinations "shall be consistent with decisions made under the federal Medicare program and in expert treatment guidelines, including those from specialty physician organizations and patient advocacy organizations, unless the committee concludes, based on its review of the systematic assessment, that substantial evidence regarding the safety, efficacy, and cost-effectiveness of the technology supports a contrary determination."

Please note, the review of this particularly therapy is quite unique given the strong Medicare, medical society and patient advocacy group standards already in place, all of which are delineated below and support appropriate use of SCS. Specifically, a very consistent pattern emerges of appropriate coverage for spinal cord stimulation systems for chronic, intractable pain of the trunk and limbs with careful consideration of the need for appropriate success through a temporary trial of the therapy prior to permanent implant.

A. Positive National Medicare Coverage Decision

CMS has issued a National Coverage Decision (NCD) for coverage of SCS for chronic, intractable pain positively governing coverage for all Medicare recipients throughout the country. We have quoted the most relevant section on use and coverage of SCS for chronic, intractable pain herein though we encourage review of the entire NCD.

http://www.cms.hhs.gov/mcd/viewncd.asp?ncd_id=160.7&ncd_version=1&basket=ncd%3A160%2E7%3A1%3AElectrical+Nerve+Stimulators

NCD for Electrical Stimulation (160.7)

Effective Date of this Version 8/7/1995

Indications and Limitations of Coverage

B - Central Nervous System Stimulators (Dorsal Column and Depth Brain Stimulators)

The implantation of central nervous system stimulators may be covered as therapies for the relief of chronic intractable pain, subject to the following conditions:

2 - Conditions for Coverage

No payment may be made for the implantation of dorsal column or depth brain stimulators or services and supplies related to such implantation, unless all of the conditions listed below have been met:

- *The implantation of the stimulator is used only as a late resort (if not a last resort) for patients with chronic intractable pain;*
- *With respect to item a, other treatment modalities (pharmacological, surgical, physical, or psychological therapies) have been tried and did not prove satisfactory, or are judged to be unsuitable or contraindicated for the given patient;*
- *Patients have undergone careful screening, evaluation and diagnosis by a multidisciplinary team prior to implantation. (Such screening must include psychological, as well as physical evaluation);*
- *All the facilities, equipment, and professional and support personnel required for the proper diagnosis, treatment training, and followup of the patient (including that required to satisfy item c) must be available; and*
- *Demonstration of pain relief with a temporarily implanted electrode precedes permanent implantation.*

B) National Medical Society Guidelines

The safety and effectiveness of spinal cord stimulation systems have been subjected to scrutiny by many other physician specialty organizations which have found SCS suitable for appropriate coverage (including treatment of chronic, intractable pain). Given the Washington State statutory language which requires significant weight be given to “*expert treatment guidelines, including those from specialty physician organizations and patient advocacy organizations,*” we will begin with a review of relevant treatment guidelines. Several various approaches might be considered with regard to attempting to appropriately answer this question. It is important to note that given this statutory requirement, and what we have learned from the HTA process and review of intrathecal drug delivery systems in summer

of 2008, in order for a positive Medicare National Coverage Decision to be trumped, the guidelines found must at least be equally weighted to “negative” conclusions. As you will see, there does not appear to be a reasonable methodology that allows for any conclusion other than treatment guidelines and coverage policies being widely in support of the positive Medicare National Coverage Determination.

Methodology #1: Washington HTA Past Vendor Approach and Results

Based on the methodology which was undertaken by the Washington HTA vendors on various therapies in the past two years, we replicated that approach for your consideration to demonstrate what the methodology will yield. Please note: for several reasons we do not believe this methodology is most reasonable as we will explain below. Nonetheless, the following table contains a list of medical society and other treatment guidelines identified by searching the National Guideline Clearinghouse (NGC) on Dec 17, 2009 using the keywords “spinal cord stimulat*”. The society or organization along with the relevant recommendation language is shown for each below. The results are very favorable to SCS despite our methodological concerns which are raised below.

Table 3. Guidelines Addressing SCS Found in Search of National Guideline Clearinghouse³

Guideline and Society/Organization	Excerpted Language on SCS	Recommendation
<p>Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin. National Institute for Health and Clinical Excellence (NICE) - National Government Agency [Non-U.S.]. 2008 Oct. 33 pages. NGC:006752</p> <p>http://www.guideline.gov/summary/summary.aspx?doc_id=13305&nbr=006752&string=%22spinal+cord+stimulat*%22</p>	<p>1 Guidance.</p> <p>1.1 Spinal cord stimulation is recommended as a treatment option for adults with chronic pain of neuropathic origin who: continue to experience chronic pain (measuring at least 50 mm on a 0–100 mm visual analogue scale) for at least 6 months despite appropriate conventional medical management, and who have had a successful trial of stimulation as part of the assessment specified in recommendation 1.3.</p> <p>1.2 [Redacted]</p> <p>1.3 Spinal cord stimulation should be provided only after an assessment by a multidisciplinary team experienced in chronic pain assessment and management of people with spinal cord stimulation devices, including experience in the</p>	<p>POSITIVE</p>

³ We again wish to mention that some of the relevant medical society and payer organization guidelines may mention uses which are not FDA-approved for any Medtronic products. It is not our intention to promote unapproved use. However, we could not provide a comprehensive list of relevant guidelines on FDA-approved uses without inclusion of these guidelines. For those guidelines addressing unapproved uses of SCS, some language has been redacted. The source documents in their entirety may be found via the adjoining web links.

Guideline and Society/Organization	Excerpted Language on SCS	Recommendation
	<p>provision of ongoing monitoring and support of the person assessed.</p> <p>1.4 When assessing the severity of pain and the trial of stimulation, the multidisciplinary team should be aware of the need to ensure equality of access to treatment with spinal cord stimulation. Tests to assess pain and response to spinal cord stimulation should take into account a person’s disabilities (such as physical or sensory disabilities), or linguistic or other communication difficulties, and may need to be adapted.</p> <p>1.5 If different spinal cord stimulation systems are considered to be equally suitable for a person, the least costly should be used. Assessment of cost should take into account acquisition costs, the anticipated longevity of the system, the stimulation requirements of the person with chronic pain and the support package offered.</p> <p>1.6 [Redacted]</p>	
<p>EFNS guidelines on neurostimulation therapy for neuropathic pain. European Federation of Neurological Societies - Medical Specialty Society. 2007 Sep. 19 pages. NGC:005909</p> <p>http://www.guideline.gov/summary/summary.aspx?doc_id=11372&nbr=005909&string=%22spinal+cord+stimulat*%22</p>	<p>Recommendations: We found level B evidence for the effectiveness of SCS in FBSS and CRPS I. The available evidence is also positive for CRPS II, ...[redacted], but still requires confirmatory comparative trials before the use of SCS can be unreservedly recommended in these conditions.</p>	<p>POSITIVE</p>

Guideline and Society/Organization	Excerpted Language on SCS	Recommendation
<p>Assessment and management of chronic pain. Institute for Clinical Systems Improvement - Private Nonprofit Organization. 2005 Nov (revised 2008 Jul). 84 pages. NGC:006693</p> <p>http://www.guideline.gov/summary/summary.aspx?doc_id=12998&nbr=006693&string=%22spinal+cord+stimulat*%22</p>	<p>Spinal Cord Stimulation (SCS): Patients with lumbar and cervical radiculopathy who are not surgical candidates, patients with postlaminectomy syndrome, and patients with complex regional pain syndrome (CRPS) type 1 or (RSD) are the best candidates for SCS.....[redacted]</p> <p>Level 1 Management of Mechanical/Compressive Pain: Invasive treatments have limited scientific evidence supporting their use. These include:...spinal cord stimulation...</p> <p>Level II Management: Interdisciplinary Team Referral, Plus a Pain Medicine Specialty Clinic, Surgical Management of Chronic Pain : Neurosurgical techniques for chronic pain that is resistant to a conservative approach hold promise, but have limited scientific evidence. These include:...spinal cord stimulation...</p>	<p>POSITIVE</p>
<p>Interventional techniques: evidence-based practice guidelines in the management of chronic spinal pain. American Society of Interventional Pain Physicians - Medical Specialty Society. 2003 (revised 2007 Jan). 105 pages. [NGC Update Pending] NGC:005510</p> <p>http://www.guideline.gov/summary/summary.aspx?doc_id=10531&nbr=005510&string=%22spinal+cord+stimulat*%22</p> <p><i>*The 2009 guidelines have been published in Pain Physician. The recommendations for SCS stayed the same.</i></p> <p>http://www.asipp.org/Guidelines.htm</p>	<p>6.7.4 Indications: While multiple indications are available, the indications in the United States are related to neuropathic pain of FBSS or CRPS.</p> <p>6.7.5 Level of Evidence: The indicated evidence for SCS is Level II-1 or II-2 for long-term relief in managing patients with FBSS.</p> <p>6.7.6 Recommendations: Based on Guyatt et al's criteria, the recommendation is 1B or 1C/strong recommendation for clinical use on a long-term basis.</p>	<p>POSITIVE</p>

Guideline and Society/Organization	Excerpted Language on SCS	Recommendation
<p>Low back disorders. American College of Occupational and Environmental Medicine - Medical Specialty Society. 1997 (revised 2007). 366 pages. NGC:006456</p> <p>http://www.guideline.gov/summary/summary.aspx?doc_id=12540&nbr=006456&string=%22spinal+cord+stimulat*%22</p> <p><i>See Appendix A for detailed discussion of the controversies surrounding ACOEM</i></p>	<p>Spinal cord stimulators are not recommended for treatment of acute, subacute, or chronic LBP. They also are not recommended for treatment of radicular pain syndromes or failed back surgery syndrome.* Not Recommended, Insufficient Evidence (I)</p> <p>* Spinal cord stimulators may be considered as a late or last resort for highly selected patients who have failed multiple other conservative treatments including a quality functional restoration program and who have had a forensic psychologic assessment (83 percent Panel agreement).</p>	<p>POSITIVE*</p> <p>*Even this guideline, considered very conservative by many, envisions appropriate use of SCS for FBSS and CRPS for certain candidates.</p>
<p>Pain (chronic). Work Loss Data Institute - Public For Profit Organization. 2003 (revised 2008 May 19). 475 pages. NGC:006564</p> <p>http://www.guideline.gov/summary/summary.aspx?doc_id=12676&nbr=006564&string=%22spinal+cord+stimulat*%22</p>	<p>Recommended only for selected patients in cases when less invasive procedures have failed or are contraindicated, for specific conditions indicated below, and following a successful temporary trial. [Remainder of the background data on history, safety and efficacy of therapy not shown here]</p> <p>Indications for stimulator implantation:</p> <p>Failed back syndrome (persistent pain in patients who have undergone at least one previous back operation and are not candidates for repeat surgery), when all of the following are present: (1) symptoms are primarily lower extremity radicular pain; there has been limited response to non-interventional care (e.g. neuroleptic agents, analgesics, injections, physical therapy, etc.); (2) psychological clearance indicates realistic expectations and clearance for the procedure; (3) there is no current evidence of substance abuse issues; (4) there are no contraindications to a trial; (5) Permanent placement requires evidence of 50% pain relief and medication reduction or functional improvement after temporary trial. Estimates are in the range of 40-60% success rate 5 years after surgery. Neurostimulation is generally</p>	<p>POSITIVE</p>

Guideline and Society/Organization	Excerpted Language on SCS	Recommendation
	<p>considered to be ineffective in treating nociceptive pain. The procedure should be employed with more caution in the cervical region than in the thoracic or lumbar due to potential complications and limited literature evidence.</p> <p>Complex Regional Pain Syndrome (CRPS)/Reflex sympathetic dystrophy (RSD), 70-90% success rate, at 14 to 41 months after surgery. (Note: This is a controversial diagnosis.)</p> <p>...[Redacted]</p>	
<p>Evidence-based clinical practice guidelines for interdisciplinary rehabilitation of chronic non-malignant pain syndrome patients. Siskin Hospital for Physical Rehabilitation (Chattanooga, TN) - Hospital/Medical Center. 1995 (revised 2005). 41 pages. NGC:004500</p> <p>http://www.guideline.gov/summary/summary.aspx?doc_id=8014&nbr=004500&string=%22spinal+cord+stimulat*%22</p>	<p>Implantable Infusion Pumps and Spine Stimulation Devices.</p> <p>Studies and systematic reviews regarding the efficacy of infusion pumps and spinal cord stimulators have increased. Thus far, they have not met the current criteria for adequate supportive evidence to recommend application to CPS* patients....Given the continued absence of quality research showing consistent and clinically significant evidence, the current guidelines do not recommend using implantable infusion pumps or spinal cord stimulators with CPS patients.</p> <p>*CPS is defined as: any set of behaviors that: 1. involves the complaint of enduring or recurring pain; 2. has persisted longer than typical for an associated condition, or is associated with an intermittent or chronic disease process; 3. has responded inadequately to appropriate medical and/or invasive care; and 4. is associated with significant and reliable impairment of functional status. Chronic nonmalignant pain syndrome patients may also demonstrate significant mood disturbance and/or anger—hostility, but these are not considered as necessary to make a</p>	<p>NEGATIVE*</p> <p>*Interestingly, this guideline speaks only to CPS and not to FBSS or CRPS which are the commonly listed indications for SCS.</p>

Guideline and Society/Organization	Excerpted Language on SCS	Recommendation
	diagnosis.	
<p>Low back - lumbar & thoracic (acute & chronic). Work Loss Data Institute - Public For Profit Organization. 2003 (revised 2008 Jun 10). 481 pages. NGC:006562</p> <p>http://www.guideline.gov/summary/summary.aspx?doc_id=12674&nbr=006562&string=%22spinal+cord+stimulat*%22</p>	<p>Recommended only for selected patients in cases when less invasive procedures have failed or are contraindicated. See the Pain Chapter for Indications for stimulator implantation.</p>	POSITIVE
<p>Complex regional pain syndrome: treatment guidelines (third edition). Reflex Sympathetic Dystrophy Syndrome Association - Private Nonprofit Organization. 2002 Feb (revised 2006 Jun). 67 pages. NGC:005233</p> <p>http://www.guideline.gov/summary/summary.aspx?doc_id=9768&nbr=005233&string=%22spinal+cord+stimulat*%22</p>	<p>Interventional Therapies:</p> <p>Our recommended strategy (and tactic) is to use interventional treatments for CRPS patients who are having difficulty either starting or progressing in the functional restoration/interdisciplinary algorithm. If patients are not progressing because of high pain levels (especially associated with autonomic dysfunction), then a stepwise progression — from the less invasive blocks, to infusions or catheter infusion therapies, and ultimately perhaps to neurostimulation — is recommended in order to facilitate the patient's functional improvement and pain control. One suggested algorithm developed by an expert panel for the integrated use of these procedures is shown below and has been previously published.</p>	POSITIVE

Guideline and Society/Organization	Excerpted Language on SCS	Recommendation
	<p>Interventional Pain Treatment Algorithm for CRPS (from Stanton-Hicks 2002)</p> <p>Step 1 Minimally Invasive Therapies Sympathetic Nerve Blocks Intravenous Regional Nerve Blocks Somatic Nerve Blocks</p> <p>Step 2 More Invasive Therapies Epidural and Plexus Catheter Block(s) Neurostimulation Intrathecal Drug Infusion (e.g., Baclofen)</p> <p>Step 3 Surgical and Experimental Therapies Sympathectomy Motor Cortex Stimulation</p> <p>Inadequate or partial response to any given therapy should lead to a stepwise progression down through these modalities (moving from less to more invasive) in conjunction with other noninterventional treatments.</p>	
<p>Diagnosis and treatment of degenerative lumbar spinal stenosis. North American Spine Society - Medical Specialty Society. 2002 (revised 2007 Jan). 262 pages. NGC:005896</p> <p>http://www.guideline.gov/summary/summary.aspx?doc_id=11306&nbr=005896&string=%22spinal+cord+stimulat*%22</p>	<p>A systematic review of the literature yielded insufficient evidence to address the role of traction, electrical stimulation or TENS in the treatment of lumbar spinal stenosis. Grade of Recommendation: I (Insufficient Evidence) An extensive review of all articles cited in the reference section found no direct comparison of ancillary treatments (traction, electrical stimulation or TENS) to an untreated control group (natural history)</p>	<p>N/A</p> <p>Note: This guideline is specific to stenosis only. Electrical stimulation named, but not spinal cord stimulation specifically.</p>

In summary, Method 1 which is based on the approach taken by the HTA’s own vendors over the past two years, yields very positive results for SCS. If one counts ACOEM Low Back as negative, even though it does envision some usage, **WORST CASE RESULTS: POSITIVE = 7, NEGATIVE = 3**. If one counts ACOEM Low Back as positive, as it envisions some usage, **BEST CASE RESULTS: POSITIVE = 8, NEGATIVE = 2**. Note: The NASS guideline specific to spinal stenosis is, arguably, not applicable. Therefore, we have not included it in the best case and worst case scenarios.

WORST CASE	POSITIVE = 7	NEGATIVE = 3
BEST CASE	POSITIVE = 8	NEGATIVE = 2

Methodology #2: Addition of ACOEM Chronic Pain Chapter Review

While the NGC appropriately includes the ACOEM Low Back Chapter discussion on spinal cord stimulation, it does not include the ACOEM Chronic Pain Chapter discussion on spinal cord stimulation for another indication (CRPS). If one reasonably concludes this is a technical oversight, and decides to include the ACOEM Chronic Pain Chapter, the guideline search would reflect Methodology #1 above plus the following in Table 4 for your consideration:

Table 4. ACOEM Chronic Pain Chapter Addressing SCS⁴

Guideline and Society/Organization	Excerpted Language on SCS	Recommendation
ACOEM Chronic Pain Chapter <i>ACOEM guidelines are for purchase only. There is no link we can provide that grants access. The general link to the ACOEM guidelines website is: http://www.acoem.org/practiceguidelines.aspx</i>	<p>Implantable Spinal Cord Stimulators for Complex Regional Pain Syndrome (CRPS) [Chronic] - Recommended - Limited Evidence (C). SCS implantation is recommended as an option for highly select CRPS patients who understand that this intervention has no demonstrated long-term benefits and is for short- to intermediate-durations during which time there is unequivocal patient commitment and adherence to a functional restoration program.</p> <p>Implantable Spinal Cord Stimulators for Complex Regional Pain Syndrome (CRPS) [Chronic] - Not Recommended - Insufficient Evidence (I). SCS implantation is not recommended for long-term relief (>3 years) of CRPS as there is no evidence that long-term benefits from SCSs are superior to those obtained from quality functional restoration programs.</p>	<p>POSITIVE*</p> <p>*Interestingly, this conservative guideline also believes SCS is supported in some circumstances.</p>

In summary, Method 2, which is the Method 1 NGC search results *plus* the ACOEM Chronic Pain Chapter, yields very positive results for SCS. If one counts the ACOEM Chronic Pain Chapter as negative, even though it envisions some usage, **WORST CASE: POSITIVE = 7, NEGATIVE = 4**, when Method 1 and 2 are combined. If one counts the ACOEM Chronic Pain Chapter as positive, as it does envision some usage, **BEST CASE: POSITIVE = 9, NEGATIVE = 2**, when Method 1 and 2 are combined.

WORST CASE	POSITIVE = 7	NEGATIVE = 4
BEST CASE	POSITIVE = 9	NEGATIVE = 2

⁴ We again wish to mention that some of the relevant medical society and payer organization guidelines may mention unapproved uses. It is not our intention to promote unapproved use. However, we could not provide a comprehensive list of relevant guidelines on FDA-approved uses without inclusion of these guidelines. For those guidelines addressing unapproved uses of SCS, some language has been redacted. We encourage you to read the source documents in their entirety.

Methodology #3: Addition of Two Recent Society Guidelines

There are two recently published guidelines by expert medical societies that have not yet been incorporated into NGC. These are from the American Pain Society (APS) and the American Society of Anesthesiologists (ASA). The recommendation language on SCS is shown in Table 5 below for your consideration.

Table 5. APS and ASA Guidelines Addressing SCS

Guideline and Society/Organization	Excerpted Language on SCS	Recommendation
<p>American Pain Society</p> <p>APS Interventional Therapies, Surgery, and Interdisciplinary Rehabilitation for Low Back Pain. An Evidence-Based Clinical Practice Guideline from the American Pain Society (Chou R, et al. Spine 2009;34(10):1066-77)</p> <p><i>A hard copy of this guideline will be sent to you as an attachment. There is no electronic link that is publicly available.</i></p>	<p>Nonradicular Low Back Pain: No trials exist for nonspecific low back pain so authors were unable to estimate net benefit. Grade I.⁵</p> <p>Radiculopathy or Spinal Stenosis: No trials for radiculopathy with prolapsed lumbar disc exist so authors were unable to estimate net benefit. Grade I. For failed back surgery syndrome with persistent radiculopathy, the level of evidence is Fair with a Moderate net benefit. Grade B. Language included in their recommendation is as follows:</p> <p>“In patients with persistent and disabling radicular pain following surgery for herniated disc and no evidence of a persistently compressed nerve root, it is recommended that clinicians discuss risks and benefits of spinal cord stimulation as an option (weak recommendation , moderate-quality evidence). It is recommended that shared decision-making regarding spinal cord stimulation include a discussion about the high rate of complications following spinal cord</p>	<p>POSITIVE*</p> <p><i>Supports use for treatment of radicular pain following surgery.</i></p>

⁵ APS Definitions: Grade I = The panel found insufficient evidence to recommend for or against the intervention. Evidence that the intervention is effective is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined. Fair = Evidence is sufficient to determine effects on health outcomes, but the strength of evidence is limited by the number, quality, size or consistency of included studies; generalizability to routine practice; or indirect nature of evidence on health outcomes (at least 1 higher-quality trial of sufficient sample size; 2 or more higher quality trials with some inconsistency, at least 2 consistent, lower-quality trials, or multiple consistent observational studies with no significant methodological flaws). Moderate = Pain scale improvement is mean 10-20-point improvement on a 100-point VAS or equivalent. Back-specific functional status is a mean 10-20-point improvement on the ODI, 2-5 points on the RDQ, or equivalent. All outcomes: standardized mean difference, 0.5-0.8. Grade B = The panel recommends that clinicians consider offering the intervention to eligible patients. The panel found at least fair evidence that the intervention improves health outcomes and concludes that benefits moderately outweigh harms, or that benefits are small but there are no significant harms, costs, or burdens associated with the intervention. Weak = Benefits and risks and burdens are finely balanced.

Guideline and Society/Organization	Excerpted Language on SCS	Recommendation
	stimulator placement.”	
<p>American Society of Anesthesiologists</p> <p>ASA Practice Guidelines for Chronic Pain Management</p> <p>http://www.asahq.org/clinical/ChronicPainUpdateGuidelinesFinal.pdf</p>	<p>Electrical Nerve Stimulation, Spinal cord stimulation: Spinal cord stimulation may be used in the multimodal treatment of persistent radicular pain in patients who have not responded to other therapies. It may also be considered for other selected patients (e.g., complex regional pain syndrome, ... [redacted]). Shared decision-making regarding spinal cord stimulation should include a specific discussion of potential complications associated with spinal cord stimulator placement. A spinal cord stimulation trial should be performed before considering permanent implantation. of a stimulation device.</p> <p>Recommendations for Electrical Nerve Stimulation, Spinal cord stimulation: One randomized controlled trial reports effective pain relief for complex regional pain syndrome patients at follow-up assessment periods of 6 months-2 years when spinal cord stimulation in combination with physical therapy is compared to physical therapy alone. [Category A3 evidence] One randomized controlled trial reports effective pain relief for an assessment period of 6 months when failed lumbosacral spine surgery patients are treated with spinal cord stimulation compared to reoperation. [Category A3 evidence] Studies with observational findings report that spinal cord stimulation also provides pain relief for other conditions (e.g., [redacted]). [Category B2 evidence] Reported side effects include insertion-site pain and infections. [Category B2 evidence] The ASA members agree, and the consultants and ASRA members strongly agree that spinal cord stimulation should be used for persistent radicular pain; and they all agree that it should be used for other conditions (e.g., [redacted])... complex regional pain syndrome, ...</p>	<p>POSITIVE</p>

Guideline and Society/Organization	Excerpted Language on SCS	Recommendation
	[redacted]). The consultants, ASA members, and ASRA members strongly agree that a spinal cord stimulation trial should be performed before considering permanent implantation of a stimulation device.	

In summary, Method 3, which includes the NGC search results in Method 1, *plus* the ACOEM Chronic Pain Chapter in Method 2, *plus* the two late-breaking society guidelines which are not yet included in the NGC yields very positive results for SCS. **WORST CASE: POSITIVE = 9, NEGATIVE = 4**, when Method 1, 2 and 3 are combined. **BEST CASE: POSITIVE = 11, NEGATIVE = 2**, when Method 1, 2 and 3 are combined.

WORST CASE	POSITIVE = 9	NEGATIVE = 4
BEST CASE	POSITIVE = 11	NEGATIVE = 2

III. Government Agency Guidelines and Policies

Methodology #4: Addition of Government Agency Guidelines

In addition to a review of the Medicare NCD and the expert physician specialty society guidelines, another reasonable approach might be to begin with the information in Section II of this response, but add to it the various evidence-based treatment guidelines that have been developed by state government. In this section, we have included all state guidelines in law or regulation, that we are aware of, that address, positively or negatively, spinal cord stimulation. For your consideration, see Table 6 below.

Table 6. State Workers' Compensation Treatment Guidelines in Law or Regulation Addressing SCS

State	Excerpted SCS Language	Recommendation
California http://www.dir.ca.gov/dwc/MedicalProvider.htm	Recommended only for selected patients in cases when less invasive procedures have failed or are contraindicated, for specific conditions indicated below, and following a successful temporary trial. Indications for stimulator implantation: <ul style="list-style-type: none"> Failed back syndrome (persistent pain in patients who have undergone at least one previous back operation), more helpful for lower extremity than low back pain, although both stand to benefit, 40-60% success rate 5 years after surgery. It works best for neuropathic pain. Neurostimulation is generally considered to be ineffective in treating nociceptive pain. The procedure should be employed with more caution in the cervical region than in the thoracic or lumbar. 	POSITIVE

State	Excerpted SCS Language	Recommendation
	<ul style="list-style-type: none"> Complex Regional Pain Syndrome (CRPS)/Reflex sympathetic dystrophy (RSD), 70-90% success rate, at 14 to 41 months after surgery. (Note: This is a controversial diagnosis.) [remainder redacted] 	
<p>Colorado</p> <p>http://www.coworkforce.com/dwc/Medical_Treatment.asp</p>	<p>Description — Neurostimulation is the delivery of low-voltage electrical stimulation to the spinal cord or peripheral nerves to inhibit or block the sensation of pain. This is a generally accepted procedure that has limited use. May be most effective in patients with chronic, intractable limb pain who have not achieved relief with oral medications, rehabilitation therapy, or therapeutic nerve blocks, and in whom the pain has persisted for longer than 6 months. Particular technical expertise is required to perform this procedure and is available in some neurosurgical, rehabilitation, and anesthesiology training programs and fellowships. Physicians performing this procedure must be trained in neurostimulation implantation and participate in ongoing injection training workshops, such as those sponsored by the Internal Society for Injection Studies or as sponsored by implant manufacturers.</p> <p>Surgical Indications — Failure of conservative therapy including active and/or passive therapy, medication management, or therapeutic injections. Preauthorization is required. Habituation to narcotic analgesics in the absence of a history of addictive behavior does not preclude the use of neurostimulation. Only patients who meet the following criteria should be considered candidates for neurostimulation:</p> <ol style="list-style-type: none"> A diagnosis of a specific physical condition known to be chronically painful has been made on the basis of objective findings; and All reasonable surgical and non-surgical treatment has been exhausted; and Pre-surgical psychiatric or psychological evaluation has been performed and has demonstrated motivation and long-term commitment without issues of secondary gain; and There is no evidence of addictive behavior. (Tolerance and dependence to narcotic analgesics are not addictive behaviors and do not preclude implantation.); and 	<p>POSITIVE</p>

State	Excerpted SCS Language	Recommendation
	<p>v. The topography of pain and its underlying pathophysiology are amenable to stimulation coverage (the entire painful area has been covered); and</p> <p>vi. A successful neurostimulation screening test of 2-3 days. A screening test is considered successful if the patient (a) experiences a 50% decrease in pain, which may be confirmed by visual analogue scale (VAS), and (b) demonstrates objective functional gains or decreased utilization of pain medications. Functional gains may be evaluated by an occupational therapist and/or physical therapist prior to and before discontinuation of the trial.</p> <p>vii. For spinal cord stimulation, a temporary lead is implanted at the level of pain and attached to an external source to validate therapy effectiveness. (For peripheral nerve screening, a nerve block is performed to define the specific nerve branch but if multiple branches are involved, a screening test for spinal cord stimulation may be indicated.) Long-term functional improvement is anticipated when objective functional improvement has been observed during time of neurostimulation screen exam.</p> <p>Contraindications — Unsuccessful neurostimulation test – either inability to obtain functional improvement or reduction of pain, those with cardiac pacemakers, patient unable to properly operate the system. It should not be used if future MRI is planned.</p> <p>e. Operative Treatment – Implantation of stimulating leads connected by extensions to either an implanted neurostimulator or an implanted receiver powered by an external transmitter. The procedure may be performed either as an open or a percutaneous procedure, depending on the presence of epidural fibrosis and the anatomical placement required for optimal efficacy.</p> <p>f. Post-Operative Considerations – MRI is contraindicated after placement of neurostimulators.</p> <p>g. Post-Operative Therapy – Active and/or passive therapy should be employed to improve function. Implantable stimulators will require frequent</p>	

State	Excerpted SCS Language	Recommendation
	monitoring such as adjustment of the unit and replacement of batteries.	
Delaware http://dowc.ingenix.com/info.asp?page=pracguid	<p>7.1 NEUROSTIMULATION (taken from Chronic Pain Guideline)</p> <p>7.1.1 Description — Neurostimulation is the delivery of low-voltage electrical stimulation to the spinal cord or peripheral nerves to inhibit or block the sensation of pain. This is a generally accepted procedure that has limited use. May be most effective in patients with chronic, intractable limb pain who have not achieved relief with oral medications, rehabilitation therapy, or therapeutic nerve blocks, and in whom the pain has persisted for longer than 6 months.</p> <p>Particular technical expertise is required to perform this procedure and is available in some neurosurgical, rehabilitation, and anesthesiology training programs and fellowships. Physicians performing this procedure must be experienced in neurostimulation implantation and participate in ongoing injection training workshops, such as those sponsored by the Internal Society for Injection Studies or as sponsored by implant manufacturers.</p> <p>7.1.2 Indications — Failure of conservative therapy including active and/or passive therapy, medication management, or therapeutic injections. Habituation to narcotic analgesics in the absence of a history of addictive behavior does not preclude the use of neurostimulation. Only patients who meet the following criteria should be considered candidates for neurostimulation:</p> <p>7.1.2.1 A diagnosis of a specific physical condition known to be chronically painful has been made on the basis of objective findings; and</p> <p>7.1.2.2 All reasonable non-surgical treatment has been exhausted; and</p> <p>7.1.2.3 Pre-surgical psychiatric or psychological evaluation has been performed and has demonstrated motivation and long-term commitment without issues of secondary gain; and</p> <p>7.1.2.4 There is no evidence of addictive behavior.</p>	<p>POSITIVE</p>

State	Excerpted SCS Language	Recommendation
	<p>(Tolerance and dependence to narcotic analgesics are not addictive behaviors and do not preclude implantation.); and</p> <p>7.1.2.5 The topography of pain and its underlying pathophysiology are amenable to stimulation coverage; and</p> <p>7.1.2.6 A successful neurostimulation screening test of 2-3 days. A screening test is considered successful if the patient (a) experiences a 50% decrease in pain, which may be confirmed by visual analogue scale (VAS).</p> <p>7.1.2.7 For spinal cord stimulation, a temporary lead is implanted and attached to an external source to validate therapy effectiveness.</p> <p>7.1.3 Operative Treatment – Implantation of stimulating leads connected by extensions to either an implanted neurostimulator or an implanted receiver powered by an external transmitter. The procedure may be performed either as an open or a percutaneous procedure, depending on the presence of epidural fibrosis and the anatomical placement required for optimal efficacy.</p> <p>7.1.4 Post-Operative Considerations – MRI is contraindicated after placement of neurostimulators.</p> <p>7.1.5 A mandatory second opinion is required to confirm the rationale for the procedure for non malignant pain.</p>	
<p>Kansas</p> <p>http://www.dol.ks.gov/WC/HTML/wc_odg.asp</p>	<p>Recommended only for selected patients in cases when less invasive procedures have failed or are contraindicated, for specific conditions indicated below, and following a successful temporary trial. [Remainder of the background data on history, safety and efficacy of therapy not shown here]</p> <p>Indications for stimulator implantation:</p> <p>Failed back syndrome (persistent pain in patients who have undergone at least one previous back operation and are not candidates for repeat surgery), when all of the following are present: (1) symptoms are primarily lower extremity radicular pain; there</p>	<p>POSITIVE</p>

State	Excerpted SCS Language	Recommendation
	<p>has been limited response to non-interventional care (e.g. neuroleptic agents, analgesics, injections, physical therapy, etc.); (2) psychological clearance indicates realistic expectations and clearance for the procedure; (3) there is no current evidence of substance abuse issues; (4) there are no contraindications to a trial; (5) Permanent placement requires evidence of 50% pain relief and medication reduction or functional improvement after temporary trial. Estimates are in the range of 40-60% success rate 5 years after surgery. Neurostimulation is generally considered to be ineffective in treating nociceptive pain. The procedure should be employed with more caution in the cervical region than in the thoracic or lumbar due to potential complications and limited literature evidence.</p> <p>Complex Regional Pain Syndrome (CRPS)/Reflex sympathetic dystrophy (RSD), 70-90% success rate, at 14 to 41 months after surgery. (Note: This is a controversial diagnosis.)</p> <p>...[Redacted]</p>	
<p>Minnesota</p> <p>http://www.dli.mn.gov/WC/PDF/treatparam.pdf</p>	<p>C. The following surgical therapies have very limited application and require a second opinion that confirms that the treatment is indicated and within the parameters listed, and a personality or psychosocial evaluation that indicates that the patient is likely to benefit from the treatment.</p> <p>(1) Dorsal column stimulator is indicated for a patient who has neuropathic pain, and is not a candidate for any other surgical therapy, and has had a favorable response to a trial screening period.</p> <p>The only surgical procedures indicated for patients with regional low back pain only are decompression of a lumbar nerve root or lumbar arthrodesis, with or without instrumentation, which must meet the parameters of subpart 6 and part 5221.6500, subpart 2, items A and C. For patients with failed back surgery, dorsal column stimulators or morphine pumps may be indicated; their use must meet the parameters of subpart 6, item C.</p> <p>C. If the patient continues with symptoms and objective physical findings after surgical therapy has</p>	<p>POSITIVE</p>

State	Excerpted SCS Language	Recommendation
	<p>been rendered, the patient refused surgical therapy, or the patient was not a candidate for surgical therapy, and if the patient's condition prevents the resumption of the regular activities of daily life including regular vocational activities, then the patient may be a candidate for chronic management. Any course or program of chronic management for patients with radicular pain, with or without regional neck pain, with static neurologic changes must meet all of the parameters of part 5221.6600.</p> <p>For patients with failed surgery, dorsal column stimulators or morphine pumps may be indicated consistent with subpart 6, item C.</p> <p>B. Dorsal column stimulator or morphine pump may be indicated for a patient with neuropathic pain unresponsive to all other treatment modalities who is not a candidate for any other therapy and has had a favorable response to a trial screening period. Use of these devices is indicated only if a second opinion confirms that this treatment is indicated, and a personality or psychosocial evaluation indicates that the patient is likely to benefit from this treatment.</p>	
<p>Nevada</p> <p>http://www.leg.state.nv.us/NAC/NA-C-616C.html</p>	<p>NAC 616C.123 <i>Occupational Medicine Practice Guidelines</i>: Adoption by reference; annual review by Administrator; use. (NRS 616A.400, 616C.250)</p> <ol style="list-style-type: none"> The most recently published edition of or update to the <i>Occupational Medicine Practice Guidelines</i>, published jointly by the American College of Occupational and Environmental Medicine and the Occupational Environmental Medicine Health Information, Inc., is hereby adopted by reference as standards for the provision of accident benefits to employees who have suffered industrial injuries or occupational diseases. <p>Excerpt from most recent ACOEM language on SCS: Spinal cord stimulators are not recommended for treatment of acute, subacute, or chronic LBP. They also are not recommended for treatment of radicular pain syndromes or failed back surgery syndrome.* Not Recommended, Insufficient Evidence (I)</p> <p>* Spinal cord stimulators may be considered as a late or last resort for highly selected patients who have</p>	<p>NEGATIVE</p> <p><i>Note: Even though ACOEM envisions some usage, we will count as both positive and negative in our best case/worst case scenario summary. ACOEM is used as a minimum standard in Nevada and we are not aware of any situation in which the state has used ACOEM to deny access to SCS.</i></p>

State	Excerpted SCS Language	Recommendation
	<p>failed multiple other conservative treatments including a quality functional restoration program and who have had a forensic psychological assessment (83 percent Panel agreement).</p>	
<p>North Dakota</p> <p>www.legis.nd.gov/information/acdata/pdf/92-01-02.pdf</p>	<p>CHAPTER 92-01-02 RULES OF PROCEDURE - NORTH DAKOTA WORKERS' COMPENSATION ACT</p> <p>Administrative Rule: 92-01-02-33 The organization may use the Official Disability Guidelines, the American College of Occupational and Environmental Medicine's Occupational Medicine Practice Guidelines, Guide to Physical Therapy Practice, The Medical Disability Advisor, Diagnosis and Treatment for Physicians and Therapists Upper Extremity Rehabilitation, Treatment Guidelines of the American Society of Hand Therapists, or any other treatment and disability guidelines or standards it deems appropriate to administer claims.</p> <p>ODG excerpt: Recommended only for selected patients in cases when less invasive procedures have failed or are contraindicated, for specific conditions indicated below, and following a successful temporary trial. [Remainder of the background data on history, safety and efficacy of therapy not shown here]</p> <p>Indications for stimulator implantation:</p> <p>Failed back syndrome (persistent pain in patients who have undergone at least one previous back operation and are not candidates for repeat surgery), when all of the following are present: (1) symptoms are primarily lower extremity radicular pain; there has been limited response to non-interventional care (e.g. neuroleptic agents, analgesics, injections, physical therapy, etc.); (2) psychological clearance indicates realistic expectations and clearance for the procedure; (3) there is no current evidence of substance abuse issues; (4) there are no contraindications to a trial; (5) Permanent placement requires evidence of 50% pain relief and medication reduction or functional improvement after temporary trial. Estimates are in the range of 40-60% success</p>	<p>POSITIVE</p> <p><i>Note: Workforce Safety & Insurance in ND noted that they officially adopted ODG as the primary guideline for decision guidance. Therefore, we are considering ND guidelines positive.</i></p>

State	Excerpted SCS Language	Recommendation
	<p>rate 5 years after surgery. Neurostimulation is generally considered to be ineffective in treating nociceptive pain. The procedure should be employed with more caution in the cervical region than in the thoracic or lumbar due to potential complications and limited literature evidence.</p> <p>Complex Regional Pain Syndrome (CRPS)/Reflex sympathetic dystrophy (RSD), 70-90% success rate, at 14 to 41 months after surgery. (Note: This is a controversial diagnosis.)</p> <p>...[Redacted]</p>	
<p>Oklahoma</p> <p>http://www.owcc.state.ok.us/guidelines.htm</p>	<p>1. NEUROSTIMULATION (from chronic pain guideline)</p> <p>a. Description C Neurostimulation is the delivery of low-voltage electrical stimulation to the spinal cord or peripheral nerves to inhibit or block the sensation of pain. This is a generally accepted procedure that has limited use. May be most effective in patients with chronic, intractable limb pain who have not achieved relief with oral medications, rehabilitation therapy, or therapeutic nerve blocks, and in whom the pain has persisted for longer than 6 months. Particular technical expertise is required to perform this procedure and is available in some neurosurgical, rehabilitation, and anesthesiology training programs and fellowships. Physicians performing this procedure must be trained in neurostimulation implantation and participate in ongoing injection training workshops, such as those sponsored by the Internal Society for Injection Studies or as sponsored by implant manufacturers.</p> <p>b. Complications: May include paraplegia, epidural hematoma, epidural hemorrhage, undesirable change in stimulation, seroma, CSF leakage, infection, allergic response, hardware malfunction or equipment migration, pain at implantation site, loss of pain relief, chest wall stimulation, and other surgical risks.</p> <p>c. Surgical Indications: Failure of conservative therapy including active and/or passive therapy, medication management, or therapeutic injections.</p> <p>Preauthorization is required. Habituation to narcotic analgesics in the absence of a history of addictive behavior does not preclude the use of neurostimulation. Only patients who meet the following criteria should be considered candidates for neurostimulation:</p>	<p>POSITIVE</p>

State	Excerpted SCS Language	Recommendation
	<p>i. A diagnosis of a specific physical condition known to be chronically painful has been made on the basis of objective findings; and</p> <p>ii. All reasonable surgical and non-surgical treatment has been exhausted; and</p> <p>iii. Pre-surgical psychiatric or psychological evaluation has been performed and has demonstrated motivation and long-term commitment without issues of secondary gain; and</p> <p>iv. There is no evidence of addictive behavior. (Tolerance and dependence to narcotic analgesics are not addictive behaviors and do not preclude implantation.); and</p> <p>v. The topography of pain and its underlying pathophysiology are amenable to stimulation coverage (the entire painful area has been covered); and</p> <p>vi. A successful neurostimulation screening test of 2-3 days. A screening test is considered successful if the patient (a) experiences a 50% decrease in pain, which may be confirmed by visual analogue scale (VAS), and (b) demonstrates objective functional gains or decreased utilization of pain medications. Functional gains may be evaluated by an occupational therapist and/or physical therapist prior to and before discontinuation of the trial.</p> <p>vii. For spinal cord stimulation, a temporary lead is implanted at the level of pain and attached to an external source to validate therapy effectiveness. (For peripheral nerve screening, a nerve block is performed to define the specific nerve branch but if multiple branches are involved, a screening test for spinal cord stimulation may be indicated.) Long-term functional improvement is anticipated when objective functional improvement has been observed during time of neurostimulation screen exam.</p> <p>d. Contraindications: Unsuccessful neurostimulation test, either inability to obtain functional improvement or reduction of pain, those with cardiac pacemakers, patient unable to properly operate the system. It should not be used if future MRI is planned.</p> <p>e. Operative Treatment: Implantation of stimulating leads connected by extensions to either an implanted neurostimulator or an implanted receiver powered by an external transmitter. The procedure may be performed either as an open or a percutaneous</p>	

State	Excerpted SCS Language	Recommendation
	<p>procedure, depending on the presence of epidural fibrosis and the anatomical placement required for optimal efficacy.</p> <p>f. Post-Operative Considerations: MRI is contraindicated after placement of neurostimulators.</p> <p>g. Post-Operative Therapy: Active and/or passive therapy should be employed to improve function. Implantable stimulators will require frequent monitoring such as adjustment of the unit and replacement of batteries.</p>	
<p>Rhode Island</p> <p>http://www.courts.ri.gov/workers/medical/protocols/Dorsal_Column_Stimulators.pdf</p>	<p>III. Conditions for which DCS placement is appropriate:</p> <ol style="list-style-type: none"> 1. The “failed back syndrome” with persistent, intractable disabling pain of nerve origin (perineural fibrosis, arachnoiditis, etc.) in spite of maximal medical, surgical or other therapies, (approximately 75% of cases). 2. Chronic and intractable pain following [redacted] (approximately 5 to 10 percent of cases). 3. Nerve disorders including [redacted], reflex sympathetic dystrophy, [redacted] which have failed to respond to the generally acceptable alternative modalities of therapy. <p>[guideline continues with other criteria to guide patient selection – not shown here]</p>	<p>POSITIVE</p>
<p>Texas</p> <p>http://info.sos.state.tx.us/pls/pub/readtac\$ext.tacpage?sl=R&app=9&pdire=&prloc=&ptloc=&pg=1&ptac=&ti=28&pt=2&ch=137&rl=100</p>	<p>Recommended only for selected patients in cases when less invasive procedures have failed or are contraindicated, for specific conditions indicated below, and following a successful temporary trial. [Remainder of the background data on history, safety and efficacy of therapy not shown here]</p> <p>Indications for stimulator implantation:</p> <p>Failed back syndrome (persistent pain in patients who have undergone at least one previous back operation and are not candidates for repeat surgery), when all of the following are present: (1) symptoms are primarily lower extremity radicular pain; there has been limited response to non-interventional care (e.g. neuroleptic agents, analgesics, injections, physical therapy, etc.); (2) psychological clearance indicates realistic expectations and clearance for the procedure; (3) there is no current evidence of substance abuse issues; (4) there are no</p>	<p>POSITIVE</p>

State	Excerpted SCS Language	Recommendation
	<p>contraindications to a trial; (5) Permanent placement requires evidence of 50% pain relief and medication reduction or functional improvement after temporary trial. Estimates are in the range of 40-60% success rate 5 years after surgery. Neurostimulation is generally considered to be ineffective in treating nociceptive pain. The procedure should be employed with more caution in the cervical region than in the thoracic or lumbar due to potential complications and limited literature evidence.</p> <p>Complex Regional Pain Syndrome (CRPS)/Reflex sympathetic dystrophy (RSD), 70-90% success rate, at 14 to 41 months after surgery. (Note: This is a controversial diagnosis.)</p> <p>...[Redacted]</p>	
<p>Wisconsin</p> <p>http://www.legis.state.wi.us/rsb/code/dwd/dwd081.pdf</p>	<p>The surgical therapies in subds. 1. and 2. have very limited application and require a personality or psychosocial evaluation that indicates the patient is likely to benefit from the treatment:</p> <p>1. Spinal cord stimulator may be necessary for a patient who has neuropathic pain and has had a favorable response to a trial screening period.</p> <p>For patients with failed surgery, spinal cord stimulators or intrathecal drug delivery systems may be necessary consistent with sub. (6) (d).</p> <p>For patients with failed back surgery, spinal cord stimulators or intrathecal drug delivery systems may be necessary consistent with the guidelines of sub. (6) (d).</p> <p>(b) There shall be appropriate psychological assessment prior to implantation of a spinal cord stimulator or intrathecal drug delivery system to determine whether the patient is a suitable candidate for this type of treatment.</p>	<p>POSITIVE</p>
<p>Wyoming</p> <p>http://doe.wyo.gov/serviceproviders/Pages/TreatmentGuidelines.aspx</p>	<p>I. Division preauthorization policy:</p> <p>A. Compensability should NOT be in question at the time of preauthorization for this procedure.</p> <p>B. All requirements raised in this form MUST be addressed prior to submitting the record for peer review.</p>	<p>POSITIVE</p>

State	Excerpted SCS Language	Recommendation
	<p>C. Physicians requesting authorization must be trained to perform that procedure.</p> <p>D. Authorization for this procedure requires prior approval by a peer physician.</p> <p>II. General indications: Implantation of a dorsal column stimulator is approved for injured workers with chronic, intractable limb pain of a radicular nature and/or intractable low back pain following failed lumbar spine surgery and/or complex regional pain syndrome in patients who have not obtained satisfactory long term relief with oral medications, rehabilitation therapy, therapeutic nerve blocks, and biofeedback or other psychological help. Whether the procedure is performed open or percutaneously depends upon the presence of epidural fibrosis and anatomical placement required for optimal efficacy. The patient must be motivated for improvement and must understand the potential for complications.</p> <p>III. Specific evaluation criteria - all must be addressed.</p> <p>A. Diagnosis of a specific physical condition known to be chronically painful made on the basis of objective findings.</p> <p>B. Pertinent history - MUST document:</p> <ol style="list-style-type: none"> 1. Detailed description of pain-character; relationship of intensity to time of day, body position and activity, and specific changes if any, during course of treatment; perceived intensity of low back and/or radicular/CRPS pain; visual analog scale > 5 pain intensity. 2. Noninvasive and invasive measures employed to reduce pain and specific response to each of these. <p>Spinal cord stimulator: Claimant name:</p> <p>C. Physical findings consistent with/corroborating lumbar axial pain/radiculitis/radiculopathy or CRPS.</p> <ol style="list-style-type: none"> 1. Lumbar range of motion (degrees) 	

State	Excerpted SCS Language	Recommendation
	<p>flexion/extension.</p> <p>2. Straight leg raise limitations (degrees).</p> <p>3. Deficits in sensation/motor/reflex functions.</p> <p>4. Distribution of sensory and sudomotor signs consistent with chronic regional pain syndrome (if applicable).</p> <p>D. Radiographic findings that are consistent with/corroborate patient complaints and above diagnosis.</p> <p>1. Plain radiographs. Date:</p> <p>2. MRI. Date:</p> <p>3. CT Scan. (if needed) Date:</p> <p>E. Procedural results consistent with and corroborate patient complaints.</p> <p>1. Nerve root blocks. Date:</p> <p>2. EMG. Date:</p> <p>3. Other.</p> <hr/> <p>Date: _____</p> <p>F. Psychiatric or psychological evaluation must document patient motivation without issues of addictive behavior or other secondary gain. Entire report must be submitted with preauthorization request.</p> <p>G. Successful trial of neurostimulation lasting 2 to 7 days. Success is defined as:</p> <p>1. At least a 50% decrease in pain as demonstrated by visual analog scale.</p> <p>2. Decreased oral pain medications.</p> <p>3. Objective functional gains—best demonstrated by a physical or occupational therapist prior to and during neurostimulator trial.</p> <p>IV. Contraindications.</p> <p>1. Unsuccessful temporary trial of neurostimulation.</p> <p>2. Cardiac pacemaker.</p> <p>3. Patient unable to understand and properly operate the system.</p> <p>4. Future MRI's anticipated.</p>	

To our knowledge, the remainder of the states either do not currently have a law or regulation regarding the use of treatment guidelines, or do not have guidelines that specifically address spinal cord

stimulation. It is worth noting that the Official Disability Guidelines promulgated by the Work Loss Data Institute are used in at least 23 states and provinces by carriers and others including many states without formal law or regulation. As shown in Section II, ODG appropriately covers SCS. Finally, through our prior authorization work, we know that with rare exception, 49 of 50 state work comp agencies/payers and the vast majority of Medicaid agencies and plans grant coverage for SCS.

In summary, Method 4 which reasonably adds guidelines developed and/or used by other state agencies, yields very positive results for SCS. When the results from Methods 1-3 are combined with those from Method 4, **WORST CASE: POSITIVE = 20, NEGATIVE = 5; BEST CASE: POSITIVE = 23, NEGATIVE = 2.**

WORST CASE	POSITIVE = 20	NEGATIVE = 5
BEST CASE	POSITIVE = 23	NEGATIVE = 2

IV. Private Payer Coverage Policies for SCS

Methodology #5: Private Payer Policy Approach

Finally, there are a number of private payer policies that appropriately cover SCS for chronic, intractable pain. Another reasonable approach might be to begin with the information in Methods 1-4 of this response, but add to it the various coverage policies that have been developed by private payers as shown in the table below. We have included all private payer coverage policies for payers that serve Washington residents, that we are aware of, that address, positively or negatively, spinal cord stimulation. For your consideration, see Table 7 below.

Table 7. Private Payer Coverage Policies for SCS

Payer and Covered Lives	SCS Language	Coverage
AETNA Health Inc. - 309,017 covered lives 151 Farmington Avenue, Hartford, CT 06156 www.aetna.com Contracted or Affiliated PBM(s): Aetna Pharmacy Management (APM) States Served: AL, AK, AZ, AR, CA, CO, CT, DE, DC, FL, GA, HI, ID, IL, IN, IA, KA, KY, LA, ME, MD, MA, MI, MN, MS, MT, NE, NV, NH, NJ, NM, NY, NC, ND, OH, OK, OR, PA, PR, RI, SC, SD, TN, TX, UT, VT, VA, WA, WV, WI,	Excerpt- Aetna considers dorsal column stimulators (DCS) medically necessary durable medical equipment (DME) for the management of members with chronic pain due to: (i) failed back surgery syndrome with low back pain and significant radicular pain, (ii) complex regional pain syndrome (also known as reflex sympathetic dystrophy), or (iii) [redacted]: -There is documented pathology, i.e., an objective basis for the pain complaint, and -Other more conservative methods of pain management have been tried and failed, and -Member does not have any untreated existing drug addiction problems (per American Society of Addiction Medicine (ASAM) guidelines), and -Member has obtained psychiatric clearance, and -Member has predominantly radiating extremity pain, and	POSITIVE

Payer and Covered Lives	SCS Language	Coverage
<p>WY</p> <p>http://www.aetna.com/cpb/medical/data/100_199/0194.html</p>	<p>-Member experienced significant pain reduction (50% or more) with a 3- to 7-day trial of percutaneous spinal stimulation. (A trial of percutaneous spinal stimulation is considered medically necessary for members who meet the above-listed criteria, in order to predict whether a dorsal column stimulator will induce significant pain relief.)</p>	
<p>Asuris Northwest Health – 57,242 covered lives</p> <p>528 East Spokane Falls Boulevard, Suite 301, Spokane, WA 99202 www.asuris.com Contracted or Affiliated PBM(s): RegenceRx States Served: 14 counties in Eastern Washington. Telephone (Automated): (888) 344-5593 Regence BlueShield. Not-Ownership: for-profit. Private.</p> <p>http://blue.regence.com/trg/medpol/surgery/sur45.html</p>	<p>Excerpt-</p> <p>I. Patient selection focuses on determining whether or not the patient is refractory to other types of treatment. The following considerations apply: A. Spinal cord stimulation may be considered medically necessary for the treatment of either of the following conditions and when all patient selection criteria in B. below have been met: 1. Severe and chronic pain of the trunk or limbs other than critical limb ischemia that is refractory to all other pain therapies, or 2. [redacted]. B. All of the following Patient Selection Criteria must be met: 1. The treatment is used only as a last resort; other treatment modalities (pharmacological, surgical, psychological, or physical, if applicable) have been tried and failed or are judged to be unsuitable or contraindicated. 2. Pain is neuropathic in nature; i.e. resulting from actual damage to the peripheral nerves. Common indications include, but are not limited to failed back syndrome, complex regional pain syndrome (i.e., reflex sympathetic dystrophy), arachnoiditis, radiculopathies, [redacted]. 3. No serious untreated drug habituation exists. 4. Patient was carefully screened, evaluated and diagnosed by a multidisciplinary pain management team prior to application of these therapies. 5. Pain relief from a temporarily implanted electrode has been demonstrated prior to permanent implantation. II. Spinal cord stimulation is considered investigational for all other indications including but not limited to treatment of the following: [redacted]</p>	<p>POSITIVE</p>
<p>Blue Cross & Blue Shield of Rhode Island - 387</p> <p>444 Westminster Street, Providence, RI 02903 www.bcbsri.com Contracted or Affiliated PBM(s): WellPoint NextRx States Served: Rhode Island. Alias(es): Coordinated Health Partners is the HMO subsidiary of Blue Cross and Blue Shield of Rhode Island. Ownership: Not-for-profit. Private.</p>	<p>Excerpt-</p> <p>Spinal cord stimulation is used to interfere with the transmission of pain signals to the brain and to provide relief from chronic pain. The sensation of pain is blocked by applying low-voltage electrical impulses to stimulate targeted nerves along the spinal cord. The repetitive electrical impulses are delivered to the spinal cord using an electronic device connected to a strip of electrodes surgically implanted in the epidural space. A magnetic remote control is used to turn the current on/off and to adjust the current for optimal pain relief. Treatment is a two-step process. Initially a trial procedure is performed to assess effectiveness in the specific patient. This surgical procedure is typically performed in an outpatient hospital or day-surgery center. Length of the trial period depends on severity of pain and physician determination, but most trials range from a few days to several weeks. A good outcome after a trial</p>	<p>POSITIVE</p>

Payer and Covered Lives	SCS Language	Coverage
<p>https://www.bcbsri.com/BCBSRIWeb/plansandservices/services/medical_policies/SpinalCordStimulation.jsp</p>	<p>procedure is defined as pain relief of 50 per cent or better. If the initial procedure is successful, a permanent stimulator is implanted. Guidelines for the use of spinal cord stimulation: -Treatment is used only as a last resort after other treatment modalities (pharmacological, surgical, psychological, or physical, if applicable) have been tried and have failed, or, are judged to be unsuitable or contraindicated; -Pain is neuropathic in nature; i.e., resulting from damage to the peripheral nerves; -No untreated drug addictions; - Demonstration of pain relief with a temporarily implanted electrode precedes permanent implantation, and -Initial trial resulted in at least 50 per cent improvement in pain relief. Spinal cord stimulation for the treatment of critical limb ischemia as a technique to forestall amputation is not covered due to insufficient evident demonstrating clinical efficacy. Spinal cord stimulators (generator or receiver) are typically replaced every two to three years.</p>	
<p>Blue Cross and Blue Shield of Nebraska - 8,647</p> <p>7261 Mercy Road, Omaha, NE 68180 www.bcbsne.com Contracted or Affiliated PBM(s): Prime Therapeutics, Inc. States Served: Nebraska. Telephone (Automated): (800) 642-8980 Mutual insurance Ownership: company. Private.</p> <p>https://www.bcbsne.com/PDFs/Provider/Library/Manuals/Medical_Policy_Manual.pdf Keyword Search "SPINAL CORD AND DEEP BRAIN STIMULATION"</p>	<p>Excerpt- The use of spinal cord and deep brain stimulation is to be utilized as follows: -The treatment is used only as a last resort; other treatment modalities (pharmacological, surgical, psychological, or physical, if applicable) have been tried and failed or are judged to be unsuitable or contraindicated; -Demonstration of pain relief with a temporary implanted electrode precedes permanent implantation; -Patients are carefully screened, evaluated, and diagnosed by a multidisciplinary team prior to application of these therapies; and -All the facilities, equipment, and professional and support personnel required for the proper diagnosis, treatment, and follow-up of the patient are available. Implantation of the spinal cord stimulator is typically a two-step process. Initially, the electrode is temporarily implanted in the epidural space, allowing a trial period of stimulation. Once treatment effectiveness is confirmed, the electrodes and radio-receiver/transducer are permanently implanted.</p>	POSITIVE
<p>BlueCross BlueShield of Tennessee – 4,818</p> <p>801 Pine Street, Chattanooga, TN 37402</p>	<p>Excerpt- A trial spinal cord stimulation associated with the following conditions/diseases is considered medically necessary if the medical appropriateness criteria are met: -Radiculopathies (diseases or conditions involving the nerve roots, including failed</p>	POSITIVE

Payer and Covered Lives	SCS Language	Coverage
<p>www.bcbst.com Contracted or Affiliated PBM(s): Caremark Rx, Inc. States Served: Tennessee. Telephone (Automated): (800) 565-9140 Alias(es): Volunteer State Health Plan, TennCare Select Ownership: BlueCross BlueShield of Tennessee, Inc. Not-for-profit. Private.</p> <p>http://www.bcbst.com/mp_manual/Spinal_Cord_Stimulation_for_Treatment_of_Pain.htm</p>	<p>back surgery syndrome [FBSS], arachnoiditis and epidural fibrosis) - Reflex sympathetic dystrophy (also known as complex regional pain syndrome type 1 -Intractable pain from severe peripheral vascular disease. Permanent implantation is considered medically necessary if the medical appropriateness criteria are met. Medical Appropriateness Criteria: Trial SCS is considered appropriate if ALL of the following criteria are met: -SCS is a late or last resort for an individual with chronic intractable pain -Other treatment modalities (e.g., pharmacologic, surgical, physical, or psychologic therapies) have been tried for at least 6 months and failed, or were judged unsuitable, or contraindicated -Careful screening, evaluation, and diagnosis by a multi-disciplinary team are undertaken prior to the implantation. Such screening must include psychological as well as physical evaluation. Permanent implantation is considered medically appropriate if there is a demonstration of pain relief for 5 to 10 days with a temporarily implanted electrode.</p>	
<p>Bluegrass Family Health, Inc. – 1</p> <p>651 Perimeter Drive, Suite 300, Lexington, KY 40517 www.bgfh.com Contracted or Affiliated PBM(s): Caremark Rx, Inc. States Served: Kentucky. Ownership: Baptist Healthcare System, Inc. (Louisville, KY). Not-for-profit. Private. Chief Executive Officer: James S. Fritz</p> <p>http://www.bgfh.com/snm.asp_3524_providers.asp Select "Coverage Issues", Keyword search: Pain Management</p>	<p>Spinal Cord Stimulation is considered medically necessary with established trial and failure of conservative therapies, who have undergone evaluation by a psychiatrist or a behavioral medicine professional specializing in pain, which has identified the member as an appropriate candidate for SCS trial, and then have undergone a trial of SCS stimulation with a reduction of >50% of pain. Patients shall have undergone careful screening and diagnosis by a multidisciplinary team before implantation, have no documented or described drug/substance abuse/addiction issues, and have demonstrated pathology as an objective source of the pain. Recognized conditions for which this modality is appropriate include: pain of neurogenic origin, extremity pain secondary to peripheral vascular disease, and pain secondary to severe disabling RSD/RCPD that has been unresponsive to conventional therapy for a minimum of six month duration.</p>	POSITIVE
<p>CIGNA HealthCare, Inc. - 130,080 covered lives</p> <p>900 Cottage Grove Road, Bloomfield, CT 06002 www.cigna.com</p>	<p>Excerpt – CIGNA covers a short-term trial of spinal cord stimulation (SCS) for the treatment of chronic intractable pain of greater than six months’ duration as medically necessary when BOTH of the following criteria are met: • There is failure of available conventional multidisciplinary medical (e.g., pharmacological,</p>	POSITIVE

Payer and Covered Lives	SCS Language	Coverage
<p>Contracted or Affiliated PBM(s): CIGNA Pharmacy Management</p> <p>States Served: AL, AK, AZ, AR, CA, CO, CT, DE, DC, FL, GA, HI, ID, IL, IN, IA, KA, KY, LA, ME, MD, MA, MI, MN, MS, MT, NE, NV, NH, NJ, NM, NY, NC, ND, OH, OK, OR, PA, PR, RI, SC, SD, TN, TX, UT, VT, VA, WA, WV, WI, WY</p> <p>Alias(es): Connecticut General Life Insurance Company, Great-West Healthcare</p> <p>Ownership: CIGNA HealthCare, Inc. For-profit. Public. NYSE: CI</p> <p>http://www.cigna.com/customer_care/healthcare_professional/coverage_positions/medical/mm_0380_coverage_positioncriteria_spinal_cord_stimulation.pdf</p>	<p>physical therapy) and surgical management. • Appropriate mental health screening has been completed, and there is no evidence of an inadequately controlled mental health problem. CIGNA covers permanent implantation of a spinal cord stimulator for the treatment of chronic intractable pain of greater than six months' duration as medically necessary when ALL of the following criteria are met: • There is failure of available conventional multidisciplinary medical (e.g., pharmacological, physical therapy) and surgical management. • Appropriate mental health screening has been completed, and there is no evidence of an inadequately controlled mental health problem. • Pain relief from a temporarily implanted electrode has been demonstrated prior to permanent implantation. CIGNA covers a short-term trial of spinal cord stimulation (SCS) for the treatment of pain secondary to [redacted]. CIGNA covers permanent implantation of a spinal cord stimulator for the treatment of pain secondary to [redacted].</p>	
<p>Group Health Cooperative - 509,208 covered lives</p> <p>320 Westlake Avenue North, Seattle, WA 98109 www.ghc.org</p> <p>Ownership: Group Health Cooperative. Not-for-profit. Private.</p> <p>Contracted or Affiliated PBM(s): MedImpact Healthcare Systems, Inc.</p> <p>States Served: Idaho, Washington.</p> <p>Alias(es): Group Health Options</p> <p>https://provider.ghc.org/all-sites/clinical/criteria/pdf/spinal_cord_stimulator_for_pain</p>	<p>Excerpt –</p> <p>Dorsal column (spinal cord) neurostimulation</p> <p>-The surgical implantation of neurostimulator electrodes within the dura mater (endodural) or the percutaneous insertion of electrodes in the epidural space.</p> <p>These implants are covered when all of the conditions listed below have been met:</p> <ul style="list-style-type: none"> - Documentation supports that the implantation is a late resort (if not a last resort) in the treatment of chronic intractable pain: - other treatment modalities (pharmacological, surgical, physical, or psychological therapies) have been tried and did not prove satisfactory, or are judged to be unsuitable or contraindicated for the given patient - Documentation shows evidence of careful screening, evaluation and diagnosis by a multidisciplinary team prior to implantation. (Such screening must include psychological, as well as physical evaluation); -Documentation that demonstrates pain relief from a temporarily implanted electrode prior to permanent implantation. 	<p>POSITIVE</p>

Payer and Covered Lives	SCS Language	Coverage
n.pdf		
<p>Group Health Incorporated (GHI) - 802</p> <p>441 Ninth Avenue, New York, NY 10001 www.ghi.com, www.emblemhealth.com Contracted or Affiliated PBM(s): Express Scripts, Inc. States Served: New York and Nationwide. Telephone (Automated): (212) 501-4444 Alias(es): GHI HMO and GHI Select Ownership: EmblemHealth, Inc. Not-for-profit. Private.</p> <p>http://www.emblemhealth.com/pdf/med_guidelines/surgical/MG_Dorsal_Column_Stimulator_aC.pdf</p>	<p>Excerpt-</p> <p>Members are eligible for coverage of DCS implantation as an in-patient procedure for the following indications (A, B or C): A. Nonmalignant pain: DCS is covered for managing chronic, intractable, nonmalignant pain in patients who meet all of the following criteria: -Conservative methods of pain management have been tried and failed. -Contraindication for further surgical intervention. -Absence of any untreated existing drug addiction problems. -Psychiatric clearance obtained (documented member assessment of emotional stability must be completed by a provider other than the surgeon, e.g., psychiatrist or psychologist). -Pain is predominantly neuropathic. -Pain reduction achieved with a 3- to 7-day trial of percutaneous spinal stimulation. OR DCS may be covered for chronic non-malignant pain patients who do not meet the above listed criteria if the psychiatrist or psychologist determines that the patient is suicidal. B. Angina: DCS is covered for the management of intractable angina in patients who are not surgical candidates and whose pain is unresponsive to all standard therapies when all of the following criteria are met: - Angiographically documented significant coronary artery disease and contraindication for revascularization procedures such as coronary artery bypass grafting or percutaneous transluminal coronary angioplasty. -Angina pectoris is New York Heart Association Functional Class III (patients are comfortable at rest; less than ordinary physical activity causes fatigue, palpitation, dyspnea, or anginal pain) or Class IV (symptoms of cardiac insufficiency or angina are present at rest; symptoms increase with physical activity). -Reversible ischemia documented by symptom-limited treadmill exercise test. -Optimal pharmacotherapy tried for at least one month. Optimal pharmacotherapy includes the maximum tolerated dosages of at least two of the following antianginal medications: long-acting nitrates, beta-adrenergic blockers, or calcium channel antagonists. -Significant pain reduction (50% or more) achieved with a 3- to 7-day trial of percutaneous spinal stimulation. C. Refractory neuropathic pain including peripheral polyneuropathy of the extremities from multiple etiologies including diabetes, toxic-metabolic, ischemic or neoplastic deafferentation syndrome (i.e. traumatic including nerve root avulsion injury), autoimmune [multiple sclerosis, Guillain Barre or chronic demyelinating polyneuropathy) or infectious (herpes zoster), spinal cord injury or cauda equina injury, chronic pain due to traumatic injuries.</p>	<p>POSITIVE</p>

Payer and Covered Lives	SCS Language	Coverage
<p>Health Net Health Plan of Oregon, Inc. - 18,000 covered lives</p> <p>13221 SW 68th Parkway, Suite 200, Tigard, OR 97223 www.healthnet.com Contracted or Affiliated PBM(s): Health Net Pharmaceutical Services; Caremark Rx, Inc. States Served: Oregon, Washington. Health Net, Inc. For-profit. Private subsidiary of Ownership: public company. NYSE: HNT</p> <p>https://www.healthnet.com/static/general/unprotected/pdfs/national/policies/dorsal_column_stimulators_apr_08.pdf</p>	<p>Excerpt-</p> <p>Health Net, Inc. considers dorsal column stimulation (DCS) medically necessary when all of the following are met: -The implantation of the stimulator is used only as a last resort for patients with chronic intractable pain; -Other treatment modalities (pharmacological, surgical, physical, or psychological therapies) have been tried and did not prove satisfactory, or are judged to be unsuitable or contraindicated for the given patient; -Patients have undergone careful screening, evaluation and diagnosis by a multidisciplinary team prior to implantation (such screening must include psychological, as well as physical evaluation); -All the facilities, equipment, and professional and support personnel required for the proper diagnosis, treatment training, and follow up of the patient must be available; and -Demonstration of pain relief with a temporarily implanted electrode precedes permanent implantation. -Patients with chronic intractable pain due to any of the following: -Lumbosacral adhesive arachnoiditis secondary to multiple myelographies or lumbar surgeries that has not responded to medical management, including physical therapy (the presence of arachnoiditis is usually documented by the presence of high levels of proteins in the CSF and/or by myelography or MRI.); - Nerve root injuries, post surgical or post traumatic (e.g., avulsion), including that of post-laminectomy syndrome (failed back syndrome); -Complex regional pain syndrome I & II (term causalgia reflex sympathetic dystrophy changed to complex regional pain syndrome I & II); -[redacted].</p>	<p>POSITIVE</p>
<p>Humana, Inc. - 79,700</p> <p>500 West Main Street, Louisville, KY 40202 www.humana.com Contracted or Affiliated PBM(s): Argus Health Systems, Inc. (retail), RightSource (mail order-in- house) States Served: Nationwide. Alias(es): This record incorporates CarePlus, CHA Health, MetCare Health Plans (aka AdvantageCare), and OSF Health Plans acquisitions, formerly listed separately, as well as KMG America acquisition.</p>	<p>Excerpt-</p> <p>Humana members MAY be eligible under the Plan for spinal cord stimulation for the following conditions: • Diabetic neuropathy; OR • Failed back surgery syndrome (FBSS) with primarily radicular pain; OR • Inoperable chronic critical limb ischemia; OR • Reflex sympathetic dystrophy (RSD)/complex regional pain syndrome (CRPS). Temporary Trial A temporary trial of spinal cord stimulation MAY be covered for any of the conditions listed above when ALL of the following criteria are met: • Implantation of the stimulator is used only as a late (if not last) resort for patients with chronic intractable pain; AND • Other treatment modalities (pharmacological, surgical, physical, or psychological therapies) have been tried and did not provide satisfactory pain control; AND • Patients have undergone careful screening, evaluation, and diagnosis by a multidisciplinary team prior to implantation (screening must include psychological as well as physical evaluations); AND • Psychological evaluation has been obtained and indicates that the member is a favorable candidate for permanent spinal cord stimulation. Permanent Implantation</p>	<p>POSITIVE</p>

Payer and Covered Lives	SCS Language	Coverage
<p>Ownership: Humana, Inc. For-profit. Public. NYSE: HUM</p> <p>http://apps.humana.com/tad/tad_new/Home.aspx</p>	<p>Permanent implantation of a spinal cord stimulator MAY be covered when a temporary trial has been successful. Successful is defined as: • A temporary trial of at least two days duration has been undertaken with ALL of the criteria listed above met; AND • Demonstration of at least a 50% reduction in pain and improved function with the temporarily implanted electrode prior to the permanent implantation. Note: These criteria for spinal cord stimulators are not consistent with the Medicare National Coverage Policy, and therefore may not be applicable to Medicare members. Refer to the CMS web site at http://www.cms.hhs.gov/ for additional information.</p>	
<p>Kaiser Foundation Health Plan of the Northwest, Inc. - 16,446 covered lives</p> <p>500 NE Multnomah, Suite 100, Portland, OR 97232 www.kaiserpermanente.org Contracted or Affiliated PBM(s): MedImpact Healthcare Systems, Inc., HealthTrans States Served: Oregon, Washington. Alias(es): Includes Kaiser Permanente Health Alternatives (KPHA Health Plans). Ownership: Kaiser Permanente. Not-for-profit. Private.</p> <p>https://members.kaiserpermanente.org/kpweb/healthency.do?hwid=tn9286</p>	<p>Excerpt- Treatment Overview Spinal cord stimulation (SCS) is a procedure that uses an electrical current to treat chronic pain. A small pulse generator, implanted in the back, sends electrical pulses to the spinal cord. These pulses interfere with the nerve impulses that make you feel pain. Implanting the stimulator is typically done using a local anesthetic and a sedative. Your doctor usually will first insert a trial stimulator through the skin (percutaneously) to give the treatment a trial run. (A percutaneous stimulator tends to move from its original location, so it is considered temporary.) If the trial is successful, your doctor can implant a more permanent stimulator. The stimulator itself is implanted under the skin of the belly (abdomen), and the small coated wires (leads) are inserted under the skin to the point where they are inserted into the spinal canal. This placement in the abdomen is a more stable, effective location. Most stimulator batteries must be replaced every 2 to 5 years. After this outpatient procedure is complete, you and your doctor determine the best pulse strength. You are then told how to use the stimulator at home. A typical schedule for spinal cord stimulation is to use it for 1 or 2 hours, 3 or 4 times a day. When in use, the spinal cord stimulator creates a tingling feeling, rather than the pain you have felt in the past.</p>	POSITIVE
<p>Lifewise Health Plan of Washington - 87,389 covered lives</p> <p>7001 220th Street, SW, Building #3, Mountlake Terrace, WA 98043 www.lifewisewa.com Contracted or Affiliated PBM(s): Medco Health</p>	<p>Excerpt- Spinal cord stimulation may be considered medically necessary for the treatment of severe and chronic pain of the trunk or limbs that is refractory to all other pain therapies, when performed according to policy guidelines. Spinal cord stimulation is considered investigational as a treatment of [redacted]. Patient selection focuses on determining whether or not the patient is refractory to other types of treatment. The following considerations may apply: • The treatment is used only as a last resort, other treatment modalities (pharmacological, surgical, psychological, or physical, if</p>	POSITIVE

Payer and Covered Lives	SCS Language	Coverage
<p>Solutions, Inc. States Served: Washington. Ownership: Premera, Inc. Not-for-profit. Private.</p> <p>https://www.lifewisewa.com/lwwa/groups/public/documents/medicalpolicy/cmi_03695.pdf</p>	<p>applicable) have been tried and failed or are judged to be unsuitable or contraindicated; • Pain is neuropathic in nature; i.e., resulting from actual damage to the peripheral nerves. Common indications include, but are not limited to, failed back syndrome, complex regional pain syndrome (i.e., reflex sympathetic dystrophy), arachnoiditis, radiculopathies, [redacted]. Spinal cord stimulation is generally not effective in treating nociceptive pain (resulting from irritation, not damage to the nerves) and central deafferentation pain (related to CNS damage from a stroke or spinal cord injury); • No serious untreated drug habituation exists; • Demonstration of at least 50% pain relief with a temporarily implanted electrode precedes permanent implantation; • All the facilities, equipment, and professional and support personnel required for the proper diagnosis, treatment, and follow-up of the patient are available.</p>	
<p>Premera Blue Cross - 1,334,000 covered lives</p> <p>7001 220th Street, SW, Mountlake Terrace, WA 98043 www.premera.com Ownership: Premera, Inc. Not-for-profit. Private Contracted or Affiliated PBM(s): Medco Health Solutions, Inc.</p> <p>States Served: Alaska, Washington. https://www.premera.com/stellent/groups/public/documents/medicalpolicy/cmi_03695.pdf</p>	<p>Excerpt - Spinal cord stimulation may be considered medically necessary for the treatment of severe and chronic pain of the trunk or limbs that is refractory to all other pain therapies, when performed according to policy guidelines. Spinal cord stimulation is considered investigational as a treatment of [redacted]</p> <p>Patient selection focuses on determining whether or not the patient is refractory to other types of treatment. The following considerations may apply: - The treatment is used only as a last resort, other treatment modalities (pharmacological, surgical, psychological, or physical, if applicable) have been tried and failed or are judged to be unsuitable or contraindicated; - Pain is neuropathic in nature; i.e., resulting from actual damage to the peripheral nerves. Common indications include, but are not limited to, failed back syndrome, complex regional pain syndrome (i.e., reflex sympathetic dystrophy), arachnoiditis, radiculopathies, [redacted]. Spinal cord stimulation is generally not effective in treating nociceptive pain (resulting from irritation, not damage to the nerves) and central deafferentation pain (related to CNS damage from a stroke or spinal cord injury); - No serious untreated drug habituation exists; - Demonstration of at least 50% pain relief with a temporarily implanted electrode precedes permanent implantation; - All the facilities, equipment, and professional and support personnel required for the proper diagnosis, treatment, and follow-up of the patient are available.</p>	POSITIVE
<p>Providence Health Plan - 34,215 covered lives</p> <p>3601 SW Murray Boulevard, Suite 10, Beaverton, OR</p>	<p>Excerpt- Implantable spinal cord stimulators may be approved subject to benefit and plan criteria listed below on an individual case-by-case basis for patients with chronic intractable radicular pain that have failed all other treatment modality and procedures and who has</p>	POSITIVE

Payer and Covered Lives	SCS Language	Coverage
<p>97005 www.providence.org/health plans States Served: Oregon, Washington. Ownership: Providence Health and Services. Not-for-profit. Private.</p> <p>NO LINK AVAILABLE</p>	<p>completed a successful trial for spinal cord stimulator. A prior authorization is required for the spinal cord stimulator trial and if all criteria met the placement of the spinal cord stimulator. All other uses for spinal cord stimulators are not covered. The efficacy has not been established for other painful syndromes such as [redacted]. The following criteria must be met for a spinal cord stimulator trial; - patients with chronic intractable back pain with associated radiating pain who have failed all other treatments and or procedures including multiple surgical interventions. - Psychological assessment may be required. - The use of the stimulator for a particular pain syndrome other than radicular back pain must be supported by scientific medical studies published in relevant medical journals. Final implantation of a spinal cord stimulator may be covered when; - the patient has completed a successful trial of 3-7 days, with a 50% decrease in pain and /or some decrease in medication use. An objective report of the results of the trial must be submitted.</p>	
<p>Regence BlueCross BlueShield of Oregon -3,138</p> <p>100 SW Market Street, Portland, OR 97207 www.or.regence.com Contracted or Affiliated PBM(s): RegenceRx States Served: Oregon. Ownership: Affiliate of the Regence Group. Not-for-profit. Private.</p> <p>http://blue.regence.com/trg/medpol/surgery/sur45.html</p>	<p>Excerpt-</p> <p>I. Patient selection focuses on determining whether or not the patient is refractory to other types of treatment. The following considerations apply: A. Spinal cord stimulation may be considered medically necessary for the treatment of either of the following conditions and when all patient selection criteria in B. below have been met: 1. Severe and chronic pain of the trunk or limbs other than critical limb ischemia that is refractory to all other pain therapies, or 2. Chronic refractory angina pectoris in patients who are not considered candidates for a revascularization procedure. B. All of the following Patient Selection Criteria must be met: 1. The treatment is used only as a last resort; other treatment modalities (pharmacological, surgical, psychological, or physical, if applicable) have been tried and failed or are judged to be unsuitable or contraindicated. 2. Pain is neuropathic in nature; i.e. resulting from actual damage to the peripheral nerves. Common indications include, but are not limited to failed back syndrome, complex regional pain syndrome (i.e., reflex sympathetic dystrophy), arachnoiditis, radiculopathies, phantom limb/stump pain, and peripheral neuropathy. 3. No serious untreated drug habituation exists. 4. Patient was carefully screened, evaluated and diagnosed by a multidisciplinary pain management team prior to application of these therapies. 5. Pain relief from a temporarily implanted electrode has been demonstrated prior to permanent implantation.</p> <p>II. Spinal cord stimulation is considered investigational for all other indications including but not limited to treatment of the following: A. Critical limb ischemia as a technique to forestall amputation B. Visceral pain C. Drug-refractory chronic cluster headaches D. Nociceptive pain (resulting from irritation, not damage to the</p>	<p>POSITIVE</p>

Payer and Covered Lives	SCS Language	Coverage
	nerves) E. Central deafferentation pain (related to CNS damage from a stroke or spinal cord injury)	
<p>Regence BlueShield - 991,337 covered lives</p> <p>1800 Ninth Avenue, P.O. Box 21267, Seattle, WA 98111 www.wa.regence.com Ownership: Affiliate of the Regence Group. Not-for-profit. Private. Contracted or Affiliated PBM(s): RegenceRx States Served: Washington.</p> <p>http://blue.regence.com/trg/medpol/surgery/sur45.html</p>	<p>Excerpt -</p> <p>I. Patient selection focuses on determining whether or not the patient is refractory to other types of treatment. The following considerations apply: A. Spinal cord stimulation may be considered medically necessary for the treatment of either of the following conditions and when all patient selection criteria in B. below have been met: 1. Severe and chronic pain of the trunk or limbs other than critical limb ischemia that is refractory to all other pain therapies, or 2. [redacted]. B. All of the following Patient Selection Criteria must be met: 1. The treatment is used only as a last resort; other treatment modalities (pharmacological, surgical, psychological, or physical, if applicable) have been tried and failed or are judged to be unsuitable or contraindicated. 2. Pain is neuropathic in nature; i.e. resulting from actual damage to the peripheral nerves. Common indications include, but are not limited to failed back syndrome, complex regional pain syndrome (i.e., reflex sympathetic dystrophy), arachnoiditis, radiculopathies, [redacted]. 3. No serious untreated drug habituation exists. 4. Patient was carefully screened, evaluated and diagnosed by a multidisciplinary pain management team prior to application of these therapies. 5. Pain relief from a temporarily implanted electrode has been demonstrated prior to permanent implantation. II. Spinal cord stimulation is considered investigational for all other indications including but not limited to treatment of the following: [redacted]</p>	<p>POSITIVE</p>
<p>Regence BlueShield of Idaho - 4,076</p> <p>1602 21st Avenue, Lewiston, ID 83501 www.id.regence.com Contracted or Affiliated PBM(s): RegenceRx; Postal Prescription Services, Inc. (mail order); Walgreens Mail Service Pharmacy (mail order) States Served: Idaho. Affiliate of the Regence Group. Not-Ownership: for-profit. Private.</p> <p>http://blue.regence.com/trg</p>	<p>Excerpt-</p> <p>I. Patient selection focuses on determining whether or not the patient is refractory to other types of treatment. The following considerations apply: A. Spinal cord stimulation may be considered medically necessary for the treatment of either of the following conditions and when all patient selection criteria in B. below have been met: 1. Severe and chronic pain of the trunk or limbs other than critical limb ischemia that is refractory to all other pain therapies, or 2. Chronic refractory angina pectoris in patients who are not considered candidates for a revascularization procedure. B. All of the following Patient Selection Criteria must be met: 1. The treatment is used only as a last resort; other treatment modalities (pharmacological, surgical, psychological, or physical, if applicable) have been tried and failed or are judged to be unsuitable or contraindicated. 2. Pain is neuropathic in nature; i.e. resulting from actual damage to the peripheral nerves. Common indications include, but are not limited to failed back syndrome, complex regional pain syndrome (i.e., reflex sympathetic dystrophy),</p>	<p>POSITIVE</p>

Payer and Covered Lives	SCS Language	Coverage
medpol/surgery/sur45.html	arachnoiditis, radiculopathies, phantom limb/stump pain, and peripheral neuropathy. 3. No serious untreated drug habituation exists. 4. Patient was carefully screened, evaluated and diagnosed by a multidisciplinary pain management team prior to application of these therapies. 5. Pain relief from a temporarily implanted electrode has been demonstrated prior to permanent implantation. II. Spinal cord stimulation is considered investigational for all other indications including but not limited to treatment of the following: A. Critical limb ischemia as a technique to forestall amputation B. Visceral pain C. Drug-refractory chronic cluster headaches D. Nociceptive pain (resulting from irritation, not damage to the nerves) E. Central deafferentation pain (related to CNS damage from a stroke or spinal cord injury)	
Tufts Associated Health Plans, Inc. – 84 705 Mt. Auburn Street, Watertown, MA 02472 www.tuftshealthplan.com Contracted or Affiliated PBM(s): Caremark Rx, Inc. States Served: Massachusetts. Telephone (Automated): (800) 462-0224 Ownership: For-profit. Private. http://www.tuftshealthplan.com/providers/pdf/mng/Spinal_Cord_Stim.pdf	Excerpt- Tufts Health Plan may authorize coverage of dorsal column stimulation for members with a diagnosis of chronic back pain due to one of the following: - Failed back surgery syndrome with predominant low back pain and secondary radicular pain. - Complex regional pain syndrome. - Inoperable chronic ischemic limb pain secondary to peripheral vascular disease. - The member must also meet all of the following criteria: - There is a documented pathology that is the objective basis of the pain. - The member has tried and failed conservative methods of pain management.1 - The member is not a candidate for further surgical intervention. - A multidisciplinary team that has evaluated the appropriateness of the device and screened for any untreated existing drug addiction and psychiatric problems has evaluated the member. - The Member's pain is predominantly radiating extremity pain. - The Member experienced significant pain reduction (50% or more) with a 3-7 day trial of percutaneous spinal stimulation.	POSITIVE
WellCare Health Plans, Inc. - 2,977 8735 Henderson Road, Tampa, FL 33634 www.wellcare.com States Served: Florida. Alias(es): Harmony Health Plan; WellCare of Florida; WellCare of New York; WellCare of Georgia; WellCare of Ohio; WellCare	Excerpt- Spinal cord stimulation of the dorsal column is considered medically necessary for the relief of chronic (greater than six months) intractable pain caused by the following conditions: -Lumbosacral arachnoiditis that has not responded to medical management including physical therapy (NOTE: Presence of arachnoiditis is usually documented by presence of high levels of proteins in the cerebrospinal fluid and/or by myelography or magnetic Resonance Imaging); OR, -Post-surgical or post-traumatic nerve root injuries, including post-laminectomy syndrome (failed back surgery syndrome [FBSS]); OR, -Complex regional pain syndrome I and II; OR, - Phantom limb syndrome that has not responded to medical	POSITIVE

Payer and Covered Lives	SCS Language	Coverage
of Connecticut; Staywell; HealthEase of Florida, Inc.; WellCare of Arizona; WellCare of Louisiana; WellCare Health Plans of New Jersey; WellCare of Texas; Wellcare of Illinois; Preferred One, First Choice. WellCare Group of Companies. For-profit. Private subsidiary of Ownership: public company. NYSE: WCG http://www.wellcare.com/WCAssets/corporate/assets/HS115_Spinal_Cord_Stimulation_Implant.pdf	management; OR, - End-stage peripheral vascular disease, when the member cannot undergo revascularization or when revascularization has failed to relieve painful symptoms and the pain has not responded to medical management; OR, - Post-herpetic neuralgia; OR, - Plexopathy; OR, - Intercostal neuralgia that did not respond to medical management and nerve blocks; OR, - Cauda equine injury; OR, - Incomplete spinal cord injury. Spinal cord stimulation of the dorsal column is considered medically necessary for the relief of chronic intractable pain caused by the above conditions if ALL of the following criteria are met: - The implantation is used as a last resort for members with chronic intractable pain; AND, - Other treatment modalities (pharmacological, surgical, physical) have been tried for a minimum of six months and did not prove satisfactory or are considered unsuitable or contraindicated for the given member; AND, - Further surgical intervention is not indicated; AND, - Psychological evaluation has been obtained and there is documentation clearly stating the pain is not psychologic in origin; AND, - No contraindications to implantation exist such as sepsis or coagulopathy; AND, - There has been a clear demonstration of pain relief (50% reduction) on a 3 to 7 day trial with a temporarily implanted electrode preceding permanent implantation.	

In addition to the private payers listed in the table above, there are other payers that serve Washington residents that had no coverage information available to us. These include: Molina Healthcare of Washington, Community Health Plan of Washington, United Healthcare, KPS Health Plans, Columbia United Providers, Inc., Sterling Life Insurance Company, Timber Products Manufacturers Trust, Coventry Health and Life Insurance Company, Puget Sound Health Partners, Washington State Auto Dealers Insurance Trust, Washington Employers Trust, PacificSource Health Plans, Arcadian Health Plan, Essence, Inc., Wellpoint, Inc., Pyramid Life Insurance Company, MVP Health Care, Union Pacific Railroad Employees Health Systems, Chesapeake Life Insurance Company, Kaiser Foundation Health Plan, Inc., Deseret Healthcare Trust, Marquette National Life Insurance Company, DAKOTACARE, Preferred Care, United Mine Workers of America, Commonwealth of Pennsylvania Public Schools Retirement System, Preferred Plus of Kansas, Inc., ConnectiCare, Inc., Health Alliance Medical Plans, Inc., and PHP Companies/dba Cariten Healthcare. Despite not having specific coverage information for the above list of plans, we were able to review our prior authorization database, which provides some indication of whether the plan has a history of allowing access to SCS. We share these data in Table 8 for your consideration.

In summary, Method 5, which reasonably adds coverage policies from private payers that cover Washington residents, yields very positive results for SCS. **WORST CASE: POSITIVE = 40, NEGATIVE = 5; BEST CASE: POSITIVE = 43, NEGATIVE = 2** when Methods 1-5 are added together.

WORST CASE	POSITIVE = 40	NEGATIVE = 5
BEST CASE	POSITIVE = 43	NEGATIVE = 2

As mentioned above, Table 8 includes prior authorization data for some of the private payers that had no specific coverage information for SCS.

Table 8. Prior Authorization Data for Select Private Payers with No Coverage Information

Payer	Prior Authorization Data for SCS	Coverage
<p>Columbia United Providers, Inc. - 36,311 covered lives</p> <p>19120 SE 34th Street, Suite 201, Vancouver, WA 98683 www.cuphealth.com States Served: Washington. Ownership: For-profit. Private.</p>	<p>.</p> <p>No published coverage policy available. No favorable or unfavorable anecdotal evidence to indicate a coverage position.</p>	<p>UNKNOWN</p>
<p>Community Health Plan of Washington (CHP) - 234,495 covered lives</p> <p>720 Olive Way, Suite 300, Seattle, WA 98101 www.chpw.org Contracted or Affiliated PBM(s): Express Scripts, Inc. States Served: Washington. Ownership: Community Health Network of Washington. Not-for-profit. Private.</p>	<p>No published coverage policy available. Confirmed 4 Spinal Cord Stimulation cases were reviewed by CHP and each received a favorable prior authorization decision.</p>	<p>History of approving prior authorizations</p>
<p>Coventry Health and Life Insurance Company - 4,451 covered lives</p> <p>6705 Rockledge Drive, Suite 900, Bethesda, MD 20817 www.coventryhealthcare.com States Served: Nationwide. Alias(es): dba Altius Health Plans in Utah, Idaho and Wyoming; Carelink Health Plans in West Virginia; Group Health Plan in Illinois and Missouri; HealthAmerica of Pennsylvania, Inc. / HealthAssurance Pennsylvania in Ohio and Pennsylvania; HealthCare USA of Missouri, LLC in Missouri; OmniCare Health Plan in Michigan; PersonalCare in Illinois; Southern Health Services in Virginia; Summit Health Plan in New Jersey, New York, Oregon, Pennsylvania, Puerto Rico, South Carolina, Tennessee and Texas; Vista Healthplans in Florida; and WellPath Community Health Plans in North and South Carolina as well as CHCcares of South Carolina. Ownership: For-profit. Public. NYSE: CVH Private.</p>	<p>No published coverage policy available. Confirmed 7 Spinal Cord Stimulation cases were reviewed by Coventry Health and each received a favorable prior authorization decision.</p>	<p>History of approving prior authorizations</p>

<p>Deseret Healthcare Trust – 122 covered lives. DMBA (Desert Mutual Benefit Administrators). www.dmba.com. 60 East South Temple, Salt Lake City, UT 84111. Serves AZ, CA, CO, HI, ID, IL, NV, OR, UT, TX, WA.</p>	<p>No published coverage policy available. 1 favorable prior authorization decision. Informal, provided verbally.</p>	<p>History of approving prior authorizations</p>
<p>Health Alliance Medical Plans, Inc. – 4 covered lives. Ownership: Care Clinic Association, P.C. For-profit. Private. www.healthalliance.org. 301 South Vine Street, Urbana, IL 61801.</p>	<p>No published coverage policy available. 1 favorable prior authorization decision. Informal, provided verbally.</p>	<p>History of approving prior authorizations</p>
<p>KPS Health Plans - 46,556 covered lives</p> <p>400 Warren Avenue, P.O. Box 339, Bremerton, WA 98337 www.kpshealthplans.com States Served: Washington. Alias(es): Kitsap Physicians Services Health Plans Ownership: Group Health Cooperative. Not-for-profit. Private.</p>	<p>No published coverage policy available. Confirmed 5 Spinal Cord Stimulation cases were reviewed by KPS Health Plans and each received a favorable prior authorization decision.</p>	<p>History of approving prior authorizations</p>
<p>Molina Healthcare of Washington - 283,173 covered lives</p> <p>21540 30th Drive SE, Suite 400, P.O. Box 1469, Bothell, WA 98041 www.molinahealthcare.com Ownership: Molina Healthcare, Inc. For-profit. Private subsidiary of public company. NYSE: MOH Contracted or Affiliated PBM(s): Rx America (Caremark Rx, Inc.) States Served: Washington.</p>	<p>No published coverage policy available. Confirmed 3 Spinal Cord Stimulation cases were reviewed by Molina Healthcare and each received an unfavorable prior authorization decision.</p>	<p>History of denying prior authorizations</p>

<p>MVP Health Care – 322 covered lives Preferred Care. Ownership: Not for profit. www.mvphealthcare.com P.O. Box 2207, Schenectady, NY 12301 Serves AL, CT, MA, NH, NY, VT.</p>	<p>No published coverage policy available. 1 favorable prior authorization decision. Informal, provided verbally.</p>	<p>History of approving prior authorizations</p>
<p>PacificSource Health Plans - 3,969 110 International Way, Springfield, OR 97477 www.pacificsource.com Contracted or Affiliated PBM(s): Caremark Rx, Inc. States Served: Oregon, Idaho. Ownership: Not-for-profit. Private.</p>	<p>No published coverage policy available. Confirmed 1 Spinal Cord Stimulation case reviewed by PacificSource Health Plans and received an unfavorable prior authorization decision.</p>	<p>History of denying prior authorizations</p>
<p>Preferred Health Systems – 12 covered lives. Ownership: For-profit. Private. www.phsystems.com. 8535 East 21st Street North, Wichita, KS 67206.</p>	<p>No published coverage policy available. Confirmed 1 Spinal Cord Stimulation case was reviewed by Coventry Health and received a favorable prior authorization decision.</p>	<p>History of approving prior authorizations</p>
<p>Puget Sound Health Partners - 4,284 covered lives 7502 Lakewood Drive West, Suite A, Lakewood, WA 98499 www.ourpshp.com States Served: Washington. Highline Medical Service Organization, Northwest Physician's Network, and Physicians of Southwest Washington. For-profit. Private.</p>	<p>No published coverage policy available. Confirmed 6 Spinal Cord Stimulation cases were reviewed by Puget Sound Health Partners and each received a favorable prior authorization decision.</p>	<p>History of approving prior authorizations</p>
<p>Sterling Life Insurance Company - 30,673 covered lives P.O. Box 1917, Bellingham, WA 98227-1917 www.sterlingplans.com States Served: Alaska, Arizona, Arkansas, Delaware, Idaho, Illinois, Iowa, Kentucky, Louisiana, Montana, Nebraska, Nevada, New Mexico, Ohio, Oklahoma, Oregon, Pennsylvania, South Carolina, Tennessee, Utah, Washington. Alias(es): Includes ESRD demonstrations marketed as Fresenius Medical Care Health Plan, Inc. - Texas and Fresenius Medical Care Health Plan, Inc. - Pennsylvania.</p>	<p>No published coverage policy available. Confirmed 9 Spinal Cord Stimulation cases were reviewed by Sterling Life Insurance Company and each received a favorable prior authorization decision.</p>	<p>History of approving prior authorizations</p>

<p>Parent company, Combined Insurance Company of America was sold by Aon Corp. in April 2008. Ownership: Munich American Holding Corporation. For-profit. Private subsidiary of public company. NYSE: ACE</p>		
<p>Timber Products Manufacturers Trust - 9,643 covered lives</p> <p>951 East Third Avenue, Spokane, WA 99202 www.tpmrs.com Contracted or Affiliated PBM(s): Caremark Rx, Inc. States Served: Idaho, Montana, Oregon, Washington, Wyoming.</p>	<p>No published coverage policy available. No favorable or unfavorable anecdotal evidence to indicate a coverage position.</p>	<p>UNKNOWN</p>
<p>United Healthcare - 47,208 covered lives</p> <p>UnitedHealth Group Center, 9900 Bren Road East, Minnetonka, MN 55343 www.uhc.com states Served: Nationwide. Alias(es): AmeriChoice; Arizona Physicians IPA; Arnett Health Plans; Better Health Plans of South Carolina, Inc.; Evercare; Fiserv; Great Lakes Health Plan; Health Plan of Nevada; John Deere Health Plan, Inc.; MAMSI; Neighborhood Health Partnership; Optimum Choice; Oxford Health Plans; PacifiCare; Sierra Health and Life Insurance Company; Sierra Spectrum; Three Rivers Health Plan; Unison Health Plan Ownership: UnitedHealth Group. For-profit. Public. NYSE: UNH</p>	<p>No published coverage policy available. Confirmed sampling of 237 Spinal Cord Stimulation cases was reviewed by UHC and each received a favorable prior authorization decision.</p>	<p>History of approving prior authorizations</p>
<p>Washington State Auto Dealers Insurance Trust - 1,943 covered lives</p> <p>P.O. Box 52848, Bellevue, WA 98015-2848 www.wsadit.org states Served: Washington. Ownership: Not-for-profit. Private.</p>	<p>No published coverage policy available. No favorable or unfavorable anecdotal evidence to indicate a coverage position.</p>	<p>UNKNOWN</p>

In summary, 10 of the 15 private payers without SCS coverage information that were in our prior authorization database have a history of approving access to SCS, while 2 consistently denied prior authorizations, and 3 had no further information. This demonstrates that even for those insurers without a specific coverage policy, the majority are approving access to SCS. In fact, of the 4,311,074 commercially-insured lives in Washington, Tables 7 and 8 demonstrate that 3,959,691 (91.8%) are definitely or, at a minimum, anecdotally allowed access to spinal cord stimulation (provided they meet

the appropriate patient selection criteria), 6.7% are definitely or, at a minimum, anecdotally denied access to spinal cord stimulation, and for the remaining 1.5%, we have no information.

There is evidence that a minimum of 91.8% of commercially-insured Washington residents have access to spinal cord stimulation as a treatment option provided they meet appropriate criteria.

Separate from the private payer coverage policies, it is worth noting that the CHAMPVA⁶ and TRICARE⁷ coverage policies appropriately cover SCS. The language is shown for your consideration in the table below.

Table 9. CHAMPVA and TRICARE Policies on SCS

Coverage Policy	Excerpted Language on SCS	Policy
<p>Civilian Health and Medical Program of the Department of Veterans Affairs (“CHAMPVA”): While we have attached the full CHAMPVA coverage policy positively governing coverage for all CHAMPVA recipients throughout the country, we have quoted the most relevant section on use and coverage of the SCS for chronic, intractable pain herein though we encourage review of the entire attached policy.</p> <p>http://www4.va.gov/HAC/forbeneficiaries/champva/policymanual/champva/chapter2/1c2s20-1.htm</p>	<p>CHAPTER: 2 SECTION: 20.1 TITLE: NERVOUS SYSTEM EFFECTIVE DATE: August 26, 1985.</p> <p>D. Spinal cord and deep brain stimulation are covered in the treatment of chronic intractable pain. Coverage includes:</p> <ol style="list-style-type: none"> 1. The accessories necessary for the effective functioning of the covered device. 2. Repair, adjustment, replacement and removal of the covered device and associated surgical costs. 	<p>POSITIVE</p>
<p>DOD Health Care Program “TRICARE”: While we have attached the full TRICARE coverage policy positively governing coverage for all TRICARE recipients throughout the country, we have quoted the most relevant section on use and coverage of the SCS for chronic, intractable pain herein though we encourage review of the</p>	<p>Chapter 4 Section 20.1 Nervous System Issue Date: August 29, 1985</p> <p>2.4 Spinal cord and deep brain stimulation are covered in the treatment of chronic intractable pain. Coverage includes: 2.4.1 The accessories necessary for the effective functioning of the covered device. 2.4.2 Repair, adjustment, replacement and</p>	<p>POSITIVE</p>

⁶ CHAMPVA is a comprehensive health care program in which the VA shares the cost of covered health care services and supplies with eligible beneficiaries.

⁷ TRICARE, formerly known as CHAMPUS, is a Department of Defense health care program for active duty and retired members of the uniformed services, their families and survivors.

Coverage Policy	Excerpted Language on SCS	Policy
entire attached policy. www.humana-military.com/southmanuals/policy/ChgOnly/C4S20_1.PDF	removal of the covered device and associated surgical costs.	

Finally, results from Methods 1-5 are summarized below for your consideration. As one can see, regardless of which method is used, there is overwhelming support for the appropriate use of spinal cord stimulation. The respective treatment guideline recommendations and policies shown above are broadly supported by the evidence on the safety, efficacy, effectiveness and cost-effectiveness of this therapy.

Method 1: NGC search	WORST CASE	POSITIVE = 7	NEGATIVE = 3
	BEST CASE	POSITIVE = 8	NEGATIVE = 2
Method 2: Method 1 + ACOEM Chronic Pain Chapter	WORST CASE	POSITIVE = 7	NEGATIVE = 4
	BEST CASE	POSITIVE = 9	NEGATIVE = 2
Method 3: Method 2 + APS & ASA treatment guidelines	WORST CASE	POSITIVE = 9	NEGATIVE = 4
	BEST CASE	POSITIVE = 11	NEGATIVE = 2
Method 4: Method 3 + State WC treatment guidelines	WORST CASE	POSITIVE = 20	NEGATIVE = 5
	BEST CASE	POSITIVE = 23	NEGATIVE = 2
Method 5: Method 4 + Private payer coverage policies	WORST CASE	POSITIVE = 40	NEGATIVE = 5
	BEST CASE	POSITIVE = 43	NEGATIVE = 2

In addition:

There is evidence that a minimum of 91.8% of commercially-insured Washington residents have access to spinal cord stimulation as a treatment option provided they meet appropriate criteria.

VI. Patient Advocacy Organization Position Statements

The American Pain Foundation

As required by law and as cited in Section II of this response, patient advocacy group positions must be weighted as well. The American Pain Foundation, the nation's largest relevant patient advocacy group, has made its public position very clear in support of spinal cord stimulation. This position statement is being submitted directly to the Washington State Health Care Authority by the American Pain Foundation. Should you have questions for the American Pain Foundation, please contact their Executive Director, Will Rowe, at wrowe@painfoundation.org.

VII. Patient Testimonials

In anticipation of this technology assessment, we thought it helpful to ask the Washington pain physician, patient community and allies to begin to identify patients willing to publicly tell their story regarding how SCS has significantly reduced their chronic, intractable pain and helped improve function. Our staff then helped various patients draft their personal stories - - in their own words. We have attached numerous examples which help to provide an important component to this overall consideration, and most importantly put real human faces to this otherwise abstract discussion. Whether injured workers or others, clearly these patients' stories help to provide additional evidence of the real effectiveness and impact these devices have on Washingtonians. ([Appendix B](#)).

VIII. Conclusion

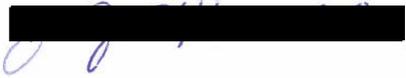
Thank you in advance for your thoughtful consideration of this information. We believe that this information provides a comprehensive summary of the current evidence for spinal cord stimulation and more specifically that it provides many specific significant and compelling provisions, several of which, under the governing EBM statute, must be presumed correct. Regardless of the methodology used to review the clinical evidence and the guidelines and recommendations put forth at a national, state and society level, there is simply no other conclusion one can make other than coverage of spinal cord stimulation for appropriately selected patients.

- An overview of the empirical clinical and cost-effectiveness literature available, which while not perfect, overall supports appropriate use of this therapy for patients in chronic pain who have failed more conservative treatment options;
- A review of the governing related Medicare National Coverage Decision which supports coverage for this therapy;
- A review of the consensus of national expert medical society guidelines and opinions which broadly support appropriate coverage for this therapy;
- Treatment guidelines and policies including state-based and private payers which broadly support appropriate coverage for this therapy;
- The opinions of a national pain patient advocacy group which support coverage of this therapy; *and perhaps most compelling*;
- The stories of Washington residents whose lives have been significantly helped by this therapy.

We stand ready to assist the Washington Health Care Authority and the Health Technology Clinical Committee in their review and delineation of a coverage policy that, hopefully, both serves to protect

patients as well as ensure that, when appropriate, they have access to this life-changing, cost-effective implantable therapy. Should you have any questions please do not hesitate to contact William Fehrenbach at 763-607-1378 or at william.fehrenbach@medtronic.com as he can best coordinate internal expertise and a timely response and best ensure your needs are met.

Sincerely,



N. William Fehrenbach
Reimbursement Director
*State Government Affairs
Evidence Based Medicine and
Coverage & Authorization Services*

Jennifer Hinnenthal
Sr. Manager
Evidence Based Medicine

7000 Central Avenue NE, RCE395
Minneapolis, MN 55432
Office: 763-526-8193
Cell: 763-607-1378
william.fehrenbach@medtronic.com

7000 Central Ave NE, RCE395
Minneapolis, MN 55432
Office: 763-526-6068
jennifer.hinnenthal@medtronic.com

Appendix A: American College of Occupational and Environmental Medicine (ACOEM)

The American College of Occupational and Environmental Medicine (ACOEM), is one of several organizations actively promoting and lobbying for official adoption and use of its own set of workers' compensation medical treatment guidelines across the country. While promulgation of "treatment guidelines" by medical professional societies is not new, there are several unique considerations and serious concerns regarding guidelines promulgated by ACOEM that must be understood. While ACOEM accurately states that a few pain-related physicians were involved in their process, that is clearly not the same as having the correct expert medical professional societies formally involved and potentially endorsing the analysis and recommendations - - which has not and will not likely occur.

What is ACOEM? ACOEM is a group of "occupational medicine" physicians that typically work either in general medicine, for corporations in risk mitigation, for workers' compensation insurance companies, or in other medical roles. More can be learned at www.acoem.com. Additionally, several articles have raised questions about the relationship between ACOEM and the insurance industries that are worthy of consideration.⁸

Are ACOEM guidelines accurate, fair and balanced, and appropriate? First, while ACOEM states its intent to employ an objective 11-point evidence ranking system, upon careful review it is clear that well done studies are not ranked equally, with some not even being included. In fact, a 2006 study in *The Spine Journal*⁹ reviewed the earlier editions of ACOEM guidelines and evaluation method and noted, "that they scored much lower in the areas of stakeholder involvement, rigor of development, application, and editorial independence." Second, medical specialty societies draft "guidelines" i.e., cardiac surgeons draft guidelines related to cardiac surgery, etc. However, ACOEM guidelines are in general not drafted, nor endorsed by, the very specialty societies most closely involved in the delivery of various therapies and related evidence. Third, and most significantly, several national professional specialty societies, the experts in the related therapies reviewed, disagree with and have significant concerns regarding these guidelines. Written concerns of which we are aware have to date been submitted by: 1) The American Academy of Pain Medicine; 2) The American Society of Interventional Pain Physicians (ASIPP has also published articles critically analyzing the ACOEM recommendations¹⁰); 3) International Spine Intervention Society; 4) The North American Neuromodulation Society and 5) The American Association of Neurological Surgeons. Upon careful consideration of the facts we believe it is clear that the guidelines are not accurate, fair, balanced, or appropriate in many cases, nor were the appropriate specialty societies significantly involved in their development. These facts are worthy of

⁸ Armstrong, David. "Amid Suits Over Mold, Experts Wear Two Hats: Authors of Science Paper Often Cited by Defense Also Help in Litigation." *The Wall Street Journal Online*. January 9, 2007.

LaDou, M.D., Josphe, et al. "American College of Occupational and Environmental Medicine (ACOEM): A Professional Association in Service To Industry." *The International Journal of Occupational and Environmental Health*. 2007;13:404-426. http://www.ijoh.com/pdfs/IJOEH_1304_LaDou02.pdf.

McLellan, M.D., Robert K. "Setting the Record Straight: A Response to IJOEH." 2007. *American College of Occupational and Environmental Medicine*. <http://www.acoem.org/ResponseToIJOEH.aspx>.

⁹ Cates J, Young D, Bowerman D and Porter R. Technical Review: An independent AGREE evaluation of the Occupational Medicine Practice Guidelines, *The Spine Journal*, 6: 72-77, 2006

¹⁰ Manchikanti, et al. *Pain Physician* 2008;11(3): 271-310 and 11(4):393-482 at <http://www.painphysicianjournal.com/>

significant consideration by those concerned with maintaining appropriate patient access to needed therapies.

How often are reviewed therapies/treatments “Recommended” by ACOEM? ACOEM guidelines reflect the very conservative “world view” of one professional society, not considered “expert” in most areas and therapies reviewed. This conservative philosophy is reflected in the narrowly-defined “medical consensus” opinions and conclusions that “Do Not Recommend” the vast majority of widely-accepted, evidence-supported treatments, procedures, tests or therapies that are currently covered under Medicare, Medicaid, most commercial policies, and Department of Defense/Veterans Affairs policies. More specifically, the recently updated ACOEM Low Back Chapter (April 2008 online version) reviews 181 treatments, procedures, tests or therapies and **“Does Not Recommend” 54% of them**; the 11/5/07 draft of the Chronic Pain Chapter reviews 200 treatments, procedures, tests or therapies and **“Does Not Recommend” 44% of them**. Simply put, use or adoption of ACOEM guidelines as coverage criteria will have significant negative impact on the ability of injured workers to receive widely-accepted medical care.

How are states using “Guidelines” such as these? While states have occasionally been developing and/or using various “guidelines” over the past 10-15 years (e.g, Colorado, Minnesota, et al.), only recently have states begun mandating use of various guidelines as “restrictive coverage policies” that supersede the expert medical opinion of the treating physician. In real terms, this new restrictive use of a conservative guideline such as ACOEM will provide a new cost containment tool by which insurers can inappropriately deny coverage for treatments “not recommended” by the respective guideline. Given this shift in “how” various “guidelines” are being used, it is extremely important to be sure that whatever guidelines are developed or used are fair and balanced and ensure that appropriate patient access to needed treatments, procedures, tests or therapies can be maintained.

Are these Guidelines free of charge? Traditionally, “guidelines” drafted by a professional medical society have been provided to the public, free of charge, in order to serve the public good and improve health care. However, ACOEM “guidelines” are not provided free of charge and in fact are being sold by the very professional society that drafted them. While this is not inappropriate, it does highlight a possible conflict of interest which at least needs to be understood.

Oct 8, 2010

Health Technology Assessment Committee

Dear Health Technology Assessment Committee,

As a resident of Washington state, I am gravely concerned about what appears to be a systematic deterioration of access to timely and appropriate pain care in Washington state. Pain care - alleviating suffering - is a basic human right. There are two key issues that are dramatically limiting this right for residents of Washington.

First, the chronic pain management bill (SL 2876) is an unprecedented effort by the Washington state government to regulate a provider's ability to prescribe. No other state has attempted to address prescription drug abuse and diversion in this way. The law will reduce provider autonomy and increase provider burden, resulting in decreased access to pain care providers who treat people who live with pain people like me.

Second, the Washington State Health Technology Assessment Clinical Committee (HTCC) recently eliminated reimbursement for spinal cord stimulation, a proven treatment for some people living with chronic pain. This decision follows a 2008 decision by the Health Technology Assessment program to eliminate reimbursement for intrathecal drug delivery systems and TENS units used for chronic pain. These decisions seriously limit the treatment options available for people like me to lead full and productive lives in spite of my constant pain. Furthermore, they limit qualified health care providers' ability to recommend or prescribe the most appropriate treatment options for the individual whose only way to afford their care hinges on these state supported insurance plans.

Pain care is important to me, personally. I have had chronic pain for over four years. Without a wonderful doctor and a few other understanding physicians, I would not be able to get up every day to take care of my two children or try to attend school to make a better life for myself. Please listen!

These two issues result in greatly limited access to pain care and treatment options for patients in Washington State. I am deeply concerned about how these decisions will affect access to the pain care I need to live a productive and fulfilled life despite my pain. Furthermore, other states are watching our state's actions, which may create a ripple effect as other states may adopt similar policies that limit access to care.

As a Washington state resident, I implore you to closely and carefully review these two issues as both affect almost two million Washingtonians and consider what you can do to help protect our rights to appropriate pain care.

Sincerely,

Ms. Rachel Dean
817 Kendall St
Port Orchard, WA 98366-4203
(360) 876-4111

October 14, 2010

I would like to comment on the recent decision by the HTA against coverage of spinal cord stimulation (SCS). I would first like to present my credentials. I am board certified by the American Board of Anesthesiology in anesthesiology and pain management and have practiced in that specialty for over 20 years. I also serve as the Chief Science Officer of Talaria, a medical research company where I am the Principal Investigator in a number of pain management related projects. I have authored numerous articles and textbook chapters on pain medicine. I was the director of Pain Management Services at the VA Puget Sound and currently direct the Evergreen Pain Management Center at Evergreen Hospital and Medical Center in Kirkland, Washington. I am the current president of the Washington Academy of Pain Management (WAPM). I do not have any financial conflict of interest to disclose and SSC accounts for less than 2% of my clinical revenues.

I have read most of the material surrounding the HTA decisions and have personally spoken to physicians who were present at the meeting. I found the process extremely biased. I will briefly summarize my objections.

1. Several world renowned experts on spinal cord stimulation attended the meeting but were allowed only 5 minutes to speak and not given any opportunity to comment about data presented to the committee by career government bureaucrats with their own biased agenda. This is not the transparent government the people deserve.
2. There are several level one studies that support use of SSC but these studies were largely dismissed in favor of a single study with multiple biases and methodological problems. The HTA has set a standard and then shifted that standard when the findings did not support their bias.
3. The HTA policy of blanket denial of coverage totally disregards the fact that there are subgroups of patients who clearly benefit from SSC namely those with inoperable radiculitis, neuropathic nerve injuries and CRPS. With the HTA decision there are simply no avenues of appeal, no medical director to discuss treatment and no appeal process that I can utilize to try to get the best care for my patient. This blanket decision basically ignores multiple scientific studies and 30 years of clinical observations by multiple pain management experts.

In summary I strongly disagree with the findings of the HTA and even more so with the process. This is not transparent government and the biased process threatens to provide my patients and the people of Washington State access to medical care and technologies more appropriate to the 1960s

Sincerely,

Charles Chabal, MD.

President, Washington Academy of Pain Management

October 14, 2010

To whom it may concern:

I am an interventional pain physician in Spokane, WA. I have been implanting SCS devices in psychologically cleared patients, since my residency in the mid 1990's. I have seen this therapy change peoples lives.

I previously practiced in Montana where I had a close working relationship with the workers compensation system. Implantable therapies are authorized by the W/C system on appropriately selected patients. I dont think anyone would disagree that a significant percentage of W/C patients are not good candidates, but to generalize this to the complete W/C population, and the entire state of WA population is ridiculous and unethical. This is exactly what is happening by using the "Turner" study, to make such an important far reaching decision.

Furthermore, the Turner study did not require psychological clearance, and in fact, it was only used in a minority of the study patients. This is an imperative step of selecting appropriate patients. Since this was not done, there is no doubt that a large number of these W/C patients were not appropriate in the first place, tainting the results of the study.

I also noticed that the proponents for spinal cord stimulation were severely limited in their ability to present their case at the August 20th hearing. On the other hand, the opposition was given a wealth of time. There was minimal notice to the public about public testimony. I would have attended had it been publicized appropriately and appropriate lead time had been given. It is very difficult for a practitioner to cancel a full day of patients with such short notice.

I have also noted that studies that were more appropriately designed than the Turner study were discounted.

There is no doubt in my mind the SCS helps a great deal of chronic pain patients get back a significant portion of their lives. These patients have few other options, and studies have shown a significant benefit with SCS.

I urge you to reverse this decision as it has such a profound affect on citizens of this state who have chronic pain. The therapy is not for everyone, but the state needs to set up guidelines for appropriate patient selection instead of denying the therapy to such a large population. Also, the HTA needs to take time and hear the story firsthand of patients who have benefitted from SCS and from providers who responsibly use it in their practice.

John A. Hatheway, MD
Diplomate of the American Board of Anesthesiology Subspecialty Certification in Pain Management Inland
Neurosurgery & Spine
509-389-2181
jhatheway@neuroandspine.com

Regence concurs with the draft findings and decisions concerning spinal cord stimulation and breast MRI.

Diane Priebe RN, BSN, CPC
Supervisor, Medical Policy
Pharmacy Services
Regence - Portland
Phone: 503.220.4766
Fax: 503.276.1894
dwprieb@regence.com

Boston Scientific

Neuromodulation

October 14, 2010

Leah Hole-Curry, JD - Program Director
Washington State Health Technology Assessment Program
676 Woodland Square Loop SE
Lacey, WA 98503

sent via email
shtap@hca.wa.gov

Ms. Hole-Curry,

On behalf of Boston Scientific Neuromodulation, I would like to thank you for the opportunity to comment on the findings and decision of the Washington State Health Care Authority related to the Health Technology Assessment (HTA) of Spinal Cord Stimulation (SCS). We would like to briefly discuss two specific areas of grave concern: 1) the weight given to the study by Turner et al¹, and 2) inaccurate morbidity data related to SCS discussed during the Committee review. Consequently, we request that the Health Technology Clinical Committee (HTCC) form an ad hoc advisory committee, as provided by WAC 182-55-045, to review deficiencies in the study by Turner et al, before a final coverage decision on spinal cord stimulation is rendered.

Neuropathic pain is difficult to manage and the pathophysiology is complex. Both of which make the determination of appropriate coverage criteria of a therapy like spinal cord stimulation that much more critical. It is Boston Scientific's position that to deny coverage of SCS outright would be detrimental to the citizens of Washington living with chronic neuropathic pain and who are covered by a state-funded health plan.

Washington is the only state in the nation to deny coverage for SCS as a late or last treatment option for sick or injured workers who are appropriate clinical candidates. There have been repeated efforts made to repute flaws in the study's methodology, design, and conclusions used to deny coverage, but Washington State Labor and Industries' (L&I) decision to deny requests for SCS remains unchanged.

Our first concern is with the weight given to the study by Turner et al. during the HTA process. There are numerous flaws with this study including the following:

- Cohort groups were not randomized. As a result, essentially non-comparable groups of patients were compared.
- The length of time after injury and before treatment (approximately 4 years for patients in the SCS cohort) undermines the efficacy of any treatment intervention.

¹ Turner JA et al. Spinal cord stimulation for failed back surgery syndrome: Outcomes in a workers' compensation setting. PAIN (2009), doi: 10.1016/j.pain.2009.08.014

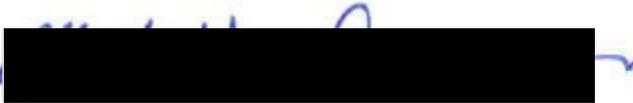
- The use of Intent-To-Treat (ITT) as a method of analysis. The purpose of ITT is to prevent selection bias in a RCT and has little relevance in a non-RCT setting. If outcomes were gauged by those patients who actually received a permanent implant (n = 27), as opposed to those who received a trial (n = 51), the results would show a statistically significant difference in the efficacy of SCS. The nine (9) successful patients would represent a 33% effective rate as opposed to the 18% identified by the study authors.

Our second concern is with the use of inaccurate mortality data during the discussion by the HTCC. During the August 20 public hearing, the Washington State Medical Director likened the mortality rate of SCS to the mortality rate of the most deadly month of fighting in Afghanistan. This, despite the findings of the outside vendor, Spectrum, that *“No deaths were attributed to SCS.”* Additionally, Spectrum found that *“There is high evidence that the rate of mortality due to SCS is low.”*

In summary, with accurate high-level data driving the assessment by an ad hoc committee, it is our hope that the same thoroughness and quality of review that have led to near-unanimous coverage policies across the country under Medicare and commercial insurance plans will result in a positive recommendation of spinal cord stimulation for patients suffering from chronic pain and who are covered by Washington State-funded health plans.

If I can be a resource during this process, please contact me at your convenience at (661) 949-4865 or Matthew.Gunderman@bsci.com. Thank you for your consideration of these comments.

Sincerely,

A black rectangular redaction box covers the signature area. Above the box, there are faint blue ink scribbles and a small blue arrow pointing to the right.

Matthew Gunderman,
Director of Health Economics and Reimbursement