Health technology assessment program

Prospective technology topics - 2020

Public comments accepted until **5:00 p.m., Tuesday July 28, 2020**
Submit all comments to: shtap@hca.wa.gov

**Background**

The Health Technology Assessment (HTA) program is a legislatively created program that seeks to ensure that health technologies purchased by state agencies are safe and effective, and that coverage decisions of state agencies are more consistent. The program relies on scientific, or evidence-based, information about safety and effectiveness to inform decisions and improve quality. An independent committee of eleven practicing health care clinicians reviews evidence regarding the safety, efficacy, and cost-effectiveness of various medical procedures and/or equipment, and determines if the state will pay for those procedures.

The Health Care Authority (HCA) in consultation with participating state agencies (Health Care Authority, Department of Labor and Industries, and Department of Corrections), selects technologies for review by the HTA program process. Agency leaders or their designees are liaisons between the HTA program and the participating agencies and provide consultation on program decisions, clinical committee membership, and to recommend and prioritize technologies.

**Interested organization/public recommendations:**

Interested individuals may petition the program to review or re-review a technology by using the [petition for health technology review](#) form located on the [HTA webpage](#) at any time.

**Prospective technology topics**

Agency medical directors and policy staff reviewed utilization, emerging technology, activity by other health technology assessment programs and public requests for a list of prospective technologies for prioritization and recommendation to the HCA director.
New proposed technology topics

<table>
<thead>
<tr>
<th>Technology</th>
<th>Safety</th>
<th>Efficacy</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-invasive testing for coronary artery disease</td>
<td>Med</td>
<td>Med</td>
<td>High</td>
</tr>
</tbody>
</table>

Coronary artery disease (CAD) is the narrowing or blockage of the coronary arteries, which over time can weaken the heart muscle. Accurate and early diagnosis of CAD can lower the risk of heart attack or the development of more severe heart disease. Many types of tests may be conducted to diagnose CAD. Some tests may be more appropriate than others depending on the indication and can support more appropriate risk stratification. This topic is proposed for medium concerns for safety and efficacy, high concerns for cost, and to support adoption of optimal testing strategies for evaluation of coronary artery disease that is evidence-based and aligns with current clinical guidelines and practice. The scope of this review will include re-reviews of prior HTCC topics (cardiac nuclear imaging and computed tomographic angiography), and may include other anatomic and/or functional imaging tests.

New technology topics considered, not proposed

<table>
<thead>
<tr>
<th>Technology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1   Allergy testing</td>
</tr>
<tr>
<td>2   Automated computed tomography (CT) perfusion imaging</td>
</tr>
<tr>
<td>3   Denervation of the sacroiliac joint</td>
</tr>
<tr>
<td>4   Fractional excretion of nitric oxide for asthma</td>
</tr>
<tr>
<td>5   Hypoglossal nerve stimulation for sleep apnea</td>
</tr>
<tr>
<td>6   Infra-low frequency neurofeedback</td>
</tr>
<tr>
<td>7   Molecular profiling of tumors</td>
</tr>
<tr>
<td>8   Multiplex respiratory viral panel testing</td>
</tr>
<tr>
<td>9   Portable magnetic resonance imaging (MRI) (Hyperfine)</td>
</tr>
<tr>
<td>10  Tissue-based regenerative therapy</td>
</tr>
</tbody>
</table>
Re-review technologies

Technologies are considered for re-review at least once every eighteen months based on availability of new evidence that may change the decision. All technologies with determinations beyond 18 months since the final determination previously reviewed by the Health Technology Clinical Committee (HTCC) are listed below, along with information on whether they have been selected for re-review.

<table>
<thead>
<tr>
<th>Technology</th>
<th>HTCC review history</th>
<th>Re-review?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Cardiac nuclear imaging</td>
<td>HTCC reviewed in 2013.</td>
<td>Yes</td>
</tr>
<tr>
<td>New literature appears to support re-review at this time. Review of cardiac imaging topics will be combined into a single, comprehensive review of non-invasive testing for coronary artery disease.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 Computed tomographic angiography (CTA)</td>
<td>HTCC reviewed in 2008.</td>
<td>Yes</td>
</tr>
<tr>
<td>New literature appears to support re-review at this time. Review of cardiac imaging topics will be combined into a single, comprehensive review of non-invasive testing for coronary artery disease.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 Artificial disc replacement</td>
<td>HTCC re-reviewed in 2017.</td>
<td>No</td>
</tr>
<tr>
<td>Review of literature submitted by stakeholder petition conducted in Spring 2020 (attached). New information does not support re-review at this time.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 Chronic migraine and chronic tension-type headache</td>
<td>HTCC reviewed in 2017.</td>
<td>No</td>
</tr>
<tr>
<td>Review of literature submitted by stakeholder petition conducted in Spring 2020 (attached). New information does not support re-review at this time.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 Coronary calcium scoring</td>
<td>HTCC reviewed in 2009.</td>
<td>No</td>
</tr>
<tr>
<td>Literature scan conducted in Spring 2020. New information does not support re-review at this time.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 Facet neurotomy</td>
<td>HTCC reviewed in 2014.</td>
<td>No</td>
</tr>
<tr>
<td>Literature scan conducted in Spring 2020. New information does not support re-review at this time.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 Peripheral nerve ablation for limb pain</td>
<td>HTCC reviewed in 2019.</td>
<td>No</td>
</tr>
<tr>
<td>Review of literature submitted by stakeholder petition conducted in Spring 2020 (attached). New information does not support re-review at this time.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 Sacroiliac joint fusion</td>
<td>HTCC reviewed in 2019.</td>
<td>No</td>
</tr>
<tr>
<td>Review of literature submitted by stakeholder petition conducted in Spring 2020 (attached). New information does not support re-review at this time.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Vertebroplasty, kyphoplasty and sacroplasty

*Literature scan* conducted in Spring 2020. New information does not support re-review at this time.

<table>
<thead>
<tr>
<th>Technology</th>
<th>HTCC review history</th>
<th>Re-review?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertebroplasty, kyphoplasty and sacroplasty</td>
<td>Literature scan conducted in 2016 and 2017. HTCC reviewed in 2011.</td>
<td>No</td>
</tr>
</tbody>
</table>

At this time, the program has not received or identified new evidence to support re-review of the following:

<table>
<thead>
<tr>
<th>HTA Decisions</th>
<th>Latest Review or Literature Scan</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Applied Behavioral Analysis (ABA) therapy for autism</td>
<td>June 2011</td>
</tr>
<tr>
<td>2 Appropriate imaging for breast cancer screening in special populations</td>
<td>March 2015</td>
</tr>
<tr>
<td>3 Arthroscopic knee surgery</td>
<td>August 2008</td>
</tr>
<tr>
<td>4 Autologous blood/platelet-rich plasma injections</td>
<td>May 2016</td>
</tr>
<tr>
<td>5 Bariatric surgery and pediatric bariatric surgery</td>
<td>May 2015</td>
</tr>
<tr>
<td>6 Bone growth stimulators</td>
<td>August 2009</td>
</tr>
<tr>
<td>7 Bone morphogenic proteins for use in spinal fusion</td>
<td>March 2012</td>
</tr>
<tr>
<td>8 Breast MRI</td>
<td>October 2010</td>
</tr>
<tr>
<td>9 Bronchial thermoplasty for asthma</td>
<td>May 2016</td>
</tr>
<tr>
<td>10 Cardiac stents</td>
<td>January 2016</td>
</tr>
<tr>
<td>11 Carotid artery stenting</td>
<td>September 2013</td>
</tr>
<tr>
<td>12 Catheter ablation procedures for supraventricular tachyarrhythmia (SVTA) including atrial flutter, atrial fibrillation</td>
<td>May 2013</td>
</tr>
<tr>
<td>13 Cervical spinal fusion for degenerative disc disease</td>
<td>March 2013</td>
</tr>
<tr>
<td>14 Cochlear implants: bilateral versus unilateral</td>
<td>May 2013</td>
</tr>
<tr>
<td>15 Computed Tomographic Angiography (CTA)</td>
<td>November 2008</td>
</tr>
<tr>
<td>16 Discography</td>
<td>February 2008</td>
</tr>
<tr>
<td>17 Electrical Neural Stimulations (ENS)</td>
<td>October 2009</td>
</tr>
<tr>
<td>18 Extracorporeal membrane oxygenation</td>
<td>March 2016</td>
</tr>
<tr>
<td>19 Extracorporeal shock wave therapy for musculoskeletal conditions</td>
<td>March 2017</td>
</tr>
<tr>
<td>20 Fecal microbiota transplantation</td>
<td>November 2016</td>
</tr>
<tr>
<td>21 Functional neuroimaging for primary degenerative dementia and mild cognitive impairment</td>
<td>January 2015</td>
</tr>
<tr>
<td>22 Gene expression profile testing of cancer tissue</td>
<td>March 2018</td>
</tr>
<tr>
<td>23 Genomic micro-array</td>
<td>January 2018</td>
</tr>
<tr>
<td>24 Glucose monitoring</td>
<td>January 2018</td>
</tr>
<tr>
<td>HTA Decisions</td>
<td>Latest Review or Literature Scan</td>
</tr>
<tr>
<td>------------------------------------------------------------------------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>25 Hip resurfacing</td>
<td>November 2013</td>
</tr>
<tr>
<td>26 Hyaluronic acid/viscosupplementation</td>
<td>November 2013</td>
</tr>
<tr>
<td>27 Hyperbaric Oxygen (HBO2) treatment for tissue damage</td>
<td>March 2013</td>
</tr>
<tr>
<td>28 Imaging for rhinosinusitis</td>
<td>May 2015</td>
</tr>
<tr>
<td>29 Implantable infusion pumps</td>
<td>August 2008</td>
</tr>
<tr>
<td>30 Intensity Modulated Radiation Therapy (IMRT)</td>
<td>September 2012</td>
</tr>
<tr>
<td>31 Knee joint replacement or knee arthroplasty (Total knee arthroplasty)</td>
<td>October 2010</td>
</tr>
<tr>
<td>32 Lumbar fusion for degenerative disc disease</td>
<td>November 2015</td>
</tr>
<tr>
<td>33 Microprocessor-controlled lower limb prosthetics - knee</td>
<td>November 2011</td>
</tr>
<tr>
<td>34 Negative pressure wound therapy</td>
<td>November 2016</td>
</tr>
<tr>
<td>35 Non-pharmacologic treatments for treatment resistant depression</td>
<td>March 2014</td>
</tr>
<tr>
<td>36 Osteochondral allograft / autograft transplantation knee</td>
<td>January 2018</td>
</tr>
<tr>
<td>37 Pharmacogenetic testing for selected conditions: behavioral health</td>
<td>January 2017</td>
</tr>
<tr>
<td>38 Pharmacogenetic testing for selected conditions / oral anticoagulants</td>
<td>May 2018</td>
</tr>
<tr>
<td>39 Positron Emission Tomography (PET) scans for lymphoma</td>
<td>November 2018</td>
</tr>
<tr>
<td>40 Robotic assisted surgery</td>
<td>May 2012</td>
</tr>
<tr>
<td>41 Routine ultrasound for pregnancy</td>
<td>October 2010</td>
</tr>
<tr>
<td>42 screening and monitoring tests for osteopenia/ osteoporosis</td>
<td>November 2014</td>
</tr>
<tr>
<td>43 Sleep Apnea Diagnosis and Treatment in Adults</td>
<td>March 2012</td>
</tr>
<tr>
<td>44 Spinal Cord Stimulation</td>
<td>July 2018</td>
</tr>
<tr>
<td>45 Spinal Injections</td>
<td>March 2016</td>
</tr>
<tr>
<td>46 Stereotactic Radiation Surgery and Stereotactic Body Radiation Therapy</td>
<td>January 2017</td>
</tr>
<tr>
<td>47 Surgery for lumbar radiculopathy/ sciatica</td>
<td>May 2018</td>
</tr>
<tr>
<td>48 Testosterone Testing</td>
<td>January 2019</td>
</tr>
<tr>
<td>49 Treatment of Chronic migraine and Chronic tension-type headaches</td>
<td>July 2018</td>
</tr>
<tr>
<td>50 Tumor Treating Fields Optune</td>
<td>November 2018</td>
</tr>
<tr>
<td>51 Tympanostomy Tubes in Children</td>
<td>November 2015</td>
</tr>
<tr>
<td>52 Upper Endoscopy for GERD and GI symptoms</td>
<td>May 2012</td>
</tr>
<tr>
<td>53 Upright / Positional MRI</td>
<td>June 2012</td>
</tr>
<tr>
<td>54 Varicose Veins</td>
<td>July 2017</td>
</tr>
<tr>
<td>55 Virtual Colonoscopy or Computed Tomographic Colonography (CTC)</td>
<td>February 2008</td>
</tr>
<tr>
<td>56 Vitamin D Screening and Testing</td>
<td>November 2012</td>
</tr>
</tbody>
</table>
Next steps:

Via this notice, prospective technology topics are posted on the HTA program webpage to gather public comment on the following:

- New topics proposed for review
- Topics selected for re-review
- Consideration of topics eligible for re-review on the basis of evidence available since the original determination

The agency recommendations and public comments will be presented to the HCA director for final selection. Selected topics are posted to the HTA program webpage.

Prioritization criteria:

HTA created a process and tools based on the legislative requirements and criteria that are widely used in technology assessment priority settings. Identification of criteria and use of priority tools makes the process explicit and increases transparency and consistency across decision-makers. The tools are intended to be used by agency liaisons when making recommendations and by the clinical committee when making comments or selections of technologies. The primary criteria are directly linked to the legislative mandates for the program to focus technology reviews where there are concerns about safety, efficacy, or cost effectiveness, especially relative to existing alternatives. See RCW 70.14.100. These criteria are also common to other technology assessment programs. The prioritization criteria tool is available on the website.

Re-review topic criteria:

Re-review criteria are directly linked to the legislative mandate that technologies shall be selected for re-review only where evidence has since become available that could change a previous determination. Technologies are considered for re-reviews at least once every 18 months. Re-reviews consider only evidence made available since the previous determination. See RCW 70.14.100. The re-review criterion is directed at identifying those situations where a technology requires a re-review to consider new evidence that was not available when the initial review was completed and the likelihood that the new evidence could result in a change to a previous determination.
Topic selection – 2020: supporting materials

*Formal stakeholder petitions, letters, review of submitted citations*

Chronic migraine and chronic tension-type headache
- Stakeholder petition
- Technology assessment center review of submitted citations

Peripheral nerve ablation for limb pain
- Stakeholder petition
- Technology assessment center review of submitted citations

Artificial disc replacement
- Stakeholder petition

Sacroiliac joint fusion
- Stakeholder petition
Submit competed petition to: shtap@hca.wa.gov; or
Atten: Health Technology Assessment
PO Box 42712, Olympia, Washington 98504-2712; or
FAX (360) 586-8827
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Atten: Health Technology Assessment
PO Box 42712, Olympia, Washington 98504-2712; or
FAX (360) 586-8827

**Petition for technology review or re-review**

*Note: Not all questions will apply to all technologies. For assistance email the HTA program at the address above, or phone (360) 725-5126 (TTY 711).*

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<table>
<thead>
<tr>
<th>Your name:</th>
<th>Charis Wolf</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mailing address:</td>
<td></td>
</tr>
<tr>
<td>E-mail address:</td>
<td><a href="mailto:mcmwolf@gmail.com">mcmwolf@gmail.com</a></td>
</tr>
<tr>
<td>Telephone number:</td>
<td></td>
</tr>
</tbody>
</table>

**Technology topic**  Click here to enter text.

*If this topic has been reviewed by the health technology assessment program in the past, skip to question 7, below. See technologies HTCC has previously reviewed.*

1. Background information
   - Does this technology have FDA approval? ☐ Yes ☐ No
   - When was this technology approved?
   - For what indications has FDA approved this technology?
   - Why do you believe this technology merits consideration for assessment?
   - Proposed research questions.

   Click here to enter text.

2. Potential patient harm(s) or safety concerns
   - What is the potential for patient harm, related to use of this technology?
   - What are the likelihood and severity of the potential harms or adverse outcomes that may result from recommended use of this technology?
   - Are there significant potential harms associated with this technology compared to alternatives?

   Click here to enter text.

3. Therapeutic efficacy, effectiveness or diagnostic accuracy
What is the potential effectiveness of this technology on the indicated clinical condition? (e.g., prevent/reduce mortality; increase quality of life)
How are indicated conditions diagnosed? Is there a consensus on diagnosis?
For diagnostic technologies: Is this technology compared to a “gold standard” technology?
What is the diagnostic accuracy or utility?
What published, peer-reviewed literature documents the efficacy of this technology or the science that underlies it? Please enclose publications or bibliography.

Click here to enter text.

4. Estimated total cost per year
What are the direct health care costs of this technology (annual or lifetime)?
What is the potential cost-effectiveness of this new technology compared with other alternatives?
Which private insurers reimburse for use of this technology? Please provide contact information and phone numbers.

Click here to enter text.

5. Secondary considerations
**Number of persons affected** - What are the numbers of people affected by this technology in the State of Washington?
**Severity of condition(s)** - What is the severity of the condition treated by this technology? Does it result in premature death; short or long term disability? How would this technology increase the quality of care for the State of Washington?
**Policy-related urgency** - Is there a particular urgency related to this technology? Is it new and rapidly diffusing? How long has this technology been in use? Is there a standard of care? Is this technology or proposed use(s) controversial?
**Potential or observed variation** - What is the observed or potential for under, or overuse of this technology? Are there any variations in use or outcomes by region or other characteristics?
**Special populations and ethical concerns** - Is use limited to small populations; what characteristics are present (e.g., race, ethnicity, religion, rare condition, socioeconomic status) that may impact policy decision?

Click here to enter text.

6. References
List other organizations that have completed technology assessments on this topic (please provide date of technology assessments and links).
Cite any Center for Medicare and Medicaid Services (CMS) national coverage decision on this topic and the date issued.
Provide list of key references used in preparing this petition.
Have any relevant medical organizations (e.g., American Medical Association) expressed an opinion on this technology? If so, please provide verification documents and contact names, numbers and links.
Bibliography or reference list of requestor attached: ☐ Yes ☐ No
7. For re-review petitions only
Re-review of a technology requires new evidence that could change a previous decision. What new evidence should be considered? Please provide specific publication information and/or references.

I am submitting a request that the evidence for the treatment of migraines and tension type headaches be re-reviewed and that the new evidence be considered. This list has also been submitted via email and a flash drive with the PDF’s has been dropped off as well.

**RCTs:**
Compared to other therapies:
(Biçer, 2017)
(Fraser, Matsuzawa, Lee, & Minen, 2017)
(X. Li, Zhang, & Cheng, 2019)
(Naderinabi et al., 2017)
(Nie, Cheng, Wen, & Li, 2019)
(Tastan, Ozer Disci, & Set, 2018)
(Yu & Salomoni, 2018)
(Zhao et al., 2017)**

Compared to Sham:
(Gildir, Tuzun, Eroglu, & Eker, 2019)
(Z. Li et al., 2016)**
(Mayrink, Garcia, Dos Santos, Nunes, & Mendonca, 2018)

  Compared to waitlist:
  (Musil et al., 2018)

**includes waitlist control

**Case Reports/Case Series**
(Allen, Deng, & Langland, 2016)
(Blome, 2017)
(Hayhoe, 2015)

**Systematic/Literature Reviews/Meta-Analysis:**
(Coeutaux & Befus, 2016)
(Linde, Allaïs, Brinkhaus, Fei, Mehring, Shin, et al., 2016)
(Linde, Allaïs, Brinkhaus, Fei, Mehring, Vertosick, et al., 2016)
(Vickers et al., 2018)
(Yin, Buchheit, & Park, 2017)
(X. T. Zhang et al., 2019)

**fMRI/Mechanisms:**
RCTs:
(Z. Li et al., 2017)
(Pei et al., 2016)
Single Arm:
(Y. Zhang et al., 2016)
Systematic Reviews:
(Xu, Zhang, Pei, & Ji, 2018)

References:


A list of 25 citations on the use of acupuncture for headache was provided to AAI by the HCA. These citations were compared against the PICOTS inclusion/exclusion criteria from the original HTA of April 14, 2017 (Appendix A). Per our usual protocol, citations were initially evaluated at title/abstract level; full text of potentially includable studies was reviewed. Based on the inclusion/exclusion criteria from the 2017 report, only two citations of new RCTs from the list provided met the inclusion criteria, bringing the total number of included trials to four. (See attached Excel spreadsheet). Both are in patients with chronic migraine headache. Table 1 below compares these trials with those from the 2017 report. The risk of bias for these trials was not assessed; overall strength of evidence was not assessed. No new systematic search was conducted by AAI. A formal signal update evaluation was not conducted.

The conclusions from the two new trials (N=186) appear to be similar to previously included trials, based on limited evaluation. Different comparators and time frames were described across trials. All trials suggest that acupuncture may improve outcomes. If the list provided was not based on a systematic search of the literature, it raises the question of whether studies that did not show an effect weren’t included. E.g. if only citations supporting acupuncture were included but those which found no difference or those finding comparative treatments to be more beneficial were omitted, this may lead to different conclusions.

Table 1. Preliminary comparison of acupuncture trials included in the previous HTA on chronic headache and list provided by the HCA

<table>
<thead>
<tr>
<th>Conclusions from CER Executive Summary</th>
<th>New Sources of Evidence and Findings</th>
<th>Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Migraine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acupuncture vs. usual care (not further defined)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 RCT (N=301) [Vickers 2004]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• No data on short- or intermediate term outcomes were available.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• In the longer term (36 weeks), acupuncture resulted in a statistically greater improvement in all outcomes measured compared with usual care: proportion of patients achieving ≥50% reduction in any, mild, and moderate/severe headache days; proportion of patients achieving ≥35% reduction in headache days; mean reduction from baseline in any, mild or moderate/severe headache days per month (low quality evidence for all outcomes).</td>
<td>Acupuncture vs. WL (w/ usual pharmacological care, not further defined)</td>
<td></td>
</tr>
<tr>
<td>1 RCT (N=86) [Musil 2018]*</td>
<td></td>
<td>• Similar conclusions; have short-term data now</td>
</tr>
<tr>
<td>• In the short- (immediately post-tx at 12 weeks) and longer-term (24 weeks): acupuncture resulted in a greater proportion of patients achieving “success” (≥50% reduction in average monthly migraine day frequency) as well as statistically greater improvement (reduction) in frequency of migraine days and migraine attacks per month, pain intensity of migraines (post-tx only) and drug consumption; no difference were seen between groups in mean duration of migraine or MIDAS score at either timepoint.</td>
<td>• No data for the intermediate-term was available.</td>
<td></td>
</tr>
</tbody>
</table>
### Conclusions from CER Executive Summary

#### Acupuncture vs. Topiramate 180
1 RCT (N=66) [Yang 2011]

- In the short-term (4 weeks), acupuncture resulted in a statistically greater improvement in all outcomes measured compared with topiramate *(low quality evidence for all): proportion of patients achieving ≥50% reduction headache days (any and moderate/severe); and mean reduction from baseline in headache days (any and moderate/severe) per month and in the Migraine Disability Assessment (MIDAS); for the latter outcome, it is unclear if the difference is clinically meaningful.
- No data on intermediate- or long-term outcomes were available

#### Acupuncture vs. Sodium valproate
1 RCT (N=100) [Naderinabi 2017]*

- In the short-, intermediate- and long-term (4, 8, 12 weeks): acupuncture resulted in statistically greater improvement (reduction) in mean VAS pain scores (clinical importance not described), mean number of headache days per month, and mean number of times needing medication per month and in the proportion of patients who were absent from work (less in the acupuncture group).

#### None identified

#### Acupuncture vs. Botulinium Toxin
1 RCT (N=100) [Naderinabi 2017]*

- In the short-, intermediate- and long-term (4, 8, 12 weeks): acupuncture resulted in statistically greater improvement (reduction) in mean VAS pain scores, mean number of headache days per month, and mean number of times needing medication per month. With exception of the 4-week results, which favored botulinium toxin, there were no significant difference between the groups in the proportion of patients who were absent from work.

#### Chronic Tension-Type Headache

#### Acupuncture vs. Sham
2 RCTs (N=69) [Karst 2000, Tavola 1992]

- In the short-term, no statistical differences were seen between the acupuncture and the sham group in the proportion of patients achieving

#### None meeting inclusion criteria in list provided

### New Sources of Evidence and Findings

<table>
<thead>
<tr>
<th>Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Similar conclusions; have intermediate- and longer-term data now.</td>
</tr>
<tr>
<td>• New comparator. Similar conclusions as other trials identified.</td>
</tr>
<tr>
<td>• NA</td>
</tr>
</tbody>
</table>

### Comparison

- RCT: Randomized Controlled Trial
- N: Number of participants
- VAS: Visual Analog Scale
- MIDAS: Migraine Disability Assessment
## Conclusions from CER Executive Summary

>33% and >50% improvement from baseline on the Headache Index (HI) in one small trial with 4 weeks of follow-up, or in the pooled mean reduction in headache episodes per month across two small trials at 4-6 weeks follow-up (insufficient evidence for all outcomes).

- In the longer term, as reported by one small trial, no statistical differences were seen between groups in the proportion of patients achieving >33% and >50% improvement from baseline on the Headache Index at 52 weeks, or in the mean reduction in headache episodes per month at 26 and 52 weeks (insufficient evidence for all).

- No data for the intermediate-term was available.

## Acupuncture vs. Physical Training/Exercise

1 RCT (N=60) [Soderberg 2006/2011]

- No data for the short- or intermediate-term were available.

- In the longer-term (12 and 26 weeks), no statistical differences were seen between the acupuncture and the physical training/exercise group in the number of headache-free periods and headache-free days per week (insufficient evidence for all).

## Acupuncture vs. Physiotherapy

1 RCT (N=62) [Carlsson 1990]

- Over the short- and intermediate term (4-9 weeks), the authors provide insufficient data to assess comparative efficacy for the reduction in number of headache episodes and overall Sickness Impact Profile (SIP) score. The authors state that the acupuncture group improved significantly more than the physiotherapy group in the SIP category Sleep and Rest but significantly less with

### New Sources of Evidence and Findings

None meeting inclusion criteria in list provided

### Comparison

- NA
Conclusions from CER Executive Summary  | New Sources of Evidence and Findings | Comparison
---|---|---
respect to the psychosocial categories Emotional Behavior, Work, Eating, and Recreation and Pastimes; no data was provided to support these statements. All evidence is insufficient for this trial.  
• No data over the longer-term were available. | None meeting inclusion criteria in list provided | • NA

**Acupuncture vs. Relaxation**  
1 RCT (N=60) [Soderberg 2006/2011]  
• No data for the short- or intermediate-term were available.  
• In the longer-term (12 and 26 weeks), no statistical differences were seen between the acupuncture and the relaxation training group in the number of headache-free periods and headache-free days per week (insufficient evidence for all).  

* Trials that met inclusion criteria from list provided:  
## Appendix A.

**PICOTS – 2017 Headache HTA**

### Table 7. Summary of inclusion and exclusion criteria

<table>
<thead>
<tr>
<th>Study Component</th>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
</table>
| **Population**  | Adults with the following chronic headache* of the following types: | • Persons <18 years old  
• Pregnant or breast-feeding women  
• Acute headache or acute migraine attacks  
• Episodic migraine (migraine occurring <15 days per month)  
• Menstrual migraine  
• New daily persistent headache  
• Hospitalized patients  
• Patients treated in the emergency department  
• Other primary headaches (e.g. trigeminal autonomic cephalgias including cluster headache)  
• Secondary headache types as defined in The International Classification of Headache Disorders, 3rd edition  
• Acute trauma-related headache  
• Medication overuse headache/medication rebound headaches as the primary population/study focus  
• Headache due to malignancy; cancer-related headache  
• Operative or procedure-related headache  
• Cervical dystonia  
• Neuropathic pain  
• Neck pain not associated with headache |
|                 | • Migraine (with or without aura)  
• Tension-type headache  
• Chronic daily headache, defined as coexistent chronic migraine and tension-type headache | |
| **Interventions** | • Botulinum toxin injection (Botox, OnabotulinumtoxinA, BoNTA)  
• Trigger point injection or dry needling  
• Acupuncture  
• Transcranial magnetic stimulation (TMS)  
• Manipulation/manual therapy (e.g. osteopathic, chiropractic) | • Treatments for acute headache; abortive treatments for acute episodes  
• Interventions that are not FDA approved and/or are not available in the U.S.  
• Dysport (abobotulinumtoxinA), incobotulinumtoxinA, RimabotulinumtoxinB) (not FDA approved for use in migraine/headache)  
• Evaluation of incremental value of combining interventions (e.g. chiropractic manipulation plus physical therapy) |
<table>
<thead>
<tr>
<th>Study Component</th>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Massage</td>
<td>• Massage</td>
<td>• Implantable devices (e.g. spinal cord stimulators, implantable occipital nerve stimulators, implantable catheters)</td>
</tr>
<tr>
<td></td>
<td>• Nerve block</td>
<td>• Nerve block</td>
</tr>
<tr>
<td></td>
<td>• Biofeedback</td>
<td>• Biofeedback</td>
</tr>
<tr>
<td></td>
<td>• TENS</td>
<td>• TENS</td>
</tr>
<tr>
<td></td>
<td>• Peripheral nerve decompression surgery</td>
<td>• Peripheral nerve decompression surgery</td>
</tr>
<tr>
<td></td>
<td>• Occipital nerve stimulation</td>
<td>• Occipital nerve stimulation</td>
</tr>
<tr>
<td></td>
<td>• Vagal nerve stimulation (implantable)</td>
<td>• Vagal nerve stimulation (implantable)</td>
</tr>
<tr>
<td></td>
<td>• Hypothalamic deep brain stimulation</td>
<td>• Hypothalamic deep brain stimulation</td>
</tr>
<tr>
<td></td>
<td>• Intranasal sphenopalatine ganglion blocks</td>
<td>• Intranasal sphenopalatine ganglion blocks</td>
</tr>
<tr>
<td></td>
<td>• Psychological therapies or behavioral interventions (e.g. cognitive behavioral therapy, education, etc.)</td>
<td>• Psychological therapies or behavioral interventions (e.g. cognitive behavioral therapy, education, etc.)</td>
</tr>
<tr>
<td></td>
<td>• Pharmacological treatment (including oral agents such as opioids, NSAIDS, beta blockers, antiepileptics, calcium channel blockers, calcium channel antagonists, antidepressants, ACE inhibitors, Angiotensin II antagonists, etc.)</td>
<td>• Pharmacological treatment (including oral agents such as opioids, NSAIDS, beta blockers, antiepileptics, calcium channel blockers, calcium channel antagonists, antidepressants, ACE inhibitors, Angiotensin II antagonists, etc.)</td>
</tr>
<tr>
<td></td>
<td>• Intervention that is part of a multi-modal treatment</td>
<td>• Intervention that is part of a multi-modal treatment</td>
</tr>
<tr>
<td></td>
<td>• Dietary supplements</td>
<td>• Dietary supplements</td>
</tr>
<tr>
<td></td>
<td>• Exercise/physical activity</td>
<td>• Exercise/physical activity</td>
</tr>
<tr>
<td></td>
<td>• Yoga, Tai Chi</td>
<td>• Yoga, Tai Chi</td>
</tr>
<tr>
<td></td>
<td>• Physical therapy</td>
<td>• Physical therapy</td>
</tr>
<tr>
<td></td>
<td>• Laser therapy</td>
<td>• Laser therapy</td>
</tr>
<tr>
<td></td>
<td>• Ultrasound</td>
<td>• Ultrasound</td>
</tr>
<tr>
<td></td>
<td>• Inferential therapy</td>
<td>• Inferential therapy</td>
</tr>
<tr>
<td></td>
<td>• Hyperbaric oxygen</td>
<td>• Hyperbaric oxygen</td>
</tr>
<tr>
<td></td>
<td>• Surgical treatment (e.g. suborbital nerve decompression, microvascular decompression of the trigeminal nerve)</td>
<td>• Surgical treatment (e.g. suborbital nerve decompression, microvascular decompression of the trigeminal nerve)</td>
</tr>
<tr>
<td></td>
<td>• Laser therapy</td>
<td>• Laser therapy</td>
</tr>
<tr>
<td></td>
<td>• Transcranial direct current stimulation</td>
<td>• Transcranial direct current stimulation</td>
</tr>
<tr>
<td></td>
<td>• Trager work/Trager approach</td>
<td>• Trager work/Trager approach</td>
</tr>
</tbody>
</table>

**Comparator**

- **Inclusion**: Usual treatment(s) (e.g. pharmacological treatment, Psychological therapies or behavioral interventions)
- **Exclusion**: Comparisons of different forms of the same treatment, Comparisons of timing interventions
<table>
<thead>
<tr>
<th>Study Component</th>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Including biofeedback, conventional physical therapy</td>
<td>• Placebo/Sham†</td>
<td>• Combined pharmacological and procedural interventions</td>
</tr>
<tr>
<td>• No treatment</td>
<td>• Combined interventions (e.g. chiropractic manipulation plus PT)</td>
<td></td>
</tr>
<tr>
<td>• Waitlist</td>
<td>• Medications that are not FDA approved for use in the United States</td>
<td></td>
</tr>
<tr>
<td>• Excluded interventions from above except as noted for inclusion</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Primary</th>
<th>Secondary or intermediate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Studies must report at least one of the following for inclusion:</td>
<td>• Proportion of responders (e.g. at least 50% reduction of headache frequency from baseline for 3-4 months following treatment)</td>
<td>• Non-clinical outcomes</td>
</tr>
<tr>
<td>• Complete cessation/prevention of headache; reduction in mean number of episodes and/or headache days</td>
<td>• Function/disability – focus on validated measures (e.g. BURMIG, burden of migraine; HADLI, Headache Activities of Daily Living Index; HDI, Headache Disability Index (Inventory); HDQ, Headache Disability Questionnaire; HIT-6, Headache Impact Test; MIDAS, Migraine Disability Scale)</td>
<td>• Intermediate outcomes</td>
</tr>
<tr>
<td>• Harms, treatment-related adverse events, treatment discontinuation due to adverse events</td>
<td></td>
<td>• Imaging outcomes</td>
</tr>
</tbody>
</table>

**Secondary or intermediate**
- Quality of life
- Patient satisfaction
- Emergency department visits
- Loss of working days
- Headache intensity
- Frequency of analgesic use
- Headache scores
<table>
<thead>
<tr>
<th>Study Component</th>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
</table>
| **Study Design** | Focus will be on studies with the least potential for bias. | • Indirect comparisons  
• Non-comparative studies (case series) (except as described to evaluate rare or long-term harms)  
• Incomplete economic evaluations such as costing studies  
• Studies with fewer than 10 patients per treatment group  
• Case reports  
• Studies in which <80% of patients have a condition or treatment of interest |

**Key Questions 1-2:**
- High quality systematic reviews of RCTs will be considered if available.
- Randomized controlled trials (RCTs)

**Key Question 2:**
- Randomized controlled trials (RCTs)
- Data from non-randomized comparative studies at low risk of bias may be considered for safety if needed to supplement RCT safety data
- Case series designed specifically to evaluate harms/adverse events may be considered only for rare events or short or long-term safety in the absence of information from high quality comparative studies

**Key Question 3:**
- RCTs which stratify on patient or other characteristics and formally evaluate statistical interaction (effect modification)

**Key Question 4:**
- Only full, formal economic studies (i.e., cost-effectiveness, cost-utility, cost-minimization, and cost-benefit studies) will be considered.

| Publication | Studies published in English in peer reviewed journals or publicly available FDA reports | Abstracts, editorials, letters  
• Duplicate publications of the same study which do not report on different outcomes  
• Single reports from multicenter trials |
<table>
<thead>
<tr>
<th>Study Component</th>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study Component</strong></td>
<td><strong>Inclusion</strong></td>
<td><strong>Exclusion</strong></td>
</tr>
</tbody>
</table>
| | • White papers  
| | • Narrative reviews  
| | • Articles identified as preliminary reports when results are published in later versions |
| **Timing** | • Focus will be on intermediate (>6 months) and long term (>12 months) for efficacy outcomes, particularly cessation/prevention; any time frame for harms | • Studies with less than 1 week follow-up past intervention |

* While chronic headache is currently defined by the International Classification of Headache Disorders, 3rd edition as 15 or more headache days each month for at least 3 months or more than 180 days a year, older studies may have used varied definitions and timeframes (e.g. 28 day period or 30 day period for a month). Given these variations, studies reporting populations with a mean of ≥12 headache days per month or ≥12 headache episodes or attacks per month or equivalent were considered to meet the criteria for chronic headache.

† Studies comparing treatments to sham treatments (even those which may be considered “active”) as one type of comparator provides valuable information regarding treatment efficacy for pain conditions. Subjective improvement in patients may result from factors other than a given procedure, whether that treatment is an “active” sham or a specified intervention. Some of these factors include the natural course of the condition, the effects of placebo, and measurement error. A placebo effect does not require a physical placebo and reflects a change in a patient’s condition attributable to the symbolic importance of a treatment versus specific physiologic or pharmacologic properties.¹⁻³

Request for re-review of decision regarding Peripheral Nerve Ablation

Purpose of request:
A request is made to re-review the recent decision by the HTCC/WA to consider Peripheral Nerve Ablation procedures as no longer being covered for treatment for chronic wrist pain, including treatment in Workers’ Compensation Claims.

Basis of request:
It is my opinion that the review by the General Practitioner representing the Center for Evidence-based Policy (CEbP) in Oregon excluded in her evaluation the nerve denervation procedure literature over the last 50+ years because those studies did not meet the review’s inclusion criteria, i.e., basically Randomized Controlled Trials (RCTs). Consequently, that review concluded that there were no acceptable studies to support surgical wrist denervation procedures.

Considering the above, the information cited below, and the references included, it is requested that the HTCC re-review the decision to deny coverage of surgical wrist denervation procedures. It is noted in the Transcript of the HTCC 20190118 meeting that the committee is “waiting for somebody to request a re-review”. And “we are looking forward to a re-review on the basis of new data.”

It is requested that the committee explain why wrist denervation procedures for alleviation of chronic wrist pain (which have been done in Washington for decades) will no longer be covered, including in Workers’ Compensation cases.

=============================================================================  
RCTs were first used to evaluated medical treatments, not surgical treatments. Although RCTs were later championed by pharmaceutical manufactures for the purpose of having their products found to be acceptable for treatment, again, the trials dealt primarily with medications, not invasive procedures like wrist surgery.

The literature is clear that RCTs are only occasionally done for evaluation efficacy, safety, and cost of surgical procedures. RCTs were not commonplace when wrist denervation procedures were developed and considered acceptable treatment for chronic wrist pain. Although early studies were done in Europe, the procedures have been done in this country since the 1980s. Because of the complexity of surgical procedure evaluations, most studies have involved case reports or case series.

The difficulties associated with RCTs for surgical procedures include the following:
Developing a study design relating to a surgical procedure that includes a comparator group is problematic since:

1) although using a sham surgical procedure would be considered for a comparator, it is considered not ethical by many surgeons,

2) participants being recruited for a study with a sham procedure, which is associated with extra risks (e.g., anesthetic risk, surgical post-op infection risk), but which includes a procedure without benefit often do not find this attractive,
3) use of a pain-relieving medication as a comparator is problematic since most patients with chronic pain being considered for a wrist denervation procedure have already tried medications without adequate relief,

4) participants being recruited for a wrist denervation study typically have had months, if not years, of non-surgical treatments (e.g., splinting, steroid injections, therapy, NSAIDs, work/activity restriction). The data from pre-operative treatments could serve as a type of comparator. Such data would be of greater value than attempting to recruit participants for a trial using “no treatment” as a comparator,

5) recruiting participants for an RCT of a surgical procedure is problematic since denervation procedures have been, and are currently being offered outside of a trial.

The following example demonstrates this recruiting difficulty. Over the last twenty (20) years, the procedure, CPT 64772 – “Transection or avulsion of other spinal nerve, extradural” (not neuroma excision), has been done for the wrist in Washington State, including in Workers’ Compensation cases (149 cases according to the Department of Labor & Industries’ SHARP division data).

Other difficulties with carrying out an RCT for a surgical procedure include:

1) having enough cases to provide sufficient data for an acceptable statistical analysis may require more than one surgeon. This introduces a variable which may be difficult to assess since there are likely differences in surgical training, surgical technique, and surgical experience,

2) assessing the outcome of many surgical procedures is somewhat dependent upon post-surgical treatments/therapy. This introduces variables not always easily addressed in the data since therapists differ in their training and experience and compliance by the participants is not always carried out according the study protocol,

3) designing and carrying out an RCT can be very expensive and thus not possible for surgeons outside of government or large institutions.

Many literature studies (see below) excluded by the CEbP review actually have had assessments of efficacy and harm/complications. Overall, the studies to date have shown that wrist denervation procedures have provided, in a majority of cases, significant, if not complete, resolution of wrist pain and many studies have provided outcome studies, some even long term outcome results. Many studies include industry-acceptable assessment metrics, such as 1) the VAS (Visual Analog Scale) for assessment of pre-op vs post-op pain, 2) objective measurements of function (e.g., grip strength, range of motion [ROM]), and 3) data regarding return to work/activities post-op compared to pre-op.

Wrist denervation procedures are appropriate in different situations. These include desire for relief of wrist pain in patients who

1) are not considered appropriate candidates (e.g., for medical conditions, perceived compliance issues) for more involved procedures,

2) cannot financially afford the prolonged limitation of wrist use/time loss after major reconstructive wrist procedures,

3) cannot likely carry out their normal job activities after major reconstructive procedures (which limit or eliminate wrist motion), or

4) simply want a simpler procedure with minimal “down time” with reasonable likelihood of moderate, if not complete relief of wrist pain.
It is noted that over the past 10 years, the American Society for Surgery of the Hand (globally the most eminent hand surgery educational society) has offered instructional course lectures regarding wrist denervation procedures. The most recent was last month, offered to surgeons from over 40 countries in the world.

It is noted that the review by CEbP did NOT provide any evidence that denervation procedures for the wrist, carried out internationally by surgeons for over fifty years, failed to provide sufficient efficacy or were associated with unacceptable harm or cost (when compared to major reconstructive procedures for pain relief).

One concern expressed, in the Transcript of the HTCC 20190118 meeting, was over how well defined is the anatomy of nerves involved in the ablation procedures. However, cadaveric dissection studies have well demonstrated the anatomy of sensory nerves (articular branches) servicing wrist joints.

References

Regarding design methodologies for evaluation of treatments vs surgical procedures


Boyce request for reevaluation of decision regarding Peripheral Nerve Ablation for Chronic Pain


New (newer) wrist denervation references


Additional references related to surgical denervation & anatomy


Peripheral Nerve Ablation For The Treatment Of Limb Pain

Review of Stakeholder Submitted New Evidence

May 2020
Peripheral Nerve Ablation For The Treatment Of Limb Pain Screening

Review of Stakeholder Submitted New Evidence

May 2020

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About the Center for Evidence-based Policy
The Center is recognized as a national leader in evidence-based decision making and policy design. The Center understands the needs of policymakers and supports public organizations by providing reliable information to guide decisions, maximize existing resources, improve health outcomes, and reduce unnecessary costs. The Center specializes in ensuring that diverse and relevant perspectives are considered and appropriate resources are leveraged to strategically address complex policy issues with high-quality evidence and collaboration. The Center is based at Oregon Health & Science University in Portland, Oregon.

Conflict of Interest Disclosures: No authors have conflicts of interest to disclose. All authors have completed and submitted the Oregon Health & Science University form for Disclosure of Potential Conflicts of Interest, and none were reported.
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Review of New Evidence Submitted by Stakeholders

In May 2019, Washington State Health Care Authority adopted a coverage decision on the use of peripheral nerve ablation (PNA) for the treatment of limb pain. The final determination stated that PNA, using any technique, to treat limb pain including for knee, hip, foot, or shoulder due to osteoarthritis or other conditions, is not a covered benefit for adults and children. The Health Technology Clinical Committee (HTCC) decision was based on an evidence review completed by the Center for Evidence-based Policy in 2018. The evidence report addressed 4 key questions:

1. What is the evidence of efficacy and effectiveness for PNA for limb pain compared to other active interventions, placebos, sham procedures, or no treatment?
2. What direct harms are associated with PNA for limb pain compared to other active interventions, placebos, sham procedures, or no treatment?
3. Do important patient efficacy/effectiveness outcomes or direct harms from PNA for limb pain vary by:
   a. Indication
   b. Patient characteristics
4. What are the cost-effectiveness and other economic outcomes of PNA for limb pain compared to other active interventions, placebos, sham procedures, or no treatment?

The PICOS used to guide the review were:

- Population
  - Adults and children with chronic limb pain caused by osteoarthritis or other conditions
- Interventions
  - PNA using any technique
- Comparators
  - Other treatments for limb pain including medication, surgery, behavioral or psychological interventions, physical therapy or other noninvasive nonmedication therapies, placebo, sham procedures, usual care or no specific treatment, and no comparator (for harms only)
- Outcomes
  - Primary outcome of short-term and long-term function measured by a validated method
  - Secondary outcomes of short-term and long-term pain measured by a validated method
  - Harms directly related to the intervention
  - Indirect outcomes of the use of subsequent interventions to control the pain that was the original indication for the initial PNA procedure
  - Cost-effectiveness outcomes (e.g., cost per improved outcome) or cost-utility outcomes (e.g., cost per quality-adjusted life year [QALY], incremental cost-effectiveness ratio [ICER])

The eligible study designs were:

- For Key Questions 1 to 4
  - Randomized controlled trials (RCTs)
o Systematic reviews that included RCTs
• For Key Questions 2 and 3, additional studies/data for harms
  o Nonrandomized comparative studies, if evidence for the intervention or device was included in Key Question 1
  o Nonrandomized studies without a comparator for harms only, if evidence for the intervention was included in Key Question 1
  o Governmental or other registries and databases containing reports of procedure-related harms or device recalls (e.g., FDA MAUDE database, FDA Medical Device Recall database)
• For Key Question 4, additional studies
  o Cost-effectiveness studies and other formal comparative economic evaluations
  o Systematic reviews of cost-effectiveness studies and other formal comparative economic evaluations

In March 2020, stakeholders submitted 31 unique references\(^3\)–\(^33\) related to the Washington State Health Care Authority HTCC coverage decision.\(^1\) We retrieved and reviewed the full-text versions of these reference in order to:
• Assess each of the newly submitted references against the eligibility criteria from the 2018 evidence review on PNA.\(^2\)
• Make an assessment of the potential impact on the final coverage decision.\(^1\)

Each assessment was done independently by 2 reviewers and any disagreements resolved, with the use of a third reviewer if needed. Full details of the individual study assessment can be seen in the Appendix.

Overall, none of the 31 newly submitted references were assessed as having any substantive impact on the overall quality of the evidence in the 2018 evidence report, nor its conclusions.\(^2\) Only 1 study was assessed as having some possible impact.

Xiao et al.\(^33\) conducted an RCT comparing highly-selective radiofrequency ablation (RFA) with hyaluronic acid injection in 96 adults with osteoarthritis of the knee.\(^33\) We did not conduct a formal assessment of study risk of bias, but generally, the study was not well-reported with key information on randomization, allocation concealment, and baseline patient characteristics missing.\(^33\) Participants in the RFA group had significantly higher levels of function, as measured by the Lysholm Knee Score (LKS), than participants in the hyaluronic acid injection group at 3 days, 3, 6, 9, and 12 months after treatment.\(^33\) Participants in the RFA group also had significantly less pain than participants in the hyaluronic acid injection group at 3 days, 3, 6, 9, and 12 months after treatment.\(^33\) Xiao et al.\(^33\) reported no adverse events in the RFA group, but no details were provided.

In the 2018 evidence report.\(^2\) 1 RCT was included comparing the same 2 interventions. Ray et al.\(^34\) evaluated RFA compared with hyaluronic acid injection in 24 adults with osteoarthritis of the knee.\(^34\) The trial was assessed as being at high risk of bias because of limited reporting of key
trial components (e.g., randomization, allocation concealment, and method of analysis), the small sample size, and few details on the baseline patient characteristics.\textsuperscript{34} Participants in the RFA group had significantly better levels of function, as measured by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), than participants in the hyaluronic acid injection group at weeks 1, 4, and 12.\textsuperscript{34} Participants in the RFA group also had significantly lower levels of pain than participants in the hyaluronic acid injection group at weeks 1, 4, and 12.\textsuperscript{34} No adverse events were observed in either treatment group (further details were not provided).\textsuperscript{34} In the prior evidence report, a review of clinical guidelines found that viscosupplementation products containing hyaluronic acid are generally not recommended because they have not been found to be effective.\textsuperscript{2}

When considering the 2018 evidence report,\textsuperscript{2} the HTCC gave greatest weight to the evidence it determined to be the most valid and reliable for the assessment of PNA for limb pain.\textsuperscript{1} The new trial by Xiao et al.\textsuperscript{33} has significant flaws that are likely to lead to a high risk of bias assessment.\textsuperscript{33} Although the sample size is larger and the study duration is longer than the single RCT considered by the HTCC, because of the potential risk of bias and the suboptimal comparator, this new evidence is unlikely to change the overall quality of evidence (GRADE rating).
References


## Appendix: References Submitted by Stakeholders

<table>
<thead>
<tr>
<th>Submitted Reference</th>
<th>Potential Impact on Final Decision</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdelaziz et al., 2019&lt;sup&gt;3&lt;/sup&gt;</td>
<td>No impact</td>
<td>A noncomparative study of an intervention without any eligible effectiveness evidence; this study would therefore not be eligible</td>
</tr>
<tr>
<td>Ahmed and Arora, 2018&lt;sup&gt;4&lt;/sup&gt;</td>
<td>No impact</td>
<td>A case series with fewer than 10 cases (N = 8)</td>
</tr>
<tr>
<td>Ajrawat et al., 2020&lt;sup&gt;5&lt;/sup&gt;</td>
<td>No impact</td>
<td>A systematic review with searches up to August 2018 (search dates in the WAHTA Final Evidence Report were through September and October of 2018)</td>
</tr>
<tr>
<td>Arboleda et al., 2019&lt;sup&gt;6&lt;/sup&gt;</td>
<td>No impact</td>
<td>Not a publication type of interest (narrative review)</td>
</tr>
<tr>
<td>Conger et al., 2019&lt;sup&gt;7&lt;/sup&gt;</td>
<td>No impact</td>
<td>Not a publication type of interest (description of surgical technique)</td>
</tr>
<tr>
<td>Davis et al., 2019&lt;sup&gt;8&lt;/sup&gt;</td>
<td>No impact</td>
<td>This study reported longer-term outcomes from an RCT included in the WAHTA Final Evidence Report. After first 6 months patients were able to crossover, with the longer-term effectiveness outcomes therefore not being comparative. At 12 months, 81 adverse events occurred among the original cooled radiofrequency ablation (CRFA) group between 6-12 months. This would only strengthen the Washington Health Technology Clinical Committee decision not to cover.</td>
</tr>
<tr>
<td>Desai et al., 2019&lt;sup&gt;9&lt;/sup&gt;</td>
<td>No impact</td>
<td>The 12 month economic outcomes are based on the follow-up by Davis et al.&lt;sup&gt;8&lt;/sup&gt; and as described above, the 6 to 12 month outcomes are primarily per protocol.</td>
</tr>
<tr>
<td>Fonkoue et al., 2019&lt;sup&gt;10&lt;/sup&gt;</td>
<td>No impact</td>
<td>Anatomical study</td>
</tr>
<tr>
<td>Fuchsberger et al., 2018&lt;sup&gt;11&lt;/sup&gt;</td>
<td>No impact</td>
<td>Excluded from the WAHTA Final Evidence Report as no outcomes of interest</td>
</tr>
<tr>
<td>Goldman et al., 2018&lt;sup&gt;12&lt;/sup&gt;</td>
<td>No impact</td>
<td>Not a publication type of interest (narrative review)</td>
</tr>
<tr>
<td>Hong et al., 2019&lt;sup&gt;13&lt;/sup&gt;</td>
<td>No impact</td>
<td>A systematic review with searches up to January 2018 (search dates in the WAHTA Final Evidence Report were through September and October of 2018)</td>
</tr>
<tr>
<td>House et al., 2019&lt;sup&gt;14&lt;/sup&gt;</td>
<td>No impact</td>
<td>Not a publication type of interest (letter)</td>
</tr>
<tr>
<td>Submitted Reference</td>
<td>Potential Impact on Final Decision</td>
<td>Rationale</td>
</tr>
<tr>
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</tr>
<tr>
<td>Hunter et al., 2020</td>
<td>No impact</td>
<td>As noted above, this study allowed patients to crossover after the initial 6 months so randomization was not preserved. Harms in original group were reported out to 24 months, observing no serious adverse events. However, no further details were reported.</td>
</tr>
<tr>
<td>Jadon et al., 2018</td>
<td>No impact</td>
<td>Not a comparison of interest (monopolar vs. bipolar RFA)</td>
</tr>
<tr>
<td>Jamison and Cohen, 2018</td>
<td>No impact</td>
<td>A systematic review with searches up to February 2018 (search dates in the WAHTA Final Evidence Report were through September and October of 2018)</td>
</tr>
<tr>
<td>Kadiyala and Lombardi, 2017</td>
<td>No impact</td>
<td>Excluded from the WAHTA Final Evidence Report as not a publication type of interest (narrative review)</td>
</tr>
<tr>
<td>Kapural et al., 2019</td>
<td>No impact</td>
<td>Noncomparative retrospective study (N = 275) No harms were reported</td>
</tr>
<tr>
<td>Kidd et al., 2019</td>
<td>No impact</td>
<td>Not a publication type of interest (narrative review)</td>
</tr>
<tr>
<td>Kim et al., 2019</td>
<td>No impact</td>
<td>Not a comparator of interest (ultrasound vs. fluoroscopy-guided genicular nerve)</td>
</tr>
<tr>
<td>Konya et al., 2020</td>
<td>No impact</td>
<td>Noncomparative (N = 48) with some mention of harms. No serious adverse events were observed. Overall, 2 patients had bruising and 1 patient had paresthesia; both are adverse events already noted well in prior literature included in the evidence report.</td>
</tr>
<tr>
<td>McCormick et al., 2018</td>
<td>No impact</td>
<td>Excluded from the WAHTA Final Evidence Report as no outcomes of interest</td>
</tr>
<tr>
<td>Milone et al., 2018</td>
<td>No impact</td>
<td>Not a publication type of interest (narrative review)</td>
</tr>
<tr>
<td>O'Shaughnessy et al., 2018</td>
<td>No impact</td>
<td>A noncomparative study of an intervention without any eligible effectiveness evidence; this study would therefore not be eligible.</td>
</tr>
<tr>
<td>Orhurhu et al., 2019</td>
<td>No impact</td>
<td>A systematic review with searches up to February 2018 (search dates in the WAHTA Final Evidence Report were through September and October of 2018)</td>
</tr>
<tr>
<td>Peltz et al., 2019</td>
<td>No impact</td>
<td>A noncomparative study of an intervention without any eligible effectiveness evidence; this study would therefore not be eligible.</td>
</tr>
<tr>
<td>Picart et al., 2019</td>
<td>No impact</td>
<td>A noncomparative study of an intervention without any eligible effectiveness evidence; this study would therefore not be eligible.</td>
</tr>
<tr>
<td>Roberts et al., 2019</td>
<td>No impact</td>
<td>A systematic review on the anatomic innervation of the knee, not a review of effectiveness. As such, this review would not be eligible.</td>
</tr>
<tr>
<td>Strand et al., 2019</td>
<td>No impact</td>
<td>Case report</td>
</tr>
<tr>
<td>Submitted Reference</td>
<td>Potential Impact on Final Decision</td>
<td>Rationale</td>
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<td>-----------------------------</td>
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<tr>
<td>Vanden Berge et al., 2017(^{31})</td>
<td>No impact</td>
<td>A systematic review with searches up to June 2016 (search dates in the WAHTA Final Evidence Report were through September and October of 2018)</td>
</tr>
<tr>
<td>Walega et al., 2019(^{32})</td>
<td>No impact</td>
<td>RCT of image-guided GN-RFA vs. simulated sham (N = 70) prior to total knee replacement. This study, although eligible, shows no significant difference between the RFA and sham procedure, in terms of function or pain at any time point. The results would have no impact on the conclusions of the evidence report or the HTCC decision.</td>
</tr>
<tr>
<td>Xiao et al., 2018(^{33})</td>
<td>Unlikely to have impact</td>
<td>RCT (N = 96) comparing highly-selective knee RFA with hyaluronic acid injection. The 2018 evidence report included 1 RCT comparing knee RFA with hyaluronic acid injection. This new study would not change the overall quality of evidence or the conclusions of the report.</td>
</tr>
</tbody>
</table>
Petition for technology review or re-review

Your name: Alan R Peper Jr
Mailing address: 
E-mail address: apeperjr@gmail.com
Telephone number: 

Note: Not all questions will apply to all technologies. For assistance email the HTA program at the address above, or phone (360) 725-5126 (TTY 711).

Technology topic 20170120B – Artificial disc replacement – Re-review

If this topic has been reviewed by the health technology assessment program in the past, skip to question 7, below. See technologies HTCC has previously reviewed.

1. Background information
   - Does this technology have FDA approval? ☐ Yes ☐ No
   - When was this technology approved?
   - For what indications has FDA approved this technology?
   - Why do you believe this technology merits consideration for assessment?
   - Proposed research questions.

   Click here to enter text.

2. Potential patient harm(s) or safety concerns
   - What is the potential for patient harm, related to use of this technology?
   - What are the likelihood and severity of the potential harms or adverse outcomes that may result from recommended use of this technology?
   - Are there significant potential harms associated with this technology compared to alternatives?

   Click here to enter text.

3. Therapeutic efficacy, effectiveness or diagnostic accuracy
   - What is the potential effectiveness of this technology on the indicated clinical condition? (e.g., prevent/reduce mortality; increase quality of life)
   - How are indicated conditions diagnosed? Is there a consensus on diagnosis?
• For diagnostic technologies: Is this technology compared to a “gold standard” technology?
• What is the diagnostic accuracy or utility?
• What published, peer-reviewed literature documents the efficacy of this technology or the science that underlies it? Please enclose publications or bibliography.

Click here to enter text.

4. Estimated total cost per year

• What are the direct health care costs of this technology (annual or lifetime)?
• What is the potential cost-effectiveness of this new technology compared with other alternatives?
• Which private insurers reimburse for use of this technology? Please provide contact information and phone numbers.

Click here to enter text.

5. Secondary considerations

• **Number of persons affected** - What are the numbers of people affected by this technology in the State of Washington?
• **Severity of condition(s)** - What is the severity of the condition treated by this technology? Does it result in premature death; short or long term disability? How would this technology increase the quality of care for the State of Washington?
• **Policy-related urgency** - Is there a particular urgency related to this technology? Is it new and rapidly diffusing? How long has this technology been in use? Is there a standard of care? Is this technology or proposed use(s) controversial?
• **Potential or observed variation** - What is the observed or potential for under, or overuse of this technology? Are there any variations in use or outcomes by region or other characteristics?
• **Special populations and ethical concerns** - Is use limited to small populations; what characteristics are present (e.g., race, ethnicity, religion, rare condition, socioeconomic status) that may impact policy decision?

Click here to enter text.

6. References

• List other organizations that have completed technology assessments on this topic (please provide date of technology assessments and links).
• Cite any Center for Medicare and Medicaid Services (CMS) national coverage decision on this topic and the date issued.
• Provide list of key references used in preparing this petition.
7. For re-review petitions only

Re-review of a technology requires new evidence that could change a previous decision. What new evidence should be considered? Please provide specific publication information and/or references.

Artificial Disc Replacement / Total Disc Replacement for the Lumbar Spine – 20170120B

The current decision by the Washington State Health Care Authority (HCA) was adopted March 17, 2018 (20170120B). However, since that time additional research, and support for Artificial Disc Replacement (ADR) as a standard of care has continued to be introduced.

A research study by Mattei, T.A., Beer, J., Teles, A.R., et. al., (2017) established ADR as having “significantly lower VAS pain scores than patients who received ALIF starting at 6 weeks (P < .001) and continuing through one year postoperatively (P = .007). Patients submitted to TDR also presented significantly lower ODI disability scores at all time points. There was a significant difference in the number of days to return to work, with TDR patients returning to work on average 65 days sooner than ALIF patients (P = .011

And, in 2018 Ziegler, F., Gornet, M.F., Ferko, N., et. al., (2018) completed a meta-analysis of 4 studies. “(ADR) patients had a significantly greater likelihood of ODI success (RR 1.0912; 95% CI 1.0004, 1.1903) and patient satisfaction (RR 1.13; 95% CI 1.03, 1.24) and a significantly lower risk of reoperation (RR 0.52; 95% CI 0.35, 0.77) than fusion patients. There was no association with improvement in back pain scores whether patients received TDR or fusion (MD −2.79; 95% CI −8.09, 2.51). Most results were robust to sensitivity analyses. Results for ODI success and patient satisfaction were sensitive to different outcome definitions but remained in favor of TDR. This study concluded stating that “TDR is an effective alternative to fusion for lumbar DDD. It offers several clinical advantages over the longer term that can benefit the patient and reduce health care burden, without additional safety consequences.

Additionally, many insurance providers consider Artificial Disc Replacement medically necessary. As an example, United Healthcare, a provider of the Apple Health Community plan, considers ADR medically necessary, but is unable to provide this service to its members due to the HCA’s current stance. Their decision to approve ADR can be found on page 13 of their Medical Policy document – CS121.L. Page 13 is excerpted below:

Lumbar Artificial Disc

Li et al. (2018) conducted an updated systematic review and meta-analysis to compare the efficacy and safety of total disc replacement (TDR) versus lumbar fusion. A total of 7 randomized controlled trials (RCTs) (1706 patients) were included. Patients in TDR group had significant improvements in
ODI, VAS scores, complication rates and had a greater percentage of being satisfied with the surgery. In addition, the clinical success in TDR group was higher than fusion group. TDR treated patients had shorter operating time and shorter duration of hospital stay. There was no clinical significance between two groups at blood loss, work status and reoperation rate. The authors concluded that the meta-analysis showed that TDR proved superiorities in improved clinical success, reduced pain, patients’ satisfaction, shortened hospital stay and operating time and lessened complication rate. But there were no benefits in blood loss. Mu et al. (2018) conducted a systematic review and meta-analysis to compare the efficacy and safety of lumbar total disc replacement (TDR) with the efficacy and safety of anterior lumbar interbody fusion (ALIF) for the treatment of lumbar degenerative disc disease (LDDD). Six studies (5 randomized controlled trials (RCT) and 1 observational study) involving 1093 patients were included. Operative time, intraoperative blood loss, hospital stay, complications and reoperation rate were without significant clinical difference between groups. Patients in the TDR group had higher postoperative satisfaction and, better improvements in ODI, VAS and postoperative lumbar mobility than did patients in the ALIF group. The authors concluded that TDR had significant reduction in clinical symptoms, improved physical function and preserved range of motion for the treatment of LDDD compared to ALIF. TDR may be an ideal alternative for the selected patients with LDDD in the short-term. More studies that are well-designed, that are of high-quality and that have larger samples are needed to further evaluate the efficacy and safety of TDR at the long-term follow-up.

Zigler et al. (2018b) conducted a meta-analysis to evaluate the long-term efficacy and safety of total disc replacement (TDR) compared with fusion in patients with functionally disabling chronic low back pain due to single-level lumbar degenerative disc disease (DDD) at 5 years. PubMed and Cochrane Central Register of Controlled Trials databases were searched for randomized controlled trials reporting outcomes at 5 years for TDR compared with fusion in patients with single-level lumbar DDD. Outcomes included Oswestry Disability Index (ODI) success, back pain scores, reoperations, and patient satisfaction. The meta-analysis included 4 studies. TDR patients had a significantly greater likelihood of ODI success and patient satisfaction and a significantly lower risk of reoperation than fusion patients. Long-term improvement in back pain scores were similar between TDR and fusion. Results for ODI success and patient satisfaction were sensitive to different outcome definitions but remained in favor of TDR. The authors concluded that TDR is an effective alternative to fusion for lumbar DDD.

Zigler et al. (2018a) conducted a network meta-analysis to compare the efficacy and safety of total disc replacement, lumbar fusion, and conservative care in the treatment of single-level lumbar degenerative disc disease (DDD). Outcomes measured at 2 year follow-up included Oswestry Disability Index (ODI) success, back pain score, patient satisfaction, employment status, and reoperation. Randomized controlled trials that included patients with discogenic low back pain due to single-level lumbar DDD, who were unresponsive to conservative therapy, were considered if they compared a TDR device (Charite, ProDisc-L, Maverick, Kineflex-L, Flexicore, activL) with other total disc replacement devices, fusion (anterior, posterior, or circumferential) or conservative care (rehabilitation, exercise). Six studies were included (1417 participants). Evidence from several studies shows that arthroplasty is superior to fusion and conservative care. The authors concluded that overall, the activL total disc replacement device had the most favorable results for ODI success, back pain, and patient satisfaction. Results for employment status and reoperation were similar across therapies.

A systematic review was conducted by Cui et al. (2018) to evaluate the mid- to long-term clinical outcomes of artificial total disc replacement (TDR) for lumbar degenerative disc diseases. Thirteen
studies, including eight prospective studies and five retrospective studies, were included. A total of 946 patients were identified who reported at least 3 years of follow-up results. A total of 1048 prostheses were implanted, single-segment TDRs were performed on 872 patients, and multi-segment TDRs were performed on 88 patients. A total of 369 prostheses were implanted into level L4/L5, 543 prostheses were implanted into level L5/S1, and 51 were implanted into other segments. Patients with lumbar TDR demonstrated significant improvements in VAS scores of 51.1 to 70.5% and of -15.6 to -44.4 for Oswestry disability index (ODI) scores at the last follow-up. Patient satisfaction rates were reported in eight studies and ranged from 75.5 to 93.3%. Complication rates were reported in 11 studies, ranging from 0 to 34.4%. The overall reoperation rate was 12.1% (119/986), ranging from 0 to 39.3%, with eight of the 13 studies reporting a reoperation rate of less than 10%. The authors concluded that the study shows that lumbar TDR effectively resulted in pain relief and an improvement in quality of life at mid- to long-term follow-up. Complication and reoperation rates were acceptable. This study did not provide sufficient evidence to show that lumbar TDR is superior to fusion surgery. A greater number of high-quality randomized controlled trials (RCTs) are needed.

A 2018 ECRI Health Technology Assessment Product Brief for ActivL artificial disc identified evidence from 1 systematic review with a network meta-analysis of 6 randomized controlled trials (RCTs) indicating that the activL artificial disc reduced back pain and improved the ability to perform daily tasks more than Prodisc-L® or Charite total disc replacements (TDR); reoperation rates were similar. Evidence on the indirect comparisons with fusion and conservative treatment was too weak to permit conclusions. The report concludes that findings warrant confirmation in additional RCTs comparing activL with other TDR systems and RCTs comparing activL with lumbar fusion and reporting longer-term outcomes (>3 years), but none are ongoing (ECRI, 2018).

A prospective study was performed by Scott-Young et al. (2018) to evaluate clinical and patient outcomes post combined total disc arthroplasty (TDA) and anterior lumbar interbody fusion (ALIF), known as hybrid surgery for the treatment of multilevel symptomatic degenerative disc disease (DDD). A total of 617 patients underwent hybrid surgery for chronic back pain between July 1998 and February 2012. Visual Analog Pain Scale for the back and leg were recorded along with the Oswestry Disability Index and Roland Morris Disability Questionnaire. The authors report both statistically and clinically significant reductions were seen in back and leg pain, which were sustained for at least 8 years post surgery. Significant improvements were also seen in self-rated physical disability and function, also maintained for at least 8 years. Patient satisfaction was rated as good or excellent in >90% of cases. They concluded that the results of this study suggest TDA with ALIF is a suitable option for patients suffering chronic back and leg pain secondary to multilevel DDD when conservative management fails. A limitation to the present study is that not all patients experienced leg pain preoperatively and, therefore, their baseline score would be zero. The findings of this study need to be validated by well-designed studies.

Formica et al. (2017) performed a systematic review to summarize the available evidence about total lumbar disc replacement (TDR), focusing on clinical and functional outcomes, comparison with fusion surgery results, rate of complications and influence on sagittal balance. Fifty-nine studies were included. Clinical and functional scores showed statistically significant improvements to baseline. There was no significant difference between TDR groups and fusion groups. There were similar rates of complications between the two surgical procedures. TDR showed significant safety and efficacy, comparable to lumbar fusion. The authors summarized that the major advantages of a lumbar TDR over fusion included maintenance of segmental motion and the restoration of the disc
height, allowing patients to find their own spinal balance. The authors concluded that disc arthroplasty could be a reliable option in the treatment of degenerative disc disease. They recommended further studies with larger groups of patients and a longer follow-up period to better evaluate the outcomes and safety of lumbar TDR.

A systematic review of overlapping meta-analyses comparing total disc replacement (TDR) with fusion for treating lumbar degenerative disc disease (LDDD) was conducted by Ding et al. (2017). Five meta-analyses only comprising randomized controlled trials (RCTs) were included. This systematic review showed that there are conflicting results among these overlapping meta-analyses. Based on this systematic review, the best available evidence indicated that TDR compared with fusion for LDDD had statistically, but not clinically, significant superiority regarding disability, pain relief, and quality of life in a selected group of patients in the short term. The prevention of adjacent segment and facet joint degeneration, as the primary reason for adopting TDR noted by the manufactures, was not appropriately evaluated. This study could not assess the long-term results, because almost all of the primary studies only have data for 2 years. The authors concluded the current best available evidence suggests that TDR may be an effective technique for the treatment of selected patients with LDDD, and is at least equal to lumbar fusion in the short term. However, considering that disadvantages may appear after years, spine surgeons should be cautious about performing TDR on a large scale.

A multicenter randomized controlled trial was conducted by Furunes et al. (2017) to assess the long-term relative efficacy of lumbar total disc replacement (TDR) compared with multidisciplinary rehabilitation (MDR). One hundred seventy-three patients with chronic low back pain (LBP) and localized degenerative changes in the lumbar intervertebral discs were randomly assigned treatment. The primary outcome was self-reported physical function (Oswestry Disability Index [ODI]) at 8-year follow-up in the intention-to-treat population. Secondary outcomes included self-reported LBP (visual analogue scale [VAS]), quality of life (EuroQol [EQ-5D]), emotional distress (Hopkins Symptom Checklist [HSCL-25]), occupational status, patient satisfaction, drug use, complications, and additional back surgery. Seventy-seven patients (90%) who were randomized to surgery and 74 patients (85%) randomized to rehabilitation responded at 8-year follow-up. Mean improvement in the ODI was 20.0 points in the surgery group and 14.4 points in the rehabilitation group. Mean difference in favor of surgery on secondary outcomes were 9.9 points on VAS and 0.16 points on HSCL-25. There were 18 patients (24%) in the surgery group and 4 patients (6%) in the rehabilitation group who reported full recovery. There were no significant differences between the groups in EQ-5D, occupational status, satisfaction with care, or drug use. Forty-three of 61 patients (70%) in the surgery group and 26 of 52 patients (50%) in the rehabilitation group had a clinically important improvement (15 ODI points or more) from baseline. Twenty-one patients (24%) randomized to rehabilitation had crossed over and had undergone back surgery and 12 patients (14%) randomized to surgery had undergone additional back surgery. One serious adverse event after disc replacement was reported. The authors concluded that long-term improvement can be expected after both disc replacement and MDR. The difference between groups is statistically significant in favor of surgery, but smaller than the prespecified clinically important difference of 10 ODI points that the study was designed to detect. Future research should aim to improve selection criteria for disc replacement and MDR.

A prospective, multicenter, randomized, controlled, investigational device exemption study with 5-year follow-up was conducted by Yue and Garcia (2017) to compare the safety and effectiveness of lumbar total disc replacement with activL (Test group) or ProDisc-L or Charité (Control group) in the
treatment of patients with symptomatic, single-level degenerative disc disease. Patients who failed at least 6 months of nonsurgical management were randomly allocated to treatment with the Test device (n=218) or Control devices (n=106). At 5-year follow-up, 185 Test patients and 90 Control patients provided 5-year follow-up data. Device effectiveness outcomes were comparable between Test and Control devices. Reductions in back pain severity were reported in 88% of Test patients and 90% of Control patients. Oswestry Disability Index (ODI) improvement was reported in 83% and 86% of patients, respectively. Patient satisfaction was very high in both groups (96% vs 94%). No significant differences were observed between groups in radiographic outcomes, including disc height, disc angle, flexion-extension ROM, translation ROM, and lateral rotation. Lack of a serious adverse event through 5 years was 58% in Test patients and 40% in Control patients. The authors concluded that total disc replacement is safe and effective for the treatment of symptomatic lumbar degenerative disc disease and is maintained through 5 years.

A prospective observational cohort study was conducted by Laugesen et al. (2017) to determine the long-term clinical results and prosthesis survival in patients treated with lumbar total disc replacement (TDR). Fifty-seven consecutive patients treated with TDR from 2003 to 2008 were invited to follow-up at a mean 10.6 years post-operatively and complete a Visual Analog Scale (VAS) for back and leg pain, the Dallas Pain Questionnaire (DPQ), and the Short Form36. These surveys were also administered to the subjects before their index TDRs. Data on reoperation were collected from the patients’ medical records. The authors report that there was a significant improvement in VAS and DPQ in the entire cohort. Nineteen patients (33%) had a revision fusion surgery after their index TDR. Patients who had revision surgery had statistically significant worse outcome scores at last follow-up than patients who had no revision. Thirty patients (52.6%) would choose the same treatment again if they were faced with the same problem. The authors concluded that this study demonstrated significant improvement in long-term clinical outcomes and two-thirds of the discus prostheses were still functioning at follow-up. They also acknowledge that there is still a lack of well-designed long-term studies, thus requiring further investigation.

A systematic review and meta-analysis was performed by Lackey et al. (2016) to assess the effect of hybrid constructs which involve a total disc arthroplasty (TDA) with stand-alone anterior lumbar interbody fusion (ALIF) versus non-hybrid constructs including posterior transpedicular fixation or multi-level stand-alone ALIF as a surgical intervention for degenerative disc disease (DDD) in the lumbar spine. Primary outcomes analyzed included the Oswestry Disability Index (ODI) and the Visual Analog Scale (VAS) for back pain. Three studies met inclusion criteria. When comparing hybrid constructs to multi-level TDA or lumbar fusion (LF) improvements in back pain were found with a VAS back pain score reduction of 1.38 postoperatively and a VAS back pain score reduction of 0.99 points at 2-years follow-up. Current results slightly favor clinically significant improved VAS back pain score outcomes postoperatively and at 2-years follow-up for hybrid constructs in multi-level lumbar DDD of the spine when compared with non-hybrid multi-level LF or TDA. The authors stated that it cannot be concluded that a hybrid construct is superior to multi-level LF or TDA based on this meta-analysis and recommend further prospective studies to delineate best practice in the management of degenerative disc disease of the lumbar spine.

Pimenta et al. (2016) conducted a prospective nonrandomized single-center study to analyze results of XL-TDR for the treatment of symptomatic degenerative disc disease. Sixty cases were enrolled. Eleven of 60 patients (18%) had not completed at least a 5-year follow-up (FUP), and 49 were enrolled in the
The mean FUP was 93 months. End points included visual analog scale (VAS) and Oswestry Disability Index (ODI) questionnaires, radiographic outcomes (radiographs and CT) such as heterotopic ossification (HO) and maintenance of disc motion, complications, reoperation, and heterotopic ossification grades. All but 3 patients stood up/walked at the same day. Five levels (10%; 5/53) required fusion. Two cases (4%; 2/49) evolved with adjacent level disease that required surgery. One case required sacroiliac fusion. One partial disc migration was identified. Flexion extension films from 38 levels were available at least at a 5-year FUP. HO grade 0 = 13%; grade I =18%; grade II = 32%; grade III = 16%; grade IV = 21% (8 cases). Most heterotopic ossification cases (85%) occurred in the lateral aspect of the disc space. Patient-reported outcomes showed significant improvement maintained up to a minimum of 5 years. VAS back pain: preoperative 8.5, postoperative early 2.5, and last FUP 3.0. ODI: preoperative 54%, postoperative early 31%, and last FUP 21%. The authors concluded that the data show satisfactory sustained pain relief and improved physical function for the patients and lumbar artificial disc replacement done by the lateral approach seems to be a feasible effective treatment for mild degenerative disc disease. Further research with larger randomized controlled trials is needed to validate these findings.

Garcia et al. (2015) conducted a prospective, multicenter, randomized, controlled, investigational device exemption (IDE) trial to evaluate the comparative safety and effectiveness of lumbar total disc replacement (TDR) in the treatment of patients with symptomatic degenerative disc disease (DDD) who are unresponsive to nonsurgical therapy. The study consisted of patients presenting with symptomatic single-level lumbar DDD who failed at least 6 months of nonsurgical management. They were randomly assigned to treatment with an investigational TDR device (activL®, n = 218) or FDA-approved control TDR devices (ProDisc-L® or Charité®, n = 106). Patient satisfaction with treatment was over 90% in both groups at 2 years. Back pain severity improved 74% with activL® and 68% with controls. Oswestry Disability Index (ODI) improved 67% with activL® and 61% with controls and Physical Component Summary score (88% vs. 81%) favored the activL® group. The percentage of patients working full-time with no restrictions increased from 33% at pretreatment to 57% at 2 years with activL® and from 33% to 49% with control. Return to work was approximately 1 month shorter with activL® versus controls. The percentage of patients with disc height increase >3mm was 94% with activL® and 87% with controls. Change in range of motion in lateral flexion–extension radiographs was statistically greater with activL® compared with controls in segmental rotation and translation but not in lateral rotation on side-bending radiographs. The rate of device-related serious adverse events was lower in patients treated with activL® versus controls (12% vs. 19%). Surgical reintervention rates were comparable (activL 2.3%, control 1.9%). The authors concluded that the single-level activL® TDR is safe and effective for the treatment of symptomatic lumbar DDD through 2 years. The long-term durability of the activL® TDR is unknown and requires further investigation.

Park et al. (2015) conducted a retrospective analysis to evaluate successful outcomes following lumbar total disc replacement (TDR) using ProDisc® II on 54 patients (81 segments) between March 2002 and February 2007. Data was reviewed at 1, 2, 5 and 7 year follow-up. Clinical outcomes were evaluated using Visual Analog Scale (VAS), Oswestry Disability Index (ODI), and subjective satisfaction (4-point scale). Radiographic results included segmental range of motion (ROM). Total VAS scores decreased significantly at postoperative 1 year and 2 year, compared with preoperative VAS score. Although total VAS scores increased until the last follow-up, they remained significantly lower than the preoperative value. All postoperative ODI scores at any follow-up time were significantly lower than the baseline value. There was significant increase in ODI scores between 2-year and last follow-up. The final range of motion (ROM) was shown to be lower than the
preoperative ROM and lumbar lordosis was increased and well-maintained during all postoperative follow-up times. Five patients (9.3%) required revision fusion surgeries.

An August 2015 Hayes Medical Technology assessment evaluated 7 randomized controlled trials (RCTs), 1 nonrandomized trial, and 6 uncontrolled studies with long-term (7 to 17 years) results published between 2002 through July 2015. A total of 2882 patients who underwent one or two level disc replacement treatment were included. The findings suggest that 1-level lumbar disc replacement (LDR) is comparable in efficacy and safety to fusion for the treatment of symptomatic degenerative disc disease in selected patients who have failed conservative treatment. Questions remain regarding the long-term safety of lumbar disc replacement and there is insufficient evidence comparing LDR with continued treatment with more conservative nonsurgical treatment options.

A July 2017 updated cumulative literature search retrieved eight abstracts, including 2 prospective randomized trials (RCTS); 1 follow-up to a multicenter randomized controlled trial; 1 prospective nonrandomized single-center study; 1 comparison study; 1 prospective observational cohort study; 1 systematic review and meta-analysis; and 1 systematic review. The available RCTs provided moderate-quality evidence that 1-level lumbar total disc replacement (LTDR) is comparable to fusion for the treatment of symptomatic degenerative disc disease (DDD) in highly selected patients who have failed conservative treatment. They found insufficient evidence to determine whether motion preservation with LTDR will prevent symptomatic adjacent segment DDD. There was insufficient evidence investigating LTDR for the treatment of 2-level DDD. The report concluded that further longer-term follow-up studies are required to determine whether LTDR poses any additional risk compared with fusion beyond 5 years.

A Cochrane review (Jacobs, et al., 2012) was conducted to determine how total disc replacement compared with other treatments for chronic low back pain. The review included seven randomized trials involving 1474 subjects in total, and involved the use of four discs: Charite®, Maverick®, Prodisc-L®, and Flexicore®. Six of the trials compared disc replacement to lumbar fusion and one compared disc replacement to nonsurgical treatment consisting of a rehabilitation protocol with cognitive treatment and physical therapy. Follow-up was 24 months in all studies with the exception of one which was five years. The subjects who had disc replacement surgery had slightly better back pain and function outcome scores compared to those who had fusion surgery; the differences did not appear clinically significant. The studies did not demonstrate any other benefit and did not provide any information regarding longterm risks. As a result, the review concluded the spine surgery community should be cautious with regards to adopting the technology on a large scale; long-term outcomes are lacking. Pain relief outcomes are short-term and studies evaluating adjacent segment degeneration and facet joint degeneration are lacking.

In 2011 Delamatter et al. published the results of a prospective randomized multicenter FDA IDE trial evaluating the ProDisc-L® compared to circumferential fusion for two-level DDD. Reported outcomes included patient selfassessments, physical, neurological and radiograph assessment preoperatively and six weeks, three, six, twelve, eighteen and twenty-four months postoperatively. Although ODI scores significantly improved in both groups from preoperative to postoperative, results were significantly better in the total disc group). A significant reduction in narcotic usage was also reported for the disc group. In the authors opinion two-level lumbar disc replacement using the ProDisc-L® device was a viable alternative to lumbar arthrodesis for the treatment of two-level disc disease.
Kim et al. (2007) completed a prospective controlled study of 32 patients who underwent lumbar total disc replacement using the ProDisc® II prosthesis. Patients were monitored for 24 months. Nineteen patients had single level total disc replacements (TDR), while 11 patients had TDR at two levels. Radiographic documentation of each patient's range of motion (ROM) was obtained prior to and every 6 months following TDR. Differences between these measures were compared and the outcomes were reported using degrees as a control measure. Visual analog and disability indexes improved significantly during the follow up period. ROM improved within the first 6 months at levels L3-4 and L4-5 being noted. ROM decreased following TDR at the L5-S1 level, with no significant improvement noted at any time. The level of the TDR was found to be a potential negative factor in the minimal gains that were achieved in ROM.

A retrospective study by Yaszay et al. (2008) of 42 patients enrolled in a prospective randomized FDA ProDisc®-L trial, were analyzed to determine factors that could influence motion and patient satisfaction following total disc replacement (TDR) at L4/5 or L5/S1. The patients selected received a TDR at L4/5 or L5-S1. Pre- and postoperative disc height and range of motion (ROM) were measured from standing lateral and flexion-extension radiographs. Anterior and posterior disc heights increased; however, the patients' ROM had decreased. Threshold factors (i.e., anterior and posterior disc heights) that were analyzed showed patients with <9 mm of anterior disc height had an increased ROM of 2.2°of disc height had a -2.2 decrease in their ROM. These findings were considered significant. While improvements were noted based on patient reported visual analog scale scores and Oswestry Disability Index measures, no significant difference between the groups could be found that would explain the average decrease in ROM from 7.0° to 5.7° patients following the use of TDR will determine if the ROM gains will be maintained.

In 2009 the National Institute for Health and Care Excellence (NICE) concluded that the current evidence on the safety and efficacy of prosthetic intervertebral disc replacement in the lumbar spine is adequate to support its use in the lumbar spine. They recommend specialist with expertise in the treatment of degenerative spine disease should be involved in patient selection and the procedure should only be carried out in patients for whom conservative treatment options have failed or are contraindicated.

Professional Societies
American Pain Society Guidelines from the American Pain Society (Chou 2007) found insufficient evidence regarding long-term benefits and harms of disc replacement to support recommendations. Vertebral fusion is the most common surgery for chronic, nonspecific low back pain. Surgical instrumentation (use of pedicle screws or other hardware) increases fusion rates, but it is not known if instrumentation improves clinical outcomes. More research with longer follow-up is needed to determine the appropriate role of artificial disc replacement versus fusion. The authors suggest that vertebral fusion be performed for patients who undergo surgical intervention for chronic low back pain.

International Society for the Advancement of Spine Surgery (ISASS)
A 2015 ISASS Policy Statement states that there is sufficient evidence-based scientific evidence to support the safety and efficacy of single level lumbar total disc replacement for patients meeting well established selection criteria. Inclusion criteria include:
- Skeletally mature patients with degenerative disc disease (DDD) at one level from L3-S1
Patients should have no more than Grade 1 spondylolisthesis at the involved level
- Patients failed at least six months of conservative treatment prior to implantation

North American Spine Society (NASS)
A 2019 NASS Coverage Policy Recommendation states that lumbar artificial disc replacement is indicated for patients with discogenic low back pain who meet all of the following criteria:
- Symptomatic single level lumbar disc disease at L3-L4, L4-L5 or L5-S1 level
- Presence of symptoms for at least 6 months or greater and that are not responsive to multi-modal nonoperative treatment over that period that should include a physical therapy/rehabilitation program but may also include (but not limited to) pain management, injections, cognitive behavior therapy, and active exercise programs
- Any underlying psychiatric disorder, such as depression, should be diagnosed and the management optimized prior to surgical intervention
- Primary complaint of axial pain, with a possible secondary complaint of lower extremity pain

Two-Level
Furthering the support of ADR as a standard of care, in April 2020, the FDA approved two-level ADR (https://centinelspine.press/2020/04/13/centinel-spine-announces-fda-approval-for-two-level-prodisc-l-total-disc-replacement/).

As described above, ADR in many cases is a superior technology to current lumbar fusion. Additionally, in the instances of younger patients, the use of ADR, where motion is preserved, reduces the potential for adjacent disc syndrome. By reducing the potential for adjacent disc syndrome, patients have a better quality of life, and reduce overall medical costs because of lower rates of operation and adjacent levels.

Given the resounding evidence for ADR; clinical stuiies and meta analysis, providers of WA Apple health being proponents of ADR, and the FDA recognizing the benefit of ADR by allowing two-level, I would please request the comittie review ADR and ultimately include it as medically necessary and a covered benefit.


Petition for technology review or re-review

Your name: Jefferson Zigler
Mailing address: [Redacted]
E-mail address: jzigler@si-bone.com
Telephone number: [Redacted]

Note: Not all questions will apply to all technologies. For assistance email the HTA program at the address above, or phone (360) 725-5126 (TTY 711).

Technology topic: Sacroiliac joint fusion (iFuse)

If this topic has been reviewed by the health technology assessment program in the past, skip to question 7, below. See technologies HTCC has previously reviewed.

1. Background information
   - Does this technology have FDA approval? ☐ Yes ☐ No
   - When was this technology approved?
   - For what indications has FDA approved this technology?
   - Why do you believe this technology merits consideration for assessment?
   - Proposed research questions.

   Click here to enter text.

2. Potential patient harm(s) or safety concerns
   - What is the potential for patient harm, related to use of this technology?
   - What are the likelihood and severity of the potential harms or adverse outcomes that may result from recommended use of this technology?
   - Are there significant potential harms associated with this technology compared to alternatives?

   Click here to enter text.

3. Therapeutic efficacy, effectiveness or diagnostic accuracy
   - What is the potential effectiveness of this technology on the indicated clinical condition? (e.g., prevent/reduce mortality; increase quality of life)
   - How are indicated conditions diagnosed? Is there a consensus on diagnosis?
• For diagnostic technologies: Is this technology compared to a “gold standard” technology?
• What is the diagnostic accuracy or utility?
• What published, peer-reviewed literature documents the efficacy of this technology or the
  science that underlies it? Please enclose publications or bibliography.

Click here to enter text.

4. Estimated total cost per year
• What are the direct health care costs of this technology (annual or lifetime)?
• What is the potential cost-effectiveness of this new technology compared with other
  alternatives?
• Which private insurers reimburse for use of this technology? Please provide contact
  information and phone numbers.

Click here to enter text.

5. Secondary considerations
• Number of persons affected - What are the numbers of people affected by this technology in
  the State of Washington?
• Severity of condition(s) - What is the severity of the condition treated by this technology? Does
  it result in premature death; short or long term disability? How would this technology increase
  the quality of care for the State of Washington?
• Policy-related urgency - Is there a particular urgency related to this technology? Is it new and
  rapidly diffusing? How long has this technology been in use? Is there a standard of care? Is this
  technology or proposed use(s) controversial?
• Potential or observed variation - What is the observed or potential for under, or overuse of this
  technology? Are there any variations in use or outcomes by region or other characteristics?
• Special populations and ethical concerns - Is use limited to small populations; what
  characteristics are present (e.g., race, ethnicity, religion, rare condition, socioeconomic status)
  that may impact policy decision?

Click here to enter text.

6. References
• List other organizations that have completed technology assessments on this topic (please
  provide date of technology assessments and links).
• Cite any Center for Medicare and Medicaid Services (CMS) national coverage decision on this
  topic and the date issued.
• Provide list of key references used in preparing this petition.
• Have any relevant medical organizations (e.g., American Medical Association) expressed an opinion on this technology? If so, please provide verification documents and contact names, numbers and links.

• Bibliography or reference list of requestor attached: ☐ Yes    ☐ No

Click here to enter text.

7. For re-review petitions only

Re-review of a technology requires new evidence that could change a previous decision. What new evidence should be considered? Please provide specific publication information and/or references.

This technology (iFuse Implant System) was reviewed by the HCA in 2018 and considered by the HTCC in January 2019. The Final Evidence Report adequately characterized the evidence to that point, however since the time of the Final Evidence Report’s literature search cut-off date (June 20, 2018), the evidence base has now been improved by 16 additional paper publications, ranging from Level I and II paper publications including long-term patient follow-up prospectively out to 5 years (LOIS study) which warrants consideration. Highlights of ongoing evaluation of iFuse patients in the LOIS study include the following:

• Persistent, long-term reduction in SI joint pain and disability
• Persistent, long-term improvements in quality of life
• Absence of device-related serious adverse events
• Absence of surgical revision
• High proportion of patients returned to work
• Marked reduction in proportion of patients using opioids

Also there have been Level III and IV papers published on case series and reviews; as well as economics and other publications such as postmarket surveillance data that would address directly some of the concerns from the HTCC when they convened on this topic in January 2019:

Level I Evidence


Level II Evidence


Level III Evidence (Comparison)


Level IV Evidence (Case Series)


Reviews


Economics


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Additional payers now cover the procedure, which were reviewed by the HTCC including Regence and Premera BCBS. Aetna, Cigna, and UHC all cover this procedure, for chronic SIJ pain patients (not only for trauma or injury patients). Per Jan 2019 HTCC worksheet, here is the revised list of covering payers that may influence future decisions:

Payor Coverage status

Medicare [no NCD; all 7 MACs allow 27279 CPT code]

Medicaid Covered in 44 states; Molina and CareSource have positive coverage policies, too

Aetna covers MIS SIJF for chronic pain; and covers for trauma

Cigna covers MIS SIJF for chronic pain; and covers for trauma

Premera covers iFuse-only for MIS SIJF for chronic pain; and covers for trauma

Regence covers iFuse-only for MIS SIJF for chronic pain; and covers for trauma

Blue Shield CA covers 27279 CPT code (per medical director Dr. Terry Gilliland)

TRICARE covers 27279 CPT code

UnitedHealthcare covers 27279 CPT code (per MCG guidelines)
Lastly, the HTCC meeting discussed issues concerning complications and revisions rates and frequency, as well as revisability of the procedure. We believe there are meaningful updates and data points on each of these topics, making the overall topic worthy of review:


UPDATE: SI-BONE postmarket surveillance of iFuse followed through April 2020 shows revision rate <3% for iFuse and iFuse-3D implants combined (iFuse: 3.3% rev rate; iFuse-3D: 1.1% rev rate). The procedure is highly revisable, and allows for the addition, adjustment, removal-and-replacement, removal-and-repositioning, removal outright, as well as removal with replacement of non-iFuse implants. The HTCC may find these data of interest, especially in light of the considerable time spent to review the revisability and the complications/revisions rates of iFuse overall.

We believe that the HTCC may have reached an alternative conclusion, had the above referenced data points been available at the time of their last meeting convened on this topic in January 2019.
June 12, 2020

Washington Health Care Authority
ATTN: Health Technology Assessment
shtap@hca.wa.gov

VIA ELECTRONIC EMAIL

RE: SI-BONE Petition for Washington HCA Technology Re-review – Sacroiliac Joint Fusion (iFuse)

Dear Josh and the Washington HCA Team,

We appreciate the opportunity to provide updates to the clinical evidence supporting the re-review by the HCA of the sacroiliac joint (SIJ) fusion topic, and specifically the triangular iFuse Implant System used for SIJ fusion procedures to treat individuals with chronic and acute SIJ pain or dysfunction. The landscape of evidence supporting this treatment option has significantly improved since June 2018 and January 2019, the dates of literature cut-off for the Final Evidence Report, and the last meeting by the HTCC on this topic, respectively. Enclosed and below is information and detail in connection with this request, along with new key evidence highlights.

New evidence enclosed: As part of the ongoing research and evaluation of this treatment option, we believe the HCA team should take careful note of Whang et al 2019, the published results from the LOIS study’s 5-year, long-term clinical and radiographic iFuse patient outcomes from a prospective, multicenter trial (ClinicalTrials.gov NCT02270203). Highlights of ongoing evaluation of iFuse patients in the LOIS study include the following:

- Persistent, long-term reduction in SI joint pain and disability
- Persistent, long-term improvements in quality of life
- Absence of device-related serious adverse events
- Absence of surgical revision
- High proportion of patients returned to work
- Marked reduction in proportion of patients using opioids

In addition to Whang et al 2019, the HCA team should consider another 15 new, peer-reviewed scientific articles published on this topic since the last review’s publication cut-off date (after June 20, 2018). This includes Level I through Level IV evidence, as well as other review articles that give helpful context as to the use and acceptance of this treatment option by clinicians around the country and around the world, for patients with acute dysfunction as well as for those with chronic SIJ pain. We have enumerated and listed each of these 15 new articles in our petition for re-review.

In total, the number and type of published papers on this topic (all-time) now includes:

10 – Level I (RCT)
9 – Level II (Prospective)
The publication of 16 new peer-reviewed articles noted above may be enough, by itself, to prompt the HCA’s re-review on this topic. However, in addition, since the time of the last HTCC meeting on this topic in January 2019, additional evidence which would have better informed the committee at that time has now become available. These new data points span the following four (4) key areas of analysis and re-review the HCA should conduct:

1. [Sept 2018 and ongoing] Published data, as well as SI-BONE postmarket surveillance, specific to iFuse complications and revisions rates discussed at the HTCC meeting;
2. [Not yet addressed] Clinical guidelines and evidence-based recommendations from professional spine societies, and more evaluations from health technology assessment organizations;
3. [Jan 2019 and ongoing] More local/area and national U.S. payers that were specifically on the HTCC worksheets in Jan 2019 now cover the procedure than were covering during the initial HTCC meeting, including Premera BCBS, the #1 commercial payer in Washington, with published clinical criteria;
4. [Eff Jan 2020] Oregon Health Authority Health Evidence Review Commission (HERC) finding for CPT 27279 on the Prioritized List of Health Services, and funding (Note 161) for chronic SIJ pain cases, with applicable Oregon Health Plan (OHP) coverage.

1. Revisions and Complications Data

Published in September 2018, Cher at al published on the SI-BONE postmarket surveillance data we maintain in compliance with FDA and other requirements.¹ Researchers found the 1-year cumulative probability of surgical revision was low (1% to 1.5%) for iFuse Implant System devices, notably finding:

✓ No implant breakages or migrations; and
✓ Overall rates of revisions and complications were similar (relatively low in spine and orthopedics), compared to previously published reporting.

As part of its ongoing commitment to the evaluation and quality of iFuse, SI-BONE continues to collect postmarket surveillance data and to track revisions (albeit uncommon), as it is an appropriate, accepted approach to estimating uncommon events. Still, iFuse continues to show

similar or lower rates of revisions as was reported in 2018. As such, this data and these updates should become part of the HCA’s update and re-review on this topic.

2. Clinical Guidelines and Recommendations

Published and updated since the June 2018 cut-off date for the HCA’s Final Evidence Report and review on this topic, the following health technology assessment organizations and clinical practice guidelines development groups have published updates on this topic of SIJ fusion for chronic SIJ pain patients, or otherwise were not reviewed by the HCA in the last review:

2. eviCore updates to MSK Spine Surgery guidelines on sacroiliac joint fusion (published revision Oct 15, 2019, effective 2/14/20)
3. MCG guidelines (provided to SI-BONE by UHC medical director Dr. Wendy MacLeod) on General Recovery Guidelines (GRG) related to SIJ fusion topic.

As it relates to professional societies’ clinical guidelines on this topic, the ISASS Policy Statement and NASS Coverage Policy Recommendations guidelines have both been widely used and cited by the nation’s payers and other HTAs / review organizations as the authoritative, evidence-based opinions directly from spine and orthopedic clinical experts. Both NASS and ISASS want payers and review organizations such as the Washington HCA to have free copies of these recommendations and guidelines. We noticed that the last review by the HCA did not include NASS guidelines, due to the perception of a paywall. In the Clinical Practice Guideline Synthesis section of the report, it was stated incorrectly that the NASS recommendations document was “only available by subscription.” However this is not the case, as NASS specifically states on its website that payers may request a free copy at all times. We highly encourage the HCA to do so. In fact, NASS’ Manager of Health Policy, Amanda Weiler, confirmed in a 6/12/20 email that “any payor can access free NASS Coverage Recommendations by going to this website https://www.spine.org/coverage. Once there, they will click on the ‘Request Access’ button for

2 NICE MTG39 Medical Technologies Guidance: iFuse for treating chronic sacroiliac joint pain: https://www.nice.org.uk/guidance/mtg39
4 SI-BONE has received a letter from UHC medical director Dr. Wendy MacLeod, regarding sacroiliac joint fusion as being covered by UHC per MCG Health (Milliman Care Guidelines). Though the MCG guidelines are proprietary, the letter provided to SI-BONE has been attached for the HCA’s review on this topic, and consideration.
6 NASS Coverage Policy Recommendations: Percutaneous Sacroiliac Joint Fusion (June 9, 2015). https://www.spine.org/Product-Details?productid=%7B9EAC3FC6-6A91-85E1-005056AF031E%7D (NOTE: the CPRs only cost money for industry. Payers (and WA HCA) may receive free access to the coverage recommendations, per NASS’ website); visit https://www.spine.org/coverage for more information.
payors and fill out the form accordingly. Once the form is submitted, we will provide them log-in information to access whichever Coverage Recommendations they select on the form.”

The rigors applied to both NASS’ and ISASS’ processes are well enumerated and relied upon broadly.⁶ We believe it would benefit the HCA to speak directly with leadership at NASS and ISASS, and to learn from them how their guidelines and recommendations coincide with the AGREE tenets. They make public their methodology and would be glad to review it with you live. In our view, both NASS and ISASS meet AGREE’s 23 tenet Items (“check the boxes”), and should be relied upon by the HCA or at least further explored by speaking to NASS and ISASS leadership, as part of the re-review.

3. Payers Now Covering SIJ Fusion for Chronic SIJ Pain Patients

Since the Jan 2019 HTCC meeting, an addition 10 payers across the U.S., several of which operate with some significance in the Washington market, have commenced covering SI joint fusion (with numerous requiring the iFuse triangular implant):

<table>
<thead>
<tr>
<th>Payers Covering (Jan 2019 to Today)</th>
<th>Date Commenced Covering</th>
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</thead>
<tbody>
<tr>
<td>BCBS-MD-CareFirst-MD, DC, VA</td>
<td>1/1/2019</td>
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<tr>
<td>BCBS-NY-Excellus BlueCross BlueShield</td>
<td>1/15/2019</td>
</tr>
<tr>
<td>BCBS-Premera</td>
<td>2/1/2019</td>
</tr>
<tr>
<td>BCBS-AL-Blue Cross and Blue Shield of Alabama</td>
<td>3/18/2019</td>
</tr>
<tr>
<td>BCBS-Wellmark Blue Cross Blue Shield (IA/SD)</td>
<td>7/1/2019</td>
</tr>
<tr>
<td>BCBS-CA-Blue Shield of California</td>
<td>7/3/2019</td>
</tr>
<tr>
<td>BCBS-RI-Blue Cross Blue Shield of Rhode Island</td>
<td>11/1/2019</td>
</tr>
<tr>
<td>CIGNA</td>
<td>12/10/2019</td>
</tr>
<tr>
<td>Oregon Medicaid</td>
<td>1/1/2020</td>
</tr>
<tr>
<td>Aetna</td>
<td>5/28/2020</td>
</tr>
</tbody>
</table>

Among the newly covering 10 payers above, Premera, Cigna and Aetna each have significant numbers of covered lives in Washington. Also, all 7 Medicare Administrative Contractors (MACs) allow coverage for CPT 27279⁷, some with criteria under applicable Local Coverage Determinations (LCDs), and some with no LCDs but which allow coverage of the CPT code.

4. OHA and HERC Analysis of SIJ Fusion Topic

Finally, during nearly the exact same time period the HCA was reviewing this topic, the Oregon Health Authority and HERC also reviewed the SI joint fusion topic. Based on a review of the evidence, HERC determined that minimally invasive joint surgery is effective in reducing pain

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⁷ MACs and current status of CPT 27279 (all cover): CGS L36494; FCSO A55120; NGS L36406; Noridian LCD; Novitas covers; Palmetto A53452; WPS A57596.
and increasing function for patients with SI joint dysfunction. In light of this evidence, HERC created a new line above the funding line for the surgical treatment of SI joint dysfunction using minimally invasive joint surgery. HERC created a guideline to prevent inappropriate use of this procedure.

We appreciate the opportunity to provide our key evidence, our thoughts, and to give inputs into the tremendous and detailed work the HCA team does in reviewing the evidence for this important therapy option. At this time, there are numerous clinical guidelines and assessments of this therapy option; there is independent clinical consensus on the diagnosis of SIJ pain as qualifying as a Clinical Diagnostic Rule 8 for low back pain, with well established clinical criteria required to identify medical necessity for the procedure by payers around the country; and importantly, there are now 83 peer-reviewed, published articles that report on iFuse patient outcomes, safety/complaints, technique, biomechanics, economics, and/or use iFuse data – 16 of which the Washington HCA has yet to review.

In light of all the reasons noted in this letter and in our petition, we believe a re-review of this topic is warranted at this time, and would appreciate your consideration for including it in the next possible upcoming opportunity for calendaring. We think the earliest possible re-review by the Washington HCA on this topic would best serve the approach currently being taken by health care providers, and the clinical need of patients actively seeking this treatment option.

Thank you again, and we look forward to learning the outcome of your re-review of sacroiliac joint fusion and iFuse.

 sincerely,

Jeffrey Zigler
Vice President, Market Access and Reimbursement
SI-BONE, Inc.

Attachments:
1. WA HCA petition for technology re-review
2. Bibliography of all known iFuse SI joint fusion publications. Includes links to open source papers where available.
3. A copy of SI-BONE’s literature synopsis and Clinical Value dossiers for iFuse Implant System®
4. A copy of the latest LOIS study results paper, Whang 2019 (Level II evidence), showing excellent 5-year results for iFuse patients.
5. Email exchange with NASS’ Manager of Health Policy, Amanda Weiler in re: WA HCA requesting a copy of the NASS CPR on sacroiliac joint fusion topic.
6. A copy of the letter from UHC medical director Dr. Wendy MacLeod referencing the MCG-GRG guidelines on this topic, which confers coverage by UHC for SIJ fusion procedures for treatment of chronic SIJ pain.

8 Laslett M. Evidence-based diagnosis and treatment of the painful sacroiliac joint. J Man Manip Ther. 2008;16(3):142-152.
<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
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<td>101</td>
<td>Dengler 2016</td>
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<td></td>
<td>Prospective, multicentric, randomized controlled trial (iFuse)</td>
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Sorted Newest to Oldest within Category

iFuse Implant System (83)

Other

Biomechanics

Economics

Reviews

Level I

Level II

Level III

Level IV
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<tr>
<td></td>
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<td>Prospective multicenter, randomized controlled trial (INSITE, ClinicalTrials.gov NCT01681004), MIS SI joint fusion (iFuse) vs. Non-surgical management (NSM), 1-year f/u.</td>
<td>Neurosurgery. 2015;77:674-91.</td>
<td>II</td>
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<td></td>
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I = Level I/IIb

ProSPEcTIVE, MULTICENTER (9)
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<td>172 (26 centers)</td>
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<tr>
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<td>Capobianco 2015</td>
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<td>20 females with PPGP (subset of 172 in SIFI)</td>
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<td>Cher 2015</td>
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<td>172 (iFuse) 3844 (NHMS)</td>
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<td>Ledonio 2014b</td>
<td>42T</td>
<td>22 Open 17 MIS (IFuse)</td>
</tr>
<tr>
<td>Ledonio 2014a</td>
<td>42T</td>
<td>22 Open 17 MIS (IFuse)</td>
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**Level II – COMPARISON (7)**

<table>
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<tr>
<th>Article</th>
<th># Patients</th>
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<tbody>
<tr>
<td>Duhon 2013</td>
<td>42T</td>
<td>32 safety 94 efficacy</td>
</tr>
<tr>
<td>Cher 2015</td>
<td>42T</td>
<td>172 (NHMS) 3944 (NHMS)</td>
</tr>
<tr>
<td>Spain 2017</td>
<td>42T</td>
<td>29 screws 263 MIS (iFuse)</td>
</tr>
<tr>
<td>Spain 2018</td>
<td>42T</td>
<td>22 Open 17 MIS (IFuse)</td>
</tr>
<tr>
<td>Spain 2019</td>
<td>42T</td>
<td>22 Open 17 MIS (IFuse)</td>
</tr>
<tr>
<td>Spain 2019</td>
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<td>22 Open 17 MIS (IFuse)</td>
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<tr>
<td>Spain 2019</td>
<td>42T</td>
<td>22 Open 17 MIS (IFuse)</td>
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**Level III – COMPARISON (7)**

<table>
<thead>
<tr>
<th>Article</th>
<th># Patients</th>
<th>Description</th>
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<tbody>
<tr>
<td>Spain 2017</td>
<td>42T</td>
<td>63 CM 47 RFA 27 iFuse</td>
</tr>
<tr>
<td>Spain 2017</td>
<td>42T</td>
<td>29 screws 263 MIS (iFuse) vs. SI joint fusion with PMMA</td>
</tr>
<tr>
<td>Description</td>
<td># Patients</td>
<td>Article</td>
</tr>
<tr>
<td>-------------</td>
<td>------------</td>
<td>---------</td>
</tr>
<tr>
<td>III Graham Smith 2013</td>
<td>149 open MIS (iFuse) Retrospective, multi-center, Open vs. MIS, 12 and 24mo f/u.</td>
<td></td>
</tr>
<tr>
<td>IV Cleveland 2019</td>
<td>50 Retrospective, single-center, grafting, and introp navigation. (Intraop measures, VAS Pain, ODI)</td>
<td></td>
</tr>
<tr>
<td>IV Bornemann 2016</td>
<td>24 Retrospective, single-center, 2-year f/u (VAS Pain &amp; ODI).</td>
<td></td>
</tr>
<tr>
<td>IV Sachs 2016</td>
<td>107 (7 sites) Retrospective cohort with prospective evaluation. 7 sites, 3 years (VAS Pain &amp; ODI).</td>
<td></td>
</tr>
<tr>
<td>IV Bornemann 2016</td>
<td>8 (10 SI joints) Assess stability and bone ingrowth using SPECT/CT.</td>
<td></td>
</tr>
<tr>
<td>IV Vanaclocha 2014</td>
<td>24 Retrospective, single-center, mean 16mo f/u.</td>
<td></td>
</tr>
<tr>
<td>IV Bornemann 2014</td>
<td>1 Case study, CT-guided.</td>
<td></td>
</tr>
<tr>
<td>IV Rudolf 2014</td>
<td>17 Retrospective, single-center, 5-year f/u.</td>
<td></td>
</tr>
<tr>
<td>IV Vanaclocha 2014</td>
<td>24 Retrospective, single-center, mean 15mo f/u (range 2-2.7 mo).</td>
<td></td>
</tr>
<tr>
<td>IV Manfré 2014</td>
<td>1 Case study, CT-guided.</td>
<td></td>
</tr>
<tr>
<td>IV Scheyerer 2014</td>
<td>8 (10 SI joints) Assess stability and bone ingrowth using SPECT/CT.</td>
<td></td>
</tr>
<tr>
<td>IV Schroeder 2013</td>
<td>6 Retrospective, single-center, Open vs. MIS, 12 and 24mo f/u.</td>
<td></td>
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</tbody>
</table>

**Level I - Case Series (19)**
<table>
<thead>
<tr>
<th>LOE</th>
<th>Article</th>
<th># Patients</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>Gaetani 2013</td>
<td>42T</td>
<td>Retrospective, single-center, 10 mo follow-up (range 8-18 mo).</td>
</tr>
<tr>
<td>IV</td>
<td>Cummings 2013</td>
<td>18</td>
<td>Retrospective, single-center, 12 mo follow-up.</td>
</tr>
<tr>
<td>IV</td>
<td>Sachs 2013</td>
<td>40</td>
<td>Retrospective, single-center, prior lumbar fusion effect, 2-year follow-up.</td>
</tr>
<tr>
<td>IV</td>
<td>Rudolf 2013</td>
<td>50</td>
<td>Retrospective, single-center, prior lumbar fusion effect, 24 mo (mean 40 mo)</td>
</tr>
<tr>
<td>IV</td>
<td>Kim 2013</td>
<td>31</td>
<td>Retrospective, single-center, range 7-50 mo.</td>
</tr>
<tr>
<td>IV</td>
<td>Lokietek 2012</td>
<td>10</td>
<td>Retrospective, single-center, min 24 mo follow-up (mean 40 mo).</td>
</tr>
<tr>
<td>IV</td>
<td>Yson 2019</td>
<td></td>
<td>Retrospective, single-center, range 2-5 mo follow-up.</td>
</tr>
</tbody>
</table>

REVIEWS

- Lodin 2019
  - Systematic review of the clinical efficacy of SI joint fusion in the treatment of LBP.

- Yson 2019
  - Review of the evidence for the various treatments of SI joint dysfunction, including conservative management, open surgical, and minimally invasive fusion.

- Whelan 2019
  - Review of the evidence for the various treatments of SI joint dysfunction, including conservative management, open surgical, and minimally invasive fusion.
<table>
<thead>
<tr>
<th>Article</th>
<th>Year</th>
<th>Description</th>
<th>Patients</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shamrock 2019</td>
<td>2019</td>
<td>Systematic review to determine the safety of minimally invasive SI joint fusion.</td>
<td>42T</td>
<td></td>
</tr>
<tr>
<td>Tran 2019</td>
<td>2019</td>
<td>Systematic review and meta-analysis: Minimally invasive SI joint fusion compared to micro lumbar discectomy.</td>
<td>20 articles</td>
<td></td>
</tr>
<tr>
<td>Lingutla 2016</td>
<td>2016</td>
<td>Systematic review and meta-analysis of observational studies describing outcome of SI joint fusion in patients with LBP.</td>
<td>405 (315 MIS, 92 Open)</td>
<td></td>
</tr>
<tr>
<td>Heiney 2015</td>
<td>2015</td>
<td>Systematic review of MIS SI joint fusion.</td>
<td>432 (368 iFuse, 64 HMA)</td>
<td></td>
</tr>
<tr>
<td>Zaidi 2015</td>
<td>2015</td>
<td>Systematic literature review of studies on SI joint fusion.</td>
<td>430 (299 MIS, 131 Open)</td>
<td></td>
</tr>
<tr>
<td>Dale 2019</td>
<td>2019</td>
<td>Review of the NICE Medical Technology Guidance for iFuse.</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Cher 2019</td>
<td>2019</td>
<td>Evaluate published evidence with respect to the clinical and economic value of treatments for SI joint pain.</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Frank 2016</td>
<td>2016</td>
<td>Costs effectiveness of MIS SI joint fusion with iFuse.</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Saavoss 2016</td>
<td>2016</td>
<td>Patients from INSITE and SIFI.</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Polly 2016</td>
<td>2016</td>
<td>Patients from INSITE and SIFI.</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Cheer 2016</td>
<td>2016</td>
<td>Patients from INSITE and SIFI.</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Zaidi 2019</td>
<td>2019</td>
<td>Pain and structural factors in chronic low back pain.</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>LOE</td>
<td>Article</td>
<td># Patients</td>
<td>Description</td>
<td></td>
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<td>------------</td>
<td>-------------</td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>Garber 2015  &lt;br&gt; <em>Int J Spine Surg</em>. 2015;9:Article 58.</td>
<td>50 MIS SIJF 89 PLD (case logs from 3 surgeons)</td>
<td>MIS SI joint fusion (SIJF) had comparable surgical time but more work effort than primary lumbar discectomy (PLD).</td>
<td></td>
</tr>
</tbody>
</table>

**BIOMECHANICS (10)**

| -   | Jeong 2018  <br> *World Neurosurg*. 2018;117:e538-43. | 8 cadavers | Biomechanical changes as assessed by 3-D motion analysis technique. |

**OTHER (13)**

<table>
<thead>
<tr>
<th>Description</th>
<th># Patients</th>
<th>Article</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prospective complainants database charactarization</td>
<td>5-319</td>
<td>Miller 2013</td>
</tr>
<tr>
<td>Interoperative neuromonitoring during MIS SI joint fusion</td>
<td>(111 implant)</td>
<td>Woods 2014</td>
</tr>
<tr>
<td>Validation of ODI as a measure of response to SI joint treatment</td>
<td>475</td>
<td>Copy 2015</td>
</tr>
<tr>
<td>4-Year surgical revision rate (or survivalship from revision) for MIS SI joint fusion</td>
<td>11,388</td>
<td>Cher 2015b</td>
</tr>
<tr>
<td>Bipolar iFuse procedure ([<a href="https://youtu.be/1XKs58kZq5">https://youtu.be/1XKs58kZq5</a>]</td>
<td>-</td>
<td>Vanaclocha 2016</td>
</tr>
<tr>
<td>Implant characteristics (TPS, 3D+HA, 3D+Autograft)</td>
<td>In vivo (osteal femoral defect) assessment of cancellous bone-implant interfaces at 6 and 12 weeks post-implantation for four implant configurations (TPS, 3D, 3D+HA, 3D+Autograft)</td>
<td>-</td>
</tr>
<tr>
<td>Utility of ODI as a measure after SI joint fusion</td>
<td>24</td>
<td>Miao 2018</td>
</tr>
<tr>
<td>Review of SI joint dysfunction – prevalence, condition, diagnosis</td>
<td>14,210</td>
<td>Cher 2015b</td>
</tr>
<tr>
<td>and treatment (including SI joint fusion) with an iFuse case study</td>
<td>-</td>
<td>Barros 2019</td>
</tr>
<tr>
<td>Algorithms the treatment of choice for sacroiliac joint dysfunction</td>
<td>-</td>
<td>Janlu 2019</td>
</tr>
<tr>
<td>Editorial Commentary: Minimally invasive sacroiliac joint fusion vs. conservative management for chronic sacroiliac joint pain</td>
<td>-</td>
<td>Polly 2019</td>
</tr>
<tr>
<td>Description</td>
<td>Article</td>
<td># Patients</td>
</tr>
<tr>
<td>-------------</td>
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</tr>
<tr>
<td>LOE Article</td>
<td>2018</td>
<td>2018</td>
</tr>
<tr>
<td>Coverage Recommendations &amp; Guidelines (2)</td>
<td>Lorio 2016</td>
<td>42T</td>
</tr>
<tr>
<td>Coverage Recommendations &amp; Guidelines (2)</td>
<td>Bono 2015</td>
<td>42T</td>
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<td>Coverage Recommendations &amp; Guidelines (9)</td>
<td>NICE</td>
<td>2018</td>
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<td>Coverage Recommendations &amp; Guidelines (1)</td>
<td>Blue Cross Blue Shield Association</td>
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<td>MCG Health</td>
<td>2018</td>
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<tr>
<td>Coverage Recommendations &amp; Guidelines (1)</td>
<td>AIM Specialty Health</td>
<td>2018</td>
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<td>Coverage Recommendations &amp; Guidelines (1)</td>
<td>Blue Cross Blue Shield Association</td>
<td>2018</td>
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</table>

- NICE: National Institute for Health and Care Excellence
- MCG Health: Medical Group of Companies
- AIM Specialty Health: American Institute for Medical Education
- Blue Cross Blue Shield Association: Blue Cross Blue Shield

- Lorio 2016: Coverage Recommendations & Guidelines (2) – ISASS;
- Bono 2015: Coverage Recommendations & Guidelines (2) – ISASS.

- Coverage Recommendations & Guidelines (9):
  - NICE: Coverage Recommendations – Percutaneous Sacroiliac Joint Fusion.
  - MCG Health: Coverage Recommendations – Percutaneous Sacroiliac Joint Fusion.
  - AIM Specialty Health: Coverage Recommendations – Percutaneous Sacroiliac Joint Fusion.

- Coverage Recommendations & Guidelines (1):
  - Blue Cross Blue Shield Association: Coverage Recommendations & Guidelines – Percutaneous Sacroiliac Joint Fusion.
  - MCG Health: Coverage Recommendations & Guidelines – Percutaneous Sacroiliac Joint Fusion.
  - AIM Specialty Health: Coverage Recommendations & Guidelines – Percutaneous Sacroiliac Joint Fusion.
<table>
<thead>
<tr>
<th>Article</th>
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<th># Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECRI Institute – Fuse Product Brief</td>
<td>Minimally Invasive Sacroiliac Joint Fusion Surgery for Chronic Sacroiliac Pain</td>
<td>-</td>
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<tr>
<td>NICE (National Institute for Health and Care Excellence, U.K.)</td>
<td>Interventional Procedures Guidance (IPG578) Minimally Invasive Sacroiliac Joint Fusion Surgery for Chronic Sacroiliac Pain</td>
<td>-</td>
</tr>
<tr>
<td>Hayes Health Technology Brief</td>
<td>Lumbar Spine Fusion for Degenerative Joint Disease of the Lumbar Spine</td>
<td>42T</td>
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<tr>
<td>Wisconsin Physicians Services – Local Coverage Determination (LCD)</td>
<td>Percutaneous minimally invasive fusion/stabilization of the sacroiliac joint for the treatment of back pain</td>
<td>L36000</td>
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<tr>
<td>Cahaba Government Services – Local Coverage Determination (LCD)</td>
<td>Minimally Invasive Surgical (MIS) Fusion of the Sacroiliac (SI) Joint</td>
<td>L36494</td>
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<tr>
<td>CMS Administrators, LLC – Local Coverage Determination (LCD)</td>
<td>Minimally Invasive Surgical (MIS) Fusion of the Sacroiliac (SI) Joint</td>
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<td>Wisconsin Physicians Services – Local Coverage Determination (LCD)</td>
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<td>L36406</td>
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<td>Reviews (4)</td>
<td>Economic (6)</td>
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<tr>
<td>Treatment options. Overviews of the anatomy, SI joint dysfunction, diagnosis, and management of sacroiliac joint dysfunction.</td>
<td>Medicare – cost comparison of non-op vs. MIS SI fusion.</td>
<td></td>
</tr>
</tbody>
</table>
| Business perspective of spine codes (127). 2

Sunday to SWSI members asking to compare CPT’s 27279 to other common spine surgery codes. CPT’s 27279 to 10 other common spine surgery codes. Survey to IJASS Surgery Committee Members asking to compare regression analysis of work RVUs for CPT’s 27279 via survey. | CPT codes 27279, 27280, 0334T. | 520, 2018 | Buysman 2018 | - |
<p>| | Medicare – cost comparison of non-op vs. MIS SI fusion. | 91, 2013 | Ackerman 2013 | - |
| | Commercial – cost of non-op care for SI pathology. | 78, 2014 | Ackerman 2014 | - |
| | Medicare – cost of non-op care for SI pathology. | 14, 2014 | Ackerman 2014 | - |
| | Commercial – cost of non-op vs. MIS SI fusion. | 78, 2014 | Ackerman 2014 | - |
| | Medicare – cost comparison of non-op vs. MIS SI fusion. | 302, 2018 | Buysman 2018 | - |
| | Regression analysis of work RVUs for CPT’s 27279 via survey. | - | Lono 2016 | - |
| | Medicare – cost comparison of non-op vs. MIS SI fusion. | - | Buysman 2018 | - |</p>
<table>
<thead>
<tr>
<th>Other (5)</th>
</tr>
</thead>
</table>
| - Petersen 2017  
BMC Musculoskelet Disord. 2017;12;18(1):188. | - 1<sup>st</sup> comprehensive systematic review of diagnostic accuracy studies for physical exam or other simple in-office tests regarding LBP diagnosis. Diagnostic algorithm for SI joint pain had sufficient clinical evidence to warrant becoming a Clinical Diagnostic Rule (CDR). |
| - MacBarb 2017 (Part 1)  
Int J Spine Surg. 2017;11:Article 15. | - In vitro investigation of human osteoblasts response to additive manufactured (AM, a.k.a. 3D-printed) trabecular-like titanium implant surfaces compared to traditionally machined base material with titanium plasma spray (TPS) coated surfaces, with and without a nanocrystalline hydroxyapatite (HA) coating. |
| - Cher 2015b  
148 INSITE (SIF)  
607 SPORT (DS)  
1244 SPORT (IDH)  
654 SPORT (SPS)  
QOL preop for SI joint dysfunction as depressed as other lumbar spinal conditions (comparison to Spine Patient Outcomes Research Trial, SPORT).  
SIFI = Sacroiliac joint fusion  
DS = degenerative spondylolisthesis  
IDH = intervertebral disc herniation  
SPS = spinal stenosis |
| - Cher 2014  
SI Joint: Burden of Disease. |
| - Lorio 2014  

*Indicates open access journal/article*
References (full citations)

iFuse Implant System Publications

Level I – RANDOMIZED CONTROLLED TRIAL [10]


http://www.painphysicianjournal.com/current/pdf?article=NDYwOQ%3D%3D&journal=107


Level II/IIb – PROSPECTIVE, MULTICENTER [9]


Level III – COMPARISON [7]


Level IV – CASE SERIES [19]


REVIEWS [8]


ECONOMICS [7]


BIOMECHANICS [10]


Other Key SI Joint Publications (full citations)

COVERAGE RECOMMENDATIONS & GUIDELINES [2]


HEALTH TECHNOLOGY ASSESSMENTS [9]


https://www.hayesinc.com/hayes/publications/health-technology-brief/htb-infuse3000/

LOCAL COVERAGE DETERMINATION (LCD) [4]
National Government Services, Inc. (NGS) – Minimally-invasive Surgical (MIS) Fusion of the Sacroiliac (SI) Joint (L36406). Effective 01 April 2016. <click here>

CGS Administrators, LLC. (CGS) – Minimally-Invasive Surgical (MIS) Fusion of the Sacroiliac (SI) Joint (L36494). Effective 2016 February 01 <click here>

Wisconsin Physicians Services Insurance Corporation (WPS) – Percutaneous minimally invasive fusion/stabilization of the sacroiliac joint for the treatment of back pain (L36000). Effective: 2015 December 17. <click here>


ECONOMIC [6]


REVIEWS [4]

OTHER [6]
Cher DJ, Reckling WC. Quality of life in preoperative patients with sacroiliac joint dysfunction is at least as depressed as in other lumbar spinal conditions. Med Devices (Auckl). 2015 Sep 16;8:395–403. DOI: 10.2147/MDER.S92070.

One or more of the individuals named may be past or present SI-BONE employees, consultants, investors, clinical trial investigators, or grant recipients. Research may have been supported in whole or in part by SI-BONE.

The iFuse Implant System is intended for sacroiliac fusion for conditions including sacroiliac joint dysfunction that is a direct result of sacroiliac joint disruption and degenerative sacroilitis. This includes conditions whose symptoms began during pregnancy or in the peripartum period and have persisted postpartum for more than 6 months. The iFuse Implant System is also intended for sacroiliac fusion to augment immobilization and stabilization of the sacroiliac joint in skeletally mature patients undergoing sacropelvic fixation as part of a lumbar or thoracolumbar fusion.

There are potential risks associated with the iFuse Implant System. It may not be appropriate for all patients and all patients may not benefit. Rx Only. For information about the risks, visit: www.si-bone.com/risks

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95050 U.S.A.

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t. 408-557-8312
info@si-bone.com
www.si-bone.com

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Patents www.si-bone.com
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DISCLAIMER

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The following information is not treatment advice for any particular patient. Physicians should use their clinical judgment and experience when deciding how to treat patients. Please reference the product IFU for full prescribing information. Suggestions offered are based on physician experience. Medical choices for patients are to be based upon their condition and the medical judgment of the treating practitioner. SI-BONE does not recommend or endorse any particular course of treatment or medical choice.
Executive Summary

Lower back pain (LBP) is one of the most prevalent musculoskeletal conditions and a significant public health burden. In the United States, LBP remains one of the most common types of pain reported by adults and is the second leading cause for primary care physician visits.

The sacroiliac (SI) joint is one of the 8 major joints in the human body and a well-recognized source of pain in many patients who present with chronic LBP. However, diagnosis of SI joint pathology is different from diagnosing lumbar spine LBP. Evidence shows diagnosis of SI joint pain is highly predictive, and as good as, or better than, most physical exams for other LBP conditions.\(^4\) Despite this, SI joint pain is still underdiagnosed and thus undertreated. \(^5\)

The SI joints are part of the pelvis, linking the iliac bones to the sacrum. The sacrum connects the pelvis to the spine. The SI joints are essential for supporting the upper body and effectively transferring loads between the spine and legs. The SI joint is a diarthrodial joint, and like other joints in the body may be damaged from acute or repetitive trauma causing disruption and/or degeneration. SI joint pathology, commonly known as SI joint dysfunction, is a condition often overlooked, as abnormalities usually do not present radiographically, and symptoms often present in a pattern similar to lumbar spine and/or hip pathology. In addition, many healthcare providers have not been educated on proper diagnosis of SI joint dysfunction. Moreover, until recently, there was no effective long-term treatment for SI joint dysfunction.

Clinical publications have identified the SI joint as a pain generator in 15-30\(^*\) of LBP patients. The prevalence of SI joint pain in symptomatic post-lumbar fusion patients is even higher, ranging from 32-43%.\(^6\) Quality of life is markedly impaired in patients with chronic SI joint pain compared with age- and gender-matched cohorts\(^7\), and the impairment is similar or worse than many musculoskeletal conditions commonly treated surgically, such as degenerative spondylolisthesis, spinal stenosis, and degenerative arthritis of the hip and knee.\(^8\)

Appropriate evaluation of patients with LBP should include assessment of the SI joint. Accurate diagnosis is directly related to positive outcomes of treatment. Inaccurate diagnosis is highly likely to lead to poor outcomes, inappropriate surgery, and a possibly increased risk of opioid abuse. Appropriate diagnosis begins with a complete patient history, followed by a comprehensive physical examination of the lumbar spine-SI joint-hip complex. A series of SI joint provocative maneuvers that stress the SI joint and that may elicit a positive pain response has been shown to have diagnostic validity.\(^9\) The diagnosis is confirmed with an intraarticular diagnostic injection of local anesthetic (i.e., SI joint block). Multiple guidelines from pain management and spine specialty societies recommend and support this diagnostic algorithm to accurately identify SI joint dysfunction and the SI joint as a source of the patient’s pain. Recent evidence suggests that clinical examination for SI joint pain is one of the most accurate office-based maneuvers to diagnose low back pain.\(^10\)

Initial treatment for patients with certain causes of SI joint dysfunction includes non-surgical options such as pain medications (e.g., NSAIDs, opioids), activity modification, physical therapy, and procedural interventions such as SI joint steroid injections and radiofrequency ablation of the dorsolateral branches of the sacral nerves. When non-surgical management fails to provide clinically important, lasting relief of symptoms, surgical options such as fusion of the SI joint should be considered.

The iFuse Implant System\(^*\) ("iFuse") (SI-BONE, Inc., Santa Clara, CA) is composed of patented triangular titanium implants with a porous titanium surface and surgical procedure instruments. The procedure is usually performed using a minimally invasive surgical (MIS) technique. The surgical goal is permanent stabilization of the SI joint through both bony adherence to the implants as well as intraarticular joint fusion. Typically, three implants are
placed across the SI joint using a lateral transarticular approach. The implants have a unique patented triangular shape designed to minimize micromotion and rotation to provide immediate joint stabilization and allow for biological fixation to support long-term fusion.

The iFuse Implant System, commercially available since 2009, is the only SI joint fusion product in the US with proven clinical safety, effectiveness, durability, biomechanics, and economic value supported by more than 70 peer-reviewed publications (www.si-bone.com/results). Key clinical evidence includes data from two randomized controlled trials (INSITE conducted in the US and iMIA in Europe), a prospective, multicenter, single-arm trial (SIFI), and a long-term prospective follow-up trial (LOIS) made up of subjects from INSITE and SIFI. Results from all trials consistently show rapid and sustained pain relief (~50-point decrease in VAS SI joint pain [0-100 scale]), functional improvement (~30-point decrease in Oswestry Disability Index or ODI), quality of life improvement, and high patient satisfaction. The two randomized controlled trials demonstrate the superiority of iFuse over non-surgical management (NSM) in decreasing pain, and improving patient function and quality of life.† 2-year results from INSITE, IMIA, and SIFI, and 4-year and 5-year results from LOIS validate the sustained clinically important outcomes patients receive after having the iFuse Procedure. Other publications report similar positive longer-term (up to 6 years)† outcomes, design confirmation through biomechanical studies, and the economic value of the procedure.

The medical community has embraced the iFuse Procedure for treating SI joint dysfunction due to sacroiliac joint disruption and/or degenerative sacroiliitis since becoming commercially available in 2009. As of June 2019, over 40,000 iFuse Procedures (using over 115,000 implants**) have been performed worldwide by over 1,900 surgeons, with the majority being performed in the United States (32,000+++ procedures; 1,300+ surgeons).

Non-surgical treatment of patients with SI joint dysfunction is costly for both Medicare and commercial insurance payors. This is because non-surgical treatment has not been shown to provide durable relief from this type of chronic pain. Economic modeling data shows MIS SI joint fusion with iFuse to be a highly cost-effective procedure and a long-term cost-savings strategy. The cost-effectiveness of the iFuse Procedure is similar to that of hip and knee arthroplasty♦, both commonly accepted and cost-effective orthopaedic procedures. Other economic studies comparing MIS SI joint fusion with non-operative care show how proper diagnosis and treatment of SI joint dysfunction can save the healthcare system money. $ A number of healthcare technology and clinical care assessment organizations, such as BCBSA, NICE, eviCore, and MCG, have published positive reports on MIS SI joint fusion with iFuse. In addition, several societies and independent specialty benefits management organizations, such as NASS, ISASS, AIM, and eviCore have published positive recommendation guidelines for MIS SI joint fusion. All U.S. Medicare Administrative Contractors (MACs) cover MIS SI joint fusion and commercial payor coverage is accelerating. In fact, many commercial payors have written positive coverage policies exclusively for the triangular-shaped iFuse Implant™ due to the overwhelming positive and high-quality clinical evidence.

This clinical value dossier details the role of the SI joint as a component of lower back pain, the prevalence of SI joint dysfunction, proper differential diagnosis, treatment options, clinical evidence and cost-effectiveness for minimally invasive SI joint fusion with the iFuse Implant System, and insurance payor coverage. Appendices provide further information on the professional medical specialty society coverage recommendations and guidelines, references, and a complete bibliography of the iFuse publications.

† Polly – IJSS 2018; Dengler – J Bone Joint Surg Am 2019
♦ Vanaclocha – Neurosurgery 2017
∇ Based on 90% of procedures using 3 implants
* Cher – Clinicoecon Outcomes Res 2016
$ Polly – Clinicoecon Outcomes Res 2016
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<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADL</td>
<td>Activities of Daily Living</td>
</tr>
<tr>
<td>APC</td>
<td>Ambulatory Payment Classification</td>
</tr>
<tr>
<td>ASC</td>
<td>Ambulatory Surgical Center</td>
</tr>
<tr>
<td>CDR</td>
<td>Clinical Diagnostic Rule</td>
</tr>
<tr>
<td>CM</td>
<td>Conservative Management (treatment term typically used in Europe for NSM)</td>
</tr>
<tr>
<td>CPT</td>
<td>Current Procedural Terminology</td>
</tr>
<tr>
<td>DSIIQ</td>
<td>Denver Sacroiliac Joint Questionnaire (test where patients evaluate 10 functional activities)</td>
</tr>
<tr>
<td>ICD-10-CM</td>
<td>International Classification of Diseases (10th revision), Clinical Modification</td>
</tr>
<tr>
<td>ICER</td>
<td>Incremental cost-effectiveness ratio</td>
</tr>
<tr>
<td>IFU</td>
<td>Indications for Use</td>
</tr>
<tr>
<td>iMIA</td>
<td>iFuse Implant System Minimally Invasive Arthrodesis (clinical trial sponsored by SI-BONE, NCT01741025)</td>
</tr>
<tr>
<td>INSITE</td>
<td>Investigation of Sacroiliac Fusion Treatment (clinical trial sponsored by SI-BONE, ClinicalTrials.gov NCT01681004)</td>
</tr>
<tr>
<td>LBP</td>
<td>Lower Back Pain (or Low Back Pain)</td>
</tr>
<tr>
<td>LOIS</td>
<td>Long-Term Follow-Up in INSITE/SIFI (clinical trial sponsored by SI-BONE, ClinicalTrials.gov NCT02270203)</td>
</tr>
<tr>
<td>LOTUS</td>
<td>Long Term Follow Up of Patients Implanted with the iFuse Implant System (clinical trial sponsored by SI-BONE)</td>
</tr>
<tr>
<td>MAC</td>
<td>Medicare Administrative Contractor</td>
</tr>
<tr>
<td>MDR</td>
<td>Medical Device Reporting</td>
</tr>
<tr>
<td>MIS</td>
<td>Minimally Invasive Surgery or Minimally Invasive Surgical</td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute for Health and Care Excellence (United Kingdom)</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Non-Steroidal Anti-Inflammatory Drugs</td>
</tr>
<tr>
<td>NSM</td>
<td>Non-Surgical Management</td>
</tr>
<tr>
<td>ODI</td>
<td>Oswestry Disability Index</td>
</tr>
<tr>
<td>EQ-5D TTO</td>
<td>EuroQoL-5 Dimension Time Trade-off index (Quality of Life measurement)</td>
</tr>
<tr>
<td>PSIS</td>
<td>Posterior Superior Iliac Spine</td>
</tr>
<tr>
<td>PT</td>
<td>Physical Therapy</td>
</tr>
<tr>
<td>QALY</td>
<td>Quality-adjusted Life Year</td>
</tr>
<tr>
<td>QOL</td>
<td>Quality of Life</td>
</tr>
<tr>
<td>RF</td>
<td>Radiofrequency Ablation or “denervation” (also known as RFA)</td>
</tr>
<tr>
<td>SALLY</td>
<td>Study of bone growth in the Sacroiliac Joint after minimally invasive surgery with titanium implants (clinical trial sponsored by SI-BONE, ClinicalTrials.gov NCT03122899)</td>
</tr>
<tr>
<td>SI</td>
<td>Sacroiliac</td>
</tr>
<tr>
<td>SIFI</td>
<td>Sacroiliac Joint Fusion with iFuse Implant System (clinical trial sponsored by SI-BONE, ClinicalTrials.gov NCT01640353)</td>
</tr>
<tr>
<td>SIJ</td>
<td>Sacroiliac Joint</td>
</tr>
<tr>
<td>SJF</td>
<td>Sacroiliac Joint Fusion</td>
</tr>
<tr>
<td>VAS</td>
<td>Visual Analog Scale</td>
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</tbody>
</table>
1 SI Joint Dysfunction: Burden of Disease

1.1 Clinical Characteristics and Presentation of Condition

The sacroiliac (SI) joint is part of the pelvic ring, linking the ilium bones of the lateral pelvis to the sacrum (lowest part of the spine). The primary role of the SI joint is to provide stability for the pelvis and to bear the load of the upper body. The SI joint is the largest joint in the human body, one of 8 major joints, and has a dual structure, with the upper part of the joint being ligamentous and the lower part being a true synovial joint. It is a diarthrodial joint (meaning that it has hyaline articular cartilage on both sides of the joint) similar to most all other joints. Multiple studies have shown the SI joint moves with normal daily activities [Sturesson 1989, 2000a, 2000b13–15; Kibsgård 2012, 201416,17] and is subject to the same internal and external forces experienced by other joints throughout the body. As such, the SI joint may be damaged from acute or repetitive trauma. The SI joint is subject to the same pathologic processes that affect other joints in the body. The ligaments and soft tissues supporting the SI joint may be stretched or damaged leading to abnormal force/load transfer. The joint may be damaged by autoimmune, inflammatory, and/or infectious processes. The SI joint is also subject to degeneration secondary to underlying osteoarthritis or increased stress at the SI joint (i.e., adjacent segment disorder) after lumbar fusion [Katz 200318, Maigne 200519, Ha 200820, DePalma 201121].

The SI joint is a proven “pain generator” or source of pain. The SI joint is highly innervated and studies demonstrate an anatomic “pain pathway” from the SI joint to the brain [Ikeda 199122; Fortin 1999, 200323,24; Vilensky 200225; Sakamoto 200126; Szadek 2008, 201027,28]. In normal volunteers, the SI joint responds to noxious stimuli, both mechanical [Dreyfuss 200929] and chemical [Fortin 1994a30], with production of SI joint pain in a typical pain referral pattern. Local anesthetic injection into the joint eliminates SI joint pain induced by noxious stimuli. The complex innervation of the SI joint has been confirmed clinically by multisite anesthetic injections in normal volunteers [Dreyfuss 200929]. The totality of evidence strongly confirms that the SI joint meets the definition of a pain generator as it: 1) demonstrates innervation and an anatomic pain pathway, 2) reproduces typical pain in response to noxious stimuli, 3) local anesthetic injection eliminates the pain, 4) the SI joint is subject to internal/external forces that could damage the joint, and 5) definitive treatment (e.g., with SI joint fusion) results in long lasting pain relief.

1.2 Epidemiology

Multiple studies have evaluated the prevalence of the SI joint as a pain generator in patients presenting with chronic lower back pain (LBP). Depending upon study methodology, the prevalence of the SI joint as a source of patients’ LBP ranges from 15% to 30% [Bernard 198731, Schwarzer 199532, Maigne 199633, Irwin 200734, Sembrano 200935]. In patients with continued or new onset LBP after lumbar fusion, the prevalence of the SI joint as the source of pain is even higher, ranging from 32% to 43% [Katz 200318, Maigne 200519, DePalma 201121, Liliang 201136].
Causes of SI joint pain include trauma, such as motor vehicle accident, fall on buttocks, lifting and twisting, or childbirth. Degenerative processes are a common cause of SI joint dysfunction, resulting from increased stresses on the joints due to previous lumbar fusion, conditions such as osteoarthritis, repetitive movements, or lingering chronic pain after giving birth known as post-partum pelvic girdle pain (PPGP). About 50% of women have pelvic girdle pain during pregnancy and 25% experience pain after pregnancy [Wu 200437]. Approximately 5% of all pregnant women continue to have PPGP 3 years following delivery [Norén 200238]. A substantial proportion of PPGP is SI joint dysfunction.

1.3 Clinical Burden of SI Joint Dysfunction

Chronic LBP carries a significant public health burden, with an estimated 83 million well-years of life lost every year due to ill health, disability, or early death [Murray 201239]. LBP is more burdensome than many other highly impactful conditions, such as cancer and chronic obstructive pulmonary disease (COPD), and it is the sixth most common cause of decrements in global disability-adjusted life years [Salomon 201240].

The SI joint is a well-recognized source of pain in many patients who present with chronic LBP. Quality of life is markedly impaired in patients with SI joint pain compared with age- and gender-matched cohorts, and the impairment is similar or even worse than many common disabling medical conditions such as cancer, COPD, and musculoskeletal conditions treated surgically [Cher 201441]. Similarly, patients with SI joint dysfunction considering surgery have decrements in quality of life as or more severe than patients with degenerative spondylolisthesis, spinal stenosis, and intervertebral disc herniation [Cher 201542].

1.4 Unmet Need

1.4.1 Diagnosis – Strong Predictive Evidence

Though the SI joint is a known source of LBP, SI joint pathology is underappreciated and underdiagnosed. This lack of recognition of the SI joint and its role in chronic LBP may lead to misdiagnosis and in turn misdirected treatment. Some SI joint pain patients may even get a lumbar fusion [Vanaclocha 201843]. All of this is true even despite the strong predictive clinical diagnostic evidence for SI joint pain. In April 2017, the first comprehensive systematic review of diagnostic accuracy studies for physical examination or other simple in-office tests regarding LBP diagnosis found a diagnostic algorithm for SI joint pain had sufficient clinical evidence to warrant becoming a Clinical Diagnostic Rule (CDR). The CDR for SI joint pain includes 3 or more positive provocative tests, lack of centralization, and pain over the posterior superior iliac spine (PSIS). This CDR was as good as or better than most physical exam tests for other low back conditions (e.g., intervertebral disc, disc herniation with nerve root involvement, spinal stenosis, and spondylolisthesis)[Petersen 201744].

SI joint pathology usually does not present radiographically, and symptoms often present in a pattern similar to lumbar spine and/or hip pathology. However, accurate diagnosis of SI joint pain can be achieved via a thorough patient history, physical exam of the lumbar spine-SI Joint-hip complex, including multiple positive provocative tests that stress the SI joint, and confirmatory diagnostic SI joint block(s). Any single physical examination provocative maneuver, which may produce mechanical stress in an adjacent structure, has limited predictive value when performed alone. However, several
Systematic reviews [Laslett 2005, Stuber 2007, Laslett 2008, Szadek 2009, Wong 2012] have demonstrated that positive findings on a cluster of provocative maneuvers (i.e., 3 or more) provide reasonable diagnostic sensitivity (85-94%) and specificity (76-78%), and thus discriminative power for diagnosing SI joint pain. Combining 3 or more positive provocative maneuvers with no centralization of pain and patients pointing to their PSIS as the area of dominant pain (Fortin Finger Test) [Fortin 1997], provides reasonable predictive power to continue along the diagnostic algorithm with SI joint injections. The reference standard for the diagnosis of SI joint dysfunction is an appropriately performed intra-articular SI joint block using short- and/or mid-acting local anesthetics [Maigne 1996, Fortin 2000]. No imaging modality(ies) definitively diagnose a dysfunctional or painful SI joint. However, it is important to note, while lumbar spine imaging is commonly used to diagnose lumbar spine pain, the accuracy is unknown and false-positive findings are very common [Boden 1996].

The diagnostic accuracy of SI joint pain is high and reliable like other major joints. As a result, assessment of LBP needs to be comprehensive and include tests specific to the SI joint. Multiple professional healthcare specialty society guidelines recommend and support this SI joint dysfunction diagnostic algorithm (see Appendix C).

1.4.2 Treatment Options for SI Joint Dysfunction

First-line treatment of patients with SI joint dysfunction typically includes non-surgical management (NSM). This treatment may consist of medications (e.g., NSAIDs, opioids), activity modification, physical therapy, or external support with an SI belt. NSM may also consist of non-operative interventional procedures, such as therapeutic (i.e., steroid) SI joint injections or radiofrequency (RF) ablation, which are often provided as the next therapeutic options. When non-surgical treatments fail to provide lasting relief of symptoms, surgical fusion of the SI joint should be considered. Minimally invasive surgical (MIS) SI joint fusion is preferred over more invasive open surgical procedures, as noted by a published utilization survey of members from the International Society for the Advancement of Spine Surgery (ISASS) and Society of Minimally Invasive Spine Surgery (SMISS) [Lorio 2012].

Non-surgical Management

Non-surgical management for SI joint dysfunction is commonly provided in modern healthcare. However, there is very little clinical evidence to support the effectiveness of NSM (see Table 1). SI joint steroid injections, are commonly performed in the United States, though there is very limited published clinical evidence supporting only modest efficacy [Kennedy 2015]. The available published randomized trial results have examined only periarticular steroid infiltration, which is not commonly performed in the US [Luukkainen 1999, 2002]. No high-quality trials of intraarticular SI joint steroid injections have been published in the United States. High-quality randomized controlled trials support the use of RF ablation of sacral nerve root lateral branches, but results are not long lasting [Cohen 2008, Patel 2012]. Two more recent published studies, however have shown RF ablation does not provide effective and durable results [van Tilburg 2016, Juch 2017].
**TABLE 1**
Non-Surgical Management Clinical Evidence

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Clinical Evidence</th>
</tr>
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<tbody>
<tr>
<td><strong>Medications</strong></td>
<td>(NSAIDs, oral steroids, pain medications)</td>
</tr>
<tr>
<td>No evidence suggests this treatment improves health outcomes.</td>
<td></td>
</tr>
<tr>
<td><strong>Physical Therapy</strong></td>
<td>No clinical trials have shown effectiveness in an SI joint dysfunction population.</td>
</tr>
<tr>
<td><strong>External SI joint stabilization</strong></td>
<td>(SI belt)</td>
</tr>
<tr>
<td>No evidence suggests this treatment improves health outcomes.</td>
<td></td>
</tr>
<tr>
<td><strong>SI joint Injections</strong></td>
<td>Little clinical evidence with only modest success rates [Kennedy 201554] and no high-quality long-term clinical trials have shown that intraarticular SI joint steroid injections are beneficial.</td>
</tr>
<tr>
<td><strong>Radiofrequency (RF) Ablation</strong></td>
<td>High-quality, short-term clinical trials have shown more pain relief than sham [Cohen 200857, Patel 201258]. Neither of these trials showed a high proportion of patients with long-term (&gt;6 months) sustained pain relief. More recent randomized trials have shown either no improvement or no clinically significant improvement with RF ablation [van Tilburg 201659, Juch 201760].</td>
</tr>
</tbody>
</table>

**Minimally Invasive SI Joint Fusion with iFuse**

The published clinical evidence supporting MIS SI joint fusion continues to grow in quantity and quality. The majority of the MIS SI joint fusion clinical evidence is based on studies performed with the iFuse Implant™, which has been commercially available since 2009, with more than 70 peer-reviewed publications (www.si-bone.com/results). The iFuse Implant is the only SI joint fusion device commercially available in the US with multiple prospective trials including two randomized controlled trials. In carefully selected patients with SI joint dysfunction caused by degeneration or disruption of the SI joint, clinical evidence from two multicenter, randomized controlled trials [Polly 20161, Dengler 2017b61], and a multicenter, prospective, single-arm 2-year outcomes trial [Duhon 20163] consistently show rapid and sustained pain relief (~50-point decrease in VAS SI joint pain [0-100 scale]), functional improvement (~30-point decrease in Oswestry Disability Index or ODI), and improved quality of life. A pooled analysis of these three prospective trials demonstrates consistent results with the iFuse Implant [Dengler 2017a5]. Prospective 3- and 4-year follow-up trial results demonstrate the improvements at 2-years are sustained [Darr 2018a62, Darr 2018b63]. Early results from the first prospective trial using iFuse-3D™ implants [Patel 20194] confirm that clinical responses are similar to those from prior trials. Other publications report similar positive longer-term outcomes [Sachs 2016 (3 years)64, Vanaclocha 2014 (4.5 years)65, Rudolf 2014 (5 years)66, Vanaclocha 2017 (6 years)68], as well as the economic value of the procedure [Cher 201611, Polly 201667, Saavoss 201668]. The safety of both the iFuse Implant [Miller 201369, Cher 201510] and iFuse-3D Implant™ [Cher 201870] has been demonstrated with low complication and revision rates. Notably, the complication and revision rates for iFuse-3D are the same as for iFuse Implants [Cher 201870]. Several biomechanical studies validate the technique and that the implants provide immediate SI joint stability as intended [Lindsey 201471,]
Minimally Invasive SI Joint Fusion – Non-iFuse Products

Outside of iFuse, there is limited clinical outcomes evidence from other MIS SI joint fusion products cleared for use in the United States. There are a few small cohort retrospective articles using Simmetry from RTI Surgical/Zyga with good results [Kube 2016, MenMuir 2017, Cross 2018]. Two retrospective studies using Rialto SI Joint Fusion System from Medtronic [Beck 2015; Rajpal 2018]. Beck presents positive outcomes and joint fusion data from 20 patients, but procedures included Bone Morphogenetic Protein (BMP) off-label. Rajpal reports pain reduction and high patient satisfaction from 24 patients along with operative measures. Another retrospective study combines outcomes from 45 total patients, 36 treated with iFuse and 9 treated with Samba Screws, with good results [Kancherla 2017].

Prospective studies include two reporting 1-year follow-up results [Rappoport 2017 (SI-LOK, Globus), Abbasi 2017 (Simmetry, RTI/Zyga)], and another with 6-month results [Araghi 2017 (Simmetry, RTI/Zyga)]. Rappoport showed significant decrease in both back and leg pain, along with mechanical joint stability at 12 months. Abbasi used a detailed CT assessment of SI joint fusion to identify bridging bone adjacent to the threaded implants and crossing the joint in most patients 12 months after surgery. Araghi reports significant improvement at 6 months in pain and disability, and reduction in opioid use in a 50-patient cohort.

Additional publications present procedure technique [Miller 2014, Beaubien 2015; both Simmetry] and biomechanical results [Bruna-Rosso 2016 (Rialto, Medtronic), Shih 2018 (Simmetry, RTI/Zyga)].

See section 4 Competition for more details.

Open Surgical SI Joint Fusion

Traditional open SI joint fusion is highly invasive and is associated with long hospital stays and recovery times, high nonunion rates, poor long-term response rates, and low patient satisfaction. As a result, unless medically necessary, MIS procedures are preferred over traditional open SI joint fusion procedures [Lorio 2012].
2 Product Information: iFuse Implant System®

2.1 Technology

The iFuse Implant System (“iFuse”) is comprised of titanium implants with a porous titanium surface and a set of surgical procedure instruments. Typically, three implants are placed across the SI joint via a lateral transarticular approach using a minimally invasive surgical (MIS) technique. The implants’ unique triangular shape, large surface area, and interference fit are designed to minimize micromotion and rotation, to provide immediate joint stability and to allow for biological fixation to support long-term fusion.

The iFuse Procedure™ is typically performed under general anesthesia with the patient in the prone position. A small incision is made in the lateral buttock through which the procedure is performed. The procedure is a typical orthopaedic pin-based technique (pin, drill, broach, implant). The entire procedure takes approximately one hour, and instrument/implant position is confirmed with intraoperative fluoroscopy or navigation-based imaging.

In March 2017, the first 3D-printed (a.k.a. additive manufactured) implant for the SI joint, iFuse-3D™ Implant, was introduced. These titanium implants have fenestrations to allow for bony through growth as well as application of bone autograft/allograft if desired. The fenestrations provide more surface area and the 3D-printing process produces a consistent and highly controlled porous surface that closely resembles cancellous bone. Overall, the iFuse-3D design allows for bony ongrowth, ingrowth, and through growth for long-term fusion [MacBarb 2017(Part 2)89].

Several other instruments, implants, and accessories to be used with the iFuse Implant System are also available. They include iFuse implant removal system and revision implants, iFuse Neuromonitoring Kit to help identify spinal nerve roots during the iFuse Procedure, iFuse-Navigation™ Instruments, and iFuse Mazor Pins. The iFuse-Navigation Instruments are designed for use with the Medtronic O-arm® Imaging System and StealthStation™ Navigation System, and the iFuse Mazor Pins are to be used with Mazor Renaissance® or Mazor X™ Robotic Guidance Systems.

The iFuse Implant System, which includes implants and other instruments and accessories for use during an iFuse Procedure, are manufactured and marketed by SI-BONE, Inc. (Santa Clara, CA, USA, www.si-bone.com).
2.2 Classification and Clearance

In the United States, the iFuse Implant System is a class II device and received FDA clearance in November 2008 (FDA 510(k) K080398) and the iFuse-3D Implant received FDA clearance in March 2017 (FDA 510(k) K162733). The indication statement was updated in 2011, 2014, 2015, and again in 2016. The iFuse implants also received clearance in April 2019 for SI joint fusion to augment immobilization and stabilization of the SI joint in patients undergoing sacropelvic fixation (FDA 510(k) K190230). The current cleared indication is:

The iFuse Implant System is intended for sacroiliac fusion for conditions including sacroiliac joint dysfunction that is a direct result of sacroiliac joint disruption and degenerative sacroiliitis. This includes conditions whose symptoms began during pregnancy or in the peripartum period and have persisted postpartum for more than 6 months. The iFuse Implant System is also intended for sacroiliac fusion to augment immobilization and stabilization of the sacroiliac joint in skeletally mature patients undergoing sacropelvic fixation.

Other instrument clearances and indications:

- Neuromonitoring Kit – October 2016 (FDA 510(k) K161893)
  The Neuromonitoring Kit is indicated for stimulation of peripheral motor nerves, including spinal nerve roots, for localization and identification during surgery.

- iFuse-Navigation – October 2017 (FDA 510(k) K172268)
  iFuse-Navigation instruments are intended to be used with the iFuse Implant System to assist the surgeon in precisely locating anatomical structures in iFuse procedures, in which the use of stereotactic surgery may be appropriate, and where reference to a rigid anatomical structure, such as the pelvis or vertebra can be identified relative to the acquired image (CT, MR, 2D fluoroscopic image or 3D fluoroscopic image reconstruction) and/or an image data based model of the anatomy. iFuse-Navigation instruments are intended to be used with the Medtronic StealthStation System.

See Indications for Use (IFU) documents at: www.si-bone.com/label
2.3 Procedure Codes

2.3.1 CPT Code

The American Medical Association established Category I CPT® Code 27279 for minimally invasive SI joint fusion effective January 1, 2015:

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>27279</td>
<td>Arthrodesis, sacroiliac joint, percutaneous or minimally invasive (indirect visualization), with image guidance, includes obtaining bone graft when performed and placement of transfixing device</td>
</tr>
</tbody>
</table>

2.3.2 Diagnosis Codes: ICD-10-CM

<table>
<thead>
<tr>
<th>ICD-10-CM</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M43.28</td>
<td>Fusion of spine, sacral and sacrococcygeal region</td>
</tr>
<tr>
<td>M46.1</td>
<td>Sacroiliitis, not elsewhere classified</td>
</tr>
<tr>
<td>M53.2x8</td>
<td>Spinal instabilities, sacral and sacrococcygeal region</td>
</tr>
<tr>
<td>M53.3</td>
<td>Sacrococcygeal disorders, not elsewhere classified</td>
</tr>
<tr>
<td>S33.2XXS</td>
<td>Dislocation of the sacroiliac and sacrococcygeal joint, sequela</td>
</tr>
<tr>
<td>S33.6XXS</td>
<td>Sprain of sacroiliac joint, sequela</td>
</tr>
<tr>
<td>S39.83XS</td>
<td>Other specified injuries of pelvis, sequela</td>
</tr>
</tbody>
</table>
### 2.3.3 ICD-10 Facility Reimbursement 2019

#### TABLE 3
Hospital Inpatient Setting (Place of Service 21)

<table>
<thead>
<tr>
<th>ICD-10-PCS</th>
<th>Description</th>
<th>Possible MS-DRG (others may apply)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0SG734Z (R)</td>
<td>Fusion of right/left sacroiliac joint with internal fixation device, percutaneous approach</td>
<td>459 – Spinal Fusion Except Cervical with MCC*</td>
</tr>
<tr>
<td>0SG834Z (L)</td>
<td>Fusion of right/left sacroiliac joint with internal fixation device, percutaneous approach</td>
<td>460 – Spinal Fusion Except Cervical without MCC*</td>
</tr>
</tbody>
</table>

*MCC = Major complications and/or comorbidities

#### TABLE 4
Hospital Outpatient Setting (Place of Service 22) Codes and Ambulatory Surgical Center (ASC) Setting (Place of Service 24) Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5116</td>
<td>Arthrodesis, sacroiliac joint, percutaneous or minimally invasive (indirect visualization), with image guidance, includes obtaining bone graft when performed, and placement of transfixing device. [For bilateral procedures, report 27279 with modifier 50] Status Indicator = J1 (see Note 2)</td>
</tr>
<tr>
<td>C1713</td>
<td>Anchor/screw for opposing bone-to-bone or soft tissue-to-bone (implantable). Status Indicator = N (see Note 3)</td>
</tr>
</tbody>
</table>

Note 1: APC 5116 is a Level 6 Musculoskeletal Procedure.
Note 2: Status Indicator J1 = Comprehensive APC. All covered under Part B services on the claim are packaged with the primary J1 service for the claim, except services with a status indicator of F, G, H, I, and U.
Note 3: Status Indicator N = Items and Services Packaged into APC Rates.
2.4 Device Components and Specifications

The iFuse Implant System consists of a surgical tray of instruments that can be re-sterilized and reused, disposables, and implants. Parts of several instruments are radiolucent to improve intraoperative visualization and reduce the amount of fluoroscopic imaging. A neuromonitoring accessories kit may be used to identify spinal nerve roots during the iFuse procedure, if desired. Additionally, iFuse-Navigation™ Instruments are designed to allow surgeons using the Medtronic O-arm® Imaging System and StealthStation™ Navigation System to perform sacroiliac joint fusion with the iFuse Implant System. For surgeons who use the Mazor Renaissance® or Mazor X™ Robotic Guidance Systems, there are iFuse Mazor Pins.

<table>
<thead>
<tr>
<th><strong>TABLE 5</strong></th>
<th>iFuse Implant System Instrumentation &amp; Implants</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Instruments</strong></td>
<td><strong>Disposables</strong></td>
</tr>
<tr>
<td>Variable Parallel Pin Guide</td>
<td>Guide Pin, 3.2 mm</td>
</tr>
<tr>
<td>Fixed Parallel Pin Guide</td>
<td>Blunt Pin, 3.2 mm</td>
</tr>
<tr>
<td>Pin Sleeve with Soft Tissue Protector</td>
<td>Exchange Pin, 3.2 mm</td>
</tr>
<tr>
<td>Soft Tissue Protector with Affixed Handle</td>
<td>Cannulated Drill Bit, 7.0 x 3.2</td>
</tr>
<tr>
<td>Drill Bit with PEEK bulb</td>
<td>Guide Pin, 2.0 mm</td>
</tr>
<tr>
<td>Sharp-tip Broach with adjustable Broach Stop</td>
<td>Blunt Pin, 2.0 mm</td>
</tr>
<tr>
<td>Blunt Dissector</td>
<td>Exchange Pin, 2.0 mm</td>
</tr>
<tr>
<td>Radiolucent-tip Clamp</td>
<td>Cannulated Drill Bit, 4.0 x 2.0</td>
</tr>
<tr>
<td>Slap Hammer</td>
<td>Neuromonitoring Kit:</td>
</tr>
<tr>
<td>iFuse-Navigation Set:</td>
<td>• Guide Pin Sleeve</td>
</tr>
<tr>
<td>• Broach</td>
<td>• Guide Pin Cap</td>
</tr>
<tr>
<td>• Impactor</td>
<td>• Guide Pin Clip</td>
</tr>
<tr>
<td>• Impactor/Removal adaptor (rod, tube, mount, and cap)</td>
<td>• Monopolar Probe</td>
</tr>
<tr>
<td>• Slap Hammer</td>
<td>iFuse Mazor Pins</td>
</tr>
<tr>
<td>• Adapter Stealth Pin Guide</td>
<td>• Short Drill Guide, 3.0 mm</td>
</tr>
<tr>
<td>• UDG Funnel and Plunger</td>
<td>• Long Drill Guide, 3.0 mm</td>
</tr>
<tr>
<td>• Implant Orientation Guide</td>
<td></td>
</tr>
<tr>
<td>• O-arm Pins, 3.1mm Threaded Sharp Tip</td>
<td></td>
</tr>
</tbody>
</table>

Titanium Triangular Shape (on cross section)
- Porous titanium surface
- Inscribed diameter: 4.0, 7.0, 7.5, and 10.75 mm
- Lengths (5 mm increments, except where indicated)

iFuse
- 4.0: 35, 45, and 55 mm
- 7.0: 30 – 70 mm
- 7.5: 35 – 70 mm
- 10.75: 35 – 70 mm

iFuse-3D
- 7.0: 35 – 90 mm
2.5 **Product Utilization**

As of June 2019, over 40,000 iFuse Procedures (over 110,000 implants**) have been performed worldwide by over 1,900 surgeons, with the majority being performed in the United States (32,000+ procedures; 1,300+ surgeons).

2.6 **SI-BONE, iFuse Implant System Manufacturer**

SI-BONE, Inc. is a medical device company in Santa Clara, CA and was founded in 2008. The company is advancing the diagnostic understanding of the sacroiliac joint and minimally invasive surgery for certain causes of SI joint disorders. SI-BONE’s mission is to dramatically raise awareness of comprehensive lower back pain differential diagnosis, to include the sacroiliac joint, and to provide access to evidence-based, safe and effective treatment solutions in the sacro-pelvic space.

More information can be found at: [www.si-bone.com](http://www.si-bone.com)

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** Based on 90% of procedures using 3 implants
Clinical Evidence for the iFuse Implant System®

The evidence supporting minimally invasive surgical (MIS) fusion of the sacroiliac (SI) joint with the iFuse Implant System is substantial and continues to grow in number and quality. iFuse is the only SI joint fusion product with clinically proven safety and effectiveness from multiple prospective trials, which includes positive outcomes from two multicenter randomized controlled trials. More than 70 peer-reviewed publications (see Table 6, Appendix D, and www.si-bone.com/results) demonstrate positive durable clinical outcomes, biomechanics, and the economic value of the iFuse Implant System. Demonstrated outcomes include:

- **Superior to Non-surgical Management**¹²
- **Pain Relief** – clinically important rapid (within 1 month) and sustained (6, 12, 24, 36, 48, and 60 months) decrease in VAS pain (~50 points on 0-100 scale)¹⁻⁶,⁶²⁻⁶⁴,⁶⁶,⁹⁰⁻¹⁰¹
- **Back Function Improvement** – clinically important reduction in disability as measured by ODI (Oswestry Disability Index) at 6, 12, 24, 36, and 48 months (~30 point reduction)¹⁻⁵,⁶²⁻⁶⁴,⁶⁶,⁹⁰⁻¹⁰³
- **Quality of Life (QOL) Improvement** – measured by SF-36, EuroQol-5D (EQ-5D), and Roland Morris Disability¹⁻³⁻⁵⁻⁶¹⁻⁻⁶³,⁹¹⁻⁹³,⁹⁶,¹⁰⁴
- **Reduction in Opioid Use**¹⁻⁴,⁸,⁶³,¹⁰⁵
- **High Patient Satisfaction** (> 90%)¹⁻³⁻⁶²⁻⁶⁶,⁹⁰⁻⁹⁴,⁹⁶,⁹⁸
- **Low Complication and Revision Rates**¹⁻³⁻⁸⁻¹⁰⁻⁶²⁻⁶⁴,⁶⁹,⁷⁰,⁹⁰,⁹¹
- **Durable Results** – sustained outcomes to 3⁶²,⁶⁴, 4⁶³,⁶⁵, 5⁶,⁶⁶ and 6 years⁸

Key publications include results from two prospective multicenter randomized controlled trials, INSITE conducted in the US (ClinicalTrials.gov identifier NCT01681004) and iMIA conducted in Europe (ClinicalTrials.gov identifier NCT01741025), as well as a prospective multicenter single-arm trial (SIFI, ClinicalTrials.gov identifier NCT01640353). A longer-term prospective trial LOIS (ClinicalTrials.gov identifier NCT02270203) is in process and is continuing follow-up for 5 years of many INSITE and SIFI patients. To date 3- and 4-year LOIS results have been published [Darr 2018a⁶², Darr 2018b⁶³]. LOIS 5-year results manuscript has been submitted and is currently under review [Whang 2019⁹]. See section 3.1 Prospective Clinical Trials.

Other publications consist of systematic reviews and meta-analyses, three studies comparing iFuse to open SI joint fusion, and multiple retrospective case series. Another publication compares the long-term results of iFuse to conservative management and radiofrequency ablation [Vanaclocha 2017⁹]. A 4-year revision rate article compares SI joint fixation with screws versus fusion with iFuse. Additional published articles address the safety, health state utility, economic value, worker productivity, work intensity/effort by surgeons, and the biomechanics of the iFuse Implant System. Finally, there are publications on bony integration with iFuse and iFuse-3D Implants [MacBarb 2017(Part 1)°⁶, MacBarb 2017(Part 2)°⁸] and the utility of intraoperative neuromonitoring [Woods 2014°⁷]. See Table 6 and Appendix D for an overview of the publications.
### TABLE 6
iFuse Implant System – Clinical Evidence Overview (June 2019)

<table>
<thead>
<tr>
<th>LOE</th>
<th>Type</th>
<th>Pubs</th>
<th>Description</th>
<th>Principle Findings</th>
</tr>
</thead>
</table>
| I   | RCT        | 10   | iMIA 24mo follow-up [Dengler 2019]
              iMIA data – risk factors of continued opioid use [Dengler 2017c]  
              iMIA 12mo follow-up [Dengler 2017b]  
              Pooled Analysis of INSITE, iMIA, and SIFI [Dengler 2017a]
              iMIA 6mo follow-up – referred leg pain [Dengler 2016]  
              iMIA 6mo follow-up [Sturesson 2016]  
              INSITE 24mo follow-up [Polly 2016]  
              INSITE and SIFI data – Correlation of SI joint block relief with SI joint fusion [Polly 2016]
              INSITE 12mo follow-up [Polly 2015]
              INSITE 6mo (102 iFuse vs. 46 NSM) [Whang 2015] |
|     |            |      |                                                                            | SI joint fusion with iFuse provided superior outcomes vs. non-surgical management. |
| II/IIb | Prospective | 9    | LOIS 5-year follow-up [Whang 2019, in review]
              SALLY 6mo interim results [Patel 2019]
              LOIS 4-year follow-up [Darr 2018b]
              LOIS 3-year follow-up [Darr 2018a]
              SIFI 24mo follow-up [Duhon 2016]
              SIFI – PPGP subset analysis, 12mo follow-up [Capobianco 2015]
              SIFI and INSITE – Health State Utility analysis [Cher 2015]
              SIFI 12mo follow-up (172 subjects) [Duhon 2016, Epub 2015 Aug 1]
              SIFI 6mo interim analysis [Duhon 2013] |
|     |            |      |                                                                            | SI joint fusion with iFuse provided durable, clinically meaningful improvements (pain, function, QOL). |
| III | Comparison Cohorts | 6    | Recognition of chronic LBP patients and high frequency of lumbar fusion [Vanaclocha 2018]
              6-yr follow-up – CM vs. RF vs. iFuse [Vanaclocha 2017]
              4-yr revision rate lower than screws [Spain 2017]
              Operative measures and ODI improvement, two centers, 12mo follow-up [Ledonio 2014b]
              Operative measures and ODI improvement, min 12mo follow-up [Ledonio 2014a]
              Operative measures and pain relief, 12 and 24mo follow-up [Graham Smith 2013] |
|     |            |      |                                                                            | Long-term sustained results, low revision rate, and minimally invasive SI joint fusion associated with better operative measures and clinical outcomes compared to open procedure. |
| IV | Retrospective | 19 | Most Recent Pubs:  
Cleveland III 2019 (50 iFuse, 12mo f/u)\(^{101}\)  
Rainov 2018 (160 iFuse, 12mo f/u)\(^{100}\)  
Bornemann 2016 (24 iFuse, 24mo follow-up)\(^{99}\)  
Sachs 2016 (3.7yr follow-up)\(^{64}\)  
Manfré 2014 (case report)\(^{114}\)  
Rudolf 2014 (5yr follow-up)\(^{66}\)  
Vanaclocha 2014 (follow-up from 1-4.5yr)\(^{65}\) | SI joint fusion provided rapid and sustained pain relief, disability reduction, and improvement in QOL. |
| Reviews | 6 | Review of evidence for surgical treatment of SI joint dysfunction [Whelan 2019\(^{115}\)]  
Systematic review to determine safety [Shamrock 2019\(^{116}\)]  
Systematic review and meta-analysis: MIS SI joint fusion compared to screw-type surgeries [Tran 2019\(^{117}\)]  
Systematic review and meta-analysis, open and MIS [Lingutla 2016\(^{118}\)]  
Systematic review and meta-analysis, MIS trans-articular technique (18 articles, 432 subjects; 85% iFuse) [Heiney 2015\(^{9}\)]  
Systematic literature review, open and MIS [Zaidi 2015\(^{119}\)] | MIS SI joint fusion is beneficial. |
| Economics | 6 | Published evidence with respect to clinical and economic value [Cher 2019\(^{120}\)]  
Work intensity [Frank 2016\(^{121}\)]  
Productivity and indirect costs [Saavoss 2016\(^{68}\)]  
Ignoring the SI joint during LBP evaluation is costly [Polly 2016\(^{67}\)]  
Cost-effectiveness [Cher 2016\(^{11}\)]  
Work effort in MIS SI joint fusion [Garber 2015\(^{122}\)] | MIS SI joint fusion is cost-effective and can be cost saving with proper evaluation of LBP and the SI joint.  
Work effort and intensity is comparable to lumbar discectomy.  
SI joint fusion may increase worker productivity in affected individuals. |
| Biomechanics | 7 | FEA model, S2AI screws and iFuse in lumbar instrumentation [Casaroli 2019\(^{123}\)]  
Changes after SI joint fusion by 3-D motion Analysis Technique [Jeong 2018\(^{124}\)]  
FEA model, assessing implant number, orientation, and length [Lindsey 2018b\(^{74}\)]  
Unilateral and bilateral stabilization [Lindsey 2018a\(^{73}\)]  
FEA model, minimal affects to adjacent lumbar segment motion [Lindsey 2015\(^{72}\)]  
Comparison of implant placement technique [Soriano-Baron 2015\(^{75}\)]  
Stability achieved & maintained post-cycles [Lindsey 2014\(^{71}\)] | 3 implants with the superior implant reaching sacral midline provided the most stable construct.  
Unilateral stabilization does not affect the non-treated joint.  
Triangular implants stabilize the SI joint, reduce range of motion, with minimal affects to lumbar spine |
| Other | 9 | Post-market surveillance of iFuse and iFuse-3D Implants [Cher 2018]  
Utility of ODI as an outcomes measure after SI joint fusion [Mao 2018]  
iFuse-3D, *in vivo* results [MacBarb 2017]  
Biplanar surgical procedure video [Vanaclocha 2016]  
4-year survivorship from revision analysis (Apr 2009 – Aug 2014) [Cher 2015]  
ODI valid measure of SI joint function [Copay 2015]  
Intraoperative neuromonitoring [Woods 2014]  
Surgical technique video [Geisler 2013]  
Complaints analysis (Apr 2009 – Jan 2013) [Miller 2013] | Implants exhibit substantial bony ongrowth/ingrowth. iFuse-3D Implants experience significantly more bony ongrowth/ingrowth, but also through growth. Favorable safety profile with low complication and revision rates. |
3.1 Prospective Clinical Trials

Several prospective clinical trials using the iFuse Implant System are in progress. The table below provides an overview of each along with links to the respective study’s registration on ClinicalTrials.gov.

<table>
<thead>
<tr>
<th>LOE</th>
<th>INSITE</th>
<th>Design</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Investigation of Sacroiliac Fusion Treatment</td>
<td>Prospective, multicenter, randomized controlled trial comparing iFuse to non-surgical management (NSM)</td>
<td>148 subjects&lt;br&gt;19 sites&lt;br&gt;Trial duration: 24-month&lt;br&gt;6-mo\textsuperscript{110}, 12-mo\textsuperscript{90}, and 24-mo\textsuperscript{1} results published&lt;br&gt;<em>Completed</em></td>
</tr>
</tbody>
</table>

| Trial | iMIA | iFuse Implant System® Minimally Invasive Arthrodesis | Prospective, multicenter, randomized controlled trial comparing iFuse to conservative management (CM) | 103 subjects<br>9 sites<br>4 European countries<br>Trial duration: 24-month<br>6-mo\textsuperscript{104}, 12-mo\textsuperscript{61}, and 24-mo\textsuperscript{2} results published<br>*Completed* |

| SIFI | Sacroiliac Joint Fusion with iFuse Implant System | Prospective, multicenter, single-arm trial | 172 subjects<br>26 sites<br>Trial duration: 24-month<br>6-mo interim\textsuperscript{113}, 12-mo\textsuperscript{91}, and 24-mo\textsuperscript{3} results published<br>*Completed* |

| LOIS | Long-Term Follow-up in INSITE/SIFI | Long-term follow-up with subjects from INSITE and SIFI | 103 subjects<br>12 sites<br>Trial duration: 5 years<br>3-yr\textsuperscript{62} and 4-yr\textsuperscript{63} results published<br>5-yr follow-up results (submitted, in review)\textsuperscript{6} |

| SALLY | Study of Bone Growth in the Sacroiliac Joint After Minimally Invasive Surgery with Titanium Implants | Studies sacroiliac joint fusion with iFuse-3D Implants | 51 subjects (enrolled and treated)<br>11 Sites<br>Trial duration: 5 years<br>6-mo interim results on 28 subjects\textsuperscript{4}<br>Follow-up ongoing for 5 years |
3.1.1 Level I – Randomized Controlled Trials

INSITE (ClinicalTrials.gov NCT01681004)

The “Investigation of Sacroiliac Fusion Treatment” (INSITE) study is a 2-year Level I randomized controlled trial (RCT) conducted in 19 centers in the U.S. and included 148 subjects that were randomized in a 2:1 ratio to either immediate SI joint fusion with iFuse (iFuse, 102 subjects) or non-surgical management (NSM, 46 subjects). Subjects were evaluated at follow-up visits scheduled at 1, 3, 6, 12, 18 and 24 months after assignment to NSM or iFuse had been performed. NSM treatments were consistent with existing US practices and directed by each site investigator for each subject. Treatments included pain medications, physical therapy following American Physical Therapy Association (APTA) guidelines, intraarticular SI joint steroid injections and radiofrequency (RF) ablation of sacral nerve roots delivered in a stepwise fashion as needed to address pain and disability according to each subject’s individual needs. Per trial protocol subjects randomized to NSM had the option to cross over to iFuse after the 6-month visit. The trial’s primary success endpoint was a binary success/failure composite measure at 6 months. A subject was considered to be a success if all of the following criteria were met: reduction in VAS SI joint pain score by at least 20 points from baseline, absence of device-related serious adverse events, absence of neurological worsening related to the lumbosacral nerve roots, and absence of surgical reintervention (i.e., removal, revision, reoperation, or supplemental fixation) for SI joint pain. Secondary outcomes measured were SI joint pain (VAS SI joint pain, 0-100 scale), back function assessment (as measured by Oswestry Disability Index, or ODI), quality of life (SF-36 and EQ-5D), patient satisfaction, and adverse events. Per protocol participating patients were to have a high-resolution CT scan at 24 months.

Two-year follow-up results were published in August 2016 in the *International Journal of Spine Surgery* [Polly 2016] the official journal of the International Society for the Advancement of Spine Surgery (ISASS). The results show iFuse provided superior clinical outcomes compared to non-surgical management in patients with SI joint dysfunction causing chronic, unremitting pain. Subjects treated with iFuse had rapid (within 1 month) improvement in both SI joint pain and disability (ODI) that was sustained through 24 months (Figures 1 and 2). From baseline to 24 months, the iFuse treated subjects improved a mean 55.8 points in VAS SI joint pain (82.3 down to 26.1) and 28.5 points in ODI (57.2 down to 28.5). In contrast, at 6 months, the NSM group had a mean decrease in SI joint pain of 12.2 points and 4.6 points for ODI. The 6-month VAS SI joint pain improvement was 38.2 points greater for the iFuse group compared to the NSM group (p<0.0001, repeated measures analysis of variance). No early crossover (before 6 months) occurred in the NSM group, but after the 6-month visit 89% (39 of 44) of NSM subjects still participating crossed over to be treated with iFuse. After crossover, both SI joint pain and ODI scores improved in a fashion similar to subjects originally treated with iFuse (dashed lines, Figures 1 and 2). After month 6, 82% of the iFuse subjects and 26% of NSM subjects met the trial’s primary success endpoint. Similar rapid and sustained improvement was seen in the iFuse group for quality of life (SF-36 and EQ-5D) which was also significantly greater improvement compared to NSM. Patient satisfaction rates were higher at 6 months for iFuse compared to NSM (77% vs. 27% very satisfied, p<0.0001), and satisfaction remained high at 12 and 24 months for the iFuse group (78% and 73%). At 6 months, the number of iFuse subjects taking opioids decreased 9% in contrast to a 7.5% increase for NSM subjects. By 24 months, there was nearly a 30% decrease in opioid users by iFuse subjects. There was no statistical difference in mean number of adverse events per subject between the iFuse and NSM groups in the first 180 days (1.5 iFuse vs. 1.3 NSM, p=0.2253). Additionally, only 3
subjects originally assigned to iFuse (or 3%) underwent revision surgery within 24 months highlighting the safety and durability of the iFuse Procedure.

A year previously, the 12-month follow-up outcomes from INSITE [Polly 201590] were published online ahead of print (August 2015) and later highlighted as “Editor’s Choice” on the cover and as the featured article of the November 2015 issue of Neurosurgery, the official journal of the Congress of Neurological Surgeons (CNS). The 12-month manuscript was accepted in the “rapid review” publication process as a “high impact manuscript,” given its importance to the neurosurgical community.

Results showed that the iFuse Procedure was more effective than NSM in relieving pain, improving patient function, and improving quality of life at 1 year in appropriately selected patients with SI joint dysfunction caused by degenerative sacroiliitis or SI joint disruption. Patients who failed NSM and opted to cross over to the iFuse Procedure also received substantial clinical benefit in pain, patient function, and quality of life similar to subjects originally randomized to surgery.
[Polly 201580]. (Note: 6-month outcomes from the trial were published earlier in March 2015 in the *International Journal of Spine Surgery* [Whang 2015110]).

**iMIA (ClinicalTrials.gov NCT01741025)**

A second, Level I RCT recently completed in Europe. This trial, entitled “iFuse Implant System Minimally Invasive Arthrodesis” (iMIA), enrolled and treated 103 patients from 9 clinical sites in 4 countries. iMIA is nearly identical in design to the U.S. trial INSITE, with subjects diagnosed by the same algorithm being assigned at random to either conservative management (CM) consistent with European guidelines or minimally invasive SI joint fusion with iFuse. (In Europe, conservative management relies primarily on physiotherapy and education and does not include SI joint steroid injections or RF ablation.) Subjects were followed for two years.

One-year results mirror those from INSITE and were published in *Pain Physician* in September 2017 [Dengler 2017b61]. Mean LBP improved by 41.6 VAS points (0 – 100 VAS pain scale) in the iFuse group compared to 14.0 points in the CM group (Figure 3), and the mean ODI improved by 25.0 points in the iFuse group compared to 8.7 points in the CM group (Figure 4). Also, mean improvements in leg pain and EuroQoL-5D quality of life (EQ-5D) were large after SI joint fusion and superior to those after CM. CM subjects were allowed to cross over to SI joint fusion after six months and subjects who crossed over to surgical treatment had no pre-crossover improvement in pain and ODI scores. After crossover, improvements in most measures were as large as those patients originally assigned to SI joint fusion.

The two-year follow-up from the iMIA clinical trial was published in the *Journal of Bone and Joint Surgery* in March 2019 [Dengler 20192]. Like the randomized controlled trial INSITE, the low back pain (VAS LB) and disability (ODI) improvement at 1-year was sustained (Figure 3). Mean VAS LB pain improvement was 45 points for the iFuse treated subjects and 11 points for those treated with conservative management (CM). Similarly, disability improved a mean of 26 points versus 8 points, iFuse versus CM, respectively. Parallel results were seen in multiple patient-reported parameters, including leg pain, quality of life, and walking distance. The iFuse subjects also had a significant improvement in work status. The low back, leg, and VAS pain component of EQ-5D graphs, along with back function/disability (ODI), quality of life (EQ-5D TTO), and Zung Depression Score results are shown below (Figure 5).
Figure 3 (iMIA 2-year Outcomes)
Previously, iMIA 6-month primary endpoint results were published in the European Spine Journal in May 2016 [Sturesson 2016]. Nearly 79% of the iFuse subjects had pain decrease of ≥20 points compared to 22% of the CM subjects. The trial included two functional assessments (SI joint function via active straight leg raise [ASLR] test and walking distance), neither of which had been previously reported, and both showed improvement in the iFuse group but not in the CM group. Frequency of adverse events did not differ between groups (number of events per subject slightly smaller in the iFuse group compared to CM: 0.19 vs. 0.2, p=0.0918).

### 3.1.2 Level II/IIb – Clinical Evidence

**SIFI (ClinicalTrials.gov NCT010640353)**

There are several publications describing results from a well-designed prospective, multicenter, single-arm study involving the iFuse Implant System (SIFI, “Sacroiliac Joint Fusion with iFuse Implant System”). SIFI is the largest iFuse prospective study with 172 subjects from 26 U.S. clinical centers. To participate, adult (age 21-70) patients had to have LBP for at least 6 months inadequately responsive to non-surgical care, a baseline SI joint pain score of at least 50 on the 0-100 mm visual analog scale (VAS), an Oswestry Disability Index (ODI) score of at least 30, and diagnosed SI joint dysfunction due to degenerative spondylitis or sacroiliac joint disruption. Subjects underwent structured assessments preoperatively and at 1, 3, 6, 12, 18 and 24 months postoperatively, including VAS SI joint pain, ODI, SF-36, EQ-5D, and patient satisfaction. Adverse events were collected throughout follow-up. Per protocol participating patients were to have a high-resolution CT scan at 1 year.

Two-year follow-up results were published in the International Journal for Spine Surgery titled “Triangular Titanium Implants for Minimally Invasive Sacroiliac Joint Fusion: 2-Year Follow-Up from a Prospective Multicenter Trial” [Duhon 2016]. Subjects treated with the iFuse Implant System had clinically important and statistically significant long-term improvements in pain, disability, and quality of life. Improvements at 6 and 12 months were maintained through 24 months, and treated subjects were approaching normal values. Mean SI joint pain improved from 79.8 at baseline to 30.0, 30.4, and 26.0 at 6, 12, and 24 months respectively (mean improvements of 49.9, 49.3, and 53.3 points, p<0.0001 each) (Figure 4). Mean ODI improved from 55.2 at baseline to 32.5, 31.5, and 30.9 at 6, 12, and 24 months (improvements of 22.7, 23.8, and 24.5 points, p<0.0001 each) (Figure 5). There was also a 28% reduction in the proportion of subjects using opioid medication from baseline to 24 months. Radiographs showed a high rate (97%) of bony apposition to at least two implants on both the iliac and sacral sides. Only 7 device-related adverse events were reported, and a low revision rate of 4.7% (8 subjects) by 24 months. Satisfaction rates were high, with 78% reporting being very satisfied with SI joint fusion treatment and 94% being very or somewhat satisfied by 24 months.
Previous SIFI results have been published in the *Global Spine Journal* (12-month follow-up) [Duhon 2016, Epub 2016 Aug 11^1^] and in *Medical Devices: Evidence and Research* (6-month interim results) [Duhon 2013^13^].

**SALLY (ClinicalTrials.gov NCT03122899)**

To date, all published triangular titanium implant studies have used solid implants (iFuse) with porous surfaces manufactured through a coating process, porous titanium plasma spray (TPS). TPS implants, while commonly used on metallic implants for the hip [Cook 1988^1^], knee, and spine [Yoon 2016^13^], typically have low interconnectivity and small pore sizes (100 - 150 μm). With the advent of 3D metal printing (also known as additive manufacturing), implants with new microstructures can be produced. In 2017, a new triangular titanium implant manufactured via 3D printing (iFuse-3D), became commercially available. In tissue culture, these implants support growth of human osteoblasts with higher calcium production vs. implants with porous spray surfaces [MacBarb 2017a^10^]. In a sheep femur model, iFuse-3D implants showed higher bone ingrowth [MacBarb 2017b^8^].

The SALLY clinical trial (“Study of Bone Growth in the Sacroiliac Joint After Minimally Invasive Surgery with Titanium Implants”) is the first prospective multicenter study using the iFuse-3D implants. This 5-year follow-up study has enrolled and treated 51 subjects at 11 sites. Six-month interim follow-up results from 28 patients has been published [Patel 2019^4^]. Pain scores decreased by 51 points and ODI decreased by 21 points (both p<0.0001). Patient’s quality of life as measured by EuroQol 5-Dimension Time Trade-off (EQ-5D TTO) also improved. The proportion of subjects able to perform various back/pelvis-related physical functions with minimal difficulty improved significantly for nearly all activities. Opioid use decreased, and physical function as assessed with three objective tests, improved.

Early results from this prospective multicenter trial confirm that clinical responses to a 3D triangular titanium implant for SI joint fusion are similar to those from prior trials. See figure 6 below comparing the prospective results from the INSITE, iMIA, SIFI, and SALLY trials.
Figure 6

The graphs show the effectiveness of different treatments for SIJ pain over time. The VAS SIJ pain graph compares non-surgical management with surgical interventions, indicating a significant reduction in pain intensity. The ODI graph highlights improvements across all treatment groups, with a marked decrease in disability. The EQ5D TTO Index shows a consistent improvement in quality of life, with all treatment groups experiencing gains in the months following treatment initiation.
3.1.3 Prospective Trials – Pooled Data

The clinical outcomes from prospective multicenter trials INSITE, iMIA, and SIFI are remarkably consistent. The combined trials provide over 320 prospectively followed subjects treated with iFuse. Results of a Level I pooled analysis were published in March 2017 in *SPINE* [Dengler 2017a].

Below are the 2-year pain and disability data as of April 2019 from INSITE, iMIA and SIFI trials demonstrating the similar results across patients and sites.

![Figure 7](image1.png)
![Figure 8](image2.png)
3.1.4 Prospective Trials – Long-Term Follow-up

LOIS (ClinicalTrials.gov NCT02270203)

The purpose of LOIS (Long-Term Follow-Up in INSITE/SIFI) is to evaluate the long-term safety and effectiveness of SI joint fusion using the iFuse Implant System. This study extended follow-up from two completed multicenter prospective US clinical trials (INSITE and SIFI, see sections above). All participants have already undergone the surgical procedure. The trial is fully enrolled (n=103 from 12 sites) and follows patients out to 5 years measuring pain, disability, and QOL. All participants had a radiographic pelvic CT scan at 5 years.

The 3-year results were published April 2018 [Darr 2018a62] and 4-year results were published in August 2018 [Darr 2018b63]. The LOIS 5-year results have been submitted and is under review at the journal Medical Devices: Evidence and Research [Whang 20196]. Results show the early statistically significant and clinically important improvements in pain, disability (ODI), and quality of life seen at 2-years were sustained out to 3, 4, and 5 years (Figure9). From baseline to 5 years, there was a 54-point mean improvement (decrease) in SI joint pain, a 26-point mean improvement (decrease) in ODI, and a quality of life improvement (increase) of 0.29 measured by EuroQoL-5D time trade-off (EQ-5D TTO). Patient satisfaction remained high, and the proportion of patients taking opioids decreased from 77% immediately prior to having the iFuse surgery to 43% at the 5-year follow-up. Only one adverse event (intermittent hip and gluteal pain) was considered device-related, and two events – both SI joint pain – were deemed related to the procedure. A total of 3 of 103 enrolled subjects in LOIS underwent SI joint revision by 5 years (3%).
Figure 9 (LOIS 5-year Outcomes)
3.1.5 Other Publications

SI Joint-related Postpartum Pelvic Girdle Pain

Postpartum pelvic girdle pain (PPGP) is a major health issue among postpartum women. A subgroup analysis of the chronic SI joint pain subjects in the SIFI trial was performed, grouping subjects to women whose pain began during pregnancy or the peripartum period (i.e., women with SI joint-related PPGP), non-PPGP women, and men. The goal of this analysis was to determine whether women whose SI joint pain began in the peripartum period experience symptom and disability relief similar to other women and men. Of 172 enrolled subjects in SIFI, 52 were men, 100 were women without PPGP, and 20 were women with PPGP (16.7% of 120 trial females, 11.6% of all 172 trial subjects). PPGP subjects were significantly younger (43.3 years, vs. 52.8 for females without PPGP and 50.5 for men, p = 0.002). There were no differences in any other demographic or baseline clinical measure.

Results were published in October 2015 [Capobianco 2015111]. Women with PPGP experienced a significant improvement in pain (51-point VAS decrease), patient function (20.6-point ODI decrease), and quality of life (SF-36 PCS +10.4, MCS +7.2, EQ-5D +0.31) at 12 months after surgery. These improvements were characteristic of the overall study results (see section 3.1.2 Level II/IIb – Clinical Evidence); no difference was detected between sub-groups. The mean adverse event rates per subject were similar across sub-groups as well (PPGP 1.8, no-PPGP 1.6, Male 1.7). The article concluded that the SI joint can be a source of pain in women with persistent PPGP and should be investigated as a pain source. As a result, women with carefully diagnosed chronic SI joint pain from PPGP recalcitrant to conservative therapies experienced clinically beneficial improvements in pain, disability and quality of life after minimally invasive SI joint fusion with iFuse.

Health State Utility

To measure the amount of improvement that is obtained following SI joint fusion with the iFuse Procedure, health state utility values from patients participating in the prospective, multicenter SIFI trial were compared to values from a normal patient cohort and published in the Global Spine Journal [Cher 2015112]. Health state utility values were calculated using the EuroQOL-5D (EQ-5D) and Short Form-36 (SF-36) scores at baseline and 6 and 12 months after SI joint fusion surgery in subjects (n=172). Values were compared with individuals who participated in a nationally representative cross-sectional survey (National Health Measurement Study [NHMS], n=3,844) after statistically adjusting for age and gender differences between the two cohorts. Baseline utility values prior to surgery were significantly depressed compared to normal populations, again highlighting quality of life is markedly impaired in patients with SI joint pain compared with age- and gender-matched cohorts. After the iFuse Procedure, patients saw substantial improvement in health state utility at 6 months that was sustained through 12 months, bringing the population back toward the expected levels of overall health.

SI Joint Block Response Predictive of SI Joint Fusion Response?

Using data from both INSITE and SIFI, Polly et al. investigated the correlation of pain relief from the SI joint block, when diagnosing SI joint pain, with SI joint fusion outcomes. A threshold of at least 50% pain relief from a SI joint block was used as inclusion criteria during diagnostic evaluation of subjects participating in INSITE and SIFI. Patients with 50% pain reduction on diagnostic injection had similar
results after MIS SI joint fusion as those with 60, 70, 80, 90, and 100% pain relief after diagnostic injection. The degree of pain improvement received from an SI joint diagnostic block did not predict improvements in pain and ODI after treatment with the iFuse Implant System. This 50% threshold resulted in subjects having excellent SI joint fusion responses. The conclusion was the ≥75% SI joint block pain relief criteria often used during SI joint pain diagnosis is overly stringent and thus will withhold a beneficial procedure from patients with chronic SI joint dysfunction [Polly 2016].

### 3.2 Level III – Comparative

#### 3.2.1 iFuse vs. Screws

Retrospective, single-center review analyzed the revision rates for SI joint fusion with iFuse compared to SI joint fixation with screws [Spain 2017]. The 4-year probability of revision was significantly lower for iFuse (5.7%) compared to screws (30.8%). Subgroup analysis showed implant used was the only predictor of revision. By year 8 post procedure, 80% of the patients treated with screws had a revision (Figure 13).

![4-year Cumulative Revision Rate: iFuse vs. Screws](image_url)

**Figure 10**

#### 3.2.2 iFuse vs. RF vs. CM

A retrospective case series reported 6-year follow-up results of patients with chronic SI joint pain treated with conservative management (CM, n=63), SI denervation (radiofrequency ablation, RF, n=47), and SI joint fusion with iFuse (n=27) [Vanaclocha 2017]. The iFuse group had markedly superior pain relief and functional improvement (ODI) compared to CM and RF treatment (Figure 14). This clinically important improvement from iFuse treatment was maintained long-term out to 6 years. Additionally, iFuse patients saw a dramatic reduction in the number of patients taking opioids from 63% at baseline down to only 7% at last follow-up. In contrast, the CM and RF patients increased use of opioids (>80%) (Figure 15). Similarly, a larger number of iFuse treated patients were able to return to full or part-time work compared to patients treated with CM and RF. Another interesting component to this study was that all patients were originally offered the iFuse treatment, but due to lack of...
insurance coverage for MIS SI joint fusion, many patients had to be treated conservatively or with SI denervation (RF).

Figure 11

Figure 12
### 3.2.3 iFuse vs. Open

Two studies show that minimally invasive SI joint fusion with the iFuse Procedure provides better operative measures and clinical outcomes than open SI joint fusion [Graham Smith 2013\(^{97}\), Ledonio 2014b\(^{103}\)]. A third study showed similar outcomes Ledonio 2014a\(^{102}\). Summary of these studies is provided in the table below.

<table>
<thead>
<tr>
<th>Article</th>
<th>Patients</th>
<th>Description</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graham Smith 2013(^{97})</td>
<td>114 iFuse 149 Open</td>
<td>Retrospective, multicenter, comparison 12- and 24-mo follow-up</td>
<td>MIS SI joint fusion provided better operative measures (intraoperative blood loss, OR time, hospital length of stay) and greater pain relief compared to open surgery at 12 and 24 mo.</td>
</tr>
<tr>
<td>Ledonio 2014a(^{102})</td>
<td>22 iFuse 22 Open</td>
<td>Retrospective, single-center comparison Minimum 12-mo follow-up</td>
<td>Patients treated with the minimally invasive SI joint fusion procedure had significantly less blood loss, shorter OR time, and shorter hospital length of stay compared to open. Both open and minimally invasive SI joint fusion provided significant ODI improvement with no difference between the groups.</td>
</tr>
<tr>
<td>Ledonio 2014b(^{103})</td>
<td>17 iFuse 22 Open</td>
<td>Retrospective, two-center, comparison 12-mo follow-up</td>
<td>Both open and minimally invasive SI joint fusion provided significant ODI improvement. Minimally invasive SI joint fusion provided significantly greater ODI improvement, and shorter OR time, and shorter hospital length of stay than open fusion.</td>
</tr>
</tbody>
</table>

### 3.3 Systematic Reviews

As part of an SI joint dysfunction focus issue in *Techniques in Orthopaedics*, Whalen and Duhon presented a review of the various treatment options which include conservative management, open surgical fusion, and minimally invasive fusion. The effectiveness of these treatment strategies including the various studies that directly compare the different modalities were reviewed. They concluded that patients with SI joint dysfunction should first undergo a 6-month trial of conservative management before being considered for surgical intervention. If surgery is being considered, they prefer minimally invasive techniques due to the lower morbidity [Whalen 2019\(^{115}\)].

February 2019, Shamrock *et al.* published a systematic review of the existing literature to determine the safety of minimally invasive SI joint fusion through the rate of procedural and device-related intraoperative and postoperative complications [Shamrock 2019\(^{116}\)]. Fourteen studies of 720 patients (499 females/221 males) with a mean follow-up of 22 months were included. Procedural-related complications was 11% with the most common adverse event being surgical wound infection/drainage (n=17). Twenty-five adverse events were attributed to be secondary to placement of the implant (3%) with nerve root impingement (n=13) being the most common. Overall revision rate was 2.56%. Additionally, a clinically important decrease in pain and disability (ODI) was reported. Author’s concluded the procedure is relatively safe but is not without certain risks. Possible areas of
improvement include preoperative patient optimization, operative technique, and use of intraoperative real-time imaging.

Tran et al. performed a systematic review and meta-analysis to evaluate treatment efficacies and patient outcomes associated with minimally invasive joint fusion in comparison to screw-type surgeries [Tran 2019117]. Data compilation, coding, and extraction were performed using MedAware Systems’ proprietary software. A total of 20 studies had adequate data to calculate a standardized mean difference and were included in the meta-analysis. Results of iFuse trials were compared to screw-type trials, pooled in three categories of outcomes. Subjects treated with iFuse showed significantly superior outcomes compared to screw-type procedures for improvement in pain (difference, p=0.01), disability/physical function (p=0.01), and global/quality of life (p=0.04).

A level II clinical evidence publication entitled, “A Systematic Review of Minimally Invasive Sacroiliac Joint Fusion Utilizing a Lateral Transarticular Technique,” was published in the International Journal of Spine Surgery [Heiney 20159]. Study authors used PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, a published standard for systematic reviews, to perform a systematic review and meta-analysis of published literature reporting clinical outcomes on subjects who underwent MIS SI joint fusion using a lateral transarticular approach. A total of 18 articles (published as of May 2015) met the inclusion criteria and after accounting for overlapping cohorts, 12 unique cohorts from 4 countries were extracted for a total of 432 subjects. Of the 12 unique cohorts, 10 were iFuse cohorts that included a total of 368 (85%) treated subjects. For the 12 unique cohorts, random effects meta-analysis (RMA) mean procedure time was 59 minutes (range 27-78), estimated blood loss was 36.9 cc (range 10-70) and hospital length of stay (LOS) was 1.7 days (range 0-7). The RMA mean pain score dropped by 5.2 points (on a 10-point scale) at 6 months and 5.3 points at 12 months (baseline score of 8.1, 12-month score of 2.7), and a 24-month score of 2.0 (Figure 16). ODI decreased by 31 points at 12 months (baseline score of 56.2, 6-month score of 30.7, and 12-month score of 25.1) (Figure 17). Two studies in the review had long-term (up to 4.5 years [Vanaclocha 201465 and 5 years [Rudolf 201466]) follow-up with consistent results.

Zaidi et al. compiled results from 16 SI joint fusion articles both open and MIS techniques (5 consecutive case series, 8 retrospective, 3 prospective) for a total of 430 subjects (131 open with mean follow-up of 60 months, 299 MIS with mean follow-up of 21 months) [Zaidi 2015119]. Five iFuse publications were included: Rudolf 201298, Cummings 201393, Duhon 2013113, Sachs 201394 and Ledonio 2014a102. Authors concluded surgical intervention for SI joint pain is beneficial in a subset of patients, however accurate diagnosis is key, and all possible causes of pain and alternate treatments should be considered before undergoing SI joint fusion.
Lingutla *et al.* published a systematic review and meta-analysis of 6 SI joint fusion articles for a total of 407 subjects (92 open, 315 MIS) with a mean follow-up of 17.6 months [Lingutla 2016][18]. Four iFuse publications were included (Duhon 2013[13], Ledonio 2014a[102], Rudolf 2014[66], Sachs 2014[92]). Outcomes reported were pain, ODI, SF-36 and Majeed Score, concluding SI joint fusion to be satisfactory in relieving SI joint pain.

### 3.4 Additional Clinical Evidence

Multiple retrospective studies demonstrate rapid and sustained clinical improvement in pain, disability, and quality life with the iFuse Procedure that are consistent with the prospective studies. The most recent retrospective publications include a 160 patient, 12-month follow-up study in Germany, reporting SI joint fusion with iFuse implants produces clinically significant decreases in pain and disability related to SI joint dysfunction [Rainov 2018][100]. A single center, two-surgeon retrospective study of 50 patients with a mean follow-up of nearly 14 months using a mini-open SI joint fusion with direct bone grafting technique. Results showed similar rapid (1 month) and sustained (1 year) improvement in pain and disability. Functional improvement was also demonstrated using the Denver Sacroiliac Joint Questionnaire (DSIJQ) that has patients evaluate 10 functional domains: sitting, sitting, getting up from a chair, walking, stairs, getting in and out of a car, bending at the waist/kneeling/squatting, lifting, work/recreation/sex/social activities, sleep, and stability [Cleveland III 2019][101].

Long-term follow-up studies have shown sustained results out to 4.5 years [Vanaclocha 2014][65] and 5 years [Rudolf 2014][66]. Additionally, patients with SI joint pain, with or without a history of prior lumbar spine fusion, show significant improvement in pain after minimally invasive SI joint fusion [Rudolf 2013][131]. Similarly, patients that developed SI joint pain after prior long-fusion to the sacrum for corrective scoliosis surgery, had significant pain reduction and quality life improvement after minimally invasive SI joint fusion [Schroeder 2013][95]. Other publications of note with similar positive outcomes include Cummings 2013[93] that reported improvement in pain (VAS) and disability (ODI), Gaetani 2013[96] reported pain relief (VAS) and quality of life improvement (Roland-Morris Questionnaire), and a multicenter retrospective analysis of 144 patients by Sachs 2014[92] reported more than 90% of the patients received clinically important pain relief after being treated with iFuse. A more recent Sachs publication [Sachs 2016][64] reported longer-term follow-up (mean 3.7 years) for 107 iFuse treated subjects. Patients experienced improved pain (mean 4.8-point decrease on a 10-point scale), low disability scores (mean 28.2-point ODI decrease), and improved ability to perform activities of daily living such as walking, sleeping and getting in and out of a car. Procedure-related complications were uncommon, and the revision rate was low (4.7%).

### 3.5 Biomechanics

Several biomechanics studies have been published on the iFuse Implant System to assess the technique and performance of the implants. Cadaveric studies have shown SI joint range of motion (ROM) significantly decreased after placement of iFuse implants and does not increase after cyclic loading [Lindsey 2014][71]. Another study assessed lateral trans-articular implant placement demonstrating that within the safe zones of the sacrum there is surgical flexibility of implant placement to provide stability [Soriano-Baron 2015][25]. Investigation of unilateral and bilateral SI joint
fusion demonstrated that single-sided SI joint stabilization significantly reduces the ROM of the treated side but does not significantly reduce or increase the ROM of the nontreated contralateral SI joint. Additionally, bilateral stabilization is necessary to significantly reduce the ROM of both SI joints [Lindsey 2018a73]. Two finite element analysis (FEA) studies have been published on SI joint stabilization with triangular iFuse implants. The first reported that SI joint stabilization has minimal (< 5% ROM increase) effect on adjacent lumbar segments [Lindsey 201572], and these minimal increases were substantially lower than the motion increases seen on adjacent lumbar segments after lumbar fusion reported in other biomechanical studies [Ha 1993132, Ivanov 2009133, Kyaw 2014134]. The second FEA study looked at the number, orientation, and length of the iFuse implants and demonstrated that placement of three implants across the SI joint using a transarticular orientation is better than two implants. Additionally the superior implant reaching the sacral midline resulted in the most stable construct and the best stabilization was achieved when the implants were placed furthest apart [Lindsey 2018b74]. Another biomechanics article assessed ROM using a 3-dimensional motion analysis technique which may provide improved insight into SI joint movement and biomechanical changes [Jeong 2018124]. The most recent article is an FEA model study that evaluated stresses when S2 alar-iliac screws and laterally placed iFuse implants for sacropelvic fixation are combined with long posterior lumbar instrumentation. The study concluded implant stresses were lower with SI joint fixation with iFuse [Casaroli 2019123].

3.6 Other Publications

There are two publications that describe the technique via a live procedure video [Geisler 2013128, Vanaclocha 2016126]. Copay validates the use of ODI as a good measure of back function for patients suffering with SI joint pain [Copay 2015127]. A retrospective study stresses ODI is a useful outcomes measurement post-SI joint fusion, but cautions the interpretation of the results in patients with a prior lumbar fusion, highlighting the importance of obtaining baseline values and subset analyses [Mao 2018125]. The utility of intraoperative neuromonitoring during an iFuse Procedure is described [Woods 2014107], and MacBarb presents data using an in vivo sheep model to demonstrate the ongrowth and ingrowth of bone to the iFuse Implant, and ongrowth, ingrowth, and through growth to the iFuse-3D Implant [MacBarb 2017(Part 1)89].

There are several publications that report the safety of the iFuse Procedure. In September 2018, a publication compared complaints related to use of the iFuse-3D Implant (3-D printed implant; commercially available since mid-2017) to the iFuse Implant (machined implant with titanium plasma spray (TPS) coating, commercially available since 2009). From January 1, 2015 to June 30, 2018, 14,210 iFuse Procedures were performed (3,140 with iFuse-3D Implants and 11,070 cases with iFuse Implants). Issues related to instruments occurred at a low and constant rate (~1.3%), while pain-related complaints were low and similar for iFuse and iFuse-3D Implants (<0.5%). Using Kaplan-Meier analysis, the one-year cumulative probability of surgical revision was low for both implants (1.5% iFuse, 1% iFuse-3D), and no implant breakages or migrations were identified [Cher 201870]. In 2013, a post-market database analysis of 5,319 patients treated between April 2009 and January 2013 detailed the 204 (3.8%) patients with complaints, finding pain with nerve impingement (0.9%) and recurrent SI joint pain (0.8%) were the most frequently cited causes. Only 1.8% of the patients had revision surgery (mean follow-up of 30 months) which was typically performed in the early postoperative period for a symptomatic malpositioned implant (0.9%) or to correct an improperly sized implant in asymptomatic
patients (0.2%) [Miller 201369]. A cumulative 4-year revision rate publication reported 96.5% of subjects treated with iFuse were free from revision surgery, representing a 3.5% revision rate. The revision rate did not differ by sex, was lower for patients >65 years of age, and the rate decreased annually since iFuse was introduced in 2009 [Cher 201510]. See also section 3.7 Safety Profile for additional information.
3.7 Safety Profile

The safety of any product and procedure is of critical importance. The safety profile for iFuse implants and the procedure is supported by multiple publications as summarized in the table below.

<table>
<thead>
<tr>
<th>Table 9</th>
<th>iFuse Implant System – Safety &amp; Revision Rate Profile</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Article</strong></td>
<td><strong>Description</strong></td>
</tr>
<tr>
<td>Whang 2019&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Prospective, multicenter (n=92) 5-year results</td>
</tr>
<tr>
<td>Dengler 2019&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Prospective, multicenter, RCT (n=52 iFuse, n=51 CM) 2-year results</td>
</tr>
<tr>
<td>Cher 2018&lt;sup&gt;70&lt;/sup&gt;</td>
<td>Postmarket surveillance of complaints for iFuse-3D Implants, and comparison to iFuse Implants (n=14,210) 11,070 cases using iFuse Implants 3,140 cases using iFuse-3D Implants</td>
</tr>
<tr>
<td>Darr 2018&lt;sup&gt;b63&lt;/sup&gt;</td>
<td>Prospective, multicenter (n=93) 4-year results</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
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<tr>
<td>---------------</td>
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</tr>
<tr>
<td>Darr 2018a62</td>
<td>Prospective, multicenter (n=103) 3-year results</td>
</tr>
<tr>
<td>Polly 20161</td>
<td>Prospective, multicenter, RCT (n=102 iFuse, n=46 NSM) 2-year results</td>
</tr>
<tr>
<td>Sachs 201664</td>
<td>Retrospective, multicenter (n=107) 3.7-year follow-up</td>
</tr>
<tr>
<td>Duhon 20163</td>
<td>Prospective, multicenter, single-arm, clinical trial (n=172) 2-year results</td>
</tr>
<tr>
<td>Cher 201510</td>
<td>4-year survivorship analysis (free from revision surgery) n=11,388</td>
</tr>
<tr>
<td>Miller 201369</td>
<td>Retrospective complaints database analysis (n=5319)</td>
</tr>
</tbody>
</table>

Specifically looking at 4-year cumulative revision rates, the 3.5% iFuse Procedure revision rate [Cher 201510] is favorable when compared with revision rates of other accepted and common lumbar surgeries: decompression (10-12%) and fusion (12-14%) [Martin 2007135, Deyo 2011136, Basques 2015137]. The revision rate also improved annually from 2009, possibly related to a surgeon learning curve and/or improved training (see figure 15 below).
Per FDA regulations (CFR - Code of Federal Regulations Title 21, 21CFR820.198), SI-BONE maintains a complaints system database. A complaint is any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution. Manufacturers and importers are required to maintain complaint files and establish and maintain procedures for receiving, reviewing, and evaluating complaints. Importers are also subject to complaint files because "initial distributors of foreign entities" fall under the definition of a manufacturer in 21 CFR 820.3.

The iFuse Implant System’s overall complaint and revision rates through May 2019 are as follows (data on file at SI-BONE, Inc.):

| Complaint Rate (Worldwide, cumulative since 2011) | 5.39% |
| Revision Rate (Worldwide, cumulative since 2011)   | 2.64% |

### 3.7.1 Instruction for Use, Information for Healthcare Professionals

The iFuse Implant System Instructions for Use (IFU) for healthcare Professionals is printed below and it along with the IFUs for all SI-BONE cleared products are also available at [www.si-bone.com/label](http://www.si-bone.com/label)

**iFuse Implant System IFU (500104 Rev. M)**

**DEVICE DESCRIPTION**

The iFuse Implant System consists of cannulated triangular, titanium (Ti 6Al4V ELI, ASTM F136) implants with a porous surface and an instrument system. Implant surface and shape are designed to prevent rotation and motion of the sacroiliac (SI) joint. The instrument system uses guide pins for accurate placement.

**INDICATIONS**

The iFuse Implant System is intended for sacroiliac fusion for conditions including sacroiliac joint dysfunction that is a direct result of sacroiliac joint disruption and degenerative sacroiliitis. This
includes conditions whose symptoms began during pregnancy or in the peripartum period and have persistied postpartum for more than 6 months.

The iFuse Implant System is also intended for sacroiliac fusion to augment immobilization and stabilization of the sacroiliac joint in skeletally mature patients undergoing sacropelvic fixation as a part of a lumbar or thoracolumbar fusion.

CONTRAINDICATIONS

1. Deformities or anatomic variations that prevent or interfere with iFuse placement.
2. Tumor of sacral or ilial bone.
3. Active infection at treatment site.
4. Unstable fracture of sacrum and or ilium involving the sacroiliac joint.
5. Allergy to metal components.

WARNINGS

1. Women of childbearing potential should be cautioned that vaginal delivery of a fetus may not be advisable following SI joint fusion. If pregnancy occurs, the woman should review delivery options with her obstetrician.

PRECAUTIONS

1. Carefully read and follow all instructions prior to use.
2. Patient adherence to post-operative physical activity instructions is important to support long-term service life of the implant.
3. Pay careful attention to selection of implant size. Pre-operative X-rays and/or CT scan may be helpful in selecting implant size.
4. Appropriate patient selection is necessary as patient factors such as size and weight may make use of iFuse more difficult or impossible.
5. Inspect iFuse Implants and delivery instruments for damage prior to use. Do not use if damaged or worn. Do not attempt to repair.
6. Do not use any component from an opened or damaged package.
7. Do not use implants after the expiration date.
8. If placing the iFuse Implants in conjunction with an open procedure, the surgeon should take care not to destabilize the joint prior to placing the implants.

MRI SAFETY INFORMATION

Non-clinical testing and MRI simulations were performed to evaluate the entire family of the iFuse implants. Non-clinical testing demonstrated that the entire family of the iFuse implants is MR Conditional. A patient with implant(s) from this family can be scanned safely in an MR system under the following conditions:

- Static magnetic field of 1.5-Tesla and 3-Tesla, only
- Maximum spatial gradient magnetic field of 4,000-Gauss/cm (40-T/m)
- Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 2-W/kg for 15 minutes of scanning (i.e., per pulse sequence) in the Normal Operating Mode

Under the scan conditions defined above, the implant(s) are expected to produce a maximum temperature rise of less than 5.4° C after 15 minutes of continuous scanning (i.e., per pulse sequence).
In non-clinical testing, the image artifact caused by the implant(s) extends approximately 20 mm from this device when imaged with a gradient echo pulse sequence and a 3-Tesla MR system.

**RISKS**

As with other surgical procedures used to treat SI joint conditions, the risks associated with the iFuse Implant System surgical procedure include, but are not limited to the following:

1. Adverse reactions to anesthesia
2. Hemorrhage
3. Muscle damage
4. Hematoma or seroma
5. Neurological deficit, nerve root or peripheral nerve injury, irritation or damage
6. Vascular injury or damage that may result in catastrophic or fatal bleeding
7. Neurovascular injury
8. Damage to lymphatic vessels and/or lymphatic fluid exudation
9. Injury to intra-pelvic structures
10. Infection of the wound, deep infection, peritonitis
11. Wound dehiscence
12. Pulmonary or systemic embolism
13. Thrombosis, thrombophlebitis
14. Death
15. Bruising
16. Local swelling
17. Radiation exposure

Potential risks specifically associated with the iFuse Implant System include, but are not limited to the following:

1. Infection
2. Pain, discomfort, or abnormal sensations due to presence of the implant
3. Instrument failure resulting in a complication
4. Migration, loosening or fracture of the implant
5. Pain in muscle(s) due to altered biomechanics
6. Nerve root or peripheral nerve root irritation due to local swelling or altered biomechanics
7. Loss of fixation / stabilization
8. Metal sensitivity or allergic reaction
9. Failure to improve symptoms and/or function
10. Increased pain at treated or adjacent levels
11. Need for re-operation or removal of the implant(s)
12. Implant rejection
13. Response to wear debris
14. Decrease in bone density due to stress shielding
15. Failure to achieve SI joint fusion
16. Potential difficulty in delivering fetus vaginally due to device-related restriction of SI joint motion
HOW SUPPLIED
iFuse Implants are provided sterile; do not resterilize. The instrumentation is provided separately, non-sterile, and must be sterilized prior to use following the SI-BONE iFuse Instruments Hospital Cleaning and Sterilization Instructions, U.S.A.

STORAGE/HANDLING
1. Store packaged implants at room temperature.
2. Handle the iFuse Implant with care to prevent damage to the surface finish.

DIRECTIONS FOR USE
1. A minimum of two (2) implants per sacroiliac joint are recommended for treatment.
2. For detailed information, refer to the relevant Surgical Technique Manual(s) prior to use of the iFuse Implant System.

GRAPHIC SYMBOLS

Manufactured for:
SI-BONE, Inc.
471 El Camino Real
Suite 101
Santa Clara, CA 95050

Customer Service:
USA: 408-207-0700 or Toll Free: 855-884-3873

Patents: www.si-bone.com

Part #: 500104 Rev. M
### 3.8 Publications in Progress

There are several additional studies and manuscripts currently in development to further expand the clinical evidence of the iFuse Implant System. Key studies are described in the table below.

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Estimated Pub Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anatomic Ethnic Differences</strong></td>
<td>Radiographic analysis of Asian versus Caucasian SI joint anatomy to confirm iFuse implants are appropriate Asian patients</td>
<td>Manuscript submitted and under review. Publication: TBD</td>
</tr>
<tr>
<td><strong>LOIS: 5-year Results</strong></td>
<td>Prospective, multicenter long-term follow-up with subjects from INSITE and SIFI. <em>Reports pain, function, QOL, patient satisfaction</em></td>
<td>5-year Follow-up results Publication: 2019</td>
</tr>
<tr>
<td></td>
<td>3-year results published [Darr 2018a]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4-year results published [Darr 2018b]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5-year results, submitted, in review [Whang 2019]</td>
<td></td>
</tr>
<tr>
<td><strong>SALLY: 1-year Results</strong></td>
<td>Prospective, multicenter long-term follow-up using the iFuse-3D implant. <em>Reports pain, function, QOL, patient satisfaction</em></td>
<td>Follow-up in progress. Publications: TBD</td>
</tr>
<tr>
<td></td>
<td>6-month interim clinical results published [Patel 2019]</td>
<td></td>
</tr>
</tbody>
</table>
3.9 Health Technology Assessments

Several independent technology and evidence-based professional organizations and medical specialty societies have reviewed minimally invasive SI joint fusion procedure and the iFuse Implant System and have published positive recommendations or guidelines. A summary of the assessments is provided in the table below. Please refer to each assessment directly for specific details.

<table>
<thead>
<tr>
<th>Assessor</th>
<th>Report</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCBS Association</td>
<td>Diagnosis and Treatment of Sacroiliac Joint Pain (6.01.023) January 2019</td>
<td>Reviews and evaluates therapeutic corticosteroid injections and minimally invasive methods (radiofrequency ablation, SIJ fusion/fixation) for the treatment of SIJ pain.</td>
</tr>
</tbody>
</table>

**Evidence Summary**

- Therapeutic corticosteroid injections – insufficient evidence
- Radiofrequency ablation – insufficient evidence
- Sacroiliac joint fusion/fixation with a triangular implant (iFuse) – sufficient to determine that the technology results in a meaningful improvement in the net health outcome
- Sacroiliac joint fusion/fixation with a cylindrical threaded implant – insufficient evidence
<table>
<thead>
<tr>
<th><strong>eviCore Healthcare</strong></th>
<th><strong>Spinal Surgery Guidelines, version 1.0.2019</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Minimally Invasive Sacroiliac Joint Fusion or Stabilization (CMM-611.2)</strong></td>
<td></td>
</tr>
</tbody>
</table>

**Indications and Criteria**

Minimally invasive sacroiliac joint (SIJ) fusion using titanium triangular implants (SI-BONE [iFuse Implant™]) for the treatment of lumbopelvic pain originating from the SI joint is considered **medically necessary** when ALL of the following are met:

- Performed by an orthopedic surgeon or neurosurgeon with specific training and expertise in percutaneous sacroiliac joint fusion surgical techniques and regularly use image-guidance for placement of implants
- Presence of non-radiating lumbopelvic pain caudal to L5, buttock, hip, and/or groin without radiation to the legs that impairs physical activities
- SIJ pain interfering with activities (sic) of daily living
- Patient localizes posterior pain to the posterior superior iliac spine (Fortin’s point)
- Localized tenderness to palpation over the sacral sulcus and posterior SIJ
- Elicitation of typical pain on three (3) or more positive provocative physical examination maneuvers/tests that stress the SIJ:
  - Thigh thrust test
  - Compression test
  - Gaenslen’s maneuver
  - Distraction test
  - FABER/Patrick’s sign
  - Posterior provocation test
- Absence of localized tenderness to palpation of similar severity to palpation of the sacral sulcus and posterior SIJ over the greater trochanter, lumbar spine, and coccyx
- Diagnostic confirmation of the SIJ as a pain generator through at least an 80% reduction in pain for the expected duration of effect of the anesthetic agent used upon two separate contrast-enhanced fluoroscopically or CT-guided intra-articular SIJ blocks using a local anesthetic performed at a minimum of two weeks apart
- Confirmation of the SIJ as a pain generator through at least a 50% reduction in pain for a minimum of two weeks following one contrast-enhanced fluoroscopically or CT guided intra-articular SIJ injection using a corticosteroid
- SIJ pain without minimal clinically important difference (MCID) from a minimum of a consecutive six (6) months of conservative, non-surgical treatment including ALL of the following unless contraindicated:
  - Non-steroidal anti-inflammatory drugs (NSAIDs)
  - Prescription medication optimization
  - Activity modification
  - Physician supervised/prescribed active physical therapy (including home exercise program) targeting lumbopelvic (core) area
  - Chiropractic care
- **Absence of generalized pain behavior (e.g., somatoform disorder) or generalized pain disorders (e.g., fibromyalgia)**
- **Unmanaged significant health disorders (e.g., major depressive disorder, drug and alcohol abuse)**
- **Alternative diagnosis more likely causing the pain**

  - **Absence of generalized pain behavior (e.g., somatoform disorder) or generalized pain disorders (e.g., fibromyalgia)**
  - **Documentation of nicotine-free status with EITHER of the following:**
    - Patient is a nonsmoker
    - Patient has refrained from smoking for at least 6 weeks prior to planned surgery as evidenced by cotinine lab results of ≤ 10 ng/mL
  - **Absence of unmanaged significant behavioral health disorders (e.g., major depressive disorder, chronic pain syndrome, secondary gain, drug and alcohol abuse)**
  - **Absence of alternative diagnoses that are a more likely cause of the patient’s ongoing pain or disability**
  - **Recent (within 6 months) diagnostic imaging studies that include ALL of the following:**
    - Plain radiographs and/or cross-sectional imaging (CT or MRI) that excludes the presence of destructive lesions (e.g., tumor, infection), acute fracture or inflammatory arthropathy that would not be properly addressed by SIJ fusion
    - Plain radiographs of the pelvis including the ipsilateral hip to evaluate potential concomitant hip pathology
    - Cross-sectional imaging (e.g., CT or MRI) of the lumbar spine to evaluate potential concomitant neural compression or other degenerative conditions
| NICE (National Institute for Health and Care Excellence, U.K.) | Medical Technologies Guidance (MTG39) October 2, 2018 | iFuse for treating chronic sacroiliac joint pain
Evidence-based recommendations:

- The case for adopting the iFuse Implant System to treat chronic sacroiliac joint pain is supported by the evidence. Using iFuse leads to improved pain relief, better quality of life and less disability compared with non-surgical management.
- iFuse should be considered for use in people with a confirmed diagnosis of chronic sacroiliac joint pain (based on clinical assessment and a positive response to a diagnostic injection of local anaesthetic in the sacroiliac joint) and whose pain is inadequately controlled by non-surgical management.
- Cost modelling indicates that after 8 years, using iFuse instead of non-surgical management will save the NHS around £129 per patient. It is likely that savings will then increase over time. Savings mainly come from fewer steroid joint injections and less pain relief medication with iFuse compared with non-surgical management.

(NOTE: The economic analysis looked at cost only. It did not consider clinical outcomes and therefore there is no cost utility information, such as QALY or ICER, available). |

| French National Healthcare System | National Commission for the Evaluation of Medical Devices and Health Technologies (CNEDIMTS) Opinion: December 5, 2017 Effective: September 6, 2018 | CNEDIMTS concluded the iFuse Procedure's observed outcomes, including improvements in quality of life and work status, are sufficient to include iFuse on the list of Products and Services provided for in Article L.165-1 of the Social Security Code.

iFuse is now on the List of Refundable Products and Services in France (Liste des Produits et Prestations Remboursables - LPPR) |
### MCG Health (Milliman Care Guidelines)

**General Recovery Care Guidelines**
- 22nd Edition
- Surgical Admission Case Management
- Published: May 7, 2018

**Care Planning – Inpatient Admission and Alternatives**

**Clinical Indications for Procedure**

Minimally invasive sacroiliac joint fusion needed as indicated by ALL of the following:

- Significant sacroiliac joint pain (pain rating of at least 5 on a 0-10 numeric scale) and/or significant activity limitations due to sacroiliac joint pain
- Unilateral pain localized over the sacroiliac joint
- Sacroiliac joint pain confirmed with response (pain) to three or more provocative examination maneuvers that stress the sacroiliac joint (e.g., FABER test, thigh thrust, pelvic gapping test, pelvic compression or Gaenslen test)
- Confirmation of diagnosis of sacroiliac disease via pain relief of at least 75 percent (i.e., on visual analogue scale) due to fluoroscopy-guided needle injection of local anesthetic into sacroiliac joint (expected time frame of pain relief depends on anesthetic chosen, dose and concentration)
- Failure to respond to at least six months of alternative treatments consisting of analgesics (e.g., nonsteroidal anti-inflammatory medication) and one or more of the following:
  - Physical therapy
  - Sacroiliac joint steroid injection
  - Radiofrequency rhizotomy
  - Alternative or contributing diagnoses absent (e.g., hip osteoarthritis, L5-S1 spine degeneration, tumor, infection or fracture)

### AIM Specialty Health

**Sacroiliac Joint Fusion**
- Effective: July 1, 2018

**Indications and Criteria**

Percutaneous/Minimally Invasive SI Joint Fusion with the **iFuse system (titanium triangular implant)** may be considered **medically necessary** when all of the following criteria are met:

- Persistent pain greater than 6 months
- Failed 6 months of conservative management
- Confirmed SI joint as a pain generator
- Diagnostic imaging studies
- Confirmation of pain relief with diagnostic SI joint injections

### Hayes

**Hayes Brief**
- November 2, 2017

**iFuse Implant System (SI-Bone Inc.) for Sacroiliac Joint Fusion for Treatment of Sacroiliac Joint Dysfunction**

Thorough evaluation of the technology, patient population, clinical evidence, and economics.
### ECRI Institute

**Product Brief**  
June 5, 2017

**iFuse Implant System (SI-BONE, Inc.) for Minimally Invasive Sacroiliac Joint Fusion**

- iFuse evidence graded as 4 out of 5, concluding iFuse significantly improves SI joint pain, disability scores, and quality of life compared to conservative management.
- 2- to 3-year follow-up data indicate the results are sustained and revision rates are low (1.8-5.7%).

### NICE (National Institute for Health and Care Excellence, U.K.)

**Interventional Procedures Guidance**  
(IPG578)  
April 5, 2017

**Minimally invasive sacroiliac joint fusion surgery for chronic sacroiliac pain**

- Current evidence on the safety and efficacy of MIS SI joint fusion surgery for chronic SI pain is adequate to support the use of this procedure.
- Patients should have a confirmed diagnosis of unilateral or bilateral SI joint dysfunction due to degenerative sacroilitis or SI joint disruption.
- This technically challenging procedure should only be done by surgeons who regularly use image-guided surgery for implant placement. The surgeons should also have had specific training and expertise in minimally invasive SI joint fusion surgery for chronic SI pain.

### 3.10 Medical Community Acceptance of Minimally Invasive SI Joint Fusion


For a comparison of the NASS and ISASS statements see Appendix E.
3.11 Economic Outcomes

Cher and Reckling present the “Health Care Economics of SI Joint Fusion” as part of the June 2019 SI joint dysfunction focus issue of *Techniques in Orthopaedics*. They concluded that substantial, high-quality evidence supports SI joint fusion with the triangular titanium iFuse implants as a valuable intervention in patients with chronic SI joint dysfunction due to degenerative sacroiliitis and sacroiliac joint disruption unresponsive to non-surgical treatment. The majority of published evidence is for iFuse Implant System, which likely explains exclusive insurance coverage for this device by many health plans in the US, UK and France [Cher 2019120].

A publication in the journal *ClinicoEconomics and Outcomes Research* [Cher 201611], used data from two prospective, multicenter, clinical trials (INSITE and SIFI described in Section 3.1) to inform a Markov process cost-utility model to evaluate cumulative 5-year health quality and costs after minimally invasive SI joint fusion with iFuse. The analysis was performed from a third-party perspective.

Minimally invasive SI joint fusion was associated with a 0.74 expected cumulative quality-adjusted life year (QALY) gain after 5 years at an incremental cost of approximately $9,800, resulting in an incremental cost-effectiveness ratio (ICER) of approximately $13,300/QALY. In multiple one-way sensitivity analyses all scenarios resulted in an incremental cost-effectiveness ratio (ICER) of < $26,000/QALY. Probabilistic analyses showed a high degree of certainty that the maximum ICER for SI joint fusion was less than commonly selected thresholds for acceptability (mean ICER =$13,687) (see Figure 18). SI joint fusion provided potential cost savings per QALY gained compared to non-surgical treatment after a treatment horizon of greater than 13 years. In conclusion, the model showed minimally invasive SI joint fusion to be a highly cost-effective, and, in the long-term, a cost-saving strategy for the treatment of SI joint dysfunction. The cost-effectiveness of minimally invasive SI joint fusion is also similar to that of hip (ICER ~$10,000) and knee (ICER ~$12,000) arthroplasty.

![Figure 16 – Cost-effective Acceptability Curve](image)

*(NOTE: The x-axis shows a range of maximum acceptable ceiling ratios; the y-axis shows the probability that siJ fusion is cost effective according to the selected maximum ratio.)*
3.12 Econometrics

LBP is burdensome and costly. Martin et al. reported US expenditures for treatment for back and neck problems accounted for approximately $86 billion in 2005 [Martin 2008141]. According to Katz, the total annual costs of LBP in the US exceeds $100 billion with indirect costs accounting for two-thirds [Katz 2006142]. In a systematic review of LBP costs studies across the world, Dagenais et al. estimates the total economic burden to consist of 15% direct and 85% indirect costs [Dagenais 2008143].

3.12.1 Indirect Costs

Indirect costs are those reflecting the economic value of consequences for which there is no direct monetary transfer. They commonly include costs related to employment (e.g., work absences resulting in lost productivity, decreased productivity) and lost household productivity. Indirect costs are thus more difficult to measure.

SI joint dysfunction has marked negative effects on a patient’s quality of life [Cher 201441], and their ability to function and lead productive lives. Additionally, due to the lack of awareness and knowledge of SI joint disorders, an exorbitant amount of costs are spent on ineffective or improper treatments [Vanaclocha 201843]. This leads to the critical need and importance of providing multi-disciplinary healthcare education on proper diagnosis and treatment options for SI joint disorders. With proper diagnosis of SI joint dysfunction, better more effective treatments can be administered in a timely fashion, which will improve the efficiency and effectiveness of the healthcare system and thus lower indirect costs.

A publication using data from the SIFI and INSITE trials shows for employees with chronic, severe SI joint dysfunction, minimally invasive SI joint fusion may improve average worker productivity compared to nonsurgical treatment. Patients who receive SI joint fusion using iFuse have an expected increase in the probability of working of 16% (95% confidence interval [CI] 11%–21%) relative to nonsurgical patients [Saavoss 201668].

3.12.2 Direct Costs

Economic studies from Ackerman et al. have shown that non-operative management of SI joint disruption and degenerative sacroiliitis has high costs and medical utilization in both the US Medicare and commercial payer patient populations. Specifically, the estimated 5-year Medicare reimbursement across practice settings is approximately $270 million or $18,527 per patient. For the patient with a prior lumbar fusion, the 5-year cumulative non-operative cost rose to nearly $64,000 per patient [Ackerman 2014b144]. Similarly, for the commercial payer, the estimated 3-year insurance payments for non-operative care attributable to treating SI joint dysfunction were $1.6 billion per 100,000 commercial payer beneficiaries. The mean 3-year non-operative care costs were $16,196 per privately-insured patient, and more than 5 times higher ($91,720) for patient with a prior lumbar spinal fusion [Ackerman 2014a145].

Non-operative care is a resource-intensive process that includes medications, physical therapy, therapeutic injections and multiple physician and clinic visits. When comparing non-operative care to minimally invasive SI joint fusion, Ackerman found treating Medicare beneficiaries with SI joint fusion in the hospital inpatient setting could save Medicare $660 million over the patients’ lifetime [Ackerman 2013146]. In the commercial setting, the cumulative 3-year and 5-year differentials in commercial insurance payments (cost of non-operative care minus cost of minimally invasive surgery)
were $14,545 and $6,137 per patient, respectively (2012 US dollars). Higher initial procedure costs for minimally invasive SI joint fusion were largely offset by decreased non-operative treatment costs over a 5-year time horizon [Ackerman 2014c147]. Cost-effective healthcare delivery can thus be achieved by proper diagnosis and effective treatment through optimizing use of both non-surgical and surgical care options.

A study published in *ClinicoEconomics and Outcomes Research* presents a retrospective observational analysis of administrative claims data from a large U.S. health insurer affiliated with Optum, Inc. (~14.6 million commercially insured adults in 2016). The database includes demographic information as well as medical claims data from physicians and facilities, and outpatient pharmacy claims data. Adult commercial health plan members with a medical claim for SI joint fusion (CPT codes 27279, 27280, 0334T) from January 1, 2011 to February 29, 2016 were identified. Associated claims data were then reviewed. This analysis shows lower post-operative low back pain-related healthcare costs compared to pre-operative costs. Median low back pain-related costs in the post-surgery period were approximately $400 per quarter overall and $250 per quarter for patients that underwent SI joint fusion in an outpatient setting. Compared with patient costs in the year prior to surgery, researchers found over a 70% reduction in patient costs in the year following outpatient-based SI joint fusion. These outpatient surgery savings provide an insurer with a breakeven timepoint of ~2.5 years (*Figure 17*) [Buysman 201812].

![Figure 17 – Break-even analysis of surgical vs non-surgical treatment in the outpatient setting.](image)

*Note: All costs are presented in US$. (from Buysman – ClinicoEcon Outcomes Res 201812)*
4  Competition

While the majority of MIS SI joint fusion literature is with iFuse, there are a few other systems cleared for use in the United States with a few articles. Most are retrospective case series, but there are a few prospective trials, and some biomechanical and technique publications.

4.1  Rialto (Medtronic)

Retrospective

Rajpal – World Neurosurg 201880
• 24 patients, 19-month mean follow-up, single center
• Results: improvement in back and leg pain; high patient satisfaction

Beck – Cureus 201579
• 20 patients, 27-month follow-up
• Results: improvement in pain, high patient satisfaction, and high radiographic fusion, however, uses Bone Morphogenetic Protein (BMP) off-label as it this product is not approved by the U.S. FDA for the use described.

Other

Lee – J Biomed Res 2016 (O-arm technique during SI joint fusion)148

4.2  SI-LOK (Globus Medical)

Rappoport—World Neurosurgery 201782
• Prospective, N=32, 12-month follow-up results of a 2-year trial
• NCT01861899

Purpose: Minimally Invasive SI joint fusion using a novel hydroxyapatite-coated screw: preliminary 1-year clinical and radiographic results of a 2-year prospective study. Study evaluated clinical and radiographic outcomes, intra-operative parameters, patient satisfaction and work status following a procedure using SI-LOK® for treatment of sacroiliac joint dysfunction with a minimum of three screws.

Results: 32 patients. Mean patient age was 55.2 ± 10.7 years. 62.5% female. Mean operating time was 42.6 ± 20.4 minutes. Overnight hospital stay for 84% of patients. VAS back and leg pain scores decreased significantly by 12 months. Mechanical stability achieved in 93.3% of patients. All employed patients returned to work within 3 months.
4.3 SImmetry (RTI Surgical, which acquired Zyga)

Prospective

Araghi—Open Orthop J 2018

- Prospective, 50 patients, 6-month follow-up
- NCT02074761

Purpose: 50 patients had minimally invasive SI joint surgery and completed a 6-month follow up. Average age at baseline at 61.5. 58% were female. Joint-related pain was ≥2 years is 54.0% of patients.

Results: At 6 months, mean VAS pain was down from 76.2 at baseline to 35.1 (54% reduction, p<0.0001). Mean ODI improved.

Abbasi—Cureus 2017

- Prospective, 19 patients, 12-month follow-up
- NCT02425631

Purpose: The success of an SI joint fusion is in part determined by whether osseous bridging occurs across the SI joint. Until now, no validated SIJF assessment method has been described. This study’s objective was to document previously described SIJF assessment methods and define and validate a detailed assessment system for SIJF. The results are only intended to establish computed tomography (CT)-based guidelines for SIJF to be used in a subsequent large clinical study to correlate them with clinical outcomes.

Results: Using the new grading system, evidence of bridging bone was observed in almost 80% of patients one year after percutaneous SIJF including decortication and bone grafting. A systematic and comprehensive assessment of bone bridging using grading systems defined beforehand and implemented by independent radiologist reviewers, such as the methodology described in this study, could help to generate reliable data that determine whether SIJFs effect clinical outcomes and may facilitate comparisons between sites and between different SIJF surgical operations.

Retrospective

Cross – Open Orthop J 2018

- 10 patients, 1 and 2-year follow-up, single center
- Results: Significant reduction in pain and 94% of subjects at 2-years had bridging bone across the SI joint

MenMuir – Int J Spine Surg 2017

- 4 iFuse patients revised by SImmetry
- Results: A more ventral-todorsal and caudal-to-cranial trajectory was established for the revision implants; by 6 to 12 months post revision and presenting symptoms were resolved
Kube – *Open Orthop J* 2016\textsuperscript{76}

- 18 patients, 12-month follow-up
- Results: 88\% fusion rate, back and leg pain improved as did disability

**Other**

Shih – *Spine J* 2018 (14 cadavers, biomechanics ROM after fixation)\textsuperscript{88}
Beaubien – *Surg Sci* 2015 (technique, decorticator)\textsuperscript{86}
Miller – *Med Device Evid Res* 2014 (technique)\textsuperscript{85}
### 5 Current Payor Coverage

#### 5.1 Medicare

As of June 1, 2016, Medicare covers minimally invasive SI joint fusion nationwide. All seven* Medicare Administrative Contractors (MACs) have established coverage positions for MIS SI joint fusion (CPT 27279).

<table>
<thead>
<tr>
<th>MAC [states]</th>
<th>Policy</th>
<th>Description</th>
</tr>
</thead>
</table>
| CIGNA Government Services (CGS) Administrators [KY, OH] | Minimally-Invasive Surgical (MIS) Fusion of the Sacroiliac (SI) Joint LCD: L36494 Effective: 02/01/2016 | Minimally-invasive surgical (MIS) fusion of the sacroiliac (SI) joint is considered medically necessary when ALL of the following criteria are met:  
  - Have moderate to severe pain with functional impairment and pain persists despite a minimum six months of intensive nonoperative treatment that must include medication optimization, activity modification, bracing, and active therapeutic exercise targeted at the lumbar spine, pelvis, SIJ and hip including a home exercise program.  
  - No mention of a requirement for SI joint imaging to demonstrate evidence of injury and/or degeneration. |
| First Coast Service Options (FCSO) [FL, PR, VI] | Medical review article for percutaneous minimally invasive fusion/stabilization of the sacroiliac joint Coverage Article: A55120 Effective: 06/01/2015 | The following patient criteria will be considered by First Coast Service Options Inc. (First Coast) medical reviewers in making clinical judgements if a prepayment or post payment audit is implemented:  
  - NASS Guidelines with the following exceptions:  
    - Positive response to the thigh thrust test OR compression test AND two of the following additional provocative tests: Gaenslen’s test, distraction test, Patrick’s sign.  
    - No mention of a requirement for SI joint imaging to demonstrate evidence of injury and/or degeneration.  
  - At least 75% reduction of pain for the expected duration of the anesthetic used during image-guided, contrast-enhanced SIJ injection on two separate occasions. |
| National Government Services (NGS) [CT, IL, MA, ME, MN, NH, NY, RI, VT, WI] | Minimally-invasive Surgical (MIS) Fusion of the Sacroiliac (SI) Joint LCD: L36406 Effective: 04/01/2016 | Minimally-invasive surgical (MIS) fusion of the sacroiliac (SI) joint is considered medically necessary when ALL of the following criteria are met:  
  - NASS Guidelines with the following exceptions:  
    - Have moderate to severe pain with functional impairment and pain persists despite a minimum six months of intensive nonoperative treatment that must include medication optimization, activity modification, bracing, and active therapeutic exercise targeted at the lumbar spine, pelvis, SIJ and hip including a home exercise program  
    - No mention of a requirement for SI joint imaging to demonstrate evidence of injury and/or degeneration. |

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* Used to be managed by 8 MACs until late February 2018 when Palmetto began managing Jurisdiction J – AL, GA, TN; formerly managed by Cahaba
<table>
<thead>
<tr>
<th>Provider</th>
<th>LCD Link</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Noridian Healthcare Solutions</td>
<td><strong>LCD Link</strong>&lt;br&gt;<strong>Effective:</strong>&lt;br&gt;01/01/2015</td>
<td>Minimally invasive sacroiliac joint fusion removed from non-coverage list</td>
</tr>
<tr>
<td>Novitas Solutions</td>
<td><strong>LCD Link</strong>&lt;br&gt;<strong>Effective:</strong>&lt;br&gt;03/17/2017</td>
<td>Novitas Medicare (has determined that minimally invasive SI joint fusion is reasonable and necessary (no longer non-covered by LCD))</td>
</tr>
<tr>
<td>Palmetto GBA</td>
<td><strong>Sacroiliac-Bone Implant System Coverage Article:</strong>&lt;br&gt;A53452&lt;br&gt;<strong>Effective:</strong>&lt;br&gt;06-09-2016</td>
<td>The sacroiliac bone implant system (SI-bone Implant System) has received 510(k) clearance from the Food and Drug Administration (FDA). The intended use of the SI-bone Implant System is for sacroiliac joint fusion for conditions including sacroiliac joint dysfunction that is a direct result of sacroiliac joint disruptions and degenerative sacroiliitis. The office outpatient AND hospital in-patient medical records must clearly document that the above indications were met. The patient’s medical records shall reflect the medical need and response to the sacroiliac joint fusion. CPT code 27279 is effective for dates of service on or after January 1, 2015.</td>
</tr>
<tr>
<td>Wisconsin Physicians Service Insurance Corporation (WPS)</td>
<td><strong>Percutaneous minimally invasive fusion/stabilization of the sacroiliac joint for the treatment of back pain</strong>&lt;br&gt;LCD: L36000&lt;br&gt;<strong>Effective:</strong>&lt;br&gt;02/01/2016</td>
<td>Percutaneous minimally invasive fusion/stabilization of the sacroiliac joint for the treatment of back pain is indicated for the treatment of SIJ pain for patients with low back/buttock pain who meet all of the following criteria: Follows NASS guidelines with the following exceptions: No mention of a requirement for SI joint imaging to demonstrate evidence of injury and/or degeneration. Covered diagnosis: M46.1</td>
</tr>
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5.2 Commercial

MIS SI joint fusion continues to gain acceptance in the medical community and is becoming the standard of care. Similarly, an increasing number of commercial payors are covering the procedure. Many payors have published policies that are exclusive to the iFuse Implant System procedure (Table 13). Several others have positive policies (Table 14), and many others are covering MIS SI joint fusion on a case-by-case basis. Policies that require the procedure to be performed by trained surgeons ONLY are indicated with a green star [ ].

| TABLE 13 Commercial Payors – MIS SI Joint Fusion
  Exclusive iFuse Implant System Coverage Policies |
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<tr>
<td><strong>Payor</strong></td>
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<td>Blue Cross Blue Shield (BCBS) Payors</td>
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<td>BCBS Arizona</td>
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<td>BCBS Florida (Florida Blue)</td>
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<td>BCBS Highmark – DE, PA, WV</td>
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<td>BCBS CareFirst (DC, MD, VA)</td>
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</tbody>
</table>
| BCBS Idaho | Diagnosis and Treatment of Sacroiliac Joint Pain  
Policy: MP 6.01.23  
**Effective:** 11/15/2018 | Minimally invasive sacroiliac joint fusion/stabilization **using a titanium triangular implant** meets the definition of medical necessity when ALL of the following criteria have been met:  
**NASS Recommendations** with the following exceptions:  
- Pain is at least 5 on a 0 to 10 rating scale that impacts quality of life or limits activities of daily living.  
- Procedure to be performed by **SURGEONS ONLY** |
|---|---|---|
| BCBS Illinois [HCSC – Health Care Service Corp] | Sacroiliac Joint Fusion or Stabilization  
**Policy:** SUR705.033  
**Effective/Revised:** 09/01/2018 | Covers minimally invasive fusion of the SI joint only using the iFuse Implant System®.  
**NASS Recommendations** with the following exceptions:  
- SI joint pain rated at least 5 on the 0-10 numeric pain rating scale.  
- Imaging of the SJ that does not indicate evidence of injury and/or degeneration.  
- **NOTE** about non-surgical management; Conservative care for a minimum of 6 month must include the following:  
  - Use of prescription strength analgesics for several weeks at a dose sufficient to induce a therapeutic response:  
    - Analgesics should include anti-inflammatory medications (NSAIDS) with or without adjunctive medications such as nerve membrane stabilizers or muscle relaxants; AND  
    - Participation in at least 6 weeks of physical therapy (including active exercise) or documentation of why the patient could not tolerate physical therapy; AND  
    - Evaluation and appropriate management of associated cognitive, behavioral, or addiction issues; AND  
    - Documentation of patient compliance with the preceding criteria.  
  (NOTE: will utilize eviCore Healthcare for prior authorizations for Musculoskeletal) |
| BCBS Kansas | Diagnosis and Treatment of Sacroiliac Joint Pain  
**Policy Link**  
**Effective/Revised:** 01/16/2019 | Minimally invasive sacroiliac joint fusion/stabilization **using a titanium triangular implant** may be considered medically necessary when ALL of the following criteria have been met:  
**NASS Recommendations** with the following exceptions:  
- Pain is at least 6 on a 1 to 10 rating scale that impacts quality of life or limits activities of daily living.  
- Procedure to be performed by **SURGEONS ONLY** |
| BCBS Kansas City | Diagnosis and Treatment of Sacroiliac Joint Pain  
**Policy 6.0123**  
**Effective/Revised:** 07/01/2018 | Minimally invasive sacroiliac joint fusion/stabilization **using a titanium triangular implant** may be considered medically necessary when ALL of the following criteria have been met:  
**NASS Recommendations** with the following exceptions:  
- Pain is at least 5 on 0 to 10 rating scale that impacts quality of life or limits activities of daily living.  
- Procedure to be performed by **SURGEONS ONLY** |
| BCBS Louisiana | Diagnosis and Treatment of Sacroiliac Joint Fusion  
Policy: 00558  
Effective/Revised: 06/01/2019 | Based on review of available data, the Company may consider percutaneous/Minimally Invasive Sacroiliac (SI) Joint Fusion with the iFuse system (titanium triangular implant) to be eligible for coverage.  
**NASS Recommendations** with the following exceptions:  
- Persistent pain greater than six (6) months’ duration that interferes with functional activities as documented by all of the following:  
  - Pain score Visual Analogue Scale (VAS) of 5 or greater  
  - Oswestry Disability Index (ODI) 30 or greater  
- Other sources of pain have been excluded as an etiology |
|---|---|---|
| BCBS Massachusetts | Diagnosis and Treatment of Sacroiliac Joint Pain  
Policy: 320  
Effective: 06/2018 | Minimally invasive sacroiliac joint fusion/stabilization using a titanium triangular implant may be considered medically necessary when ALL of the following criteria have been met:  
**NASS Recommendations** with the following exceptions:  
- Pain is at least 5 on 0 to 10 rating scale that impacts quality of life or limits activities of daily living.  
- Procedure to be performed by **SURGEONS ONLY** |
| BCBS Minnesota | Sacroiliac Joint Fusion  
Policy: IV-126  
Effective/Revised: 08/27/2018 | Minimally invasive or percutaneous sacroiliac joint fusion/stabilization using a titanium triangular implant may be considered MEDICALLY NECESSARY AND APPROPRIATE when ALL of the following are met:  
**NASS Recommendations** with the following exceptions:  
- Pain is at least 5 on 0 to 10 rating scale that impacts quality of life or limits activities of daily living.  
(Note: Effective 8/1/2018 will utilize eviCore Healthcare for prior authorizations for Musculoskeletal) |
| BCBS Mississippi | Diagnosis and Treatment of Sacroiliac Joint Pain  
Policy: L.6.01.413  
Effective: 01/31/2018 | Minimally invasive fusion/stabilization of the sacroiliac joint using a titanium triangular implant may be considered medically necessary when ALL of the following criteria have been met:  
**NASS Recommendations** with the following exceptions:  
- Pain is at least 5 on a 0 to 10 rating scale that impacts quality of life or limits activities of daily living. |
NASS Recommendations with the following exceptions:  
- SI joint pain rated at least 5 on the 0-10 numeric pain rating scale.  
- Imaging of the SJ that does not indicate evidence of injury and/or degeneration.  
- NOTE about non-surgical management; Conservative care for a minimum of 6 month must include the following:  
  - Use of prescription strength analgesics for several weeks at a dose sufficient to induce a therapeutic response:  
    - Analgesics should include anti-inflammatory medications (NSAIDS) with or without adjunctive medications such as nerve membrane stabilizers or muscle relaxants; AND  
    - Participation in at least 6 weeks of physical therapy (including active exercise) or documentation of why the patient could not tolerate physical therapy; AND  
    - Evaluation and appropriate management of associated cognitive, behavioral, or addiction issues; AND  
    - Documentation of patient compliance with the preceding criteria.  
(NOTE: will utilize eviCore Healthcare for prior authorizations for Musculoskeletal) |
|---|---|---|
| BCBS New Jersey [Horizon] | Sacroiliac Joint Fusion/Stabilization Policy: 139 Effective: 01/09/2018 | Minimally invasive fusion/stabilization of the sacroiliac joint using a titanium triangular implant is considered medically necessary when ALL of the following criteria have been met:  
NASS Recommendations with the following exceptions:  
- Pain is at least 5 on 0 to 10 rating scale that impacts quality of life or limits activities of daily living.  
- Procedure to be performed by SURGEONS ONLY |
| BCBS New Mexico [HCSC – Health Care Service Corp] | Sacroiliac Joint Fusion or Stabilization Policy: SUR705.033 Effective/Revised: 09/01/2018 | Covers minimally invasive fusion of the SI joint only using the iFuse Implant System®.  
NASS Recommendations with the following exceptions:  
- SI joint pain rated at least 5 on the 0-10 numeric pain rating scale.  
- Imaging of the SJ that does not indicate evidence of injury and/or degeneration.  
- NOTE about non-surgical management; Conservative care for a minimum of 6 month must include the following:  
  - Use of prescription strength analgesics for several weeks at a dose sufficient to induce a therapeutic response:  
    - Analgesics should include anti-inflammatory medications (NSAIDS) with or without adjunctive medications such as nerve membrane stabilizers or muscle relaxants; AND  
    - Participation in at least 6 weeks of physical therapy (including active exercise) or documentation of why the patient could not tolerate physical therapy; AND  
    - Evaluation and appropriate management of associated cognitive, behavioral, or addiction issues; AND  
    - Documentation of patient compliance with the preceding criteria.  
(NOTE: will utilize eviCore Healthcare for prior authorizations for Musculoskeletal) |
| BCBS New York, Western [HealthNow NY] | Diagnosis and Treatment of Sacroiliac Joint Pain  
[Policy Link]  
**Effective:** 07/01/2018 | Minimally invasive fusion/stabilization of the sacroiliac joint using a titanium triangular implant may be considered medically necessary when ALL of the following criteria have been met:  
**NASS Recommendations** with the following exceptions:  
- Pain is at least 5 on 0 to 10 rating scale that impacts quality of life or limits activities of daily living. |
|---|---|---|
| BCBS Excellus (New York) ★  
[includes Univera] | Sacroiliac Joint Fusion/Stabilization: Open and Percutaneous Methods  
**7.01.93**  
**Effective/Revised:** 12/20/2018 | Minimally invasive sacroiliac joint (SIJ) fusion using titanium triangular implants (SI-BONE (IFUSE Implant™)) for the treatment of lumbopelvic pain originating from the SIJ is considered medically necessary when ALL of the following criteria are met:  
**NASS Recommendations** with the following exceptions:  
- Performed by an orthopedic surgeon or neurosurgeon with specific training and expertise in percutaneous SIJ surgical techniques and who regularly uses image-guidance for placement of implants;  
- Diagnostic confirmation of the SIJ as a pain generator through at least an 80% reduction in pain for the expected duration of effect of the anesthetic agent used upon two separate contrast-enhanced fluoroscopically or CT-guided intra-articular SIJ blocks using a local anesthetic performed at a minimum of two weeks apart;  
- Confirmation of the SIJ as a pain generator through at least a 50% reduction in pain for a minimum of two weeks following one contrast-enhanced fluoroscopically or CT-guided intra-articular SIJ injection using a corticosteroid;  
- Documentation of nicotine-free status with EITHER of the following:  
  - Patient is a nonsmoker; or  
  - Patient has refrained from smoking for at least 6 weeks prior to planned surgery as evidence by cotinine lab results of less than or equal to 10ng/mL;  
- Absence of unmanaged significant behavioral health disorders (e.g., major depressive disorder, chronic pain syndrome, secondary gain, drug and alcohol abuse); and  
- Recent (within 6 months) diagnostic imaging studies |
| BCBS North Carolina ★ | Sacroiliac Joint Fusion/Stabilization  
**Policy:** 139  
**Effective:** 01/09/2018 | Treatment for back pain presumed to originate from the sacroiliac joint, using a minimally invasive, titanium triangular implant when ALL of the following criteria have been met:  
**NASS Recommendations** with the following exceptions:  
- Pain is at least 5 on 0 to 10 rating scale that impacts quality of life or limits activities of daily living.  
- Procedure to be performed by SURGEONS ONLY (trained in neurosurgery or orthopedic spine surgery and have completed procedure-specific training or has been granted hospital privileges to perform minimally invasive SI joint surgery). |
| BCBS Oklahoma [HCSC – Health Care Service Corp] | Sacroiliac Joint Fusion or Stabilization  
Policy: SUR705.033  
Effective: 01/01/2017  
Updated: 08/01/2018 | Covers minimally invasive fusion of the SI joint only using the iFuse Implant System®.  
NASS Recommendations with the following exceptions:  
- SI joint pain rated at least 5 on the 0-10 numeric pain rating scale.  
- Imaging of the SJ that does not indicate evidence of injury and/or degeneration.  
- NOTE about non-surgical management; Conservative care for a minimum of 6 month must include the following:  
  - Use of prescription strength analgesics for several weeks at a dose sufficient to induce a therapeutic response:  
    - Analgesics should include anti-inflammatory medications (NSAIDS) with or without adjunctive medications such as nerve membrane stabilizers or muscle relaxants; AND  
    - Participation in at least 6 weeks of physical therapy (including active exercise) or documentation of why the patient could not tolerate physical therapy; AND  
    - Evaluation and appropriate management of associated cognitive, behavioral, or addiction issues; AND  
    - Documentation of patient compliance with the preceding criteria.  
  (NOTE: will utilize eviCore Healthcare for prior authorizations for Musculoskeletal) |
|---|---|
| BCBS Pennsylvania [Capital BlueCross]  
(Central PA) | Diagnosis and Treatment of Sacroiliac Joint Pain  
Policy: MP-5.048  
Effective: 05/01/2018 | Minimally invasive fusion/stabilization of the sacroiliac joint using a titanium triangular implant may be considered medically necessary when ALL of the following criteria have been met:  
NASS Recommendations with the following exceptions:  
- Pain is at least 5 on 0 to 10 rating scale that impacts quality of life or limits activities of daily living.  
- Surgeons ONLY to perform the procedure; must have specific training and expertise in MIS SI joint fusion surgery.  
- Procedure to be performed by a SURGEONS ONLY |
| BCBS Pennsylvania [Independence Blue Cross]  
(Philadelphia, Southeast PA) | Minimally invasive fusion/stabilization of the sacroiliac joint using a titanium triangular implant  
Policy: 00.01.66a  
Effective: 05/14/2018 | Capital BlueCross MIS SI joint Fusion policy is managed by TurningPoint Healthcare effective 1/1/2019  
Note: TurningPoint does not have a published policy |
| BCBS Premera ★ (Alaska, Washington) | Diagnosis and Treatment of Sacroiliac Joint Pain  
Policy: 6.01.524  
Effective: 02/01/2019 | Minimally invasive fixation/fusion of the sacroiliac joint using a titanium triangular implant, (e.g., iFuse®), may be considered medically necessary when ALL of the following criteria have been met:  
**NASS Recommendations** with the following exceptions:  
- Pain is at least 5 on 0 to 10 rating scale that impacts quality of life or limits activities of daily living.  
- Procedure to be performed by a **SURGEONS ONLY** |
|---|---|---|
| BCBS Regence (Idaho, Oregon, Utah, and select counties of Washington) | Sacroiliac Joint Fusion Surgery, Policy: 193  
Effective: 07/01/2018 | Minimally invasive fusion/stabilization of the sacroiliac joint using a titanium triangular implant may be considered medical necessary when ALL of the following criteria have been met:  
**NASS Recommendations** with the following exceptions:  
- Clinical documentation pain limits activities of daily living (ADL) defined as feeding, bathing, dressing, grooming, meal preparation, household chores, and occupational risks that are required for daily functioning |
| BCBS South Carolina | Sacroiliac Joint Fusion or Stabilization  
Policy: CAM 187  
Effective: 01/23/2018 | Minimally invasive sacroiliac joint (SIJ) fusion or stabilization, using titanium triangular implants or devices, for the treatment of back pain presumed to originate from the SIJ is considered MEDICALLY NECESSARY when meeting ALL of the following criteria:  
**NASS Recommendations** with the following exceptions:  
- Pain is at least 5 on 0 to 10 rating scale that impacts quality of life or limits activities of daily living. |
| BCBS Tennessee | Diagnosis and Treatment of Sacroiliac Joint Pain  
Policy: DMP0118-18  
Effective: 05/01/2018  
Note: TurningPoint Healthcare Solutions, LLC, will continue administering these prior-authorizations | Minimally invasive fusion/stabilization of the sacroiliac joint is considered medically necessary if ALL of the following is met:  
**NASS Recommendations** with the following exceptions:  
- Titanium triangular implant is used (i.e. iFuse Implant System)  
- Pain is at least 5 on 0 to 10 rating scale that impacts quality of life or limits activities of daily living. |
<table>
<thead>
<tr>
<th>Payor</th>
<th>Procedure Description</th>
<th>Criteria</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCBS Texas [HCSC – Health Care Service Corp]</td>
<td>Sacroiliac Joint Fusion or Stabilization &lt;br&gt;Policy: SUR705.033 &lt;br&gt;Effective: 01/01/2017 &lt;br&gt;Updated: 09/01/2018</td>
<td>Covers minimally invasive fusion of the SI joint only using the iFuse Implant System®. &lt;br&gt;NASS Recommendations with the following exceptions: &lt;br&gt;• SI joint pain rated at least 5 on the 0-10 numeric pain rating scale. &lt;br&gt;• Imaging of the SIJ that does not indicate evidence of injury and/or degeneration. &lt;br&gt;• NOTE about non-surgical management; Conservative care for a minimum of 6 month must include the following: &lt;br&gt;  o Use of prescription strength analgesics for several weeks at a dose sufficient to induce a therapeutic response: &lt;br&gt;  ▪ Analgesics should include anti-inflammatory medications (NSAIDS) with or without adjunctive medications such as nerve membrane stabilizers or muscle relaxants; AND &lt;br&gt;  ▪ Participation in at least 6 weeks of physical therapy (including active exercise) or documentation of why the patient could not tolerate physical therapy; AND &lt;br&gt;  ▪ Evaluation and appropriate management of associated cognitive, behavioral, or addiction issues; AND &lt;br&gt;  ▪ Documentation of patient compliance with the preceding criteria.</td>
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<td>BCBS Vermont ★</td>
<td>Diagnosis and Treatment of Sacroiliac Joint Pain &lt;br&gt;Policy: UM.SURG.08 &lt;br&gt;Effective: 07/01/2017</td>
<td>Fusion/stabilization of the SI joint via open, percutaneous or minimally invasive technique may be considered medically necessary for members with low back/buttock pain that meet ALL of the following criteria: &lt;br&gt;NASS Recommendations &lt;br&gt;• Procedure to be performed by SURGEONS ONLY</td>
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<tr>
<td>BCBS Wyoming ★</td>
<td>Diagnosis and Treatment of Sacroiliac Joint Pain &lt;br&gt;Policy: 6.01.23.0 &lt;br&gt;Effective: 01/23/2018</td>
<td>Minimally invasive fusion/stabilization of the sacroiliac joint using a titanium triangular implant may be considered medically necessary when ALL of the following criteria have been met: &lt;br&gt;NASS Recommendations with the following exceptions: &lt;br&gt;• Pain is at least 5 on a 0 to 10 rating scale that impacts quality of life or limits activities of daily living. &lt;br&gt;• Procedure to be performed by SURGEONS ONLY</td>
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<tr>
<td>Capital Health Blue Cross – Florida (follows Florida Blue)</td>
<td>Minimally Invasive Fusion Techniques: Sacroiliac Joint Fusion/Stabilization &lt;br&gt;Policy: 02-61000-36 &lt;br&gt;Effective/Revised: 01/01/2019</td>
<td>Minimally invasive sacroiliac joint fusion/stabilization using a titanium triangular implant meets the definition of medical necessity when ALL of the following criteria have been met: &lt;br&gt;NASS Recommendations with the following exceptions: &lt;br&gt;• Pain is at least 5 on a 0 to 10 rating scale that impacts quality of life or limits activities of daily living.</td>
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<tr>
<td>Other Payors</td>
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<tr>
<td>Insurance Provider</td>
<td>Description</td>
<td>Coverage Details</td>
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| AmeriHealth (Caritas, NJ and PA) | Minimally invasive fusion/stabilization of the sacroiliac joint using a titanium triangular implant | Minimally invasive stabilization/fusion/fixation of the sacroiliac joint using a titanium triangular implant, (**i.e.,** iFuse® Implant System (SI-Bone)), is considered medically necessary and, therefore, covered when all of the following criteria have been met:  
**NASS Recommendations** with the following exceptions:  
- Pain is at least 5 on a 0 to 10 rating scale that impacts quality of life or limits activities of daily living  
**NOTE:** Beginning 01/14/2019 “Sacroiliac Joint Fusion” is being added to the Spine Surgical Procedures’ section for this utilization management program through AIM Specialty Health. |
| Molina Healthcare | iFuse Implant System (SI-BONE Inc.) for Sacroiliac Joint Fusion for Treatment of Low Back Pain | Covers minimally invasive fusion of the sacroiliac (SI) joint only using the iFuse Implant System® as a proven technology.  
**ISASS Guidelines** with the following exceptions:  
- 80% or greater acute decrease in pain on diagnostic SI joint injection  
- Procedure to be performed by SURGEONS ONLY |
| AllWays Health Partner (formerly Neighborhood Health Plan) (Massachusetts) | Minimally Invasive Fusion of the Sacroiliac Joint (CPT 27279) | AllWays Health Partners covers minimally invasive sacroiliac joint fusion surgery with a titanium triangular implant as a treatment for chronic sacroiliac joint pain in members when all the following are met:  
**NASS Recommendations** with the following exceptions:  
- Pain is at least 5 on a 0 to 10 rating scale that impacts quality of life or limits activities of daily living.  
- Doesn’t require imaging of the SI joint that shows injury and/or degeneration.  
- Procedure to be performed by SURGEONS ONLY |
| SelectHealth | Minimally Invasive Fusion of the Sacroiliac Joint | Covers minimally invasive fusion of the sacroiliac (SI) joint only using the iFuse Implant System® as a proven technology.  
**ISASS Guidelines** with the following exceptions:  
- Patients aged 21-70 with confirmed diagnosis of SI joint mediated pain based on history and physical exam.  
- Neurological testing.  
- Persistent SJ pain of moderate to severe despite conservative therapy (Baseline score of 30 or greater on the ODI and/or numeric pain score in the last week of 5 or higher on a 10 VAS scale.  
- Complete or near complete (>79%) relief of typical pain on CT or fluoroscopic confirmed injection. |

* Indicates procedure to be performed by SURGEONS ONLY
Several other commercial payors have positive coverage policies as note in the table below.

<table>
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<tr>
<th>Payor</th>
<th>Policy Description</th>
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<tbody>
<tr>
<td><strong>TABLE 14</strong> Commercial Payors – MIS SI Joint Fusion Coverage</td>
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</tr>
<tr>
<td><strong>Payor</strong></td>
<td><strong>Policy</strong></td>
</tr>
<tr>
<td>BCBS Positive Coverage Policies</td>
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</tbody>
</table>
| BCBS Alabama                               | Sacroiliac Joint Fusion Policy: MP-555 Effective: 03/18/2019                     | Minimally invasive fusion/stabilization of the SI joint using an FDA approved device may be considered medically necessary when ALL of the following criteria are met:  
  **NASS Recommendations** with the following exceptions:  
  • Pain is at least 5 on a 0 to 10 rating scale that impacts quality of life or limits activities of daily living. |
| BCBS Michigan [Blue Care Network of Michigan] | Sacroiliac Joint Fusion for the Treatment of Low Back Pain Policy: 2092573 Effective: 03/01/2017 | Procedure is indicated for the treatment of SI joint pain for patients with low back/buttock pain who meet ALL of the following criteria:  
  **ISASS guidelines** with the following exceptions:  
  • Controlled sacroiliac joint blocks, using local anesthetic agents of different duration of action for controlled comparison with or without placebo, are recommended to confirm the diagnosis when clinical findings are consistent with disabling sacroiliac joint pain.  
  • Achieving 75% or greater pain relief, with the ability to perform previously painful movements after injection is considered a positive response. |
| BCBS Nebraska                              | Diagnosis and Treatment of Sacroiliac Joint Pain Policy: III.189 Effective: 01/01/2016 | Fusion/stabilization of the SI joint for the treatment of back pain is scientifically validated when ALL criteria is met:  
  • Patient has had a positive result with dual diagnostic blocks using 2 anesthetic agents with different duration of action used; AND  
  • Patient has tried and failed therapeutic injections; AND  
  Patient had tried and failed 12 weeks of conservative management which must consist of documented physical therapy and nonsteroidal anti-inflammatory medications. |
| BCBS North Dakota                          | Lumbar Spine/Sacroiliac Joint Fusion Surgery and Axial-Lumbosacral Interbody Fusion Surgery Policy: ND1-S-230.013 Effective: 07/01/2018 | Percutaneous or minimally invasive SI joint fusion using FDA-cleared implant may be considered medical necessary when ALL of the following criteria are met:  
  **NASS Recommendations** with the following exceptions:  
  • Pain is at least 5 on a 0 to 10 rating scale that impacts quality of life or limits activities of daily living. |
<p>| Other Payors                                |                                        |                                                                                |</p>
<table>
<thead>
<tr>
<th>Health Plan</th>
<th>Sacroiliac Joint Fusion</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>EmblemHealth (New York)</td>
<td></td>
<td>All of the following criteria must be met:</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>NASS Recommendations</strong> with the following exceptions:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Doesn’t require imaging of the SI joint that shows injury and/or degeneration.</td>
</tr>
<tr>
<td>Geisinger Health Plan</td>
<td>Sacroiliac Joint Fusion</td>
<td>Minimally invasive fusion of the SI joint is considered to be medically necessary for the treatment of SI joint syndrome and SI joint mediated mechanical low back pain when all of the following criteria as recommended by the International Society for the Advancement of Spine Surgery (ISASS) are met.</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>ISASS Guidelines</strong> with the following exceptions:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 75% or greater acute decrease in pain on diagnostic SI joint injection</td>
</tr>
<tr>
<td>Health New England</td>
<td>Clinical Review Criteria Related to Sacroiliac Joint Fusion for the Treatment of Adult Low-Back Pain</td>
<td>Sacroiliac Joint Fusion will be approved for members over 18 years of age if the following criteria are met:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Attempted and failed conservative treatment (muscle relaxants, NSAIDs, PT, activity modification, bracing, therapeutic intra-articular injections, RF)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• All other pain generators have been eliminated</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• If previous lumbar fusion, CT scan must show solid fusion</td>
</tr>
<tr>
<td>HealthPartners</td>
<td>Clinical Review Criteria Related to Sacroiliac Joint Fusion for the Treatment of Adult Low-Back Pain</td>
<td>Minimally invasive or percutaneous sacroiliac joint fusion is covered when all of the following criteria are met:</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>NASS Recommendations</strong> with the following exceptions:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Reported reduction in pain from SI injection on two separate occasions for the requested side</td>
</tr>
<tr>
<td>Location</td>
<td>Procedure Description</td>
<td>Details</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>---------------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Kaiser – California</td>
<td>Minimally Invasive Sacroiliac Fusion (SI Fusion)</td>
<td>For Non-Medicare Members: Sacroiliac joint fusion is medically necessary when ALL of the following are met: 1. Appropriate imaging studies demonstrate localized sacroiliac joint pathology 2. The individual is a nonsmoker, or in the absence of progressive neurological compromise will refrain from use of tobacco products for at least 6 weeks prior to the planned surgery 3. And ONE of the following: • Post-traumatic injury of the SI joint (e.g., following pelvic ring fracture) • As an adjunctive treatment for sacroiliac joint infection or sepsis • Management of sacral tumor (e.g., partial sacrectomy) • When performed as part of multisegmental long fusions for the correction of spinal deformity (e.g., idiopathic scoliosis, neuromuscular scoliosis)</td>
</tr>
<tr>
<td>Kaiser – Northwest</td>
<td>Minimally Invasive Sacroiliac Fusion (SI Fusion)</td>
<td>For Non-Medicare Members: Sacroiliac joint fusion is medically necessary when ALL of the following are met: 1. Appropriate imaging studies demonstrate localized sacroiliac joint pathology 2. The individual is a nonsmoker, or in the absence of progressive neurological compromise will refrain from use of tobacco products for at least 6 weeks prior to the planned surgery 3. And ONE of the following: • Post-traumatic injury of the SI joint (e.g., following pelvic ring fracture) • As an adjunctive treatment for sacroiliac joint infection or sepsis • Management of sacral tumor (e.g., partial sacrectomy) • When performed as part of multisegmental long fusions for the correction of spinal deformity (e.g., idiopathic scoliosis, neuromuscular scoliosis)</td>
</tr>
<tr>
<td>Kern Health Systems</td>
<td>MIS SI Joint Fusion</td>
<td>Prior authorization is required.</td>
</tr>
<tr>
<td>Medical Mutual of Ohio</td>
<td>Sacroiliac joint fusion</td>
<td>Minimally invasive sacroiliac joint fusion (CPT 27279) removed from “Investigational/Experimental Services” list. NOTE: Switched to MCG Health for guidelines.</td>
</tr>
<tr>
<td>Network Health (Wisconsin)</td>
<td>Minimally-invasive Surgical (MIS) Fusion of the Sacroiliac (SI) Joint</td>
<td>The procedure requires a pre-authorization and will be reviewed by Network Health’s outside orthopedic review group, eviCore, using the NGS Medicare LCD L36406 patient selection criteria.</td>
</tr>
<tr>
<td>Paramount</td>
<td>Sacroiliac Joint Fusion</td>
<td>Percutaneous or minimally invasive sacroiliac joint stabilization (e.g., iFuse Implant System™) for sacroiliac joint fusion (27279) requires a prior authorization for Advantage &amp; Elite. Percutaneous or minimally invasive sacroiliac joint stabilization (e.g., iFuse Implant System™) for sacroiliac joint fusion (27279) is non-covered for HMO, PPO, Individual Marketplace</td>
</tr>
</tbody>
</table>
| Priority Health (Michigan) | Lumbar Fusion  
**Policy: 91590-R5**  
**Effective: 05/01/2017** | Sacroiliac (SI) joint fusion (open or minimally invasive percutaneous procedure including implants [e.g., iFuse Implant System]) may be covered when all of the following are met:  
1. Patient is skeletally mature  
2. Patient has lower back pain for >6 months inadequately responsive to conservative care  
3. Diagnosis of sacroiliac joint disruption or degenerative sacroiliitis based on BOTH of the following:  
   a. Patient has pain at or close to the posterior superior iliac spine (PSIS) with possible radiation into buttocks, posterior thigh or groin and can point with a single finger to the location of pain (Fortin Finger Test), and  
   b. Patient has improvement in lower back pain numeric rating scale (NRS) of at least 80% after a minimum of two local anesthetic blocks into affected SI joint(s)  
| United Healthcare (UHC) | Current Coverage Position on Minimally Invasive Sacroiliac Joint Fusion  
**April 20, 2018**  
Minimally invasive sacroiliac joint fusion needed as indicated by ALL of the following:  
- Significant sacroiliac joint pain (pain rating of at least 5 on a 0-10 numeric scale) and/or significant activity limitations due to sacroiliac joint pain  
- Unilateral pain localized over the sacroiliac joint  
- Sacroiliac joint pain confirmed with response (pain) to three or more provocative examination maneuvers that stress the sacroiliac joint (e.g., FABER test, thigh thrust, pelvic gapping test, pelvic compression or Gaenslen test)  
- Confirmation of diagnosis of sacroiliac disease via pain relief of at least 75 percent (i.e., on visual analogue scale) due to fluoroscopy-guided needle injection of local anesthetic into sacroiliac joint (expected time frame of pain relief depends on anesthetic chosen, dose and concentration)  
- Failure to respond to at least six months of alternative treatments consisting of analgesics (e.g., nonsteroidal anti-inflammatory medication) and one or more of the following:  
  - Physical therapy  
  - Sacroiliac joint steroid injection  
  - Radiofrequency rhizotomy  
  - Alternative or contributing diagnoses absent (e.g., hip osteoarthritis, L5-S1 spine degeneration, tumor, infection or fracture) |
| Utah’s Public Employee Health Plan (PEHP) | Back Pain – Invasive Procedures  
**Prior Authorization Form Link** | Sacroiliac Fusion:  
CPT code 27279 covered with prior authorization for iFuse. |
TRICARE
(coverage for U.S. uniformed service members)

Minimally Invasive Surgery for sacroiliac Joint pain
Policy:
Manual 6010.57-M
Effective: 03/17/2017

TRICARE is the healthcare program providing comprehensive coverage for uniformed service members and their families around the world, including active duty and retired members of the:
- U.S. Army
- U.S. Air Force
- U.S. Navy
- U.S. Marine Corps
- U.S. Coast Guard
Commissioned Corps of the U.S. Public Health Service
Commissioned Corps of the National Oceanic and Atmospheric Association.
Retroactive coverage for dates of service beginning August 23, 2016

Many payors are paying for MIS SI joint fusion on a prior authorization and/or case-by-case basis:

- Aetna
- Anthem
- CIGNA
- Humana
5.3 Medicaid

As of June 30, 2019, 43 states (AL, AK, AR, AZ, CA, CT, CO, DE, FL, GA, HI, ID, IL, IN, IA, KS, KY, LA, ME, MA, MI, MN, MO, MT, NE, NV, NH, NJ, NM, NY, NC, ND, OH, OK, RI, SC, SD, UT, VA, VT, WV, WI, WY) and the District of Columbia Medicaid programs cover MIS SI joint fusion.

Note, coverage may vary due to a state’s specific policy criteria and/or because the state has multiple Medicaid programs with varying policies. For example, special circumstances exist for Indiana, Oregon, Pennsylvania, and Tennessee.

- **Indiana** – all programs cover except CareSource
- **Oregon** will begin covering MIS SI joint fusion (CPT 27279), effective January 1, 2020.
- **Pennsylvania** covers under the 1150 Administrative Waiver.*
- **Tennessee** has three Medicaid programs and two of the three currently cover 27279.
- **California** – IEHP covers MIS SI joint fusion.

See Figure below.

* PA Department of Human Services (DHS) has “made a decision to not add procedure code 27279 to the MA program fee schedule as procedure code 27280 (Arthrodesis, open sacroiliac joint, including obtaining bone graft, including instrumentation, when performed), which may also be used for this procedure, is currently open on the MA program fee schedule.” As an alternative to reporting CPT 27279, “a prescriber may request a program exception if it is determined that the procedure represented by procedure code 27279 is medically necessary, by following the 1150 Administrative Waiver Process outlined in their MA provider handbook.
5.4 Medical Specialty Society Guidelines/Recommendations and Health Technology Assessments

Summarized below are guidelines/recommendations followed by several of the policies noted above.

See also section 3.8 Health Technology Assessments.

5.4.1 NASS Recommendations

In June 2015, the North American Spine Society (NASS) Coverage Committee published coverage policy recommendation for “Percutaneous Sacroiliac Joint Fusion” [Bono 2015]. The recommendations include a list of eight criteria, specifically intended to ensure appropriate patient selection for minimally invasive SI joint fusion. Below is summary text from the policy:

Percutaneous (also referred to as minimally invasive) SIJ fusion (e.g. insertion of a metallic device across the SIJ that is intended to fuse to the bone or lead to fusion of the joint itself, in distinction from insertion of screws without bone graft across the SIJ which are intended to stabilize but not fuse the joint) is indicated for the treatment of SIJ pain for patients with low back/buttock pain who meet ALL of the following criteria:

a) Have undergone and failed a minimum six months of intensive nonoperative treatment that must include medication optimization, activity modification, bracing, and active therapeutic exercise targeted at the lumbar spine, pelvis, SIJ and hip including a home exercise program

b) Patient’s report of typically unilateral pain that is caudal to the lumbar spine (L5 vertebrae), localized over the posterior SIJ, and consistent with SIJ pain

c) A thorough physical examination demonstrating localized tenderness with palpation over the sacral sulcus (Fortin’s point, i.e. at the insertion of the long dorsal ligament inferior to the posterior superior iliac spine or PSIS) in the absence of tenderness of similar severity elsewhere (e.g. greater trochanter, lumbar spine, coccyx) and that other obvious sources for their pain do not exist

d) Positive response to a cluster of 3 provocative tests (e.g. thigh thrust test, compression test, Gaenslen’s test, distraction test, Patrick’s sign, posterior provocation test). Note that the thrust test is not recommended in pregnant patients or those with connective tissue disorders

e) Absence of generalized pain behavior (e.g. somatoform disorder) or generalized pain disorders (e.g. fibromyalgia)

f) Diagnostic imaging studies that include ALL of the following:
   1. Imaging (plain radiographs and a CT or MRI) of the SI joint that excludes the presence of destructive lesions (e.g. tumor, infection) or inflammatory arthropathy that would not be properly addressed by percutaneous SIJ fusion
   2. Imaging of the pelvis (AP plain radiograph) to rule out concomitant hip pathology
   3. Imaging of the lumbar spine (CT or MRI) to rule out neural compression or other degenerative condition that can be causing low back or buttock pain
   4. Imaging of the SI joint that indicates evidence of injury and/or degeneration

g) At least 75 percent reduction of pain for the expected duration of the anesthetic used following an image-guided, contrast-enhanced intra-articular SIJ injection on two separate occasions
h) A trial of at least one therapeutic intra-articular SIJ injection (i.e., corticosteroid injection)

**Percutaneous SIJ fusion for SIJ pain is NOT** indicated in ANY of the following scenarios:

- Any case that does not fulfill ALL of the above criteria
- Presence of systemic arthropathy such as ankylosing spondylitis or rheumatoid arthritis
- Presence of generalized pain behavior (e.g., somatoform disorder) or generalized pain disorder (e.g., fibromyalgia)
- Presence of infection, tumor, or fracture
- Presence of acute, traumatic instability of the SIJ
- Presence of neural compression as seen on an MRI or CT that correlates with the patient’s symptoms or other more likely source for their pain.

### 5.4.2 ISASS Guidelines

The International Society for the Advancement of Spine Surgery (ISASS) developed and published a policy statement regarding minimally invasive SI joint fusion. Initial guidelines published in 2014 [Lorio 2014\(^{139}\)]. In 2015, the policy statement was updated in March and then again in December. The current policy and latest update was published in July 2016 [Lorio 2016\(^{149}\)]. Below is a summary of the current policy:

Patients who have all of the following criteria may be eligible for minimally invasive SIJ fusion:

- Significant SIJ pain that impacts quality of life or significantly limits activities of daily living;
- SIJ pain confirmed with at least 3 physical examination maneuvers that stress the SIJ (e.g., distraction test, compression test, thigh thrust, FABER (Patrick’s) test, Gaenslen’s maneuver) and reproduce the patient’s typical pain.
- Confirmation of the SIJ as a pain generator with ≥50% acute decrease in pain upon fluoroscopically guided diagnostic intra-articular SIJ block using local anesthetic. Prospective trials have shown that patients with SIJ pain responses of 50-75% respond to MIS SIJ fusion as well as those with 75-100% acute responses.
- Failure to respond to at least 6 months of non-surgical treatment consisting of non-steroidal anti-inflammatory drugs and physical therapy. Failure to respond means continued pain that interferes with activities of daily living and/or results in functional disability;
- Additional or alternative diagnoses that could be responsible for the patient’s ongoing pain or disability have been considered. Physicians should take into account that patients can have multiple pain generators and addressing just one pain generator may not adequately relieve disability or all back pain.

**Minimally invasive SIJ fusion is NOT indicated for patients with the following:**

- Less than 6 months of SIJ pain and/or functional impairment;
- Failure to pursue conservative treatment of the SIJ (unless contra-indicated);
• Pain not confirmed with a diagnostic SIJ block;
• Existence of other pathology that would substantially prevent the patient from deriving benefit from SIJ fusion.

5.4.3 BlueCross BlueShield Association (BCBSA)

In December 2016, BlueCross BlueShield Association (BCBSA) launched Evidence Street™ website (https://app.evidencestreet.com/) to streamline evaluations of medical devices, diagnostics and pharmaceuticals. The platform Evidence Street™ was created to make BCBSA’s evidence review process of medical technologies and therapies more transparent, efficient and comprehensive. BCBSA collects and analyzes available peer-reviewed evidence on devices, diagnostics and pharmaceuticals, then synthesizes that data and ascertains if the evidence is sufficient or insufficient to determine the effect on health outcomes.

In January 2019, BCBSA published its latest evidence summary report on “Diagnosis and Treatment of Sacroiliac Joint Pain” with the objective to evaluate therapeutic corticosteroid injections and minimally invasive methods (radiofrequency ablation, SIJ fusion/fixation) for the treatment of SIJ pain. Below are key elements and conclusions of the report:

• BCBSA uses a four-level evidence rating scale of Substantial, Moderate, Low to None, and Uncertain.
• To receive a Moderate or Substantial rating, there must be sufficient clinical evidence to determine the positive effects of the technology on health outcomes.
• Rating for MIS SI joint fusion with triangular implants was Moderate.
• ONLY triangular implants (iFuse Implants™) have the high-quality evidence that, according to BCBSA, is “sufficient to determine that the technology results in a meaningful improvement in the net health outcome.”
• Cylindrical threaded implants (e.g., screws) used for SI joint fusion were given an Uncertain rating because the evidence is insufficient.

5.4.4 AIM Specialty Health®

AIM Specialty Health® (AIM, www.aimspecialtyhealth.com) provides clinical solutions that drive appropriate, safe, and affordable care. Serving more than 50 million members across 50 states, D.C. and U.S. territories, AIM promotes optimal care through use of evidence-based clinical guidelines and real-time decision support for both providers and their patients.

At the end of 2017, AIM completed a review and published positive clinical appropriateness guidelines for Sacroiliac Joint Fusion (Percutaneous/Minimally Invasive Techniques) that became effective July 1, 2018. These AIM guidelines are utilized by some Anthem plans, Independence BCBS, AmeriHealth and Others. The complete guidelines can be found at http://www.aimspecialtyhealth.com/PDF/Guidelines/2018/Jul01/AIM_Guidelines_MSK_Sacroiliac-Joint-Fusion.pdf

Below is a summary:

Percutaneous/Minimally Invasive SI Joint Fusion with the iFuse system (titanium triangular implant) may be considered medically necessary when all of the following criteria are met:
• Persistent pain greater than six (6) months’ duration that interferes with functional activities as documented by all of the following:
  o Pain score (VAS) of 5 or greater
  o ODI 30 or greater
• Failure of at least six (6) months of conservative management
• Confirmation of the SI joint as a pain generator as demonstrated by all of the following:
  o Pain pattern consistent with SI joint pain (typically unilateral pain caudal to L5 vertebrae, localized over posterior SI joint)
  o Positive finger Fortin test (localized tenderness with palpation over the sacral sulcus)
  o Absence of tenderness of similar severity elsewhere in the pelvic region (e.g., greater trochanter, lumbar spine, coccyx)
  o Positive response from at least three (3) of the following provocative tests:
    ▪ Long ligament test
    ▪ Faber’s test/Patrick’s sign
    ▪ Active straight leg raise
    ▪ Compression test
    ▪ Distraction test
    ▪ Thigh thrust test (not recommended for those who are pregnant or those with connective tissue disorder)
    ▪ Gaenslen’s test
  o Other sources of pain have been excluded as an etiology
• Diagnostic imaging studies that include all of the following:
  o Imaging (plain radiographs and a CT) or MRI of the SI joint that excludes the presence of destructive lesions (e.g., tumor, infection) or inflammatory arthropathy that would not properly be addressed by percutaneous SI joint fusion
  o Imaging of pelvis (AP plain radiograph) to rule out concomitant hip pathology
  o Imaging of lumbar spine (CT or MRI) to rule out neural compression or other degenerative condition that can be causing low back or buttock pain
  o Imaging of SI joint that indicates evidence of injury and/or degeneration
• Diagnostic confirmation of the SI joint as the pain generator demonstrated by at least 75% reduction of pain for the expected duration of the anesthetic used following an image-guided, contrast-enhanced intra-articular SI joint injection on two (2) separate occasions

Exclusions

Indications other than those addressed in this guideline are considered not medically necessary, including but not limited to the following:

• Presence of infection, tumor, or fracture
• Presence of acute, traumatic instability of the SI joint
• Presence of neural compression as seen on imaging that correlates with symptoms or other more likely source of pain
• Presence of generalized pain behavior (e.g., somatoform disorder) or generalized pain disorders (e.g., fibromyalgia)
• Presence of ankylosing spondylitis or rheumatoid arthritis
5.4.5 Milliman Care Guidelines (MCG)


Minimally invasive sacroiliac joint fusion needed as indicated by ALL of the following:

- Significant sacroiliac joint pain (pain rating of at least 5 on a 0 to 10 numeric scale) and/or significant activity limitations due to sacroiliac joint pain
- Unilateral pain localized over the sacroiliac joint
- Sacroiliac joint pain confirmed with response (pain) to 3 or more provocative examination maneuvers that stress the sacroiliac joint (e.g., FABER test, thigh thrust, pelvic gapping test, pelvic compression, Gaenslen test)
- Confirmation of diagnosis of sacroiliac disease via pain relief of at least 75% (i.e., on visual analogue scale) due to fluoroscopy-guided needle injection of local anesthetic into sacroiliac joint (expected time frame of pain relief depends on anesthetic chosen, dose, and concentration)
- Failure to respond to at least 6 months of alternative treatments consisting of analgesics (e.g., nonsteroidal anti-inflammatory medication) and 1 or more of the following[A]:
  - Physical therapy
  - Sacroiliac joint steroid injection
  - Radiofrequency rhizotomy
- Alternative or contributing diagnoses absent (e.g., hip osteoarthritis, L5-S1 spine degeneration, tumor, infection, fracture).

5.4.6 eviCore Healthcare

EviCore Healthcare is a specialty benefits manager that contracts with various payors who cover more than 100 million lives. In 2018, eviCore updated its Clinical Guidelines for Spine Surgery (Version 1.0.2018) which became effective October 22, 2018 [eviCore 2018150].

CMM-611.2: Minimally Sacroiliac Joint Fusion or Stabilization

Minimally invasive sacroiliac joint (SIJ) fusion using titanium triangular implants (SI-BONE [iFuse Implant™]) for the treatment of lumbopelvic pain originating from the SIJ is considered medically necessary when ALL of the following are met:

- Performed by an orthopedic surgeon or neurosurgeon with specific training and expertise in percutaneous sacroiliac joint fusion surgical techniques and regularly uses image-guidance for placement of implants
- Presence of non-radiating lumbopelvic pain caudal to L5, buttock, hip, and/or groin pain without radiation into the leg(s) that impairs physical activities
- SI joint pain interfering with activities of daily living
- Patient localizes posterior pain to the posterior superior iliac spine (Fortin’s point)
- Localized tenderness to palpation over the sacral sulcus and posterior SI joint
• Elicitation of typical pain on three (3) or more provocative physical examination maneuvers/test that stress the SI joint:
  - Thigh thrust test
  - Compression test
  - Gaenslen’s maneuver
  - Distraction test
  - FABER/Patrick’s sign
  - Posterior provocation test
• Absence of localized tenderness to palpation of similar severity to palpation of the sacral sulcus and posterior SIJ over the greater trochanter, lumbar spine, and coccyx
• Diagnostic confirmation of the SIJ as a pain generator through at least an 80% reduction in pain for the expected duration of effect of the anesthetic agent used upon two separate contrast-enhanced fluoroscopically or CT-guided intra-articular SIJ blocks using a local anesthetic performed at a minimum of two weeks apart
• Confirmation of the SIJ as a pain generator through at least a 50% reduction in pain for a minimum of two weeks following one contrast-enhanced fluoroscopically or CT-guided intra-articular SIJ injection using a corticosteroid
• SIJ pain without minimal clinically important difference (MCID) improvement from a minimum of a consecutive six (6) months of conservative, non-surgical treatment including ALL of the following unless contraindicated:
  - Non-steroidal anti-inflammatory drugs (NSAIDs)
  - Prescription medication optimization
  - Activity modification
  - Physician supervised/prescribed active physical therapy (including home exercise program) targeting lumbopelvic (core) area
  - Chiropractic care
• Absence of generalized pain behavior (e.g., somatoform disorder) or generalized pain disorders (e.g., fibromyalgia)
• Documentation of nicotine-free status with EITHER of the following:
  - Patient is a nonsmoker
  - Patient has refrained from smoking for at least 6 weeks prior to planned surgery as evidenced by cotinine lab results of ≤ 10ng/mL
• Absence of unmanaged significant behavioral health disorders (e.g., major depressive disorder, chronic pain syndrome, secondary gain, drug and alcohol abuse)
• Absence of alternative diagnoses that are a more likely cause of the patient’s ongoing pain or disability
• Recent (within 6 months) diagnostic imaging studies that include ALL of the following:
  - Plain radiographs and/or cross-sectional imaging (CT or MRI) that excludes the presence of destructive lesions (e.g., tumor, infection), acute fracture or inflammatory arthropathy that would not be properly addressed by SIJ fusion
  - Plain radiographs of the pelvis including the ipsilateral hip to evaluate potential concomitant hip pathology
  - Cross-sectional imaging (e.g., CT or MRI) of the lumbar spine to evaluate potential concomitant neural compression or other degenerative conditions
6 Appendices

Appendix A – Literature Search Methodology

Appendix B – References

Appendix C – Sacroiliac Joint Diagnosis: Summary of Guidelines and Clinical Evidence for Provocative Maneuvers and Diagnostic Injections

Appendix D – iFuse Implant System® and Other Key SI Joint Publications

Appendix E – Comparison of ISASS and NASS Coverage Criteria for Minimally Invasive SI Joint Fusion
6.1 Appendix A – Literature Search Methodology


The search resulted in 353 publications. Three publications were removed because two were responses to a published article and the third was an erratum to a previous publication. Of the 350 remaining publications, abstracts were reviewed, and 127 articles specifically reported on SI joint fusion, whereas the other 223 covered a wide range of topics such as ankylosing spondylitis, spondyloarthropathy, pelvic ring instability/fractures/tumors, deformity/scoliosis, sacral fractures, and even tuberculosis and ankle conditions.

The 127 SI joint fusion publications can be sorted by design and type of article as shown in the table below. Only 61% (78) of the articles report/discuss products or systems indicated and cleared for SI joint fusion in the United States, with the iFuse Implant System making up 76% (58 articles) of these publications.

<table>
<thead>
<tr>
<th>Article Count</th>
<th>iFuse (%)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>353</td>
<td></td>
<td>Search Terms “sacroiliac joint” AND “fusion”</td>
</tr>
<tr>
<td>350</td>
<td></td>
<td>Search Terms “sacroiliac joint” AND “fusion” (minus 3: two responses and an erratum)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>223 = not related to SI joint fusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>127 = SI joint fusion</td>
</tr>
<tr>
<td>127</td>
<td>58 (46%)</td>
<td>Reporting on SI joint fusion</td>
</tr>
</tbody>
</table>

Various sorting of the 123 SI joint fusion publications

<table>
<thead>
<tr>
<th>Article Count</th>
<th>iFuse (%)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>78</td>
<td>58 (74%)</td>
<td>Products indicated/cleared in the US for SI joint fusion</td>
</tr>
<tr>
<td>21</td>
<td>16 (76%)</td>
<td>Prospective or Randomized Controlled Trials</td>
</tr>
<tr>
<td>50</td>
<td>21 (42%)</td>
<td>Retrospective</td>
</tr>
<tr>
<td>9</td>
<td>2 (22%)</td>
<td>Technique, no clinical outcomes</td>
</tr>
<tr>
<td>9</td>
<td>6 (67%)</td>
<td>Biomechanics</td>
</tr>
<tr>
<td>11</td>
<td>4 (36%)</td>
<td>Reviews</td>
</tr>
<tr>
<td>8</td>
<td>4 (50%)</td>
<td>Economics</td>
</tr>
<tr>
<td>18</td>
<td>6 (33%)</td>
<td>Miscellaneous (policy, survey, condition, case report, comments, etc.)</td>
</tr>
</tbody>
</table>

There are 14 known iFuse Implant System publications that were not identified with the above search (13 published and 1 submitted and in review).

Published


Submitted, in review:


6.2 Appendix B – References


42. Cher DJ, Reckling WC. Quality of life in preoperative patients with sacroiliac joint dysfunction is at least as depressed as in other lumbar spinal conditions. *Med Devices Evid Res.* 2015;8:395-403.


47. Laslett M. Evidence-based diagnosis and treatment of the painful sacroiliac joint. *J Man Manip Ther.* 2008;16(3):142-152.


130. Yoon BJV, Xavier F, Walker BR, Cammisa FP, Abjornson C. Optimizing surface characteristics for cell adhesion and proliferation on titanium plasma spray coatings on PEEK. Spine J. May 2016. doi:10.1016/j.spinee.2016.05.017


6.3 Appendix C – Sacroiliac Joint Diagnosis: Summary of Guidelines and Clinical Evidence for Provocative Maneuvers and Diagnostic Injections

This document is intended to provide the reader with a summary of the peer-reviewed published literature that supports the diagnosis of sacroiliac (SI) joint disorders using physical provocative maneuvers and diagnostic injections. Citations are provided and hyperlinks to the references as indexed on PubMed and society websites, as applicable.

Society Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAOS</td>
<td>American Academy of Orthopaedic Surgeons</td>
</tr>
<tr>
<td>AAPM&amp;R</td>
<td>American Academy of Physical Medicine and Rehabilitation</td>
</tr>
<tr>
<td>APS</td>
<td>American Pain Society</td>
</tr>
<tr>
<td>ASA</td>
<td>American Society of Anesthesiologists</td>
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<tr>
<td>ASIPP</td>
<td>American Society of Interventional Pain Physicians</td>
</tr>
<tr>
<td>ASRA</td>
<td>American Society of Regional Anesthesia and Pain Medicine</td>
</tr>
<tr>
<td>IASP</td>
<td>International Association for the Study of Pain</td>
</tr>
<tr>
<td>IPM</td>
<td>Interventional Pain Management</td>
</tr>
<tr>
<td>ISASS</td>
<td>International Society for the Advancement of Spine Surgery</td>
</tr>
<tr>
<td>SIS</td>
<td>Spine Intervention Society (formerly ISIS, International Spine Intervention Society)</td>
</tr>
</tbody>
</table>

I. Provocative Maneuvers – The following authors have published studies on the usefulness of a cluster of physical examination maneuvers in diagnosing SI joint disorders.

<table>
<thead>
<tr>
<th>Reference / Title</th>
<th>Statement on Provocative Maneuvers</th>
</tr>
</thead>
</table>
| **Petersen et al. 2017**<sup>1</sup> *Clinical Classification in Low Back Pain: Best-evidence Diagnostic Rules Based on Systematic Reviews* | First comprehensive systematic review of diagnostic accuracy studies for physical examination or other simple in-office tests regarding low back (LBP) pain diagnosis with the goal to develop best-evidence **Clinical Diagnostic Rules (CDR)**. A CDR is a guideline that aids in the diagnosis and/or management of a condition.  
- Sufficient evidence for CDRs for  
  - symptomatic intervertebral disc  
  - sacroiliac (SI) joint  
  - disc herniation with nerve root involvement  
  - spinal stenosis  
  - spondylolisthesis  
- SI joint test includes 3 or more positive provocative tests, lack of centralization, and pain over the posterior superior iliac spine (PSIS).  
- The SI joint pain CDR is as good or better than most physical exam tests for other low back conditions. |
<table>
<thead>
<tr>
<th>Reference / Title</th>
<th>Statement on Provocative Maneuvers</th>
</tr>
</thead>
</table>
| **Lorio 2016**<sup>2</sup>  
**ISASS Policy 2016 Update – Minimally Invasive Sacroiliac Joint Fusion**  
(See also the original policy: **Lorio & Rashbaum 2014**<sup>3</sup>  
**ISASS Policy Statement – Minimally Invasive Sacroiliac Joint Fusion**) | Indications for surgery include:  
1. SIJ pain confirmed with at least 3 physical examination maneuvers that stress the SIJ (see list provided above) and reproduce the patient's typical pain.  
2. Confirmation of the SIJ as a pain generator with ≥50% acute decrease in pain upon fluoroscopically guided diagnostic intra-articular SIJ block using local anesthetic. Prospective trials have shown that patients with SIJ pain responses of 50-75% respond to MIS SIJ fusion as well as those with 75-100% acute responses. |
| **Wong & Johnson 2012**<sup>4</sup>  
**A narrative review of evidence-based recommendations for the physical examination of the lumbar spine, sacroiliac and hip joint complex** | • As low back pain can stem from the spine, sacroiliac and hip joints in various combinations, efficiently identifying contributing structures enables the physician to direct effective treatment.  
• The 5 sacroiliac joint pain provocation tests utilized have substantial inter-rater reliability and consist of the distraction test, compression test, thigh thrust test, FABER and Gaenslen test.  
• The thigh thrust test has the highest reported sensitivity of any sacroiliac joint test (88%) with a 69% specificity.  
• Optimally, tests have both high sensitivity and specificity, and thus a positive likelihood ration (+LR) of 2 or more.  
• A combination of 3 of 5 positive tests for sacroiliac joint-related pain has discriminative power for sacroiliac joint pathology in 2 meta-analyses of SI joint tests with +LR = 3.2 |
| **Szadek et al. 2009**<sup>5</sup>  
**Diagnostic validity of criteria for sacroiliac joint pain: a systematic review** | • Systematic literature review was conducted to determine the diagnostic validity of the criteria for sacroiliac joint pain as proposed by the International Association for the Study of Pain (IASP)  
• In all studies, the SI joint selective infiltration was used as gold standard.  
• Taking the double infiltration technique as a reference test, the pooled data of the thigh thrust test, compression test and 3 or more positive stressing tests showed discriminative power for diagnosing SI joint pain. |
| **Vleeming et al. 2008**<sup>6</sup>  
**European Guidelines for the diagnosis and treatment of pelvic girdle pain** | • Pelvic girdle pain is defined by pain experienced between the posterior iliac crest and gluteal fold, particularly in the vicinity of the sacroiliac joints  
• PGP can be diagnosed by pain provocation tests: P4/thigh thrust, Patrick’s Faber, Gaenslen’s test, and modified Trendelenburg’s test |
<table>
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<tr>
<th>Reference / Title</th>
<th>Statement on Provocative Maneuvers</th>
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</table>
| Laslett 2008<sup>7</sup> | • This study examined the diagnostic power of pain provocation SI joint tests singly and in various combinations, in relation to an accepted criterion standard.  
• The sacroiliac pain provocation tests used were: distraction, right-sided thigh thrust, ride-sided Gaenslen’s test, compression and sacral thrust.  
• The thigh thrust test is the most sensitive test and the distraction test is the most specific.  
• Sensitivity and specificity for 3 or more of 6 positive SI joint tests were 94% and 78% respectively; for 2 positive tests of distraction, thigh thrust, compression and sacral thrust, sensitivity was 88% and specificity was 78%.  
• 2 of 4 positive tests (distraction, compression, thigh thrust or sacral thrust) or 3 of 6 tests are the best predictors of a positive intra-articular SI joint block.  
• When all 6 provocation tests do not provoke familiar pain, the SI joint can be ruled out as a source of current LBP (low back pain). |
| Stuber 2007<sup>9</sup> | • A systematic review of the literature was conducted to determine the sensitivity, specificity, and predictive values of any clinical SI joint tests when compared to the gold standard of an SI joint block (injection). Five studies were included in the analysis.  
• The study by Laslett et al.<sup>8</sup> had the highest methodological quality score.  
• Specificity: The thigh thrust/posterior shear test had specificity of 50%, 100% (with both 70% and 90% pain relief criteria), and 69% in three different studies. Differences in results between studies may be explained by different pain relief standards required for the injection to be considered positive and by other methodological differences.  
• The specificity of numerous positive results generally increased as the number of positive tests increased.  
• From the results of this review, it appears that two trends can be discerned. First, employing a group of tests with a requisite number of positive tests (such as 2 out of 4 or 3 out of 5) in order to diagnose a SI joint injury may be desirable as Laslett et al. demonstrate that employing this approach results in adequate sensitivity, specificity and predictive values, and Slipman et al. demonstrated an acceptable positive predictive value when 3 out of 5 tests were positive. Second, certain tests appear to have higher sensitivity and specificity than others. |

### II. Diagnostic Injections

The following societies have developed guidelines on diagnostic injections of the sacroiliac joint.

<table>
<thead>
<tr>
<th>Society: Year / Title</th>
<th>Statement on Diagnostic Injections</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISASS Statement: 2016&lt;sup&gt;2&lt;/sup&gt;</td>
<td>The diagnosis of SI joint pain is confirmed by performing a fluoroscopy guided intra-articular SI joint block with local anesthetic (e.g., lidocaine). An acute reduction in typical pain indicates a positive test, suggesting that the injected joint is a pain generator. Confirmation of the SIJ as a pain generator with ≥50% acute decrease in pain upon fluoroscopically guided diagnostic intra-articular SIJ block using local anesthetic. Prospective trials have shown that patients with SIJ pain responses of 50-75% respond to MIS SIJ fusion as well as those with 75-100% acute responses (ref Polly. Int J Spine Surg. 2016;10:Article 4).</td>
</tr>
<tr>
<td>Society: Year / Title</td>
<td>Statement on Diagnostic Injections</td>
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| Simopoulos et al. 2015<sup>10</sup>  
*Systematic Review of the Diagnostic Accuracy and Therapeutic Effectiveness of Sacroiliac Joint Interventions* | **OBJECTIVE:** To evaluate the diagnostic accuracy and therapeutic effectiveness of sacroiliac joint interventions.  
**STUDY DESIGN:** A systematic review of the diagnostic accuracy and therapeutic effectiveness of sacroiliac joint interventions.  
**METHODS:** The available literature on diagnostic and therapeutic sacroiliac joint interventions was reviewed. The quality assessment criteria utilized were the Quality Appraisal of Reliability Studies (QAREL) checklist for diagnostic accuracy studies, Cochrane review criteria to assess sources of risk of bias, and Interventional Pain Management Techniques – Quality Appraisal of Reliability and Risk of Bias Assessment (IPM – QRB) criteria for randomized therapeutic trials and Interventional Pain Management Techniques – Quality Appraisal of Reliability and Risk of Bias Assessment for Nonrandomized Studies (IPM – QRBNR) for observational therapeutic assessments.  
The level of evidence was based on a best evidence synthesis with modified grading of qualitative evidence from Level I to Level V.  
Data sources included relevant literature published from 1966 through March 2015 that were identified through searches of PubMed and EMBASE, manual searches of the bibliographies of known primary and review articles, and all other sources.  
**OUTCOME MEASURES:** For the diagnostic accuracy assessment, and for the therapeutic modalities, the primary outcome measure of pain relief and improvement in functional status were utilized.  
**RESULTS:** A total of 11 diagnostic accuracy studies and 14 therapeutic studies were included. The evidence for diagnostic accuracy is Level II for dual diagnostic blocks with at least 70% pain relief as the criterion standard and Level III evidence for single diagnostic blocks with at least 75% pain relief as the criterion standard.  
The evidence for cooled radiofrequency neurotomy in managing sacroiliac joint pain is Level II to III. The evidence for conventional radiofrequency neurotomy, intraarticular steroid injections, and periarticular injections with steroids or botulinum toxin is limited: Level III or IV.  
**LIMITATIONS:** The limitations of this systematic review include inconsistencies in diagnostic accuracy studies with a paucity of high quality, replicative, and consistent literature. The limitations for therapeutic interventions include variations in technique, variable diagnostic standards for inclusion criteria, and variable results. |
<table>
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<tr>
<th><strong>Society: Year / Title</strong></th>
<th><strong>Statement on Diagnostic Injections</strong></th>
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</table>
| **SIS Appropriate Use Criteria: 2015**<sup>11</sup>  
*Fluoroscopically Guided Diagnostic and Therapeutic Sacroiliac Joint Injections: A Systematic Review* | **OBJECTIVE:** To assess the validity of fluoroscopically guided diagnostic intra-articular injections of local anesthetic and effectiveness of intra-articular steroid injections in treating sacroiliac joint (SIJ) pain.  
**DESIGN:** Systematic review.  
**INTERVENTIONS:** Ten reviewers independently assessed 45 publications on diagnostic validity or effectiveness of fluoroscopically guided intra-articular SIJ injections.  
**OUTCOME MEASURES:** For diagnostic injections, the primary outcome was validity; for therapeutic injections, analgesia. Secondary outcomes were also described.  
**RESULTS:** Of 45 articles reviewed, 39 yielded diagnostic data on physical exam findings, provocation tests, and SIJ injections for diagnosing SIJ pain, and 15 addressed therapeutic effectiveness. When confirmed by comparative local anesthetic blocks with a high degree of pain relief, no single physical exam maneuver predicts response to diagnostic injections. When at least three physical exam findings are present, sensitivity, and specificity increases significantly. The prevalence of SIJ pain is likely 20-30% among patients that have suspected SIJ pain based on history and physical examination. This estimate may be higher in certain subgroups such as the elderly and fusion patients. Two randomized controlled trials and multiple observational studies supported the effectiveness of therapeutic sacroiliac joint injections.  
**CONCLUSIONS:** Based on this literature, it is unclear whether image-guided intra-articular diagnostic injections of local anesthetic predict positive responses to therapeutic agents. The overall quality of evidence is moderate for the effectiveness of therapeutic SIJ injections. |
| **AAOS: 2014**<sup>12</sup>  
*Sacroiliac Joint Injections* | Sacroiliac joint (SI joint) injections are similar to facet joint injections in many ways. The SI joints are located between the sacrum and ilium (pelvic) bones.  
- Problems in the SI joints have been shown to cause pain in the low back, buttock, and leg. Typically, one joint is painful and causes pain on one side of the lower body. It is less common for both SI joints to be painful at the same time |
Evidence: Lumbar Spine

The evidence for diagnostic lumbar facet joint nerve blocks and diagnostic sacroiliac intraarticular injections is good with 75% to 100% pain relief as criterion standard with controlled local anesthetic or placebo blocks.

3.1 Diagnosis of Sacroiliac Joint Pain

There is no universally accepted gold standard for the diagnosis of low back pain stemming from sacroiliac joints. In a systematic review evaluating a battery of tests to identify the disc, sacroiliac joint, or facet joint as the source of low back pain, Hancock et al. (375) suggested that a combination of sacroiliac joint pain provocative maneuvers appears to be useful in pinpointing the sacroiliac joint as the principal source of symptoms in patients with pain below the fifth lumbar vertebra. They also concluded that although a positive bone scan has high specificity, it is associated with a very low sensitivity, which means that the majority of patients with the sacroiliac joint pain will not be accurately identified.

A systematic review by Szadek et al. (397) evaluated the diagnostic validity of the IASP criteria for sacroiliac joint pain. The meta-analysis showed that the thigh thrust test, the compression test, and 3 or more positive stressing tests contain sufficient discriminative power for diagnosing sacroiliac joint pain. They concluded that in view of the lack of a gold standard for sacroiliac joint pain, the diagnostic validity of tests for sacroiliac joint pain should be regarded with caution.

3.1.1.5 Recommendations

- Controlled sacroiliac joint blocks with placebo or controlled comparative local anesthetic blocks are recommended when indications are satisfied with suspicion of sacroiliac joint pain, except when required by regulation or guidance, a positive response is considered ≥ 75% relief (good evidence) or with ability to perform previously painful movements.
<table>
<thead>
<tr>
<th>Society: Year / Title</th>
<th>Statement on Diagnostic Injections</th>
</tr>
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</table>
| **SIS: 2013**<sup>14</sup>  
**Practice Guidelines for Spinal Diagnostic and Treatment Procedures: Sacroiliac Joint Access (2nd Edition)** | **DEFINITION** – Sacroiliac joint blocks are a diagnostic procedure performed to test the hypothesis that a sacroiliac joint is the source of a patient’s pain and involve injecting an aliquot of local anesthetic into the cavity of the joint in order to anesthetize it.  
**VALIDITY** – Sacroiliac joint blocks have concept and face validity. Construct validity must be secured in each and every patient. This means that in order to be valid, sacroiliac joint blocks must be subjected to controls (anatomical or physiological) every time that they are applied.  
**UTILITY** – Sacroiliac joint blocks have diagnostic utility. Establishing a diagnosis of sacroiliac joint pain protects patients from further pursuing a diagnosis, and from undergoing futile treatment that will not relieve sacroiliac joint pain.  
**INDICATIONS** – In the simplest terms, the indication for a sacroiliac joint block is the need, or desire, to know if a sacroiliac joint is the source of a patient’s pain. No clinical features are diagnostic of sacroiliac joint pain. However, positive responses are more likely to occur in patients who are positive to three or more provocative tests of the sacroiliac joint. In the interest of professional efficiency, sacroiliac joint blocks should be reserved, in the first instance, to such patients who have positive sacroiliac joint signs. Patients with sacroiliac joint pain typically do not complain of pain rostral to L5.  
**EVALUATION** – It is prudent to consider a response negative if there is < 50% relief, equivocal if there is 51-74% relief, and positive if there is a least 75% improvement, with increased confidence that the response is truly positive as the percentage relief approaches 100%. Moreover, any apparently positive response should be tested with a subsequent, control block. |
| **ASA and ASRA: 2010**<sup>15</sup>  
**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** | **Interventional diagnostic procedures:**  
Based on a patient’s clinical presentation, appropriate diagnostic procedures may be conducted as part of a patient’s evaluation. The choice of an interventional diagnostic procedure (e.g., selective nerve root blocks, medial branch blocks, facet joint injections, sacroiliac joint injections, or provocative discography) should be based on the patient’s specific history and physical examination and the anticipated course of treatment. Interventional diagnostic procedures should be performed with appropriate image guidance.  
Diagnostic sacroiliac joint injections or lateral branch blocks may be considered for the evaluation of patients with suspected sacroiliac joint pain.  
Findings from patient history, physical examination, and diagnostic evaluation should be combined to provide the foundation for an individualized treatment plan focused on the optimization of the risk–benefit ratio with an appropriate progression of treatment from a lesser to a greater degree of invasiveness. |
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<tr>
<th>Society: Year / Title</th>
<th>Statement on Diagnostic Injections</th>
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<tbody>
<tr>
<td><strong>Manchikanti 2010:</strong> Comment / Reassessment of APS 2009 Guideline[^16]</td>
<td>Reassessment states there is fair to poor evidence for SI joint blocks to diagnose SI joint pain. Manchikanti states, “The development process of the guidelines by APS appears to be superior to the ACOEM guideline process and others. However, there were deficiencies and inappropriate evaluation in almost all areas; inappropriate studies were included, and appropriate studies were excluded.” Concludes with, “there was no consistency as literature was reviewed inappropriately with inclusion and exclusion criteria based on convenience rather than a standardized approach.” CONCLUSION: The reassessment, using appropriate methodology and including high quality studies, shows evidence that differs from published APS guidelines.</td>
</tr>
<tr>
<td><strong>ASIPP – IPM: 2009[^17]</strong> Comprehensive Evidence-Based Guidelines for Interventional Techniques in the Management of Chronic Spinal Pain</td>
<td>Due to the inability to make the diagnosis of sacroiliac joint-mediated pain with non-invasive tests, sacroiliac joint blocks appear to be the evaluation of choice to provide appropriate diagnosis. Further, controlled studies have established sacroiliac joints as a potential source of low back and lower extremity pain. Based on the controlled diagnostic blocks, the sacroiliac joint block has been implicated as the primary source of pain. RECOMMENDATION – Controlled sacroiliac joint blocks with placebo or controlled comparative local anesthetic blocks are recommended when indications are satisfied. A positive response is considered ≥ 80% relief with ability to perform previously painful movements. • The primary indication for sacroiliac joint blocks is the need to know if a patient’s pain is arising from the sacroiliac joint or not. • Sacroiliac joint injections are indicated in patients - with chronic low back pain that is maximal below the level of L5 vertebra extremity - with or without somatic referred pain in the lower limb, in whom no other diagnosis is readily apparent - no other possible diagnosis is more likely - a diagnosis has been made or cannot be made using less invasive options - lack of resolution of pain with the passage of time or conservative therapy</td>
</tr>
<tr>
<td><strong>APS: 2009[^18]</strong> Guideline for the Evaluation and Management of Low Back Pain Evidence Review</td>
<td>There are no studies on how use of sacroiliac joint blocks to evaluate patients for sacroiliac joint pain affects choice of therapy and clinical outcomes compared to use of non-invasive methods alone. It did not include any study that evaluated whether use of a diagnostic sacroiliac joint block to select patients for procedures intended to treat presumed sacroiliac joint pain improves clinical outcomes compared to relying on other methods to select patients for such procedures.</td>
</tr>
</tbody>
</table>
## Statement on Diagnostic Injections

**AAPM&R: 2008**

**Educational Guidelines for Interventional Spinal Procedures**

Diagnostic block of the SI joint is the only means available to confirm or deny the SI joint as a pain generator, although a single sacroiliac joint diagnostic block may have a false positive response of 7.7-20.5%.

SI joint Injections are primarily diagnostic and may facilitate other treatment options such as manual or physical therapy. Indications for therapeutic sacroiliac joint injections also included those patients with sacroiliitis as well as sacroiliac joint dysfunction.

**IASP: 2002**

**Classification of Chronic Pain: Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms**

Sacroiliac Joint Pain (XXVII-10)

Definition – Spinal pain stemming from a sacroiliac joint.

Clinical Features – Pain perceived in the region of the sacroiliac joint with or without referred pain into the lower limb girdle or lower limb itself.

**Diagnostic Criteria**

The following criteria should all be fulfilled.

1. Pain is present in the region of the sacroiliac joint.
2. Stressing the sacroiliac joint by clinical tests that are selective for the joint reproduces the patient’s pain,
3. Selectively infiltrating the putatively symptomatic joint with local anesthetic completely relieves the patient of the pain.

### References – Appendix C


### 6.4 Appendix D – iFuse Implant System® and Other Key SI Joint Publications

June 30, 2019

**Sorted Newest to Oldest within Category**

**iFuse Implant System Publications (73)**

<table>
<thead>
<tr>
<th>LOE</th>
<th>Article</th>
<th># Patients</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level I</td>
<td>Randomized Controlled Trials</td>
<td>103 (52 iFuse, 51 CM)</td>
<td>Prospective, multicenter, randomized controlled trial (iMIA, clinicaltrials.gov NCT01741025), MIS SI joint fusion (iFuse) vs. conservative management (CM), 2-year f/u</td>
</tr>
<tr>
<td>Level I</td>
<td>Dengler 2019 (iMIA 2yr)</td>
<td>103 (52 iFuse, 51 CM)</td>
<td>Secondary analysis of data from prospective, multicenter, randomized controlled trial (iMIA, clinicaltrials.gov NCT01741025), to identify risk factors for continued opioid use after MIS SI joint fusion (iFuse) and conservative management (CM), 6mo f/u</td>
</tr>
<tr>
<td>Level I</td>
<td>Dengler 2017c (iMIA opioid risk factors)</td>
<td>101 (52 iFuse, 49 CM)</td>
<td>Prospective, multicenter, randomized controlled trial (iMIA, clinicaltrials.gov NCT01741025), MIS SI joint fusion (iFuse) vs. conservative management (CM), 6mo f/u</td>
</tr>
<tr>
<td>Level I</td>
<td>Dengler 2017b (iMIA 1yr)</td>
<td>103 (52 iFuse, 51 CM)</td>
<td>Prospective, multicenter, randomized controlled trial (iMIA, clinicaltrials.gov NCT01741025), MIS SI joint fusion (iFuse) vs. conservative management (CM), 1-year f/u</td>
</tr>
<tr>
<td>Level I</td>
<td>Dengler 2017a [Pooled Analysis] (INSITE, iMIA, SIFI)</td>
<td>326 iFuse 97 NSM</td>
<td>Pooled analysis of iFuse patients from 2 multicenter, randomized controlled trials (INSITE and iMIA) and 1 multicenter prospective trial (SIFI)</td>
</tr>
<tr>
<td>Level I</td>
<td>Dengler 2016</td>
<td>101 (49 iFuse, 51 CM)</td>
<td>Prospective, multicenter, randomized controlled trial (iMIA, clinicaltrials.gov NCT01741025). Referred leg pain (RLP) is a frequent phenomenon in patients with SIJ-associated pain. At 6mo, iFuse helped relieve RLP more effectively than CM.</td>
</tr>
<tr>
<td>Level I</td>
<td>Polly 2016</td>
<td>148 (102 iFuse, 46 NSM)</td>
<td>Prospective, multicenter, randomized controlled trial (INSITE, clinicaltrials.gov NCT01681004), MIS SI joint fusion (iFuse) vs. Non-surgical management (NSM), 24 mo f/u</td>
</tr>
<tr>
<td>Level I</td>
<td>Sturesson 2016</td>
<td>103 (52 iFuse, 51 CM)</td>
<td>Prospective, multicenter, randomized controlled trial (iMIA, clinicaltrials.gov NCT01741025), MIS SI joint fusion (iFuse) vs. conservative management (CM), 6 mo f/u</td>
</tr>
<tr>
<td>LOE</td>
<td>Article</td>
<td># Patients</td>
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<tr>
<td>I</td>
<td>Polly 2015&lt;br&gt;&lt;i&gt;Neurosurgery. 2015;77:674-91. [Epub 2015 Aug 19]&lt;/i&gt;</td>
<td>148 (102 iFuse, 46 NSM)</td>
<td>Prospective, multicenter, randomized controlled trial (INSITE, clinicaltrials.gov NCT01681004), MIS SI joint fusion (iFuse) vs. Non-surgical management (NSM), 12 mo f/u</td>
</tr>
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</table>

**Level II/IIb – CLINICAL EVIDENCE (9)**

<p>| II  | Whang 2019&lt;br&gt;(LOIS 5yr)&lt;br&gt;&lt;i&gt;Med Devices (Auckl). 2019 [submitted, in review]&lt;/i&gt; | 92 (12 centers) | 5-year follow-up report from 92 of 103 subjects (89%) of the LOIS trial (patients from INSITE and SIFI). |
| II  | Patel 2019&lt;br&gt;(SALLY 6mo-interim)&lt;br&gt;&lt;i&gt;Med Devices (Auckl). 2018;11:287-289.&lt;/i&gt; | 28 (8 centers) | Prospective, multicenter, trial (SALLY, ClinicalTrials.gov NCT03122899) in which patients had minimally invasive SI joint fusion with iFuse3D Implants™, Interim 6-month f/u results from 28 of the 51 patients enrolled. |
| II  | Darr 2018b&lt;br&gt;(LOIS 4yr)&lt;br&gt;&lt;i&gt;Med Devices (Auckl). 2018;11:287-289.&lt;/i&gt; | 93 iFuse (12 centers) | 4-year follow-up report from 93 of 103 subjects (90.3%) of the LOIS trial (patients from INSITE and SIFI). |
| II  | Darr 2018a&lt;br&gt;(LOIS 3yr)&lt;br&gt;&lt;i&gt;Med Devices (Auckl). 2018;11:113-121.&lt;/i&gt; | 103 iFuse (12 centers) | Long-term (3 year) prospective results of patients with 2-year results from INSITE and SIFI. |
| IIb | Capobianco 2015&lt;br&gt;&lt;i&gt;SpringerPlus. 2015;4:570.&lt;/i&gt; | 20 females with PPGP (subset of 172 in SIFI) | Females with postpartum pelvic girdle pain (PPGP) from prospective, multicenter study (SIFI), 12 mo f/u results |
| IIb | Duhon 2015&lt;br&gt;(SIFI 2yr)&lt;br&gt;&lt;i&gt;Global Spine J. 2016;6:257-69. [Epub 2015 Aug 11]&lt;/i&gt; | 172 | Prospective, multicenter trial (SIFI, ClinicalTrials.gov NCT01640353), 12 mo f/u results |
| IIb | Cher 2015a&lt;br&gt;&lt;i&gt;Global Spine J. 2016;6(2):100-107. [Epub 2015 Jun 25]&lt;/i&gt; | 172 (iFuse) 3844 (NHMS) | Health state utility before and after SI joint fusion (patients from SIFI, 6 and 12 mo f/u results), comparison to normal cohort (NHMS). |
| IIb | Duhon 2013&lt;br&gt;&lt;i&gt;Med Devices (Auckl). 2013;6:219-29.&lt;/i&gt; | 94 efficacy 32 safety | Prospective, multicenter (SIFI, ClinicalTrials.gov NCT01640353), interim 6 mo f/u results |</p>
<table>
<thead>
<tr>
<th>LOE</th>
<th>Article</th>
<th># Patients</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Level III – CLINICAL COMPARISON (6)</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>III</td>
<td>Vanaclocha 2018</td>
<td>103 CM 56 RFA 30 iFuse</td>
<td>Assesses recognition of SI joint pain in chronic LBP patients and the high frequency of lumbar fusion in patients denied SI joint fusion. [Conservative management (CM), radiofrequency ablation (RFA), and iFuse.]</td>
</tr>
<tr>
<td>III</td>
<td>Vanaclocha 2017</td>
<td>63 CM 47 RFA 27 iFuse</td>
<td>Long-term outcomes for conservative management (CM), radiofrequency ablation (RFA), and iFuse. 6-year f/u results.</td>
</tr>
<tr>
<td>III</td>
<td>Spain 2017</td>
<td>29 screws 263 MIS (iFuse)</td>
<td>4-year cumulative revision rate comparison of SI joint fixation with screws vs. SI joint fusion with iFuse</td>
</tr>
<tr>
<td>III</td>
<td>Ledonio 2014b</td>
<td>22 Open 17 MIS</td>
<td>Retrospective comparison of Open vs. MIS (periop and ODI), 12mo f/u</td>
</tr>
<tr>
<td>III</td>
<td>Ledonio 2014a</td>
<td>22 Open 22 MIS</td>
<td>Retrospective, single-center, Open vs. MIS</td>
</tr>
<tr>
<td>III</td>
<td>Graham Smith 2013</td>
<td>149 open 114 MIS</td>
<td>Retrospective, multicenter, Open vs. MIS, 12 and 24mo f/u</td>
</tr>
<tr>
<td><strong>Level IV – CLINICAL EVIDENCE (19)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Cleveland 3rd 2019</td>
<td>50</td>
<td>Retrospective, single-center, 12-mo f/u. Mini-open, grafting, and introp navigation. (Intraop measures, VAS Pain, ODI)</td>
</tr>
<tr>
<td>IV</td>
<td>Rainov 2018</td>
<td>160</td>
<td>Retrospective, single-center, 12-mo f/u (VAS Pain, ODI, and CT scan at 1 year).</td>
</tr>
<tr>
<td>IV</td>
<td>Bornemann 2016b</td>
<td>24</td>
<td>Retrospective, single-center, 2-year f/u (VAS Pain &amp; ODI)</td>
</tr>
<tr>
<td>IV</td>
<td>Sachs 2016</td>
<td>107</td>
<td>Retrospective cohort with prospective evaluation, 7 sites, ≥ 3 years f/u (mean 3.7 years, range 3.0-4.7 years)</td>
</tr>
<tr>
<td>IV</td>
<td>Bornemann 2016a</td>
<td>24</td>
<td>Retrospective, single-center, 12 mo f/u</td>
</tr>
<tr>
<td>IV</td>
<td>Manfré 2014</td>
<td>1</td>
<td>Case study, CT-guided</td>
</tr>
<tr>
<td>IV</td>
<td>Rudolf 2014</td>
<td>17</td>
<td>Retrospective, single-center, 5-year f/u</td>
</tr>
<tr>
<td>IV</td>
<td>Vanaclocha 2014</td>
<td>24</td>
<td>Retrospective, single-center, mean 23 mo f/u (range 1-4.5 years)</td>
</tr>
<tr>
<td>IV</td>
<td>Sachs 2014</td>
<td>144</td>
<td>Retrospective, multicenter, iFuse, mean 16 mo f/u</td>
</tr>
<tr>
<td>IV</td>
<td>Scheyerer 2014</td>
<td>8 (10 SI joints)</td>
<td>Assess stability and bone ingrowth using SPECT/CT, mean 5.8 mo f/u (range 2-7 mo)</td>
</tr>
<tr>
<td>LOE</td>
<td>Article</td>
<td># Patients</td>
<td>Description</td>
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<tr>
<td>-----</td>
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</tr>
<tr>
<td>IV</td>
<td>Schroeder 2013</td>
<td>6 (10 cases)</td>
<td>Retrospective, single-center, iFuse post long-fusion in adult deformity, mean 10.25 mo f/u (range 4-15 mo)</td>
</tr>
<tr>
<td>IV</td>
<td>Gaetani 2013</td>
<td>10</td>
<td>Retrospective, single-center, 10 mo f/u (range 8-18 mo)</td>
</tr>
<tr>
<td>IV</td>
<td>Cummings 2013</td>
<td>18</td>
<td>Retrospective, single-center, 12 mo f/u</td>
</tr>
<tr>
<td>IV</td>
<td>Sachs 2013</td>
<td>40</td>
<td>Retrospective, single-center, 12 mo f/u</td>
</tr>
<tr>
<td>IV</td>
<td>Rudolf 2013</td>
<td>40</td>
<td>Retrospective, single-center, prior lumbar fusion affect, 24 mo f/u</td>
</tr>
<tr>
<td>IV</td>
<td>Kim 2013</td>
<td>31</td>
<td>Retrospective, single-center, radiographs and CT scans evaluated at 6 and 12 months post-operatively</td>
</tr>
<tr>
<td>IV</td>
<td>Sachs 2012</td>
<td>11</td>
<td>Retrospective, single-center, 12 mo f/u</td>
</tr>
<tr>
<td>IV</td>
<td>Lokietek 2012</td>
<td>10</td>
<td>Retrospective, single-center, range 2-5 mo f/u</td>
</tr>
<tr>
<td>IV</td>
<td>Rudolf 2012</td>
<td>50</td>
<td>Retrospective, single-center, min 24 mo f/u (mean 40 mo)</td>
</tr>
</tbody>
</table>

**REVIEWS (7)**

- **Yson 2019**
  PM R. 2019 [Epub 2019 Jun 16].
  Review: Sacroiliac Joint Fusion: Approaches and Recent Outcomes.

- **Whelan 2019**
  Review: Review of the evidence for the various treatments SI joint dysfunction, including conservative management, open surgical fusion, and minimally invasive fusion. Part of a 5 article SI joint focus series in Techniques in Orthopaedics (June 2019).

- **Shamrock 2019**
  Global Spine J. 2019;[Epub 2019 Feb 14].
  Systematic Review to determine the safety of minimally invasive SI joint fusion.

- **Tran 2019**
  Systematic Review and meta-analysis: Minimally invasive SI joint fusion compared to screw-type surgeries.

- **Lingutla 2016**
  Systematic review and meta-analysis of observational studies describing outcome of SI joint fusion in patients with LBP.

- **Heiney 2015**
  Systematic review of MIS SI joint fusion.

- **Zaidi 2015**
  Systematic literature review of studies on SI joint fusion (open and MIS).

**ECONOMICS (6)**
<table>
<thead>
<tr>
<th>LOE</th>
<th>Article</th>
<th># Patients</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cher 2019</td>
<td>-</td>
<td>Evaluates published evidence with respect to the clinical and economic value of treatments for SI joint pain. Part of a 5 article SI joint focus series in <em>Techniques in Orthopaedics</em> (June 2019)</td>
</tr>
<tr>
<td></td>
<td>Frank 2016</td>
<td>Patients from INSITE and SIFI</td>
<td>RVUs, compared to micro lumbar discectomy</td>
</tr>
<tr>
<td></td>
<td>Saavoss 2016</td>
<td>Patients from INSITE and SIFI</td>
<td>Productivity and indirect costs</td>
</tr>
<tr>
<td></td>
<td>Polly 2016</td>
<td>Patients from INSITE and SIFI</td>
<td>Ignoring the SI joint during LBP evaluation is costly</td>
</tr>
<tr>
<td></td>
<td>Cher 2016</td>
<td>Patients from INSITE and SIFI</td>
<td>Cost-effectiveness of MIS SI joint fusion with iFuse</td>
</tr>
<tr>
<td></td>
<td>Garber 2015</td>
<td>50 MIS SIJF 89 PLD</td>
<td>MIS SI joint fusion (SIJF) had comparable surgical time but more work effort than primary lumbar discectomy (PLD).</td>
</tr>
</tbody>
</table>

**BIOMECHANICS (7)**

|     | Casaroli 2019 | FEA model | Evaluation of S2AI screws and iFuse during sacropelvic fixation in combination with posterior fusion instrumentation. |
|     | Jeong 2018 | 8 cadavers | Biomechanical changes as assessed by 3-D motion analysis technique |
|     | Lindsey 2018b | FEA model | Finite element analysis of implant number, orientation, and superior implant length |
|     | Lindsey 2018a | 8 cadavers | Compares unilateral and bilateral SI joint fusion |
|     | Lindsey 2015 | FEA model | Adjacent lumbar segment affects after iFuse |
|     | Soriano-Baron 2015 | 7 cadavers | Analysis of the stability of the SI joint using two lateral implant placement techniques: Posterior and Transarticular |
|     | Lindsey 2014 | 7 cadavers | Biomechanical analysis of the iFuse System |

**OTHER (9)**

<p>|     | Cher 2018 | 14,210 (3,140 iFuse-3D, 11,070 iFuse) | Analysis of complaints related to 3D-printed iFuse implants (iFuse-3D) compared to TPS-coated implants (iFuse) |
|     | Mao 2018 | 24 | Utility of ODI as a measure after SI joint fusion |
|     | MacBarb 2017 (Part 2) | - | <em>In vivo</em> (ovine distal femoral defect) assessment of cancellous bone-implant interfaces at 6 and 12 weeks post-implantation for four implant configurations (TPS, 3D, 3D+HA, 3D+Autograft) |
|     | Vanaclocha 2016 | - | Biplanar iFuse procedure (<a href="https://youtu.be/TX5g8c765M">https://youtu.be/TX5g8c765M</a>) |</p>
<table>
<thead>
<tr>
<th>LOE</th>
<th>Article</th>
<th># Patients</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cher 2015b</td>
<td>11,388</td>
<td>4-year surgical revision rate (or survivorship from revision) for MIS SI joint fusion</td>
</tr>
<tr>
<td></td>
<td>Copay 2015</td>
<td>155</td>
<td>Validation of ODI as a measure of response to SI joint treatment</td>
</tr>
<tr>
<td></td>
<td>Woods 2014</td>
<td>37 (111 implants)</td>
<td>Intraoperative neuromonitoring during MIS SI joint fusion</td>
</tr>
</tbody>
</table>

 Indicates open access article

## Other Key SI Joint Publications

### Coverage Recommendations & Guidelines (2)

<table>
<thead>
<tr>
<th>LOE</th>
<th>Article</th>
<th># Patients</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lorio 2016 (July 5, 2016 update)</td>
<td>-</td>
<td>ISASS policy 2016 Update – Minimally Invasive Sacroiliac joint Fusion: Coverage Indications, Limitations, and/or Medical Necessity</td>
</tr>
<tr>
<td></td>
<td>Bono 2015</td>
<td>-</td>
<td>NASS Coverage Policy Recommendations – Percutaneous Sacroiliac Joint Fusion</td>
</tr>
</tbody>
</table>

### Health Technology Assessments (9)

<table>
<thead>
<tr>
<th>LOE</th>
<th>Article</th>
<th># Patients</th>
<th>Description</th>
</tr>
</thead>
</table>
|    | NICE (National Institute for Health and Care Excellence, U.K.) Medical Technologies Guidance (MTG39) | - | iFuse for treating chronic sacroiliac joint pain Evidence-based recommendations:  
• Case for adopting the iFuse Implant System to treat chronic SI joint pain is supported by the evidence.  
• iFuse should be considered for use in people with a confirmed diagnosis of chronic SI joint pain.  
• Cost modelling indicates that after 8 years, using iFuse instead of non-surgical management will save the NHS money. |
<p>|    | French National Healthcare System List of Refundable Products and Services in France (Liste des Produits et Prestations Remboursables - LPPR) Effective: September 6, 2018 | - | Reimbursement, which is exclusive to the iFuse Implant™, established following the favorable opinion of the National Commission for the Evaluation of Medical Devices and Health Technologies (CNEDIMTS) |
|    | eviCore Healthcare Spinal Surgery Guidelines, Version 1.0.2018 Minimally Invasive Sacroiliac Joint Fusion or Stabilization (CMM-611.2) Effective: October 22, 2018 | - | Minimally invasive sacroiliac joint (SI) fusion using titanium triangular implants (SI-BONE [iFuse Implant™]) for the treatment of lumbopelvic pain originating from the SIJ is considered medically necessary when ALL of the following are met. |
|    | AIM Specialty Health Musculoskeletal Program: Clinical Appropriateness Guidelines – Sacroiliac Joint Fusion Effective: July 1, 2018 | - | Percutaneous/Minimally Invasive SI Joint Fusion with the iFuse system (titanium triangular implant) may be considered medically necessary when all criteria are met. |</p>
<table>
<thead>
<tr>
<th>LOE</th>
<th>Article</th>
<th># Patients</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCG Health</td>
<td>General Recovery Care 22nd Edition (2018)</td>
<td>-</td>
<td>Musculoskeletal Surgery or Procedure GRG [GRG: SG-MS (ISC GRG)] Care Planning - Inpatient Admission and Alternatives Clinical Indications for Procedure Minimally invasive sacroiliac joint fusion needed as indicated by ALL criteria are met.</td>
</tr>
<tr>
<td>BlueCross BlueShield Association</td>
<td>Diagnosis and Treatment of Sacroiliac Joint Pain (6.01.023) January 1, 2018</td>
<td>-</td>
<td>Reviews and evaluates therapeutic corticosteroid injections and minimally invasive methods (radiofrequency ablation, SI fusion/fixation) for the treatment of SIJ pain.</td>
</tr>
<tr>
<td>ECRI Institute – iFuse Product Brief (<a href="http://www.ecri.org">www.ecri.org</a>) May 2016</td>
<td>-</td>
<td>iFuse Implant System (SI-BONE, Inc.) for Minimally Invasive Sacroiliac Joint Fusion</td>
<td></td>
</tr>
<tr>
<td>Hayes</td>
<td>Health Technology Brief November 2, 2017</td>
<td>-</td>
<td>iFuse Implant System (SI-BONE, Inc.) for Sacroiliac Joint Fusion for Treatment of Low Back Pain</td>
</tr>
</tbody>
</table>

Local Coverage Determination (LCD) (4)

<p>| | CGS Administrators, LLC – Local Coverage Determination (LCD) L36494. Effective 2016 Feb 01. | - | Minimally-Invasive Surgical (MIS) Fusion of the Sacroiliac (Si) Joint (L36494). Effective: 2016 February 01 Medicare Administrative Contractor (MAC) for: KY and OH |</p>
<table>
<thead>
<tr>
<th>LOE</th>
<th>Article</th>
<th># Patients</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECONOMIC (6)</td>
<td>Buysman 2018 Clinicoecon Outcomes Res. 2018;10:643-651.</td>
<td>302</td>
<td>Retrospective observational study analysis of administrative claims data from a large U.S. health insurer affiliated with Optum, looking at CPT codes 27279, 27280. 0334T.</td>
</tr>
<tr>
<td></td>
<td>Lorio 2016 Int J Spine Surg. 2016;10:40.</td>
<td>-</td>
<td>Regression analysis of work RVUs for CPT® 27279 via survey. 1st survey to ISASS surgeon committee members asking to compare CPT® 27279 to 10 other common spine surgeries codes. 2nd Survey to SMISS members asking to compare CPT® 27279 to broader spectrum of spine codes.</td>
</tr>
<tr>
<td></td>
<td>Ackerman 2014c Clinicoecon Outcomes Res. 2014;6:283-96.</td>
<td>78,533</td>
<td>Commercial – cost of non-op vs. MIS SIJ fusion</td>
</tr>
<tr>
<td></td>
<td>Ackerman 2014a Clinicoecon Outcomes Res. 2014;6:63-74.</td>
<td>78,533</td>
<td>Commercial – cost of non-op care for SIJ pathology</td>
</tr>
<tr>
<td>Other (5)</td>
<td>Petersen 2017 BMC Musculoskelet Disord. 2017 May 12;18(1):188.</td>
<td>-</td>
<td>1st comprehensive systematic review of diagnostic accuracy studies for physical exam or other simple in-office tests regarding LBP diagnosis. Diagnostic algorithm for SI joint pain had sufficient clinical evidence to warrant becoming a Clinical Diagnostic Rule (CDR)</td>
</tr>
<tr>
<td>LOE</td>
<td>Article</td>
<td># Patients</td>
<td>Description</td>
</tr>
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<td>-----</td>
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</tr>
<tr>
<td>-</td>
<td>MacBarb 2017 (Part 1)</td>
<td>-</td>
<td>In vitro investigation of human osteoblasts response to additive manufactured (AM, a.k.a. 3D-printed) trabecular-like titanium implant surfaces compared to traditionally machined base material with titanium plasma spray (TPS) coated surfaces, with and without a nanocrystalline hydroxyapatite (HA) coating.</td>
</tr>
<tr>
<td>-</td>
<td>Cher 2015b</td>
<td>155  SIFI 607  SPORT (DS) 1244  SPORT (IDH) 654  SPORT (SPS)</td>
<td>QOL preop for SI joint dysfunction as depressed as other lumbar spinal conditions (comparison to Spine Patient Outcomes Research Trial, SPORT). DS = degenerative spondylolisthesis IDH = intervertebral disc herniation SPS = spinal stenosis</td>
</tr>
<tr>
<td>-</td>
<td>Cher 2014</td>
<td>198</td>
<td>SI Joint: Burden of Disease</td>
</tr>
<tr>
<td>-</td>
<td>Lorio 2014</td>
<td>-</td>
<td>Prevalence of MIS SI Joint fusion over time – ISASS / SMISS survey</td>
</tr>
</tbody>
</table>

Indicates open access article
References (full citations) – Appendix D

iFuse Implant System Publications

Level I – RANDOMIZED CONTROLLED TRIAL [10]


http://www.painphysicianjournal.com/current/pdf?article=NDYwOQ==&journal=107


Level II/Ib – CLINICAL EVIDENCE [9]


Level III – CLINICAL COMPARISON (Open vs. MIS) [6]


Level IV – CLINICAL [19]


REVIEWS [7]


**ECONOMICS [6]**


**BIOMECHANICS [7]**


**OTHER [9]**


Other Key SI Joint Publications

**COVERAGE RECOMMENDATIONS & GUIDELINES [2]**


**HEALTH TECHNOLOGY ASSESSMENTS [9]**


**LOCAL COVERAGE DETERMINATION (LCD) [4]**

National Government Services, Inc. (NGS) – Minimally-invasive Surgical (MIS) Fusion of the Sacroiliac (SI) Joint (L36406). Effective 01 April 2016. <click here>

CGS Administrators, LLC. (CGS) – Minimally-Invasive Surgical (MIS) Fusion of the Sacroiliac (SI) Joint (L36494). Effective 2016 February 01 <click here>

Wisconsin Physicians Services Insurance Corporation (WPS) – Percutaneous minimally invasive fusion/stabilization of the sacroiliac joint for the treatment of back pain (L36000). Effective: 2015 December 17. <click here>


**ECONOMIC [6]**


**REVIEWS [4]**


**OTHER [6]**


Cher DJ, Reckling WC. Quality of life in preoperative patients with sacroiliac joint dysfunction is at least as depressed as in other lumbar spinal conditions. *Med Devices (Auckl).* 2015 Sep 16;8:395–403. DOI: [10.2147/MDER.S592070](https://doi.org/10.2147/MDER.S592070).


### 6.5 Appendix E – Comparison of ISASS and NASS Coverage Criteria for Minimally Invasive SI Joint Fusion

<table>
<thead>
<tr>
<th>Criteria</th>
<th>International Society for the Advancement of Spine Surgery (ISASS)</th>
<th>North American Spine Society (NASS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GUIDELINES</td>
<td><strong>ISASS Policy Statement – Minimally Invasive Sacroiliac Joint Fusion (Updated July 5, 2016)</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td><strong>NASS Coverage Policy Recommendations: Percutaneous Sacroiliac Joint Fusion (June 9, 2015)</strong>&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Patients who have all of the following criteria may be eligible for minimally invasive SIJ fusion:</td>
<td><strong>Percutaneous (also referred to as minimally invasive) SIJ fusion (e.g., insertion of a metallic device across the SIJ that is intended to fuse to the bone or lead to fusion of the joint itself, in distinction from insertion of screws without bone graft across the SIJ which are intended to stabilize but not fuse the joint) is indicated for the treatment of SIJ pain for patients with low back/buttock pain who meet ALL of the following criteria:</strong></td>
</tr>
<tr>
<td>CONSERVATIVE</td>
<td>Failure to respond to at least 6 months of non-surgical treatment consisting of non-steroidal anti-inflammatory drugs and physical therapy. Failure to respond means continued pain that interferes with activities of daily living and/or results in functional disability; Note: Additional ISASS Documentation Requirements are outlined on page 4 of this document.</td>
<td>Have undergone and failed a minimum six months of intensive nonoperative treatment that must include medication optimization, activity modification, bracing, and active therapeutic exercise targeted at the lumbar spine, pelvis, SIJ, and hip including a home exercise program. <strong>Note: Traditional care for the treatment of pain arising from the sacroiliac joint not due to an infectious or neoplastic process begins with physical therapy and activity modification. Analgesic medication including NSAIDS, acetaminophen, or opioids could be considered depending on each patient’s medical history and symptom severity. Alternative treatments such as sacroiliac support belts and manual medicine may be considered as well. It is important to note that while these treatments are utilized routinely, no comparative effectiveness study has been published to establish their efficacy.</strong></td>
</tr>
<tr>
<td>SI JOINT PAIN</td>
<td>Significant SI joint pain that impacts quality of life or significantly limits activities of daily living. (Patients with SI joint pain typically report pain in the buttocks, with possible radiation into the groin or upper legs.)</td>
<td>Patient’s report of typically unilateral pain that is caudal to the lumbar spine (L5 vertebrae), localized over the posterior SIJ, and consistent with SIJ pain.</td>
</tr>
<tr>
<td>Criteria</td>
<td>International Society for the Advancement of Spine Surgery (ISASS)</td>
<td>North American Spine Society (NASS)</td>
</tr>
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<tr>
<td>PHYSICAL EXAM</td>
<td>SIJ pain confirmed with at least 3 physical examination maneuvers that stress the SIJ the patient’s typical pain. &lt;br&gt;Note: Specific physical examination tests that stress the SIJ (e.g., distraction test, compression test, thigh thrust, FABER (Patrick’s) test, Gaenslen’s maneuver) are typically performed in the physician’s office; in combination, these tests are thought to be predictive of SIJ pain.</td>
<td>Positive response to a cluster of 3 provocative tests (e.g., thigh thrust test, compression test, Gaenslen’s test, distraction test, Patrick’s sign, posterior provocation test). &lt;br&gt;(Note that the thrust test is not recommended in pregnant patients or those with connective tissue disorders.) &lt;br&gt;A thorough physical examination demonstrating localized tenderness with palpation over the sacral sulcus (Fortin’s point, i.e., at the insertion of the long dorsal ligament inferior to the posterior superior iliac spine or PSIS) in the absence of tenderness of similar severity elsewhere (e.g., greater trochanter, lumbar spine, coccyx) and that other obvious sources for their pain do not exist</td>
</tr>
<tr>
<td>DIAGNOSTIC IMAGING</td>
<td>Note: ISASS does not require diagnostic imaging. In many cases, imaging can show non-specific findings in the SIJ. Rather, imaging is used to ensure that the patient does not have alternative diagnoses that could mimic SIJ pain (e.g., hip osteoarthritis, occasionally L5/S1 spine degeneration).</td>
<td>Diagnostic imaging studies that include ALL of the following: &lt;br&gt;- Imaging (plain radiographs and a CT or MRI) of the SI joint that excludes the presence of destructive lesions (e.g., tumor, infection) or inflammatory arthropathy that would not be properly addressed by percutaneous SIJ fusion. &lt;br&gt;- Imaging of the pelvis (AP plain radiograph) to rule out concomitant hip pathology. &lt;br&gt;- Imaging of the lumbar spine (CT or MRI) to rule out neural compression or other degenerative condition that can be causing low back or buttock pain. &lt;br&gt;- Imaging of the SI joint that indicates evidence of injury and/or degeneration. &lt;br&gt;Note: NASS guidance - Diagnostic imaging studies have not been shown to reliably predict SI joint pain. &lt;br&gt;Note: NASS guidance – Diagnostic imaging studies have not been shown to reliably predict SI joint pain.</td>
</tr>
<tr>
<td>Criteria</td>
<td>International Society for the Advancement of Spine Surgery (ISASS)</td>
<td>North American Spine Society (NASS)</td>
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<tr>
<td>----------</td>
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</tbody>
</table>
| DIAGNOSTIC INJECTIONS | Confirmation of the SIJ as a pain generator in ≥ 50% acute decrease in pain upon fluoroscopically guided diagnostic intra-articular SIJ block using local anesthetic.  
*Note: Prospective trials have shown that patients with SIJ pain responses of 50-75% respond to MIS SIJ fusion as well as those with 75-100% acute responses.*  
[Sources: Polly 2016; Dengler 2019; Duhon 2016] | At least 75 percent reduction of pain for the expected duration of the anesthetic used following an image-guided, contrast-enhanced intra-articular SIJ injection on two separate occasions.  
A trial of at least one therapeutic intra-articular SIJ injection (i.e. corticosteroid injection). |
| OTHER DIAGNOSES CONSIDERED | Additional or alternative diagnoses that could be responsible for the patient’s ongoing pain or disability have been considered. Physicians should take into account that patients can have multiple pain generators and addressing just one pain generator may not adequately relieve disability or all back pain. | Absence of generalized pain behavior (somatoform disorder) or generalized pain disorders (e.g., fibromyalgia). |
| **Not indicated for patients with the following scenarios:** | Minimally invasive SIJ fusion is NOT indicated for patients with the following:  
- Less than 6 months of SIJ pain and/or functional impairment;  
- Failure to pursue conservative treatment of the SIJ (unless contra-indicated);  
- Pain not confirmed with a diagnostic SIJ block;  
- Presence of other pathology that would substantially prevent the patient from deriving benefit from SIJ fusion. | Percutaneous SIJ fusion for SIJ pain is NOT indicated in ANY of the following scenarios:  
- Any case that does not fulfill ALL of the above criteria  
- Presence of systematic arthropathy such as ankylosing spondylitis or rheumatoid arthritis  
- Presence of generalized pain behavior (e.g., somatoform disorder) or generalized pain disorder (e.g., fibromyalgia)  
- Presence of infection, tumor, or fracture  
- Presence of acute, traumatic instability of the SIJ  
- Presence of neural compression as seen on an MRI or CT that correlates with the patient’s symptoms or other more likely source for the pain. |
ISASS Documentation Requirements (July 5, 2016):

- Significant SIJ pain that impacts quality of life or significantly limits activities of daily living;
- SIJ pain confirmed with at least 3 physical examination maneuvers that stress the SIJ (see list provided above) and reproduce the patient’s typical pain.
- Confirmation of the SIJ as a pain generator with ≥50% acute decrease in pain upon fluoroscopically guided diagnostic intra-articular SIJ block using local anesthetic. Prospective trials have shown that patients with SIJ pain responses of 50-75% respond to MIS SIJ fusion as well as those with 75-100% acute responses.
- Failure to respond to at least 6 months of non-surgical treatment consisting of non-steroidal anti-inflammatory drugs and physical therapy. Failure to respond means continued pain that interferes with activities of daily living and/or results in functional disability;
- Additional or alternative diagnoses that could be responsible for the patient’s ongoing pain or disability have been considered. Physicians should take into account that patients can have multiple pain generators and addressing just one pain generator may not adequately relieve disability or all back pain.

Minimally invasive SIJ fusion is NOT indicated for patients with the following:

- Less than 6 months of SIJ pain and/or functional impairment
- Failure to pursue conservative treatment of the SIJ (unless contra-indicated);
- Pain not confirmed with a diagnostic SIJ block;
- Presence of other pathology that would substantially prevent the patient from deriving benefit from SIJ fusion

REFERENCES

1. ISASS Policy Statement – Minimally Invasive Sacroiliac Joint Fusion (July 2016): Coverage Indications, Limitations, and/or Medical Necessity
   Updated July 5, 2016
   PDF version click here
   Author: ISASS Task Force (Coding & Reimbursement) Chair; Morgan P. Lorio, MD, FACS.

The iFuse Implant System is intended for sacroiliac fusion for conditions including sacroiliac joint dysfunction that is a direct result of sacroiliac joint disruption and degenerative sacroiliitis. This includes conditions whose symptoms began during pregnancy or in the peripartum period and have persisted postpartum for more than 6 months. The iFuse Implant System is also intended for sacroiliac fusion to augment immobilization and stabilization of the sacroiliac joint in skeletally mature patients undergoing sacropelvic fixation.

iFuse-Navigation™

iFuse-Navigation™ instruments are intended to be used with the iFuse Implant System® to assist the surgeon in precisely locating anatomical structures in iFuse procedures, in which the use of stereotactic surgery may be appropriate, and where reference to a rigid anatomical structure, such as the pelvis or vertebra can be identified relative to the acquired image (CT, MR, 2D fluoroscopic image or 3D fluoroscopic image reconstruction) and/or an image data based model of the anatomy. iFuse-Navigation instruments are intended to be used with the Medtronic StealthStation™ System.

Neuromonitoring Kit
The Neuromonitoring Kit is indicated for stimulation of peripheral motor nerves, including spinal nerve roots, for localization and identification during surgery.

There are potential risks associated with the iFuse Implant System. It may not be appropriate for all patients and all patients may not benefit. For information about the risks, visit: www.si-bone.com/risks

Reimbursement information is provided for convenience only. It is neither legal advice nor official payor guidance. SI-BONE does not warrant or guarantee that the use of the information will result in coverage or payment. Providers are solely responsible for determining medical necessity and for being in compliance with Medicare and other payor rules and requirements, as well as for the information they submit with claims and appeals. Before any claims or appeals are submitted, providers should review official payor instructions and requirements, confirm the accuracy of their coding or billing practices with these payors, and use independent judgment when selecting codes that most appropriately describe the services or supplies provided to a patient.

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Long-Term Prospective Clinical And Radiographic Outcomes After Minimally Invasive Lateral Transiliac Sacroiliac Joint Fusion Using Triangular Titanium Implants

Background: Accumulating evidence supports the long-term safety and effectiveness of minimally invasive sacroiliac joint fusion (SIJF) for sacroiliac joint dysfunction.

Objective: To report 5-year clinical and radiographic follow-up in patients undergoing SIJF using triangular titanium implants (TTI).

Methods: One hundred and three subjects at 12 centers treated with SIJF using TTI in two prospective clinical trials (NCT01640353 and NCT01681004) were enrolled and followed in the current study (NCT02270203) with clinic visits at 3, 4 and 5 years. CT scans performed at 5 years were compared to prior CT scans (at 1 or 2 years) by an independent radiologist.

Results: Compared to baseline scores, SIJ pain scores at 5 years decreased by a mean of 54 points, disability scores (Oswestry Disability Index) decreased by 26 points, and quality of life scores (EuroQOL-5D time trade-off index) increased by 0.29 points (0–1 scale) (all p<0.0001). Satisfaction rates were high and the proportion of subjects taking opioids decreased from 77% at baseline to 41% at 5-year follow-up. Independent radiographic analysis showed a high rate (98%) of bone apposition to implants on both the sacral and iliac sides of the SI joint, with a high rate of bony bridging (87%) and a low rate of radiolucencies suggestive of loosening (5%).

Conclusion: A 5-year follow-up showed continued excellent clinical responses in patients with SIJ pain treated with SIJF using triangular titanium implants along with a high rate (88%) of joint fusion.

Level of evidence: Level II.

Keywords: sacroiliac joint pain, sacroiliac joint degeneration, arthrodesis, sacroiliac joint fusion

Introduction

A 15–30% of patients with chronic low back pain have pain originating from the sacroiliac joint (SIJ).1–5 SIJ pain impairs quality of life similarly to other spine conditions.6,7 Non-surgical treatments, such as physical therapy, chiropractic, intraarticular SIJ steroid injections, prolotherapy, and radiofrequency neurotomy of sacral nerve root branches, have minimal evidentiary support.8–13 No available high-quality studies support the long-term effectiveness of any non-surgical treatment.

Minimally invasive sacroiliac joint fusion (MIS SIJF) is an increasingly accepted surgical option for SIJ dysfunction. While some available devices and
allograft products are placed through a dorsal surgical approach, the evidence base supporting the safety and effectiveness of such strategies is minimal. Most commercially available implant systems for MIS SIJF are placed with a lateral transarticular approach, and triangular titanium implant (TTI) remains the most thoroughly studied device. MIS SIJF using this approach has been evaluated and found to be both safe and effective as documented by multiple health technology assessments including BCBSA and National Institute for Health and Care Excellence (NICE, UK, see IPG 578).

To date, the vast majority of published evidence for lateral transiliac SIJF involves the use of porous triangular titanium implants (TTI, iFuse Implant System, SI-BONE, Inc., Santa Clara, CA, USA). Evidence supporting improvement in pain, disability and quality of life after SIJ fusion with TTI derives from 3 prospective clinical trials, and numerous case series and comparative case series. Herein, we report 5-year prospective follow-up from two multicenter clinical trials of TTI for SIJF: INSITE (NCT01681004, a prospective, randomized controlled trial of SIJ fusion vs non-surgical management) and SIFI (NCT01640353, a prospective multicenter single-arm study). Both studies enrolled patients with chronic SIJ pain diagnosed via history, physical examination and confirmatory diagnostic SIJ block with a local anesthetic. In the feeder studies, subjects underwent SIJF with TTI in a brief minimally invasive surgery and had structured follow-up visits to 2 years. Published reports showed marked, immediate and sustained improvements in pain, disability and quality of life throughout follow-up. Herein, we report 5-year clinical and radiographic follow-up from the same cohort.

Methods
Participants
Subjects included in the current study (LOIS, Long Term Outcomes from INSITE and SIFI, NCT02270203) were enrolled at 12 centers who participated in either INSITE or SIFI (Appendix 1). INSITE is a prospective multicenter randomized trial of SIJF vs non-surgical management whose 2-year results showed considerable improvements in pain, disability and quality of life in the surgical group but only modest responses in the non-surgical group. SIFI is a prospective multicenter single-arm clinical trial evaluating the same procedure/device with an identical follow-up and assessment schedule; 2-year results were similarly positive. A pooled analysis of these trials (along with a randomized trial from Europe) confirmed marked homogeneity of study results. As reported previously, patients enrolling in INSITE and SIFI were diagnosed with SIJ dysfunction due to degenerative sacroilitis or sacroiliac joint disruption based upon medical history, a positive Fortin Finger test, at least 3 positive physical examination signs suggestive of SIJ dysfunction, and a positive diagnostic SIJ block performed under fluoroscopic or CT guidance. Key INSITE/SIFI exclusion criteria were severe low back or hip pain due to other conditions, SIJ dysfunction due to autoimmune or inflammatory conditions and osteoporosis (see previously publications for details).

Participating LOIS sites had to have enrolled and treated at least 5 patients with SIJF with sufficient clinical trial resources, including a dedicated study investigator and coordinator who could carry out trial requirements and the ability to maintain meaningful enrollment and follow-up for this long-term study. Of the 39 sites participating in INSITE and SIFI, 12 sites met study participation criteria. To qualify for LOIS, a subject had to have undergone SIJF with TTI within the INSITE or SIFI studies and sign a LOIS-specific informed consent form. Potential study participants were screened for study eligibility criteria and reasons for non-participation (not meeting criteria or refusal to participate) were captured.

Interventions And Assessments
LOIS assessments included in-person study visits that took place at years 3, 4 and 5 during which time subjects completed surveys to assess SIJ pain and low back pain scores (a 100-mm visual analog scale [0–100 scale]); disability (Oswestry Disability Index, a validated measure of disability due to back pain); quality of life (EuroQOL-5D, a commonly used generic quality of life survey that produces a health state utility value ranging from 0 [death; values <0 are possible, representing health states worse than death] to 1 [perfect health])); and satisfaction. All questionnaires were administered by trained study research coordinators. In addition, phone calls to subjects were completed at years 2.5, 3.5 and 4.5; these were intended to maintain subject contact and assess adverse events. Adverse events were assessed during both in-clinic and phone visits using a broad definition from an international clinical trial standard (ISO14155:2011). Study site personnel and study monitors also reviewed medical records to ensure complete adverse event reporting during the study follow-up. For each event, the site investigator was
required to assess the severity and relatedness of the adverse event to the SIJF or a pre-existing condition; the relatedness to device or procedure was characterized as definitely, probably, possibly, unlikely or not related. The study did not incorporate any structured program to promote opioid cessation.

Radiographic Analysis

As part of INSITE and SIFI, all LOIS participants had undergone high-resolution (<1 mm slice thickness) CT scans of the pelvis without contrast at either 2 years (INSITE) or 1 year (SIFI). LOIS participants also underwent a similar CT scan at 5 years. All radiographic analysis was performed by an independent musculoskeletal radiologist (author TH). The primary radiographic endpoint was the proportion of subjects undergoing 5-year CT scan who show at least 30% apposition of bone to both the iliac and sacral sides of at least 2 of 3 iFuse implants at 5 years. Additional radiographic endpoints included the following: radiolucencies consistent with device loosening, bridging bone across the SIJ, assessed as continuous bridging across the treated joint, occurring either adjacent to implants, distant from implants and/or adjacent/distant from implants, degree of bridging (<5% of joint, 5–15%, 15–30%, or 30–100%), signs of both positive and/or adverse bone remodeling, device failure or migration, and heterotopic ossification. Positive bone remodeling was defined as presence of increased bone density adjacent to the implant that appears to be due to new bone formation and an increase in mechanical demand at the bone–implant interface. Adverse bone reaction was defined as presence of new erosions, cysts, signs of infection, osteolysis or other pathologic reactions in the bone adjacent to the implant. Analysis was conducted on a per-side or, in some cases, per-implant basis. Twelve subjects underwent unplanned contralateral SIJ fusion between years 1 and 5, resulting in iFuse or iFuse-3D devices (11 of 12 cases) evident on 5-year CT scans. However, since these implants do not represent 5-year residence in the body, these treated sides were excluded from the analysis.

Study Ethics

All centers obtained study-specific institutional review board (IRB) approval prior to study initiation. Subjects were paid nominal amounts for their time and expenses required to complete study visits and call requirements, as approved by each site’s governing IRB. The study was sponsored by the device manufacturer (SI-BONE, Inc., Santa Clara, CA).

Data Collection And Monitoring

All study data were entered into an electronic data capture system. All study sites underwent remote and regularly scheduled on-site data monitoring visits by sponsor representatives so that all collected data could be verified against source documents maintained at the sites.

Endpoints

The primary efficacy success endpoint for this study is a composite, defined as a reduction from pre-operative VAS SIJ pain score of at least 20 points in the absence of device-related serious adverse event, absence of neurological worsening, and absence of surgical revision. This endpoint is identical to that used in the component trials (INSITE, SIFI) and was assessed at 3, 4 and 5 years in the LOIS trial. Other outcomes include improvements in SIJ pain scores (VAS), disability (Oswestry Disability Index), and quality of life (EuroQOL-5D) across all time points; proportion of non-working subjects who return to work; and occurrence of serious adverse events. The study’s primary radiographic endpoint (i.e. the proportion of treated sides with at least 30% apposition of bone to both the iliac and sacral sides of at least 2 of 3 iFuse devices on 5-year CT scans) was designed to be consistent with literature from other metallic devices showing the adequacy of this level of bone binding for positive patient outcomes.

Statistical Analysis

A standard approach to statistical analysis was employed to calculate standard aspects of change scores and binary outcomes. Repeated-measures analysis of variance was used to evaluate changes from baseline over time in continuous measures. Where relevant, binary outcomes were evaluated with a chi-squared test, McNemar test, or exact binomial confidence intervals.

Data Availability

The study sponsor (SI-BONE) will share full, deidentified study data with physicians proposing specific analyses through Yale University’s Yale Open Data Access (YODA) program.

Results

Participants

Of 127 potentially eligible INSITE/SIFI subjects, 103 were enrolled in LOIS. Reasons for non-participation included inability to participate due to health issues (n=2), death prior to screening (3), lost to follow-up during
the previous study (4), moved out of state (1), refused study participation (11), planning pregnancy (1), previous withdrawal from INSITE or SIFI (1), and unlikely to be compliant (1).

Patient Flow
A 5-year follow-up was available in 93 (90%) subjects. Reasons for attrition include loss to follow-up (n=6), death due to other causes (n=2), and withdrawal of consent (n=2, Figure 1).

Baseline Characteristics
Subjects (mean age 51 years) were mostly Caucasian (97%) and female (73%, Table 1). Subjects had high preoperative pain scores (mean [SD] of 81.5 [12.7]) and high levels of disability (ODI score 56.3 [12.1]). The duration of pain prior to enrollment averaged 5.7 years. EQ-5D at baseline was 0.45 (0.17), indicating a very poor quality of life.6 A 77% of subjects were taking opioids for back or SIJ pain preoperatively and 45% had a history of lumbar fusion, and concomitant spine and hip disease was common. Most (93, 90.3%) patients underwent unilateral SIJF on either of the treatment studies; 10 (9.7%) exhibited pain, physical examination signs and appropriate responses to diagnostic blocks consistent with bilateral SIJ dysfunction and therefore underwent bilateral SIJF.

Clinical Outcomes
At 5 years, the mean SIJ pain score had decreased from 81.5 (SD 12.7) to 27.1 (29.4), a mean change from baseline of 54.1 (32.3) points (p<0.0001, Figure 2). Seventy-seven (82.8%) subjects had improvements of at least 20 points in SIJ pain scores. Study success (VAS improvement of at least 20 points in the absence of severe device-related adverse event, neurologic adverse event and revision surgery) was observed in 76 subjects at 60 months (81.7%, 95% CI 72.4–89.0%); one subject underwent early revision for implant malposition but otherwise had marked improvements in pain and disability. Oswestry Disability Index, a measure of disability due to back pain, decreased from 56.3 (12.1) pre-operatively to 29.9 (21.2) at 5 years, an improvement of 26.2 (21.6) points (p<0.0001). Sixty-four (68.8%) subjects had an improvement in ODI scores of at least 15 points from their pre-operative score. EuroQOL-5D time trade-off index score, a

Table 1 Baseline And Surgical Characteristics Of Study Participants (n=103)

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean (SD)</td>
<td>50.8 (10.8)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>75 (72.8%)</td>
</tr>
<tr>
<td>Body mass index, mean (SD)</td>
<td>31.0 (7.4)</td>
</tr>
<tr>
<td>Non-white race, n (%)</td>
<td>3 (2.9%)</td>
</tr>
<tr>
<td>Hispanic, n (%)</td>
<td>3 (2.9%)</td>
</tr>
<tr>
<td>History of prior lumbar fusion</td>
<td></td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>19 (18.4%)</td>
</tr>
<tr>
<td>Pain began in peripartum period, n (%)</td>
<td>14 (13.6%)</td>
</tr>
<tr>
<td>Pain duration, years, mean (SD)</td>
<td>5.7 (6.8)</td>
</tr>
<tr>
<td>Visual analog scale SIJ pain, mean (SD)</td>
<td>81.5 (12.7)</td>
</tr>
<tr>
<td>Oswestry Disability Index, mean (SD)</td>
<td>56.3 (12.1)</td>
</tr>
<tr>
<td>EuroQOL-5D, TTO index</td>
<td>0.45 (0.17)</td>
</tr>
<tr>
<td>Taking opioids, n (%)</td>
<td>79 (76.7%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Surgical characteristics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Right side, n (%)</td>
<td>42 (40.8%)</td>
</tr>
<tr>
<td>Bilateral SIJ fusion, n (%)</td>
<td>10 (9.7%)</td>
</tr>
<tr>
<td>Operative duration (minutes), mean (SD)</td>
<td>46.3 (16.4)</td>
</tr>
<tr>
<td>Hospital length of stay (days), mean (SD)</td>
<td>0.72 (0.93)</td>
</tr>
<tr>
<td>Number of implants, n (%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2 (1.9%)</td>
</tr>
<tr>
<td>3</td>
<td>80 (77.7%)</td>
</tr>
<tr>
<td>4</td>
<td>21 (20.4%)</td>
</tr>
</tbody>
</table>

Figure 1 Patient follow-up in LOIS study.
measure of health state utility, improved from 0.45 (0.17) at baseline to 0.75 (0.22) at 5 years, an improvement of 0.29 (0.26) points (p<0.0001).

Satisfaction rates with SIJF were high at 6 months and remained high throughout the entire follow-up period (Figure 3). The proportion of patients who would definitely undergo the procedure again was high at 24 months (85%) but decreased somewhat at 5 years (75%). The proportion who would not have the procedure again was very low throughout the follow-up period (2–6%). Satisfaction rates correlated with improvement in SIJ pain and ODI. Opioid use decreased progressively over time (Figure 4).

The proportion of subjects who were working full time decreased perioperatively but returned to preoperative levels by 6 months (Figure 5). The proportion not working due to back pain was 16.5% at baseline and 15.1% at 5 years (McNemar p=0.6056).

Three hundred and twenty-eight adverse events were reported in 95 participating subjects, most of which were unrelated to the pelvis or spine. Forty-eight events in 42 subjects involved the pelvis; these included SIJ pain (16), contralateral SIJ pain (18); buttock pain and thigh numbness/tingling (1); hip and leg pain radicular hip pain (3), trochanteric bursitis (7), hip gluteus minimus tear (1), pelvic floor

Figure 2 Improvement in SIJ pain (by visual analog scale, top), disability (Oswestry Disability Index, middle) and quality of life (EuroQOL-5D TTO Index, bottom) over time.
Figure 3 Left: satisfaction levels by study visit. Right: whether the subject would have the procedure again by study visit.

Figure 4 Proportion of subjects taking opioids by study visit.
nerve impingement after lumbar fusion unrelated to index SIJ fusion (1) and pelvic organ prolapse (1). Only 1 event – intermittent hip and gluteal pain likely to be trochanteric bursitis – was rated as related to the study device. One event – SIJ pain – was deemed related to the study procedure; this subject underwent placement of an additional TTI due to prior partial resolution of SIJ pain. Of 43 severe adverse events, most were unrelated to the pelvis and none were device-related. One event was classified as being probably procedure-related (the previously described revision due to poor implant placement). Including 1 subject who underwent SIJ revision surgery during the SIFI study, a total of 3 of 103 enrolled subjects in LOIS underwent SIJ revision by 5 years (3%). Three subjects reported exacerbations of their SI joint pain related to falls. By 5 years, 2 subjects died from conditions unrelated to the SIJ (lung cancer and myocardial infarction).

Radiographic Outcomes
Five-year CT scans for radiographic analysis were available in 93 (90%) enrolled subjects comprising 121 treated sides. In 67 cases, CTs were available at 12 and 60 months; in 25 cases, studies were available at 24 and 60 months; and in 1 case, a CT was available only at 60 months. Reasons for a CT scan not being available included: loss to follow-up (6); voluntary withdrawal prior to 5 years (2); early termination (2). Sample findings from CT scan analysis are shown in Figures 6 and 7. Detailed results are provided below.

10 subjects underwent interim SIJF between 2 and 5 years; these sides were eliminated from radiographic analysis as their 5-year CT scans do not represent 5 years of residence in the body. All analysis therefore included in 111 sides. Of 111 sides, 109 (98%) met the primary radiographic endpoint with >30% apposition of bone to the ilial and sacral sides of at least 2 implants. In one instance of a single side not meeting the primary endpoint, the subject had undergone explantation of iFuse implants against the recommendations of the investigator. In addition, evaluation of another construct showed the second and third implants inadequately placed into the sacrum, possibly resulting in suboptimal SIJ stabilization that prevented bony apposition in the sacrum. Compared to 1- or 2-year scans, bony integration of implants with adequate apposition remained stable at 5 years with no deterioration.

Radiolucencies suggesting failure of implant integration were seen in 6 sides (5%); in all cases lucencies were seen only in the sacrum; in 5 of 6 cases, one or more implants associated with radiolucencies were inadequately placed into the sacrum.

Bridging of bone within the SIJ was seen in 45% of sides at 12 months, 71% at 24 months and 88% at 60 months. Of 277 implants analyzed on year 5 scans, bridging bone was present adjacent to the implants in 91%, or both adjacent and distant to implants in 25 cases (9%).
Seven percent of treated sides showed bridging judged as >15% of the SIJ volume.

Positive bone remodeling was seen in 95% of sides at 60 months. No other adverse bone reactions were seen.

No device migrations or failures were observed and heterotopic ossification was uncommon. Small bone growths abutting the lateral aspect of the implants were frequently noted, occurring in 54/93 (58%) of sides. Small islands of ossification present in the soft tissue adjacent to the implants but not attached to the implant were seen in 4 cases.

Discussion

Until recently, surgeons have ignored the SIJ as a source of low back and/or buttock pain, possibly because of surgical treatments perceived as safe and effective were not available. Porous TTI have been commercially available since 2009 and their use is supported by a growing body of evidence. The current study contributes substantially to the evidence base by reporting the long-term (5-year) outcomes from prospective multicenter clinical trials in conjunction with an independently adjudicated radiographic analysis. Participants in our study had previously participated in two prospective multicenter trials evaluating SIJF with TTI and returned for 3-, 4- and 5-year follow-up visits. We observed durable long-term improvements in pain, disability and quality of life with sustained high levels of satisfaction such that most patients would elect to undergo the procedure again. Furthermore, opioid use progressively decreased over time following the procedure.
SIJF with TTI appears to be at least as efficacious as other commonly performed spine surgery procedures (e.g. spinal fusion, total joint replacement). The long-term safety profile of the procedure and device also appears reasonable, with a low rate of subjects undergoing revision surgery in the current study (3/103, 3%). In fact, revision surgery was performed in only one case because initial implant placement was suboptimal.

Our clinical outcome data are also consistent with a European randomized trial, a long-term case series, and other reports which strongly corroborate the long-term safety and effectiveness of SIJF with TTI.
These findings argue strongly against an apparent bias by many physicians that SIJ-mediated back and/or buttock pain is challenging to diagnose and treat. Indeed, these various studies suggest that SIJ pain can be reliably diagnosed and successfully addressed over the long term through a combination of diagnostic modalities (composed primarily of history, physical examination and response to diagnostic SIJ blocks) and a definitive, anatomically based surgical procedure. The results of surgery are significantly better compared to non-surgical treatments for SIJ dysfunction, none of which have been shown to provide long-term benefits; in general, the evidence supporting commonly performed non-surgical treatments (e.g., intraarticular corticosteroids, physical therapy) is largely scant or non-existent.

In our study, contralateral SIJ pain was observed in 18 (17%) of study participants. Our study cannot discern which of the following reason serves as the primary rationale for this finding: 1) the same degenerative process that involved the index side subsequently affected the contralateral side; 2) the subject had bilateral pain at baseline but only one (the index) side was found to be eligible for surgery within the study; 3) increased activity as a result of successful index side surgery exacerbated the contralateral SIJ; or 4) fusion of the index side altered the biomechanical forces across the contralateral SIJ and hastened the development of degeneration, i.e., a cross-body variant on adjacent segment disease. Since SIJF does not appear to increase motion or stress across the contralateral SIJ, it is unlikely that this procedure would result in adjacent segment degeneration. Similarly, there is little evidence that SIJF increases the risk of hip or lumbar spine pathology.

An important unique feature of our study is an independent comparative analysis of CT scans performed at 1 or 2 years in the initial studies to images obtained at 5 years in the current study. The CT analysis revealed positive findings including a very high rate of bone apposition to implants in both the sacrum and ilium, a low rate of radiolucencies suggestive of implant loosening, and progressive fusion of the SIJ. Radiolucencies typically occurred around the distal (leading) ends of implants, most commonly when they were not introduced far enough into the sacrum. It is hypothesized that shallow implant placement gives rise to poor fixation and allows for residual joint motion which may prevent bony apposition. In theory, the incidence of implant loosening may be lowered even further by improving the accuracy of implant placement with full engagement into the sacrum. The low revision rate observed in our study is consistent with previous publication of safety analyses which also demonstrated very low cumulative revision rates. The low revision rate also suggests that progressive fusion evident in 5-year CT scans is clinically relevant and establishes the efficacy of this procedure. Furthermore, the radiographic findings from this study are consistent with high fusion rates observed in a smaller retrospective cohort.

The major advantage of our study is prospective long-term follow-up of a relatively large number of subjects from two clinical trials (one a randomized trial) conducted in a variety of clinic settings as well as detailed independent radiographic analysis. It is also important to emphasize that our data derive from procedures performed by surgeons; it is not current practice for these implants to be placed by non-surgeons and their use by other practitioners is not recommended. Moreover, the results presented herein apply to only to TTI placed through a lateral transiliac approach and not to other devices advocated for lateral transiliac SIJF, for which long-term data supporting safety and effectiveness have not been published. The TTI used in our study are not only designed to confer immediate stability by resisting joint motion (i.e., rotation) but they also have a porous surface specifically designed to promote bone apposition, a finding which was demonstrated on 5-year CT scans. Thus, it is unclear whether the results of our study would be applicable to other devices placed through a lateral transiliac approach and it is highly unlikely that they would be germane to other implant/products inserted posteriorly for which there is a paucity of published clinical data.

The primary limitation of this study is the lack of long-term data from a concurrent control group receiving only non-surgical treatments for SIJ dysfunction. Nevertheless, the majority of subjects in the non-surgical control cohort of the INSITE study experienced inadequate pain relief at 6 months and analogous findings were also observed in the non-surgical control group of a European randomized controlled trial involving the same implant system. It should be noted that long-term non-surgical care in this patient population is associated with very poor outcomes in terms of worsening pain, increased opioid use, and poor work status. In contrast to non-surgical care, which provides little benefit to patients with chronic SIJ pain, our collective results suggest that SIJF with TTI gives rise to marked improvements in pain, disability, and quality of life, with high rates of satisfaction and decreased opioid use. In
addition, the radiographic analysis confirmed high rates of bony apposition to implants and joint fusion.

Conclusions
Prospective long-term (5-year) follow-up of subjects undergoing SIJF with TTI demonstrate significant improvements in pain, disability and quality of life, excellent patient satisfaction, low risk of complications, and high rates of bony apposition to implants (98%) and joint fusion (88%).

Disclosure
All authors conduct clinical research as part of prospective trials sponsored by SI-BONE. Peter Whang, Philip Ploska, S Craig Meyer and Clay Frank are paid consultants of SI-BONE. Harry Lockstadt reports non-financial support from SI-BONE, during the conduct of the study and personal fees from SI-BONE, outside the submitted work. Andy Redmond is an investor for Statera Spine, a company involved in spinal imaging. He is also a partner in West End Bay Partners LLC., a start up company dedicated to the treatment of sacroiliac joint pain. Dr. Redmond has a patent pending for sacroiliac joint stabilization and fixation devices and related methods. Application number 16/418,619. Daniel Cher is an employee for SI-BONE, Inc. Travis Hillen was paid for independent radiographic reads as part of this study and a consultant for Medtronic, outside the submitted work. The authors report no other conflicts of interest in this work.

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April 20, 2018

Judy Dean
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Miami Beach, FL 33141-0157

RE: Your Inquiry Regarding Minimally Invasive Sacroiliac Joint Fusion Using Triangular Titanium Implants

Dear Ms. Dean,

Thank you for contacting us regarding UnitedHealthcare’s clinical coverage position on minimally invasive sacroiliac joint (MIS SIJ) fusion. In your email dated April 10, 2018, you shared with us recently published data from the new Lois 3-year study on the long-term safety and effectiveness of sacroiliac joint fusion with the iFuse® Implant System. We appreciate your insights and want to give you some background information on our policy.

How We Determine Coverage
Benefits for members are determined by the provisions of their specific health plan with safety and efficacy of the covered health care services as guiding standards. When deciding coverage, the member’s specific benefit plan document and UnitedHealthcare Medical Policy are referenced. In the event of a conflict, the member’s specific benefit plan document supersedes the UnitedHealthcare Medical Policy. Medical Policy coverage decisions are based on scientifically proven clinical evidence.

In general, UnitedHealthcare defines “unproven services” as those determined to be ineffective for the treatment of the medical condition or not to have beneficial effect on the health outcomes due to insufficient and inadequate clinical evidence from well-conducted randomized controlled trials or cohort studies in prevailing published peer-reviewed medical literature. These are defined as follows:

- **Well-conducted randomized controlled trials.** Two or more treatments are compared to each other, and the patient is not allowed to choose which treatment is received.
- **Well-conducted cohort studies from more than one institution.** Patients who receive study treatment are compared to a group of patients who receive standard therapy. The comparison group must be nearly identical to the study treatment group.

Our Current Clinical Coverage Position on MIS-SIJ
Our Medical Policy department recently reviewed current scientific literature on MIS-SIJ. We also reviewed the updates introduced in the MCG™ Care Guidelines, 22nd edition, 2018. In this updated edition of MCG, clinical coverage criteria have been added for MIS-SIJ within the Musculoskeletal Surgery or Procedure General Recovery Guideline (GRG), SG-MS.
At this time, UnitedHealthcare has elected not to manage a UnitedHealthcare Medical Policy for MIS-SIJ as we have chosen to adopt the MCG GRG SG-MS, Musculoskeletal Surgery or Procedure for our clinical coverage criteria. Those criteria are as follows:

- Minimally invasive sacroiliac joint fusion needed as indicated by ALL of the following:
  o Significant sacroiliac joint pain (pain rating of at least 5 on a 0-10 numeric scale) and/or significant activity limitations due to sacroiliac joint pain
  o Unilateral pain localized over the sacroiliac joint
  o Sacroiliac joint pain confirmed with response (pain) to three or more provocative examination maneuvers that stress the sacroiliac joint (e.g., FABER test, thigh thrust, pelvic gapping test, pelvic compression or Gaenslen test)
  o Confirmation of diagnosis of sacroiliac disease via pain relief of at least 75 percent (i.e., on visual analogue scale) due to fluoroscopy-guided needle injection of local anesthetic into sacroiliac joint (expected time frame of pain relief depends on anesthetic chosen, dose and concentration)
  o Failure to respond to at least six months of alternative treatments consisting of analgesics (e.g., nonsteroidal anti-inflammatory medication) and one or more of the following:
    ▪ Physical therapy
    ▪ Sacroiliac joint steroid injection
    ▪ Radiofrequency rhizotomy
  o Alternative or contributing diagnoses absent (e.g., hip osteoarthritis, L5-S1 spine degeneration, tumor, infection or fracture)

We Welcome Further Information
We’ll continue to review published clinical evidence for MIS-SIJ and will reassess our position as the evidence and guidance evolves. If additional published, peer-reviewed clinical evidence that you haven’t previously submitted becomes available and you would like to share it with us, please submit the information to UnitedHealthcare’s Medical Policy Department at mpq@uhc.com. Thank you.

Sincerely,

Wendy MacLeod MD
National Medical Director