WASHINGTON STATE HEALTH CARE AUTHORITY

Spinal Cord Stimulation

Peer Review and Public Comments & Responses

Health Technology Assessment

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Health Technology Assessment

Peer Review, Public and Washington State Agency Comments and Responses for Spinal Cord Stimulation

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1. SPECTRUM RESEARCH RESPONSE TO PEER REVIEW COMMENTS

Andrew Friedman, M.D., Virginia Mason Medical Center

Introduction, comment: We agree, and tried to make it clear throughout the report that the studies included for Key Question 1 evaluated FBSS patients with leg pain that met or exceeded back pain.

Report objectives and key questions, comment: Our inclusion and exclusion criteria limited the studies evaluated in key question 1 to patients with CRPS and FBSS with leg pain that met or exceeded back pain. For key questions 2 and 3, we included studies with 75% or more of patients having neuropathic pain; the patient diagnoses varied in these studies and included many different types of neuropathic pain (see Supplemental Tables 5 and 7). Due to the varying indications for SCS in these key questions, it would have been difficult to separate the results out by indication.

Hugh Allen, M.D., Virginia Mason Medical Center

Spectrum Research was unable to respond to Dr. Allen's peer review, as we did not receive it before the final report was published.

2. SPECTRUM RESEARCH RESPONSE TO PUBLIC COMMENTS

A. Responses to authors of included studies

Judith A. Turner, Ph.D., University of Washington School of Medicine

General response:

We made all of the suggested corrections <u>except</u> the following:

In Supplemental Table 3 (pg 37-41 of the final version of the tables), we found our usage of "per-protocol analysis" (where patients with permanent SCS implants (n = 27) were compared with patients who received at least some Pain Clinic treatment (n = 22) to be correct.

B. Responses to Industry

- ***Boston Scientific***

1. *Comment 1:* Mortality strength of evidence of "high" could be misconstrued to inappropriately conclude that there is a significant mortality risk with SCS

therapy. For other key questions it is clearer what the strength of evidence is regarding.

Response: We clarified the rating in the strength of evidence tables (pg 15 & pg 125 (Table 11) of the final report by adding the following text: "There is high evidence that the rate of mortality due to SCS is low."

2. *Comment 2, part 1:* Inclusion of a LoE III study in evaluating efficacy and effectiveness is not appropriate as it could skew the findings in the report.

   Response: The rating of the Turner study as LoE III was a typographical error on our part and has been correctly rated as a LoE II study in the final report. Please see the LoE critical appraisal checklist on page 150 of the final report (Appendix E).

   Comment 2, part 2: The Turner study was the sole study used to evaluate effectiveness.

   Response: The Turner study was the only study that met our inclusion criteria for the effectiveness portion of Key Question 1: we required studies to be comparative cohort studies and excluded case series. We added text throughout the report to make it clear to the reader that the study was conducted among workers' compensation patients. The best type of study to help answer KQ3 is one where patients with an exposure (in this case, workers' compensation) and those without the exposure (patients without workers' compensation) are both given the treatment and the outcomes are compared. The Turner study did not set out to answer the question of whether SCS was more or less effective among workers' compensation patients compared with non-workers' compensation patients. Rather, theirs was an effectiveness study among that group of patients; the results of which are best generalized to a similar population.

3. *Comment:* SCS clinical studies treating both FBSS and CRPS were aggregated inappropriately and could skew the results; these are separate and unique indications with the possibility of vastly differing outcomes.

   Response: For key question 1, we did not pool the data for CRPS (Kemler RCT) and FBSS (Kumar, North RCTs and Turner cohort study) patients. We tried to include clarifying language throughout but needed to summarize outcomes for the efficacy of SCS in some way that would be useful to the Health Technology Clinical Committee (HTCC). For key questions 2 and 3, we included studies that clearly established that 75% or more of patients having neuropathic pain; the patient diagnoses varied in these studies and included many different types of neuropathic pain (see Supplemental Tables 5 and 7).

Due to the varying indications for SCS in these key questions, it would have been difficult to separate the results out by indication.

- ***Medtronic***

1. *Comments on appraisal and background section of draft report, Sections 1.1, 1.2, 2.1, 2.4*

   Response: corrections, clarifications, and additions made

2. *Comments on clinical guidelines, section 2.5:* Additional guidelines should be included from: (1) ACOEM Chronic Pain Chapter, (2) American Pain Society, and (3) American Society of Anesthesiologists. Guideline on spinal stenosis is not relevant and should be removed; Sanders guideline should be removed.

   Response: The guidelines from the American Pain Society and American Society of Anesthesiologists were added; the spinal stenosis guideline was removed. We did not include the guideline from the ACOEM Chronic Pain Chapter, as it was not freely available for download. While the Sanders guideline (2005) is not associated with a larger society or organization, it is an evidence-based practice guideline published in a peer-reviewed journal and indexed in PubMed and thus remains in our final report.

3. *Comments on previous systematic reviews/technology assessments, section 2.6:* (1) The NICE guideline was not included; (2) the economic endpoints for the Simpson systematic review were incorrectly listed.

   Response: (1) The NICE guideline is listed in the Clinical Guidelines section (2.5, page 26 of the final report); (2) corrections were made.

4. *Comments on Medicare and representative private insurer coverage policies, section 2.7:* (1) SCS used as late or last resort, or if deemed appropriate; (2) selection of payers not comprehensive.

   Response: (1) corrections made; (2) the payers were selected using broad searches (i.e., google) and by searching the websites of payers included in previous HTAs; selection of payers for inclusion was limited to the ones that were easily identifiable by these methods.

5. *Comments on methods of the review, section 3.1:* (1) data from FBSS and CRPS patients were inappropriately combined; (2) observational data in the form of the Turner cohort study were included, thus <u>all</u> observational data should

be considered; (3) cost-benefit, cost-effectiveness, and cost-utility studies should all have been included.

Response: (1) see response to Boston Scientific (comment 3) above; (2) all comparative studies identified via the search methods described (PubMed and hand-searching, see Appendix B) were reviewed for inclusion using the methods described (see Appendix A), studies not included if they did not meet our pre-defined inclusion criteria (see Table 3); (3) Please see our inclusion criteria on pages 44 and 45 of the final report (Table 3).

6. *Comments on clinically meaningful improvement*, section 3.2.3: section was too limited; other key outcomes should be discussed as well.

   Response: We attempted to report results as given by the authors. In general for SCS, pain was most often used as the primary outcome. We have a short discussion on the clinically meaningful improvement for that outcome in the final report. In general, a 30% change from baseline is considered by some to represent clinically meaningful improvement for a range of patient reported outcomes when comparing before and after measures for individual patients. It would be helpful if studies would report the proportion of patients that achieve a 30% change so that a comparison between groups could be made more easily.

   (Ostelo RW, Deyo RA, Stratford P, Waddell G, Croft P, Von Korff M, Bouter LM, de Vet HC. Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. Spine (Phila Pa 1976). 2008 Jan 1;33(1):90-4.)

7. *Comment:* the disaggregation of efficacy and effectiveness is inappropriate and the PROCESS trial had few inclusions/exclusions (making it unnecessary to include non-RCTs to evaluate efficacy/effectiveness); unreasonable to assume for any technology that efficacy data for mid- and long-term are readily available and conclusions should be informed by a larger body of longitudinal, observational data.

   Response: In general, we use RCTs to inform us with respect to efficacy and comparative cohort studies to provide evidence on effectiveness. We provide the results separately to allow the HTCC the opportunity to decide how each will inform the policy decision.

8. *Comment:* The draft report fails to include an important discussion about the generalizability of data for the Turner cohort study.

   Response: Several points were added to the section on Turner (4.1.2) as well as the discussion on contrasting the RCTs to the cohort study.

9. *Comment:* (1) Incorrect LoE used for Turner study (pg 51); (2) statement about the PROCESS trial analyses should be corrected (pg 59).

   Response: corrections made.

10. *Comment:* The limitations of the Turner cohort study (pg 74) should include a discussion on the use of the composite measure as well as the limitations in evaluating opioid use on a less than daily basis.

    Response: The Turner article used as their primary outcome a composite measure assessing pain, function and daily opioid use. These were selected to meet the clinical goals of SCS in that population. The effect of using a composite score is to reduce the power of a study compared with using a single component. Wherever possible we included the components of the composite outcome that were also reported by Turner so the HTCC can see effect on the component scores as well.

11. *Comment:* The discussion about funding source should be balanced to recognize that L & I is a payer and that their financial support leaves them with a vested interest (pg 77).

    Response: The source of funding of all studies evaluated for efficacy and effectiveness is included; this information is required by the HTCC and taken into consideration during the review process.

12. *Comment:* The information on Medtronic's involvement in the PROCESS trial (Kumar RCT) is incomplete.

    Response: The following text was added to the section on this study (pg 59 of the final report (italics added for emphasis): "Of note, the study was managed in part and funded by Medtronic, Inc., *although additional independent researchers were involved in the oversight of the study and data analysis*; the study was conducted in an international (non-US) setting."

13. *Comment:* implanter experience may vary between RCTs and Turner cohort study (pg 77).

    Response: This was noted in the section on differences between the RCTs and the cohort study (#3, pg 77 of the final report).

14. *Comment:* the criteria for the 'overall strength of evidence' requiring three or more appropriately powered studies is unusual. Where does this crierion

come from? It is at odds with the expectancy of the FDA and EMEA for two confirmatory RCTs for licensing.

Response: The strength of evidence summary is intended to assess the body of published literature and takes into account those domains identified by the AHRQ and GRADE system: the quality of the evidence, the quantity (number) of studies and the consistency of the results of the studies. These systems are designed to assist clinicians and policy makers in translating clinical research. The purpose of the FDA/EMEA is different.

West S, King V, Carey TS, et.al. Systems to Rate the Strength of Scientific Evidence. Evidence Report/Technology Assessment No. 47 (Prepared by the Research Triangle Institute-University of North Carolina Evidence-based Practice Center, Contract No. 290-97-0011): Agency for Healthcare Research and Quality, Rockville, MD; 2002.

Atkins D, Best D, Briss PA, et al. Grading quality of evidence and strength of recommendations. *Bmj*. Jun 19 2004;328(7454):1490.

15. *Comment:* The level of evidence (LoE) ratings for the Kemler and Kumar RCTs are inaccurate (pg 147).

    Response: After re-evaluation, these studies have been re-graded as LoE I.

16. *Comment:* The evaluation methodology between the hip resurfacing HTA and the spinal cord stimulation HTA are not equivalent.

    Response: The same evaluation methodologies were used for both of the HTAs indicated. To evaluate safety for both HTAs, all RCTs and cohort studies included in key question 1 were used. For the previous report on hip resurfacing, three national registry studies were identified; none were identified using our search methodology for spinal cord stimulation (outlined in Appendix B). For hip resurfacing, more cohort studies met our inclusion criteria compared with the one cohort study identified for this HTA. Finally, for both HTAs, case series with a mean follow-up of ≥ 5 years were included in order to provide mid- and long-term data for safety outcomes.

17. *Comment:* Mortality strength of evidence of "high" is misleading and could be misconstrued to inappropriately conclude that there is a significant mortality risk with SCS therapy (pg 16). For other key questions it is clearer what the strength of evidence is regarding.

    Response: We clarified the rating in the strength of evidence tables (pg 15 & pg 125 (Table 11) of the final report by adding the following text: "There is high evidence that the rate of mortality due to SCS is low." The determination

of the overall strength of evidence is based on the criteria outlined in Appendix D (pg 144 of the final report).

18. *Comment:* (1) Statement should be added to the summary statement to indicate that no deaths were attributed to SCS; (2) it is inappropriate to include comment about a life-threatening complication that arose from trial stimulation.

    Response: (1) statement added; (2) trial stimulation is part of the process of receiving permanent SCS, thus no changes were made to the text.

19. *Comment:* Summary section on mortality includes an inaccurate data point for the pooled control patients of 1/149 (pg 16).

    Response: Correction made.

20. *Comment:* Missing from the mortality section is a discussion about the mortality risk associated with other surgical procedures as well as non-operative treatments.

    Response: The mortality rate of the pooled control groups from the comparative studies is included to inform the reader.

21. *Comment:* The reference to and discussion of the Coffey study should be removed from the section on mortality, as the study did not meet the inclusion criteria.

    Response: The reference to the study remains to provide important context to the HTCC around cumulative mortality rates from all causes in patients receiving SCS 3 days, 30 days and 1 year following hospital discharge. However, the discussion of the study has been moved to the appendix (Appendix F in the final report).

22. *Comment:* The SCS technology used in the RCTs included older non-rechargeable generators, but today, rechargeable generators are commonly used.

    Response: The information remains as it was included in the studies evaluated; however, in the background section (pg 24 of the final report), the following text was added (italics added for emphasis): "Reoperation may be necessary to replace the battery *(although many current systems utilize rechargeable batteries which could decrease or eliminate this need for revision)…,"*

23. *Comment:* Other observational sources and systematic reviews provide a more complete picture for the revision rate and other SCS-related events and should be taken into consideration.

    Response: All observational studies identified via the search methods described (PubMed and hand-searching, see Appendix B) were reviewed for inclusion using the methods described (see Appendix A), studies not included if they did not meet our pre-defined inclusion criteria (see Table 3);

24. *Comment:* The assessment of the quantity of evidence for safety (Table 11) is inconsistent with Table 10; there is evidence of variation of the frequency of complications of SCS across studies, therefore consistency should be graded as low.

    Response: Both Table 10 and Table 11 were evaluated using the predefined criteria for determining the overall strength of evidence (Appendix D); while there is some variability in the frequency of complications associated with SCS across studies, we found consistency in the types of complications reported.

25. *Comment:* Medtronic uses a prospective, long-term multi-center registry study (ISPR) to monitor the performance of products at selected centers throughout the US.

    Response: Unfortunately, the registry study was not identified during our search process (see Appendix A and B), and we are not able to evaluate this registry study as needed at this point in the review process due to time constraints. In general, we include registry studies to help inform us on long-term safety issues that are often not available from published studies. For example, with hip resurfacing, revision surgery (determined by the clinical expert) was deemed a safety issue. Registry data were available on revisions over several years.

26. *Comment:* (1) The differential efficacy and effectiveness of technologies should be addressed by pre-defined subgroup (interaction) analyses undertaken within RCTs, as they outweigh the findings of observational (prognostic) studies as undertaken by the authors of this report; the report does not systematically review the RCT subgroup evidence. (2) If other analyses of prognostic factors are to be considered, there were some that were excluded from the analysis due to being LoE III or were missing.

    Response: Prognostic information recorded in the exploratory analyses of two RCTs was inadvertently omitted. The following summarizes these results:

- North 2005 reported that patients using narcotic analgesics before surgery were more likely to cross over from their randomized treatment than those who were not using narcotics.
- Kumar 2007 evaluated whether the number of previous back surgeries (<3 vs. ≥3) or duration of diagnosis of FBSS (<12 vs. ≥12 months) was associated with achieving the primary outcome. Neither was statistically significant.

27. *Comment:* The Kumar 22-yr experience paper from Neurosurgery 2006 should be included in key question 3.

    Response: The study was reviewed but did not meet our pre-defined criteria for inclusion, as it was not a LoE I or II study (retrospective, no multivariate analysis).

28. *Comment:* Research presented at the 2009 North American Neuromodulation Society regarding time to SCS implant and outcomes should be included.

    Response: This information does not meet our pre-defined inclusion criteria (see Table 3).

29. *Comment:* The Burchiel 1995 study (under the workers' compensation section, pg 95) is cited as the only study; Turner 2010 should be included in this study.

    Response: We added a brief summary about the Turner study to this section to remind the reader about the outcomes from this study (as evaluated in Key Question 1). However, The best study to help answer the KQ3 is one where patients with an exposure (in this case, workers' compensation) and those without the exposure (patients without workers' compensation) are both given the treatment and the outcomes are compared. The Turner study did not set out to answer the question of whether SCS was more or less effective among workers' compensation patients compared with non-workers' compensation patients. Rather, theirs was an effectiveness study among that group of patients; the results of which are best generalized to a similar population.

30. *Comment:* Research presented at the 2010 HTAi conference regarding adapting the UK cost effectiveness model to the US healthcare system should be included.

    Response: This information does not meet our pre-defined inclusion criteria (see Table 3).

- ***St. Jude Medical***

1. *Comment:* (1) Grades assigned for the strength of evidence were inconsistent with the explanation in Appendix D; (2) the report does not make clear how the individual studies were evaluated and graded.

   Response: (1) The grades assigned for the overall strength of evidence were reviewed and found to be consistent with the criteria outlined in Appendix D; (2) the criteria used to evaluate the individual studies are outlined in Appendix D, and the LoE grading is outlined in Appendix E. We have added our rationale for not giving credit for any criteria for the studies included in key question 1.

2. *Comment:* A single LoE III study was used to evaluate effectiveness and is the sole reason for assigning a "low" evidence grade for the effectiveness of SCS.

   Response: The rating of the Turner study as LoE III was a typographical error on our part and has been correctly rated as a LoE II study in the final report; the Turner study was the only study that met our inclusion criteria for evaluating the effectiveness in Key Question 1.

3. *Comment:* The report does not explain why the RCT data are not considered in addressing the effectiveness of SCS, as they used standard practice guidelines in selecting patients and the results are applicable to normal practice.

   Response: In general, we use RCTs to inform us with respect to efficacy and comparative cohort studies to provide evidence on effectiveness. We provide the results separately to allow the HTCC the opportunity to decide how each will inform the policy decision.

4. *Comment:* The reliance on the single prospective cohort study should be questioned because of a series of study limitations; troubling that only this study was used to conclude that there is only "low" evidence of SCS effectiveness.

   Response: See note on comment 3 above. Unfortunately, we were only able to identify one comparative cohort study that met our inclusion criteria to assess SCS.

5. *Comment:* The single prospective study concentrates on the workers' compensation subpopulation of patients, and this study is best used to address key question 3.

Response: We added text throughout to make it clear to the reader that the study was conducted in a subpopulation of patients (workers' compensation patients). Because the study did not compare workers' compensation patients to patients not receiving workers' compensation (or other disability) payments, it did not fit our criteria for inclusion in Key Question 3.

6. *Comment:* (1) For key question 2, evidence was graded on matters (such as mortality) that could give a distorted view of the evidence supporting SCS procedures; (2) the strength of evidence grade of "high" for mortality was arbitrary.

   Response: Don't confuse the rate of mortality (low) with the strength of evidence (high). The strength of evidence was based on the pre-defined criteria outlined in Appendix D. In order to clarify the meaning of the strength of evidence grade of "high" for mortality (pg 15 & pg 125 (Table 11) we added the following text: "There is high evidence that the rate of mortality due to SCS is low."

7. *Comment:* There is irregularity associated with the grading of the evidence relating to the sponsorship of certain studies cited; the results of the high-quality studies were discounted because they were sponsored by a manufacturer, yet the study commissioned by the Washington Department of L & I was used as the single study to support a low evidence grade for SCS effectiveness.

   Response: The sponsorship of studies was not used to grade the evidence of any of the studies (see Appendixes D and E). The source of funding of <u>all</u> studies evaluated for efficacy and effectiveness is included; this information is required by the HTCC and taken into consideration during the review process.

8. *Comment:* The desired endpoint for SCS is the reduction in pain, and this should be the main determinant of the procedure's efficacy and effectiveness (pages 7 & 22).

   Response: The reduction of pain is one of the main outcomes evaluated for efficacy and effectiveness; however, the HTCC is also interested in other outcomes, including (but not limited to) function and quality of life (see Key Questions, 1.2, pg 18 of the final report).

9. *Comment:* (1) Additional guideline from the American Society of Anesthesiologists should be included; (2) the University of Sheffield report (ScHARR) was not used in consideration for key questions 1, 2, and 3.

Response: (1) ASA guideline added; (2) The outcomes from this HTA are included in Table 1 (pg 28 of the final report), but systematic reviews were not used to evaluate key questions 1, 2, and 3. Rather, the RCTs evaluated in this report were individually assessed in key question 1.

C. Responses to non-profit organizations

- ***Neuromodulation Therapy Access Coalition (NTAC)***

1. *Comment 1:* The presentation of the strength of evidence of "high" for mortality should be amended to emphasize the absences of SCS-related mortality and to ensure that the limited evidence is not inappropriately interpreted to indicate a significant mortality risk from SCS.

   Response: We clarified the rating in the strength of evidence tables (pg 15 & pg 125 (Table 11) of the final report by adding the following text: "There is high evidence that the rate of mortality due to SCS is low." In addition, we added the following sentence to the discussion on mortality in the results section (pg 93 of the final report): "It should be noted that in general, mortality is not discussed in the studies we identified as an SCS-related adverse event."

2. *Comment 2:* The 2010 Turner study contains a number of methodological limitations that undermine its utility in assessing the clinical role of SCS, and its inclusion is inappropriate. Undue weight is given to this LoE III study well beyond its limited focus on the workers' compensation subpopulation. Its application should be limited to key question 3.3 only.

   Response: The Turner study was the only study that met our inclusion criteria for evaluating the effectiveness in Key Question 1. We added text throughout to make it clear to the reader that the study was conducted in a subpopulation of patients (workers' compensation patients). A discussion of many of the limitations noted was included in the section contrasting the RCTs with the cohort study, and a discussion on the lack of psychiatric evaluation in the cohort study was added here. In addition, we added a more robust section on the rate of surgery and other therapies on pages 76-77. Because the study did not compare workers' compensation patients to patients not receiving workers' compensation (or other disability) payments, it did not fit our criteria for inclusion in Key Question 3. In addition, the

rating of the Turner study as LoE III in the draft report was a typographical error on our part and has been correctly rated as a LoE II study in the final report.

3. *Comment 3:* The entire Sheffield University technology assessment should be included, noting its applicability to the key questions.

   Response: This HTA was included in Table 1 (pg 28 of the final report). We had it listed by its author, Simpson. Note that systematic reviews were not critically appraised for our evaluation of key questions 1, 2, and 3. Rather, the RCTs evaluated in this and other HTAs were individually assessed to answer the key questions.

4. *Comment 4:* The report presents an imbalanced and partial view of sponsorship of clinical studies.

   Response: The source of funding of <u>all</u> studies evaluated for efficacy and effectiveness is included; this information is required by the HTCC and taken into consideration during the review process.

5. *Comment 5:* The report mischaracterizes the clinical role of SCS in treating chronic pain conditions; the report should be amended at pages 7 and 22 to emphasize that the first goal of treatment for chronic pain conditions is to reduce pain.

   Response: The reduction of pain is one of the main outcomes evaluated for efficacy and effectiveness; however, the HTCC is also interested in other outcomes, including (but not limited to) function and quality of life (see Key Questions, 1.2, pg 18 of the final report).

6. *Comment 6:* Clinical treatment guidelines that fall outside the scope of the assessment were included (spinal stenosis); the relevant guideline by the American Society of Anesthesiologists should be included.

   Response: Changes were made as recommended.

7. *Comment 7:* The presentation of the strength of evidence of "high" for mortality should be amended to emphasize the absences of SCS-related mortality and to ensure that the limited evidence is not inappropriately interpreted to indicate a significant mortality risk from SCS.

   Response: We clarified the rating in the strength of evidence tables (pg 15 & pg 125 (Table 11) of the final report by adding the following text: "There is high evidence that the rate of mortality due to SCS is low." In addition, we

added the following sentence to the discussion on mortality in the results section (pg 93 of the final report): "It should be noted that in general, mortality is not discussed in the studies we identified as an SCS-related adverse event."

8. *Comment 8:* Submission included correspondence between NTAC and Washington State Department of Labor and Industries which discusses previous L&I coverage decision basis. This correspondence predates the HTA. Those comments are included in the attachment entitled "Attachment of Public Comments".

   Response: Correspondence occurred prior to the commissioning of the HTA and does not address the HTA report.

D. SPECTRUM RESEARCH RESPONSE TO WASHINGTON STATE AGENCY COMMENTS

	Section (page)	HTA text of interest	State Agency Comment	Spectrum Research Response
1.	Executive Summary (p14) and throughout	Short-term: < 5 yrs Mid-term: 5 to < 10 yrs Long-term: ≥ 10 yrs	Classification of short- versus mid-term invalid (suggest short > 3 yrs, mid 3-5 yrs, and long >5 yrs)	We found no clinical standard defining short, mid or long term. Therefore, we chose these time periods *a priori* as they have been useful in other HTAs (see Hip Resurfacing). The report is careful to identify the follow-up periods from each clinical trial so that the HTCC can identify when the effect is reported in absolute years versus the descriptive terms.
2.	Executive Summary (p8, p14) and throughout	Order in which outcomes are presented (varies)	Summary of results and anywhere outcomes are listed should describe pain first, then function, then other outcomes.	Reorganized order of outcomes in summaries; for the strength of evidence, the outcomes were highlighted with bold text but were left as is in order to group by level of evidence rating (i.e., moderate versus low)
3.	Results (p52-57) and throughout	Outcomes presented for Kemler RCT	No section on physical function for Kemler (Kemler reported no improvement in function)	Kemler did not evaluate functional status using patient- or clinician-reported outcome measures. Rather, it was reported using a variety of physiologic tests (time to

	Section (page)	HTA text of interest	State Agency Comment	Spectrum Research Response
				perform a subtest, range of motion, grip strength or strength of flexion). These are surrogate measures and how well they translate into function is not known.
4.	Results (p67-71) and throughout	Outcomes presented for North RCT	North reported no improvement in function	We agree; the results reported for activities of daily living and neurological status (pg 71) were classified as "function" in the overall strength of evidence and other summaries.
5.	Summary strength of evidence (p14) and elsewhere	Function:	Three of the four RCT/cohort studies reported no improvement in function	Two RCTs reported function: Kumar had improved function in the SCS group (ODI); North reported no difference between groups. One cohort reported no improvement in function with SCS.
6.	1.1 Rationale (p18) and elsewhere	SCS used as part of multidisciplinary pain program	SCS is almost never done as part of a multidisciplinary pain program.	The use of the term "multidisciplinary pain program" does not refer to a structured formal program but rather an individualized multidisciplinary treatment program that employs SCS as well as other modes of usual care, such as physical therapy, medication usage, etc. Thus, SCS is used in addition to other therapies, as described in the surrounding text and on page 22 of the final report.
7.	2.4 Technology and comparators (p24)	Implantation of SCS is minimally invasive	Term "minimally invasive" should be deleted, as SCS involves surgical procedure.	Deleted "minimally invasive".
8.	4.3 KQ3 (p93) and throughout	Subpopulation: "Workers' compensation" patients	Burchiel study included patients in other disability programs, which could include other types of disability payments besides workers' compensation.	Corrected title of subpopulation being evaluated to "Workers' compensation or other disability payments".
9.	4.3 KQ3 (p93) and	Subpopulation: "Workers'	Turner cohort study is a study of a workers'	We added a sentence to this section indicating that Turner

	Section (page)	HTA text of interest	State Agency Comment	Spectrum Research Response
	throughout	compensation" patients	comp population and should be highlighted here.	evaluated workers' compensation patients and reported similar outcomes between treatment groups and that the rate of success was low. Turner was evaluated thoroughly in Key Question 1 (Effectiveness) and not in Key Question 3, as it did not compare outcomes between patients receiving to those not receiving workers' compensation payments.
10.	4.4 KQ4 (p106-108) and throughout	We found that SCS cost-effectiveness increases and may be dominant over time compared with control treatments (i.e., CMM or reoperation), and 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.	If there is no evidence of longer term (> 3 yrs) improvement in pain and little evidence of improved function short or long term, then any projected savings over more than 2-3 yrs is not supportable.	Added statement to qualify our conclusions in this section and throughout: "However, the assumption of continued efficacy past 3 years is questionable from the only RCT reporting pain 5-10 years after implantation."
11.	4.4 KQ4 (p106-108) and throughout	We found that SCS cost-effectiveness increases and may be dominant over time compared with control treatments (i.e., CMM or reoperation), and that there is some evidence that SCS is cost-effective at	The revision and removal rates in the cohort study were very high within 18 months, similar to other studies. Are these costs accurately reflected in the cost-effectiveness studies?	As indicated in Table 9, two of the economic studies evaluated (Taylor and Taylor; Simpson) included complications were part of the model inputs; the third study (North) utilized all hospital charge data through a mean 3.1-yr follow-up. All three economic studies utilized data from the same RCTs we included in Key Question 1.

	Section (page)	HTA text of interest	State Agency Comment	Spectrum Research Response
		moderate (<$20,000) incremental cost effectiveness ratio (ICER) levels compared with CMM or reoperation.		
12.	Table 10 Summary Strength of Evidence (pg 123 and throughout)	Effectiveness: Strength of evidence: Low	The Turner cohort study is deemed low evidence, but consistent with the evidence classification in the report and other society classifications, it should be considered a class II study.	We incorrectly classified the study as LoE III in our draft report; the study is correctly graded as LoE II in the final report (Appendix E, pg 150 of final report, and throughout). Regarding the overall strength of evidence being "low" for effectiveness, this is consistent with our grading system (see Appendix D, pg 145 of final report). (We could not grade consistency as + since there was only one study included for Effectiveness, thus the overall strength of evidence was graded as "Low" instead of "Moderate".)
13.	Table 1 (pg 27)	Previous health technology assessments and systematic reviews	Table should be moved to appendix; not appropriate to include all systematic reviews unless there is description of rigor of review and whether formal evidence was conducted.	This section is an overview of the summary of HTAs and systematic review (SRs) published. If we use an SR as primary evidence to answer key questions, it is critically appraised and evaluated. Since there were so few studies in the SRs, we chose to evaluate the individual studies themselves.
14.	Table 2 (pg 40)	Rationale for WA State L&I policy	Rationale/comments should include description of committee that made the policy.	This description was not part of the main document of the policy; similar descriptions were not included for other payer policies.
15.	4.2 KQ2 (pg 79-93)	Complications assessed	Was any search and/or analysis of FDA MAUDE adverse events or of device recalls performed?	Section added in final report (4.2.5 pg 93 of final report).
16.	4.2.4	"the reason for	Can't assume conclusion	Text left as is, as study was

	Section (page)	HTA text of interest	State Agency Comment	Spectrum Research Response
	Mortality (pg 91)	SCS was not reported; therefore it is likely that a good percentage of the patients included in these rates were being treated for ischemic pain, and these patients are more likely to have cardiovascular-related deaths than those being treated from neuropathic pain…"	to be true; what are the population estimates for the percentage of patients with ischemia treated with SCS compared with FBSS/CRPS, when were SCS devices approved for this use?	moved to Appendix F in final report. Initially this study was excluded as it did not meet our inclusion criteria for safety (Pain diagnosis was not reported; ≥75% of patients need to be diagnosed with neuropathic pain for inclusion, see Appendix C). There was not sufficient time to verify the diagnosis of the patients included so we could not rule out patients receiving SCS for other than neuropathic pain. The use of SCS for treatment of ischemic pain or angina has been recommended by third-party payers and the American College of Cardiology (ACC) and American Heart Association (AHA) for a number of years, and SCS is approved by at least some insurance companies for use in chronic angina patients with pain refractory to other treatments or who are not candidates for percutaneous intervention or revascularization by at least some insurance companies. (REFERENCES LISTED AT BOTTOM OF TABLE)*
17.	4.2.4 Mortality (pg 91)	Coffey study	A description of the Coffey study objectives and purpose of the publication would be helpful. Why did they do the study in light of the weaknesses? Seems this may be the best estimate of mortality associated with SCS.	They report all cause mortality at 3 different time frame up to 1 year, and these are included in Appendix F.
18.	4.4 KQ4 (pg 106-115)	Table 9: Summary of economic studies	Is there a table with individual grading of the cost effectiveness studies?	QHES grading of each of the three econ studies has been added to Appendix D (pgs 147-149 of the final report).

	Section (page)	HTA text of interest	State Agency Comment	Spectrum Research Response
19.	4.4 KQ4 (pg 106-115)	Key question 4	Weaknesses could be better described	See #10, above.

* References:

Anderson, J. L., Adams, C. D., Antman, E. M. et al.: ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-Elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction) developed in collaboration with the American College of Emergency Physicians, the Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation and the Society for Academic Emergency Medicine. J Am Coll Cardiol, **50:** e1, 2007

Gibbons, R. J., Abrams, J., Chatterjee, K. et al.: ACC/AHA 2002 guideline update for the management of patients with chronic stable angina--summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Chronic Stable Angina). Circulation, **107:** 149, 2003

Cigna Medical Coverage Policy; Coverage Policy Number 0380; available at http://www.cigna.ca/customer_care/healthcare_professional/coverage_positions/medical/mm_0380_coveragepositioncriteria_spinal_cord_stimulation.pdf

Regence Medical Policy; Policy Number 45; available at http://blue.regence.com/trgmedpol/surgery/sur45.html

3. Peer Review Comments

See Attachment entitled “Attachment of Public Comments”