Washington State Health Care Authority

Sacroiliac Joint Fusion Update

Peer review and public comment on draft evidence report

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Health Technology Assessment Program (HTA)

Washington State Health Care Authority

PO Box 42712
Olympia, WA 98504-2712
(360) 725-5126
www.hca.wa.gov/hta
shtap@hca.wa.gov

Prepared by:
RTI International–University of North Carolina Evidence-based Practice Center
Research Triangle Park, NC 27709
www.rti.org

This document was created in response to peer review and public comments on a Draft Health Technology Assessment (HTA) report prepared by the RTI-UNC Evidence-based Practice Center through a contract to RTI International from the State of Washington Health Care Authority (HCA). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the State of Washington HCA and no statement in this document should be construed as an official position of the State of Washington HCA.

The information in the document is intended to help the State of Washington's independent Health Technology Clinical Committee make well-informed coverage determinations. This document and its associated Evidence Report are not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this document and the associated Evidence Report in the same way as any medical reference and in conjunction with all other pertinent information (i.e., in the context of available resources and circumstances presented by individual patients).

Acknowledgments

The following individuals contributed to the report associated with this document:
Lead Investigator: Eva Chang, PhD, MPH
Co-Investigators: Leila Kahwati, MD, MPH; Roberta Wines, MPH
Project Coordinator: Rania Ali, MPH
Analyst: Caroline Rains, MPH
Scientific Reviewer: Meera Viswanathan, PhD
Library/Document Preparation: Mark Howell, MLS; Loraine Monroe; Sharon Barrell, MA

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Peer Review Comments and Responses

Two independent, external peer reviewers were invited to provide comments on the Draft Evidence Report and were provided with an honorarium for their review. The peer reviewer's name, affiliations, and conflicts of interest are reported in ***Table 1***.

Table 1. External Peer Reviewer of the Draft Evidence Report

Name	Title/Affiliation	Summary of Conflicts of Interest Reported
William Cross, MD (Reviewer 1)	Mayo Clinic Department of Orthopedic Surgery	Financial conflicts: Designed and uses a minimally invasive sacroiliac joint fusion system in partnership with Mayo Clinic and Lincotek Incorporated. Once this device is sold, Mayo Clinic and peer reviewer will receive royalties. Non-financial conflicts: Peer reviewer believes in fairness with coverage of minimally invasive sacroiliac joint fusion surgery for all patients regardless of the implant used. States that sole-vendor coverage is inappropriate and has not been demonstrated in any other orthopedic technology (i.e., hip replacement, knee replacement, ankle fusion products, etc.) to his knowledge. Is an orthopedic trauma surgeon with specialty focus on derangements of the pelvis and has subspecialty interest in the treatment of pathological conditions of the SI joint. Performs SI joint fusions on carefully selected patients who have failed all non-operative measures to address the dysfunction. Has authored peer reviewed papers on the topic of SI joint fusion and is currently conducting research related to SI joint fusion surgery.
Bradley Weiner, MD (Reviewer 2)	Houston Methodist	Financial conflicts: None reported Non-financial conflicts: Reports primary clinical specialty is orthopedics and spinal surgery; rarely performs sacroiliac joint fusion.

The peer reviewers did not identify any missing studies and did not identify any studies that should have been excluded from the report. We addressed many of the comments submitted by the reviewers in the Final Evidence Report; though some comments or suggestions were outside the scope of the HTA. We considered the revisions made based on peer review comments as minor revisions. Specific peer review comments and responses are provided in ***Table 2***.

Table 2. Peer Reviewer Comments on Draft Evidence Report and Response

Item	Comment	Response
Introduction		
Are there any additional issues you think we should cover in the introduction?	Reviewer 1: None. Reviewer 2: It looks good.	Thank you.
Do you see anything inaccurate, superfluous, or unclear?	Reviewer 1: Nothing came to mind. Much attention is paid to the MAUDE database and it is clear why this was omitted. A potential reference to the revisions noted in MAUDE may be considered if there was a significant trend noted. Reviewer 2: Since the diagnosis is fuzzy at best, with lots of overlap (facet joint pain, proximal sciatica, etc); most doctors / surgeons feel that true SI joint pain is uncommon, if not rare, as opposed to the very high percentages quoted.	Thank you for this suggestion. We did not review the revisions in MAUDE because a previous check we performed found that several publications reported higher rates of revision than reported in MAUDE.
Any additional comments?	Reviewer 1: Very comprehensive and no edits needed. Reviewer 2: Perhaps comment on whether the RCTs were company sponsored and whether (and how much) the authors were reimbursed for their work. This is ubiquitous in spine surgery and has been a major problem in biased publications in the past.	We have included information about study sponsorship for all included studies when reported by study authors; we have also noted study author financial relationships disclosed in controlled studies even when the study was not reported as sponsored by a manufacturer. The issue of industry conflicts of interest is discussed in the discussion section.
Methods		
Do you see any problems with our methods?	Reviewer 1: None. Originally disappointed that MAUDE was not included but methods very clearly detail why this decision was made and I support fully (as noted above in my comments). Reviewer 2: No. Look good.	Thank you.
Any additional comments about the Methods section?	Reviewer 1: No. Reviewer 2: No.	Thank you.
Results		
Are there any studies you believe we may have missed?	Reviewer 1: None. Reviewer 2: Not that I'm aware of.	Thank you.

Are there studies that you believe we should have excluded?	None.	Thank you.
Are there studies that you believe we should have excluded?	Reviewer 1: No Reviewer 2: No	Thank you.
Do you believe we have inaccurately described any studies?	Reviewer 1: No Reviewer 2: Yes. But corporate sponsorship and disclosure of payments is important.	We have included information about study sponsorship for all included studies when reported by study authors; we have also noted study author financial relationships disclosed in controlled studies even when the study was not reported as sponsored by a manufacturer. The issue of industry conflicts of interest is discussed in the discussion section.
Any additional comments about the Results?	Reviewer 1: There has been some discussion on results based on surgical approach with some societies starting to advocate certain approaches and with billing/coding differences based on the approach chosen. Thus, it may be considered to add a portion of the review on outcomes based on surgical approach. Reviewer 2: No comments.	We found one controlled cohort study that compares the Rialto Implant System to the iFuse Implant System which use different approaches (dorsal vs. transiliac, respectively). This study did not find any differences in efficacy and safety. Among the uncontrolled studies, we categorized the studies by device rather than approach because the studies did not reliably report surgical approach.
Discussion		
Do you think we missed any important points?	Reviewer 1: There is no mention of industry bias amongst the higher-level studies. As with all peer-reviewed literature, great attention must be paid to the study and its author/industry bias. Reviewer 2: Just as above. Otherwise, quite good.	We have included information about study sponsorship for all included studies when reported by study authors; we have also noted study author financial relationships disclosed in controlled studies even when the study was not reported as sponsored by a manufacturer. The issue of industry conflicts of interest is discussed in the discussion section.
Do you disagree with any of the discussion items?	Reviewer 1: No. Reviewer 2: My disagreement is: Diagnosis is fuzzy at best since there is no gold standard; observed outcomes in the 'real world' are minimal at best; and the procedure is generally performed at a few select centers. This procedure is often not performed at most centers because many doctors and surgeons believe that true SI joint pain is very uncommon. As a result, quality RCTs will not be available simply because there is no way to have equipoise—many physicians would not find it ethical to conduct an RCT to perform SI joint fusion.	Thank you.

Any additional comments about the Discussion?	Reviewer 1: None. Reviewer 2: No comments.	Thank you.
Other Sections		
Any comments on the structured abstract, conclusion, figures, tables and appendices?	Reviewer 1: I appreciated the abstract and executive summary. The presentation and table formats are very clear and comprehensive. Reviewer 2: Looks good.	Thank you.
General Comments		
Is the report clearly written, adequately detailed and of an appropriate length?	Reviewer 1: Very much so. I appreciate addressing the MAUDE database in particular and also the brief discussion on the complication/adverse event reporting. Reviewer 2: Yes.	Thank you.
Please make any additional comments you feel would help us improve the report.	Reviewer 1: Adding comments on bias, based upon your expertise with identifying bias, should be noted within this report. This would include comments on study sponsorship trends, interpreting statistics and reporting of data by potentially-biased researchers. Reviewer 2: No comments	We have included information about study sponsorship for all included studies when reported by study authors; we have also noted study author financial relationships disclosed in controlled studies even when the study was not reported as sponsored by a manufacturer. The issue of industry conflicts of interest is discussed in the discussion section.

Public Comments and Responses

The Draft Evidence Report was posted for public comment from April 2, 2021, to May 3, 2021. One public comment was submitted. The names and affiliations of those submitting comments are summarized in ***Table 3.***

Table 3. Individuals or Organizations Submitting Public Comments on the Draft Evidence Report

Name	Title/Affiliation
Jeffrey Zigler	Vice President, Market Access and Reimbursement, SI-BONE, iFuse Implant System

Public comments and responses to comments are detailed in ***Table 4***. Complete copies of the comments submitted by individuals follow the table.

Table 4. Public Comments on Draft Evidence Report and Specific Responses

Public Comment	Response
Evidence for SIJ fusion (iFuse Implant System) Recent clinical reviews have focused extensively on SIJ pain and noted that physical examination maneuvers for SIJ pain were amongst the most accurate of all tests for establishing the etiology of chronic low back pain. This is identified in Table 21 of the RTI report, entitled "Diagnostic accuracy of common sacroiliac joint clinical tests…" The Level I and II long-term outcomes evidence available for iFuse-treated patients suffering from chronic SIJ pain related to degenerative sacroiliitis and/or SIJ disruption clearly shows immediate, and sustained benefit of this treatment option which should be supported by the HCA. As the RTI report notes, of the 8 controlled studies evaluating minimally invasive SIJ fusion, all evaluated iFuse procedures, which limits the generalizability of findings to other minimally invasive procedures. Therefore, the immediate and sustained results of iFuse-treated patients (now evaluated prospectively out to 5 years) can, and should, stand alone.	Thank you for this comment.
The evidence summaries in the RTI report are quite thorough, and for the most part we agree with them. However, despite Level I evidence from multiple RCTs, Level II evidence from prospective studies, case series and professional spine societies' guidelines, as well as the experience of over 19,000 iFuse cases' post-market surveillance in the U.S., the RTI report still characterizes some of the follow-up for iFuse patients as "low quality" or "very low quality" due to the strictures of the GRADE scale for evaluating evidence. This would suggest to you that the true effect of iFuse might somehow be "markedly different from the estimated effect." We are concerned that this mischaracterizes the substantial evidence base for SIJ fusion, as multiple studies have each shown an immediate, and sustained true effect of iFuse procedures.	We have revised the terminology used to describe the GRADE ratings to 'certainty' instead of 'quality' consistent with recent guidance. Current GRADE methodology assesses the certainty of the existing evidence considering study design, risk of bias limitations, precision, consistency, directness of measures used, and publication bias. We provide the ratings for each domain that go into the overall certainty rating for transparency along with documentation justifying any downgrading for serious or very serious concerns in a domain. Bodies of evidence comprised of observational studies will rarely be assessed as anything higher than a low certainty rating under GRADE because of limitations inherent in that study design. The RCT evidence included in the report had risk of bias limitations from lack of blinding (including outcome assessor blinding) and extensive crossovers. Our conclusions were moderate certainty for benefit from surgery for pain, physical function, and quality of life outcomes compared to conservative management at 6 months. The interpretation of moderate certainty is "**We are moderately confident that the estimate of effect lies close to the true effect for this outcome.** The body of evidence has some deficiencies. We believe that the findings are likely to be stable, but some doubt remains."

	Effectiveness outcomes at timepoints longer than 6 months were downgraded to low certainty because of crossover contamination and the analyses used to account for crossovers were not robust in addition to the issue of no blinding. Safety outcomes were downgraded to very low certainty for a variety of reasons documented in the report, including inconsistency in data reported for such outcomes across multiple study publications associated with each trial. We contacted study authors of the iMIA and INSITE trials for clarifications about the safety data; they acknowledged the inconsistencies but did not provide any updated data to clarify the inconsistencies.
The designs of the RCTs and prospective studies evaluating iFuse procedures are industry standard and were well-vetted by investigators and their institutional review boards. Since the commercialization of iFuse over 10 years ago, the real-world evidence now available via post-market surveillance and administrative claims databases (e.g., Optum, Blue Health Intelligence) further reinforces its net effect for patients. Over 100 commercial, Medicare and Medicaid payers cover the procedure for chronic SIJ pain patients (more about this below). Further, the BCBSA Evidence Street Opinion on this topic confers favorable conclusions about the same evidence base for iFuse; as do evaluations of this evidence by AIM Specialty Health, eviCore, Magellan Healthcare, and most recently by Hayes, Inc.	We acknowledge that blinding of an intervention in an RCT of a surgical procedure or device can be challenging. However, this does not negate the impact that lack of blinding can have on a trial, especially when outcome assessors cannot be blinded, which is the case when using patient-reported outcomes. We identified an ongoing trial of iFuse compared to sham surgery that is currently recruiting and that should be able to overcome the limitations posed by lack of blinding and will also help elucidate the magnitude of bias potentially introduced from lack of blinding. We do not have access to how payors described in this comment make their coverage decisions but can confirm that based on our scan of the payors most relevant to the State of Washington, all but Kaiser do cover the procedure when clinical criteria are met.
We believe the totality of the evidence for chronic SIJ pain patients, and the continued reliance upon it by so many payers and specialty benefits management companies, suggests a clear effect of the procedure for well-selected chronic SIJ pain patients. This is because these groups all recognize that published research from the study of iFuse procedures reaches the highest Levels of Evidence which are universally adopted by academic journals, government research institutions, the AMA, commercial U.S. payers and technology assessment organizations. We therefore disagree with the summation in the RTI report that the published evidence of iFuse procedures at 1 and 2 years' follow-up, including results published in such high-impact journals as *Journal of Bone and Joint Surgery*, is of "low" or "very low" quality. We hope that you and your team may find the evidence base to be of relatively	Please see response to earlier similar comment. We use internationally recognized and recommended tools for assessing risk of bias and use dual independent review. We rated the 6-month and earlier outcomes from both RCTs as having some concerns for bias because treatment and outcome assessment was not blinded. We considered outcomes reported after 6 months as high risk of bias because of extensive crossovers. Although both RCTs appropriately attempted to mitigate the bias introduced from crossover, these methods do not fully mitigate potential

high quality by accepted standards, and factor this into your consideration of this topic.	biases. Further the evidence for safety outcomes is limited by inconsistency in reporting across multiple papers for the same trial and presented/analyzed in multiple ways posing a risk for selected outcome reporting. Finally, the impact factor of journals where studies are published and whether societies, payors, or organizations cite a study in their guidelines are not factors that we (or anyone in the evidence synthesis arena) use to determine whether a study has risk of bias limitations.
RTI concerns about clinical study of iFuse procedures Specifically, the RTI report notes a concern for bias in results from the RCTs of iFuse vs. non-surgical management (INSITE study). The report specifically notes a high concern for bias because of no masking and cross-over. Our responses to those two specific concerns are summarized as follows: **RTI concern about "no masking":** As a study design consideration, blinding was not possible in the RCTs of iFuse, since the implants are radiopaque; it was deemed too easy for participants to gain access to their X-rays or CTs, which clearly show the presence/absence of highly radiopaque iFuse implants. **RTI concern about cross-over to surgery:** Importantly, and ethically, the study protocols for iFuse allowed conservative care-treated patients to cross over to surgery if their symptoms did not improve after 6 months. Patients enrolled in the iFuse RCTs after first having failed at least 6 months of non-surgical treatment. Then, for the conservative care group, cross-over occurred after 6 more months of non-surgical treatment delivered by the investigators. It would be highly unusual to expect that such patients would improve substantially after the combined amount of non-surgical treatment they had already received by that point. Patients who crossed over did as well as patients initially assigned to surgical treatment. Taken together, these data provide very strong evidence for the efficacy of surgery over non-surgical treatment. Analyses published at 1 year and 2 years in *Journal of Bone and Joint Surgery* show that the superiority of SI joint fusion persists at 2 years. Finally, there is no published evidence that SIJ pain, once it becomes chronic, resolves on its own. Thus, the expectation in the control group is continued pain and disability. Surgeon investigators would have refused to enroll patients on ethical grounds had cross-over not been allowed, because of the high degree of pain and dysfunction suffered by their patients with chronic SIJ pain. Disallowing cross-over would have resulted in massive study withdrawal and out-of-study surgery.	Thank you. We believe most of these comments have been addressed above but will provide some additional response. Based on comments received from 1 of our peer reviewers without any conflicts of interest related to this procedure or device, there is some debate over whether SI joint pain/dysfunction can be reliably diagnosed, whether it is a common source of low back pain, and some concern that doing surgery for this procedure might not be ethical for those reasons. The issue of allowing crossovers is a particularly challenging problem for studies of devices, which often receive FDA 510k clearance and become commercially available before rigorous trials of efficacy and safety are conducted to establish a definitive lack of equipoise between surgery and non-surgical treatment. And, as the commenter notes, the availability of a device commercially has an impact on the ability to recruit investigators and patients to participate in a trial when there is a chance of being randomized to the nonsurgical arm. However, the integrity of results from an RCT (particularly one that is not blinded) demands upholding the belief of equipoise from recruitment throughout followup to avoid introducing bias. For these reasons, studies should not recruit investigators who have a strong opinion about the benefits or harms of the intervention and investigators should not enroll patients into a study who have strong treatment preferences. We commend the study authors for maintaining allocated treatment groups through 6 months followup. We understand the decision to allow crossovers after 6 months was a choice to

	maximize recruitment and retention. However, these considerations do not remove the bias introduced by crossovers. One-way crossovers (as is commonly seen in studies comparing surgery to non-surgical management) are particularly problematic because the reasons people crossover are directly related to the severity of symptoms and will always result in an underestimate of the effect of nonsurgical management. The interpretation of results involving one-way crossovers must be nuanced because of this. When crossovers occur at a low rate it is possible to assess the impact of them using multiple and different sensitivity analyses. However, it is much harder to have confidence in the analyses when the crossover rate is very high (43% in iMIA and 80% in INSITE by 1 year) and crude approaches to analyses are used (e.g., LOCF, stratified analyses by crossover status).
We also want to comment on the 3.8% revision rate referenced in Table C-4 of the RTI report. Even as reported, this revision rate is very low relative to other orthopedic surgical procedures. In 2015, the 4-year revision surgery rate after SIJ fusion with iFuse was reported to be even lower, at 3.5%.1 This rate compares favorably to published 4-year revision rates in the state of Washington for surgery for lumbar stenosis (11%)2 and for lumbar spine surgery for degenerative spine disorders (~13%).3	Thank you for this comment. We agree the rate of revision is likely in line with other spine-related surgeries; however, a formal analysis of this was outside of the scope of the review.
Additional payers covering iFuse procedures (for chronic SIJ pain) There are now over 100 commercial and government payers that have published coverage policies related to the MIS SIJ fusion procedure. This does not include insurers who also allow case-by-case coverage of certain MIS SIJ fusion candidates as a result of claims denial appeal processes- including numerous workers' compensation claims initially denied per the current Washington State Department of Labor & Industries policy (following strictly the HTCC coverage determination which excludes MIS SIJ fusion for chronic SIJ pain). Since the HTCC's decision in May 2019 to limit coverage for these patients, we are aware of numerous examples where patients' denials were later overturned by the State of Washington Board of Industrial Insurance Appeals. This further underscores the importance of a revised policy, and an expanded coverage position by the HCA and HTCC for MIS SIJ fusion, to include chronic SIJ pain patients.	Thank you for the additional information. Our report focuses primarily on payors in the State of Washington. The coverage policy is determined by the HTCC.
The RTI report notes how major insurers continue to revise coverage criteria in favor of iFuse, including Humana which now covers the MIS SIJ fusion procedure for chronic SIJ pain, exclusively when triangular implants (iFuse) are used. However, we wanted to point out that the RTI report states "No policy identified" as it relates to Medicare, which does not reflect for your team all of the access to this procedure available to Medicare patients, either as a medically necessary service under Title XVIII of the Social Security Act, or via Local Coverage Determinations published by Medicare Administrative Contractors (MACs). As of June 1, 2016, Medicare supports minimally invasive SIJ fusion nationwide. All MACs have created pathways for beneficiaries' access to MIS SI joint fusion (CPT 27279):	We have modified the table to clarify that all 8 of the Medicare MACs cover this procedure on a case-by-case basis. However, there remains no national coverage determination for this procedure from Medicare.

We would welcome the opportunity to join in the next HTCC meeting, alongside other professional societies, clinician experts and researchers on this topic, to present on any and all iFuse device and/or clinical data the Committee may find relevant to its decision making process. Thank you again for continuing to work on getting the Washington HCA position on this important topic right, and for the opportunity to comment. Please let us know what additional information might support the decision to cover this important treatment option for chronic SIJ pain patients.	Thank you for your comments. Information about participating in the June 2021 HTCC meeting is available at the State's Health Technology Assessment website.