Review report of MTG39: iFuse for treating chronic sacroiliac joint pain

This medical technology guidance was published in October 2018.

All medical technology guidance is usually reviewed 3 years after publication, unless NICE become aware of significant new information before the expected review date.

This review report summarises new evidence and information that has become available since this medical technology guidance was published, and that has been identified as relevant for the purposes of this report. This report will be used to inform NICE's decision on whether this guidance will be updated, amended, remain unchanged (static list) or withdrawn.

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1. Original objective of guidance

To assess the clinical and cost effectiveness of iFuse for treating chronic sacroiliac joint pain.

2. Current guidance recommendations

The current recommendations as outlined in NICE MTG39 (NICE 2018) are:

- 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

3. Methods of review

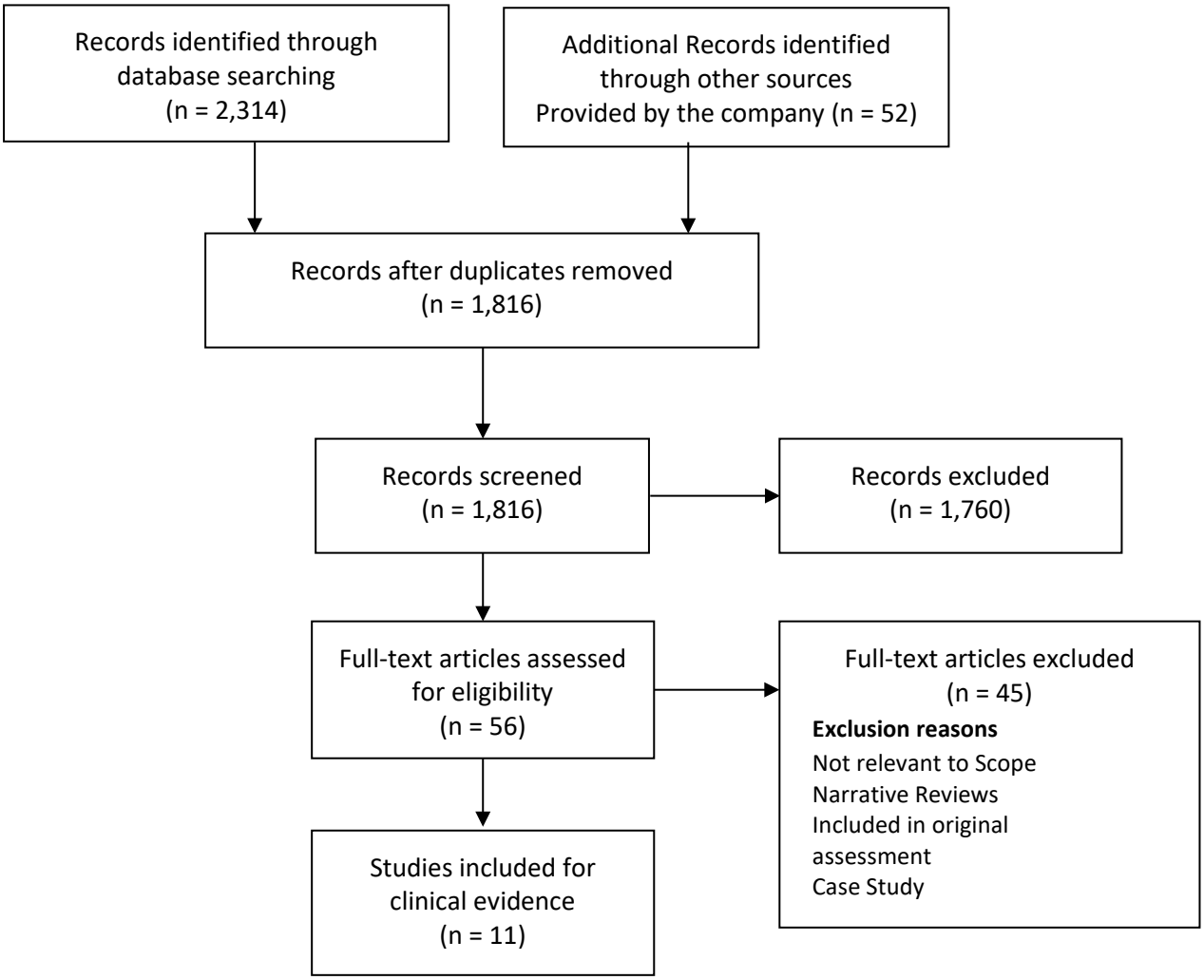
Update searches, based on the original EAC searches for this guidance, were conducted by information specialists at NICE on 9th November 2021 and covered the period November 2017 to November 2021. Details are provided in Appendix D.

NICE searches identified 2,314 records, from which duplicates were removed (n=505). Search results provided to Cedar were imported into Endnote (n=1,809). The company submitted a list of 52 studies, 7 of which had not been identified by the literature searches and were added to the Endnote library. Following de-duplication, a total of 1,816 publications were included for title and abstract sift.

One researcher reviewed all records and 56 were selected as being relevant for full review. A second researcher reviewed the 56 selected publications to confirm relevance. Full texts of the 56 studies were obtained and were reviewed and discussed by two researchers after which 11 studies were considered relevant for inclusion. These were reviewed and are summarised in Appendix C, together with EAC comments.

Searches were also conducted for ongoing and/or unpublished trials in ClinicalTrials.gov, ISRCTN and WHO International Clinical Trial Registry Platform (ICTRP).

Figure 1: EAC Study Selection



4. New evidence

4.1. Changes in technology

The technology is the iFuse implant system which consists of a sterile, cannulated titanium implant and a surgical instrument system for implantation. It is used for the treatment of chronic sacroiliac joint pain specifically after conservative management, analgesia, physical therapy and joint injections or ablative techniques have proved unsuccessful. The company provided information on the changes to the manufacturing process of the iFuse implant, outlining that the iFuse 3D implant is a second-generation triangular porous implant that is very similar to the original implant. The company report that the implant is equivalent to the original iFuse implant in terms of clearance,

indication, biomechanical properties, materials, and dimensions. The primary difference between iFuse-3D and the original iFuse implant is in the manufacturing process. The original implant was manufactured from machined titanium bar stock and the porous surface coating was applied as a titanium plasma spray. The iFuse-3D implant is 3D printed (additive manufactured) from titanium powder. This manufacturing process allows for greater uniformity of the porous surface and also allows for fenestrations. The company report that the majority of sales are now the 3D implant. One clinical expert also reported that they have moved to using 3D printed implants.

4.2. Changes in care pathways

Since the development of the guidance in 2018 there have been no changes to the clinical pathway. Open surgery is still not considered to be a valid comparison in the NHS and therefore remains excluded.

The company indicated there have been no changes to the iFuse implant system since publication of the guidance. The EAC noted that 3D printed implants were excluded in the original assessment due to lack of evidence but note it would fit into the pathway identically to the original implant. The EAC has reported on any evidence relating to 3D printed implants in section 4.3.

The company described two expanded indications:

1. placement of an iFuse triangular titanium implant in a sacro-alar iliac trajectory adjacent to an S2AI screw placed as pelvic fixation for long construct deformity surgery.

2. use of iFuse implant in trauma: high and low energy fractures of the pelvic ring.

Neither of these indications were included in the original scope and the company has indicated that the current review should exclude these expanded indications and should include only minimally invasive sacroiliac joint fusion performed with the lateral transiliac placement of iFuse implants as described in the scope (NICE 2017).

One clinical expert noted that placement of an iFuse triangular titanium implant in a sacro-alar iliac trajectory adjacent to an S2AI screw placed as pelvic fixation for long construct deformity surgery is a different sacroiliac joint (SIJ) fusion technique called ‘Bedrock’ which is used to protect iliac bolts from breakage and reduce SIJ pain in long lumbar fusions and adult deformity corrections. Although not reviewed in this report, the EAC note that there are a number of studies published and ongoing which investigate this technique and therefore this could be an area to consider expansion of the scope in the future (appendix C). This is supported by one expert who reported that

expanding the scope to include patients who have SIJ pain after lumbar fusion would be useful.

4.3. New studies

The EAC identified 7 studies reported in 10 publications relevant to the scope, including 1 trial protocol (Randers 2021) which is discussed in section 4.4. One additional publication identified is a systematic review and meta-analysis (Tran 2019) reporting outcomes for iFuse compared with other surgical approaches. In total, 11 publications are included in this review.

Systematic review and meta-analysis

Tran 2019 is a systematic review evaluating treatment efficacies and patient outcomes associated with minimally invasive joint fusion in comparison to screw type surgeries including open surgical approaches. Fourteen publications reported an iFuse treatment implant, 8 of which were included in the original assessment report (Duhon 2013; Duhon 2016; Polly 2015; Polly 2016; Rudolf 2014; Sachs 2016; Smith 2013; Sturesson 2016). Results of iFuse trials compared with screw type trials were pooled for the outcomes pain, disability and global quality of life and results indicated significantly better outcomes for patients with iFuse. It should be noted that one of the comparators, open surgery, is not considered a valid approach for NHS practice which means the review may have limited applicability.

Long Term Outcomes from INSITE and SIFI (LOIS)

Whang 2019, Darr (2018a) and **Darr (2018b)** report results from the LOIS study. LOIS reports long term outcomes for patients undergoing sacroiliac joint fusion using triangular titanium implants from two previous prospective clinical trials INSITE and SIFI, (reviewed in the original EAC assessment report) and followed up in a single long-term follow-up study (Table 1). Whang 2019 reports up to 5-year outcomes in 93 patients, Darr 2018a reports up to four-year outcomes in 93 patients and Darr 2018b reports 3-year outcomes in 96 patients.

In the original assessment, 6, 12- and 24-month results from the INSITE RCT (Polly 2016a) reported significant improvements in SIJ pain score, Oswestry Disability Index (ODI) score, and EQ-5D TTO index (table 1 and EAC Assessment Report). Further long-term follow-up results from the LOIS study (table 1) indicate that the improvements in pain scores, ODI scores and quality of life scores from baseline to year 2 observed in the SIFI and INSITE studies are maintained through years 3 to 5.

Opioid use reduced from baseline to 6 months in the INSITE study and from baseline to 25 months in the SIFI study. Results from the LOIS study indicate that further reductions were observed to year 5.

The proportion of participants working full time decreased perioperatively but returned to preoperative levels by 6 months. Patient satisfaction was high throughout (Whang 2019).

Table 1: Long term outcomes from INSITE and SIFI (LOIS)

	INSITE & SIFI*	LOIS Study (INSITE and SIFI)			
	EAC Assessment Report (table 4)	**Preoperative**	**3 Years**	**4 Years**	**5 Years**
Sacroiliac joint (SIJ) pain score	INSITE (Polly 2016a) • Baseline: 82.3 • 6 month: 30.1 • 12 month: 28.6 • 24 month: 26.7 (p<0.001) SIFI (Duhon 2016) • Baseline: 79.8 • 1 month: 37 • 3 month: 30.7 • 6 month: 30 • 12 month: 30.4 • 18 month: 28.1 • 24 month 26 p<0.0001 between baseline and 24 months.	81.5 (SD 12.7)	26.2	Improvements in score were maintained (actual score not reported)	27.1 (29.4)
Oswestry Disability Index (ODI) score	INSITE (Polly 2016a) • Baseline: 57.2 • 6 month: 29.9 • 12 month: 28.3 • 24 month: 28.7 (p<0.0001).	56.3 (SD 12.1)	28.0	Improvements in score were maintained (actual score not reported)	29.9 (SD 21.2)

	INSITE & SIFI*	LOIS Study (INSITE and SIFI)			
	EAC Assessment Report (table 4)	**Preoperative**	**3 Years**	**4 Years**	**5 Years**
	SIFI (Duhon 2016) • Baseline: 55.2 • 1 month: 42.6 • 3 month: 33.8 • 6 month: 32.5 • 12 month: 31.5 • 24 months: 30.9 p<0.0001 between baseline and 24 months				
Quality of Life	INSITE (Polly 2016a) • 6 month: 0.29 • 12 month: 0.31 • 24 month: 0.28 SIFI (Duhon 2016) • Baseline: 0.43 • 6 month: 0.69 • 12 month: 0.71 • 24 months: 0.71 p<0.0001 between baseline and 24 months	0.45 (SD 0.17)		Improvements in score were maintained (actual score not reported)	0.75 (SD 0.22)

	INSITE & SIFI*	LOIS Study (INSITE and SIFI)			
	EAC Assessment Report (table 4)	**Preoperative**	**3 Years**	**4 Years**	**5 Years**
Patient Satisfaction			73% would definitely undergo the procedure again (figure 3, Whang 2019)	Satisfaction rates remained high, except for a slight reduction in the proportion who were very satisfied. 76% would definitely undergo the procedure again (figure 3, Whang 2019)	75% of participants would definitely undergo the procedure again
Opioid Use	INSITE (Polly 2016a) • Baseline: 68.6% • 6 months: 58.4% SIFI (Duhon 2016) • Baseline: 76.2% • 25 months: 55%	76.7% (Whang 2019)	47.4% (Whang 2019)	43% (Darr 2018a)	41.3% (Whang 2019)
Abbreviations: ODI, Oswestry Disability Score; SD, standard deviation; SIJ, sacroiliac joint					
*iFuse results reported here for reference only, for full results refer to EAC assessment report					

Study of Bone Growth in the Sacroiliac Joint after Minimally Invasive Surgery with Titanium Implants (SALLY - NCT03122899)

Patel 2019, Patel 2020 and **Patel 2021** report 6-month, 12-month and 24-month outcomes respectively from the SALLY study (Table 2). SALLY is a prospective, single arm study including 51 patients undergoing SIJ fusion using 3D printed implants. Results from the study indicate improvements in pain scores, ODI scores and quality of life scores from baseline to 6 months, with improvements maintained at 24 months. The largest improvement was observed from baseline to 6 months. Physical activity scores (Active straight leg raise (ASLR), five times sit-to-stand, transitional up and go) all showed statistically significant improvements from baseline to 12 months. Opioid use reduced from 59% at baseline to 18% at 24 months. The authors concluded that SIJ fusion using 3D printed implants provided immediate and sustained benefits to patients with SIJ pain and that the results were similar to those of trials using a predecessor device (presumed to be non 3D printed implants though this is not explicitly stated).

Table 2: Long term outcomes from SALLY

	Preoperative	6 months	12 months	24 months
	Changes in the mean are reported from baseline to each timepoint			
Mean sacroiliac joint (SIJ) pain score	78.5 (79.1 Patel (2019), based on 28 subjects)	28.1 (p<0.0001)	21 (p<0.0001)	21.5 (p<0.0001)
Mean Oswestry Disability Index (ODI) score	52.8 (49.9 Patel (2019), based on 28 subjects)	26.3 p<0.0001)	27.9 (p<0.0001)	28.3 (p<0.0001)
Mean Active straight leg raise (on the most painful side)	2.7 (for n=28 patients)	0.9 (p<0.0001)	Improved for both most painful and least painful side (p<0.0001)	N/R
Mean five times sit-to-stand	23.4 seconds (26 seconds when looking at 6-month follow-up)	21 seconds (p=0.0298)	17.8 seconds (0.0053)	N/R
Mean times transitional up and go	22.6 seconds (24 seconds when looking at 6-month follow-up)	18 seconds (p=0.0076)	15.6 seconds (p<0.0001)	N/R

	Preoperative	6 months	12 months	24 months
	Changes in the mean are reported from baseline to each timepoint			
Mean quality of Life (EuroQOL-5D TTO)	0.47		0.74	0.81
Patient Satisfaction			Satisfaction rates were high throughout	
Opioid Use	59% (57% Patel (2019))	21%	22%	18%

Additional Studies

Dengler 2019 and corresponding conference abstract (Dengler 2018) is a randomised controlled trial comparing sacroiliac joint fusion with conservative management in 103 patients. Low back pain improved significantly in the iFuse group compared with the conservative management group (iFuse 43.3 points compared with CM 5.7 points ($p<0.0001$)) with improvements maintained at 24-month follow-up. ODI scores were significantly improved in the iFuse group compared with conservative management at 24 months (26-point improvement (95% CI 21 to 32 points) at 24 months for iFuse and 8-point improvement for CM). Opioid use decreased from 56% at baseline to 33% at 24 months ($p=0.009$) with no change observed in the conservative management group.

Schmidt 2021 is a retrospective cohort study including 19 patients who underwent sacroiliac join fusion. Physical function scores improved significantly postoperatively (40 vs 55 $p=0.016$) and post-operative VAS scores were significantly improved compared with pre-operative scores (7 vs 3 $p=0.0001$). Role limitations due to physical and emotional health were significantly improved at follow-up.

4.4. Ongoing trials

NICE and EAC searches identified 2 ongoing studies relevant to the scope (appendix C).

One ongoing randomised clinical trial (NCT03507049) was identified (Randers 2021), the aim of which is to examine whether there is a difference in pain reduction between patients treated with a minimally invasive fusion of the sacroiliac joint compared with patients undergoing a sham operation.

One prospective cohort study (NCT04824534) aims to determine spatiotemporal parameters, pelvic obliquity, center of gravity and load

capacity in patients suffering from SIJ dysfunction before and after MISJF surgery.

4.5. Adverse Events

No safety alerts were identified from searches (03/11/21) of the MHRA website related to iFuse by information specialists at NICE. No product recalls were identified from searches (08/11/21) of the FDA MAUDE database by information specialists at NICE. A search (31/05/22) by the EAC of the FDA MAUDE medical device reports restricted to ‘malfunction’ type identified one report, this report was received on 30th March 2020. A broad MAUDE search returned over 500 results primarily reporting injury, with 1 death which was unrelated to the SI joint placement. The event description states that the 'si-bone cannulated impactor' tip broke off while the surgeon was using it, broken items were placed in specimen bag and held for operating room manager. It was reported that there was no known impact or consequence to the patient.

Adverse events reported in three studies (table 3) indicate 1 device-related adverse event (Patel 2020) and 8 procedure-related events (Patel 2020, Patel 2021). An additional 4 adverse events were considered to be probably or definitely procedure-related (Patel 2019) and 4 were probably or definitely device or procedure-related (Dengler 2019).

One post-market surveillance study (Cher 2018) compared iFuse and iFuse 3D and reported that the 3D printed version was associated with similar complaint and adverse event rates as the non-3D printed version. Complaints related to the use of iFuse occur at a low rate and appear similar for iFuse-3D. Use of iFuse-3D did not result in any new complaint types. Pain-related complaints occurred at a low and similar rate in both groups (<0.5%). The 1-year cumulative probability of surgical revision was low in both the 3D and machined versions of the device (1.5% for machined and 1% for 3D printed, p=0.0408). No implant breakages or migrations were identified in either group.

Table 3: Adverse events

Follow-up Duration	3 Years	3-4 Years	5 Years
LOIS (Whang 2019, Darr 2018a, Darr 2018b)	168 adverse events reported in 75 subjects (from surgery to year 3) 0 device-related 0 procedure-related	114 adverse events between years 3 and 4 0 device-related 1 surgical revision	Not reported
Follow-up Duration	**Up to 6 months**	**Up to 12 months**	**12-24 months**
SALLY (Patel, 2019, 2020, 2021)	46 in 19 participants 0 device-related 4 probably or definitely procedure-related	112 in 43 participants 1 was device-related 6 were procedure-related	30 in 18 participants 0 device-related 2 were procedure-related
Follow-up Duration	**24 months**		
Dengler 2019	iFuse: 39 events rated severe 4 probably/definitely related to device or procedure CM: 27 severe adverse events 1 related to study procedure		

4.6. Changes in cost case

The results indicate that iFuse is now cost incurring (-£323 per patient) at an 8-year time horizon however it becomes cost saving at 9 years (£230 per patient).

The company included an additional iFuse-3D printed implant which is more expensive (£1,395 compared with £1,212 for a standard implant). The company claims that the iFuse-3D implant makes up the majority of sales and one clinical expert indicated they were using the 3D printed implants. The EAC also investigated the impact of using the cost of the 3D implant and found it to be cost incurring until year 10 when iFuse-3D becomes cost saving (£172 per patient).

The EAC consider the current model to be valid however this assumes that the iFuse-3D implant is clinically equivalent to the iFuse implant. The 3D printed implants were excluded from the original assessment due to a lack of evidence. Current evidence from the SALLY study (Patel 2019, Patel 2020, Patel 2021) suggests that clinical outcomes using 3D implants are similar to the predecessor device however this was not a comparative study.

As in the original cost modelling, savings mainly come from fewer steroid joint injections and less pain relief medication with iFuse compared with non-surgical management. iFuse is likely to be cost saving over time, although it may take longer for it to become cost saving, particularly if there has been a shift to using iFuse-3D.

4.7. Other relevant information

None

5. Conclusion

Evidence in the initial assessment report indicated that for patients undergoing surgery with iFuse implants experience improvements in outcomes such as pain scores, ODI scores and quality of life. Reductions in opioid use were also reported. Long-term follow-up was limited at time of original assessment. More recently, studies reporting long-term follow-up in the same cohorts (Whang 2019, Darr 2018a, Darr 2018b) suggest that the improvements observed in the short term are maintained in the years following surgery.
One study using 3D printed implants (Patel 2021, Patel 2020, Patel 2019) reported similar improvements in outcomes for people undergoing SIJ fusion over 24-month follow-up however, there are no studies comparing 3D printed implants with standard implants. One comparative study (Dengler 2019) reported improved low back pain, ODI scores and reduced opioid use at 24 months compared with conservative management.
Cost modelling indicated that iFuse implants would be cost saving after 8 years compared with surgical management. Updated costs indicate that iFuse will still be cost saving however it may not become cost saving until 9 years after surgery due to increases in device costs.
Overall, the EAC considers that iFuse results in pain relief, less disability, reduction in opioid use and improved quality of life. It has the potential to save £230 per patient around 9 years following surgery. SIJ fusion surgery using iFuse is safe with reports of device and procedure related adverse events rare.

The EAC conclusion is therefore that the current recommendations remain valid at this time (table 4).

Table 4: Potential Impact on Recommendations

MT39 Recommendation	Potential Impact on Recommendation
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.	No change to recommendation More recent evidence, including long-term follow-up suggests that iFuse leads to improved pain relief, better quality of life and less disability.
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.	No change to recommendation Currently no change needed to the population however an area for future consideration/scope expansion may be around the placement of an iFuse triangular titanium implant in a sacro-alar iliac trajectory adjacent to an S2AI screw placed as pelvic fixation for long construct deformity surgery and/or in trauma setting.
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	The EAC considers this recommendation may need to be amended as it is possible that iFuse is no longer cost saving at 8 years as currently stated. An update of the costs (appendix B) indicates that iFuse may not becoming cost saving until 9 years after surgery. Reasons for this may include increases in costs of the iFuse technology as well as a move to the use of the costlier iFuse 3D implant however the full impact of these changes cannot be stated without first assessing all other model inputs, including clinical inputs, for any changes.

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Appendix A – Relevant guidance

Supplied by the NICE gIS team

NICE guidance – published

Low back pain and sciatica in over 16s: assessment and management (2016) NICE guideline NG59

Spondyloarthritis in over 16s: diagnosis and management. (2017) NICE guideline NG65

NICE quality standards

Low back pain and sciatica in over 16s. (2017) NICE Quality standard QS155

NICE technology appraisals and highly specialised technologies

None identified

NICE interventional procedures, medical technologies or diagnostics guidance

iFuse for treating chronic sacroiliac joint pain. (2018) NICE Medical technologies guidance MTG39

Transaxial interbody lumbosacral fusion for severe chronic low back pain (2018) NICE Interventional procedures guidance IPG620

Minimally invasive sacroiliac joint fusion surgery for chronic sacroiliac pain (2017) NICE Interventional procedures guidance IPG578

Lateral interbody fusion in the lumbar spine for low back pain (2017) NICE Interventional procedures guidance IPG574

Epiduroscopic lumbar discectomy through the sacral hiatus for sciatica (2016) NICE Interventional procedures guidance IPG570

Percutaneous transforaminal endoscopic lumbar discectomy for sciatica (2016) NICE Interventional procedures guidance IPG556

Percutaneous interlaminar endoscopic lumbar discectomy for sciatica (2016) NICE Interventional procedures guidance IPG555

Percutaneous coblation of the intervertebral disc for low back pain and sciatica (2016) NICE Interventional procedures guidance IPG543

Percutaneous electrothermal treatment of the intervertebral disc annulus for low back pain and sciatica (2016) NICE Interventional procedures guidance IPG544

Percutaneous intradiscal radiofrequency treatment of the intervertebral disc nucleus for low back pain (2016) NICE Interventional procedures guidance IPG545

Insertion of an annular disc implant at lumbar discectomy (2014) NICE Interventional procedures guidance IPG506

Peripheral nerve-field stimulation for chronic low back pain (2013) NICE Interventional procedures guidance IPG451

Non-rigid stabilisation techniques for the treatment of low back pain (2010) NICE Interventional procedures guidance IPG366

Percutaneous intradiscal laser ablation in the lumbar spine (2010) NICE Interventional procedures guidance IPG357

Prosthetic intervertebral disc replacement in the cervical spine (2010) NICE Interventional procedures guidance IPG341

Prosthetic intervertebral disc replacement in the lumbar spine (2009) NICE Interventional procedures guidance IPG306

Percutaneous endoscopic laser cervical discectomy (2009) NICE Interventional procedures guidance IPG303

NICE pathways

Spondyloarthritis. (2021) NICE Pathway

Low back pain and sciatica (2020) NICE Pathway

All other NICE guidance and advice products - MedTech, ESNM / Evidence Summary, ESUOM, Key Therapeutic Topic, QOF Indicator, and NICE CKS

None identified

NICE guidance – in development

NICE guidelines

None identified

NICE quality standards

None identified

NICE technology appraisals and highly specialised technologies

None identified

NICE interventional procedures, medical technologies or diagnostics guidance

None identified

NICE pathways

None identified

All other NICE guidance and advice products - MedTech, ESNM / Evidence Summary, ESUOM, Key Therapeutic Topic, QOF Indicator, and NICE CKS

None identified

Guidance from other professional bodies

None identified

Appendix B – Costing report

Costing update report of MTG39: iFuse implant system for treating chronic sacroiliac joint pain

This medical technology guidance was published in October 2018.

All medical technology guidance is reviewed 3 years after publication according to the process described in the MTEP Interim addendum on guidance reviews.

This report is part of the information considered in the guidance review. It describes an update of the cost model so that it reflects any new relevant information including revising the cost and resource parameters to current values. The results from the updated cost model are used to estimate the current savings associated with the use of the technology.

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7. Background

The technology is the iFuse implant system which consists of a sterile, cannulated titanium implant and a surgical instrument system for implantation for the treatment of chronic sacroiliac joint pain specifically after conservative management, analgesia, physical therapy and joint injections or ablative techniques have proved unsuccessful. The comparators defined in the 2017 scope are open sacroiliac joint fusion surgery using screw or cage systems; non-surgical or conservative management including optimisation of medical therapy, individualised psychological and physical therapy with provision of adequate information and reassurance, steroid injections; or sacroiliac joint denervation using radiofrequency ablation.

As part of the 2018 assessment, the company (SI-Bone Inc., USA) submitted a model with two comparators:

- SIJ fixation surgery using screw or cage systems (open surgery)

- Steroid injections with the option of progression to RF ablation, with opioid medical therapy used when these are not effective (stepped pathway)

Physical therapy is not included in the model as it was assumed be offered prior to any of the treatment options

The company chose a 7-year time horizon and an NHS and social care perspective was used. Discounting was applied at 3.5%.

The company provided up-to-date costs for inclusion in the model and clinical inputs were taken from published studies.

Assumptions made in the iFuse versus open surgery model included:

- 50% of open surgeries use an anterior approach, the remainder use a posterior approach

- Patients with a good response post-surgery remain in this health state for the duration of the model unless they were to have a revision surgery

- 50% of patients who have a surgical revision will move into a chronic pain health state and the remainder will have a good response. This assumption was applied to both iFuse and open surgery

- Patients with a “good response” do not require any pain medication at all

- The cost of revision surgery is assumed to be the same as the original surgical procedure minus the training costs and the cost of early revision

- Risk of revision is constant. It does not vary with time and is not dependant on any previous revision surgeries.

- Patients living with chronic pain are treated with an opioid base regimen; 50% of patients are on a daily regimen = co-codamol 4 x 8/500 mg + naproxen 2 x 500 mg + Omeprazole 20 mg. The other 50% are on a daily regimen = tapentadol 2 x 200 mg + naproxen 2 x 500 mg + Omeprazole 20 mg

- All patients suffering with chronic pain will see their GP once every six months to obtain a repeat prescription for their pain medication regimen. In addition, patients on strong slow release opioids will also

attend an outpatient visit with a pain management consultant every six-months to review their medication regimen.

Assumptions made in the iFuse versus stepped pathway model included:

- Patients being treated with repeat steroid injections will not be in chronic pain while in this repeat steroid injection health state as treatment provides temporary pain relief
- Patients being treated with repeat steroid injections will not be on an opioid pain management regimen

The EAC consider these assumptions to remain valid at this time but note that there is new clinical evidence available (see section 2) which may lead to some assumptions being revised.

The company's base-case showed a cost saving of £4,273 per patient for iFuse compared to open surgery and a cost saving of £325 per patient for iFuse compared to a stepped pathway.

The EAC assessment also identified some additional assumptions including:

- All patients are alive for the duration of the 7-year model.
- The cost of adverse events is entirely captured in length of hospital stay.
- Physical therapy is not included in the model.
- The model structure and use of surgery as a tunnel state means that patients do not arrive in mild or severe pain states for 6 months, and fewer revisions occur in the first year.
- Patients on the stepped pathway who move into a chronic pain state would not be considered for further therapy, and would remain in the chronic pain state for the rest of the model duration, receiving pain management with opioids.
- Probability of continuing with either steroid injections or ablation is constant over time.

The EAC corrected two model errors and amended model inputs (as detailed in the EAC assessment report). This resulted in an EAC base case with a reduced cost saving compared with open surgery (£3,163) and a change to being cost incurring for the stepped pathway (£557), at a time horizon of 7 years, although this would also become cost saving at a time horizon of 9 years (£495).

The NICE committee concluded that the comparator of open surgery was no longer relevant to NHS practice, and therefore the only comparator

considered in the final recommendations was the stepped pathway. During the consultation phase the company amended the costs of consumable items used during iFUSE surgery, resulting in an overall cost saving at an 8-year time horizon of £129 for iFUSE compared with the stepped pathway. During consultation the EAC carried out a limited exploratory analysis to extend the time horizon to 30 years. The committee considered it likely that cost savings would increase over time.

NICE MTG39 (2018a) recommends that:

- 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.

While noting that

- 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.

The purpose of this 2022 report is to investigate changes to the costs in the original model and the potential impact these changes have on the original results to determine whether the current guidance for the iFuse implant system should be reviewed or remain as it is.

8. Published Evidence

Neither the company nor the EAC identified any economic evidence relevant to the decision problem during original guidance development. The company provided details of three potentially relevant economic publications during the review process (table 1).

Table 1: Published Economic Studies

Study	Study Details	EAC Comment
Cher (2019)	Review Article	Not included – Review article discussing the value of surgical treatments for sacroiliac joint pain.
Dale (2019)	Review Article	Not included as this is a manuscript summarising the MTG39 guidance.

Blissett (2020)	Cost utility analysis (NHS Perspective)	Included

Only one of the economic studies identified was considered relevant to the current review (Blissett 2020). The aim of the study was to identify the cost-effectiveness of minimally invasive sacroiliac joint (MI SIJF) surgery titanium triangular implants (presumed to be iFuse) for patients with sacroiliac joint (SIJ) pain who have failed conservative management, compared to non-surgical management (NSM) from an NHS England perspective. A Markov model including adults with chronic, disabling SIJ pain unrelated to acute trauma or underlying inflammatory disease who have failed conservative management was constructed to compare MISIJF to three treatment strategies:

1. A stepped pathway (patients initially treated with combination of conservative techniques such as physical therapy and corticosteroids (PTSI) and can transition from PTSI to radiofrequency ablation RF).

2. A combination pathway (50% of patients start the model being treated with PTSI and 50% start treatment with RF)

3. Treatment with RF only

The model was adapted from the model submitted by the company in the original guidance, as described in MTG39 EAC assessment report (EAC 2018), which was adapted to capture health state utility. As much of the data and costs included in the model were derived from NICE MTG39, the analysis is not discussed in detail in this review. Results from the cost-effectiveness analysis, at a 5-year time horizon, indicate:

- patients undergoing MI SIJF accrued total procedure-related and pain-management costs of £8358 compared with £6880 for non-surgical management (NSM) treatment strategy 1 (stepped care).

- the MI SIJF cohort had 2.98 QALYs compared to 2.30 QALYs with strategy 1, resulting in an ICER of £2164/QALY gained for MI SIJF.

- Strategy 2 (combination pathway) of the NSM arm had lower costs than strategy 1 (£6564) and 2.26 QALYs resulting in an ICER of £2468/QALY gained for MI SIJF.

- Strategy 3 (radiofrequency ablation) of the NSM arm had lower costs than strategy 1 (£6580), and this resulted in 2.28 QALYs and an ICER of £2518/QALY gained for MI SIJF.

- Probabilistic sensitivity analysis shows that at a threshold of £20,000/QALY gained, MI SIJF has a probability of being cost-effective versus NSM strategies of 96%, 97%, and 91% for strategies 1, 2, and 3, respectively, at 5 years.

In the original economic analysis, the key drivers for incurring costs identified by the EAC included total pain management and the number of steroid injections in 6 months. Other important drivers included length of stay for iFuse, % good response to steroid injection treatment, unit cost of theatre time and steroid injection procedure costs.

New clinical evidence identified by the company included a randomised controlled, post-market clinical follow-up trial comparing iFuse with conservative management (Dengler 2019) and a number of prospective multi-centre studies including one (Whang 2019) which reports 5-year outcomes from the INSITE/SIFI studies (LOIS) which had not been published at the time of the original assessment. The availability of longer-term data may result in changes to the cost savings but it should be noted that clinical evidence has not been reviewed at this time.

9. Current validity of model

Since the development of the guidance in 2018 there have been no changes to the clinical pathway. Open surgery is still not considered to be a valid comparison in the NHS and therefore remains excluded. For the stepped pathway, clinical experts noted that steroid injections would be used only as long as they were beneficial after which they would stop and surgery would be considered. Updated clinical expert input indicates that this remains the case, with one expert reporting that patients in their service would receive a maximum of 2 to 3 steroid injections.

The company indicated there have been no changes to the iFUSE implant system since publication of the guidance. The company described two expanded indications:

1. placement of an iFuse triangular titanium implant in a sacro-alar iliac trajectory adjacent to an S2AI screw placed as pelvic fixation for long construct deformity surgery

2. use of iFuse implant in trauma: high and low energy fractures of the pelvic ring

Neither of these indications were included in the original scope and the company has indicated that the current review should exclude these expanded indications and should include only minimally invasive sacroiliac

joint fusion performed with the lateral transiliac placement of iFuse implants as described in the scope (NICE 2017).

The EAC noted that the updated price list included an iFUSE 3D implant and queried this with the company. The company provided information on the changes to the manufacturing process of the iFuse implant, outlining that the iFuse 3D implant is a second generation triangular porous implant that is very similar to the original implant. According to the company, the implant is equivalent to the original iFuse implant in terms of clearance, indication, biomechanical properties, materials, and dimensions. The primary difference between iFuse-3D and the original iFuse implant is in the manufacturing process. The original implant was manufactured from machined titanium bar stock and the porous surface coating was applied as a titanium plasma spray. The initial RCT trials (INSITE and iMIA) studied the original iFuse implant. The iFuse-3D implant is 3D printed (additive manufactured) from titanium powder. This manufacturing process allows for greater uniformity of the porous surface and also allows for fenestrations. Currently, the 3D implant comprises the large majority of iFuse sales. The 3D implant would fit into the pathway identically to the original implant. In the original Assessment Report, the EAC considered the iFuse-3D implant to be out of scope however, if the majority of sales are now the 3D implant, this may need to be reconsidered and a review of the clinical evidence, including safety data may be required.

No new guidance which might potentially impact the use of the device has been published. There have not been any changes to the clinical pathway since publication of the original guidance.

10. Updated input parameters

The company has provided updated costs for the iFuse implant system (table 2) and the EAC has obtained updated costs for all other costs and resources in the model (table 3 and table 4). The clinical parameters in the model have not been updated at this time. The EAC noted there were different costs for different implant sizes however the company confirmed that the most common sizes would be the 7x55 mm, 7x45 mm, and 7x40 mm implants and it is the cost for these sizes that has been used in the updated costs. This is consistent with the approach in the original guidance.

As the company noted that the majority of iFuse sales are 3D printed iFuse implants and these are more expensive (£1,395) and the impact of using the cost of the 3D implants is also reported.

The surgical accessories are not included in the price list provided by the company, and have therefore been inflated using the PSSRU index. It should

be noted that no clear description of what is covered by the accessories cost has been provided by the company.

Table 2: iFuse Costs

Parameter	Units	Cost per unit (2018)	Cost per Unit (2022)	Source
Unit cost Surgical Implants	3	£1,155.00	£1,212/£1,395)	SI-Bone List Price
Surgical Accessories (post consultation cost)		£136.00	£146	Inflated using PSSRU index (2020/21)
Unit cost steinmann pins	3	£47.00	£50	SI-Bone List Price
Unit cost exchange pin	1	£47.00	£50	SI-Bone List Price
Unit cost drills	1	£131.00	£140	SI-Bone List Price
Total consumables		**£3,920.00**	**£4,122.60**	**SI-Bone List Price**
Training costs per procedure		£6.09	£6.89	PSSRU

Non-surgical costs are detailed in table 3. Total pain management costs comprised cost of a low or high medication regiment and also included costs a GP visit, assessment visits and outpatient visit. Low and high medication costs were based on the cost of medication for a 6-month period. Low medication costs included 4 x 8/500 mg cocodamol tablets plus 2 x 500 mg naproxen tablets plus 1 x 20 mg Omeprazole capsule per day for 6 months. High medication costs included 1 x 200 mg tapentadol tablet plus 2 x 500 mg naproxen tablets plus 1 x 20 mg Omeprazole capsule per day for 6 months. The EAC has used the cost of capsules in line with the original guidance however there are also costs for tablets which are much expensive.

Table 3: Non-Surgical Costs for the stepped pathway

Parameter	Cost per unit (2018)	Source	Cost per Unit (2022)	Source
Procedure Cost				
Steroid Injection Procedure Cost	£500	NHS reference cost 2015-16 – Day case HC29B	£473.89	NHS reference cost 2019-20 – Day case HC29B
RF Ablation Procedure Cost	£773.67	NHS reference cost 2015-16 – Day case (Weighted average of AB15Z, AB16Z)	£1,066.85	NHS reference cost 2019-20 – Day case (Weighted average of AB15Z, AB16Z)
Pain Management Cost				
	Pack size / per pack / per tablet		Pack size / per pack / per tablet	
Cocodamol (8mg/500mg)	500 / £5.70 / £0.1	NHS Indicative price, BNF 2017	30 / £1.14 / £0.04	Drug Tariff cost, BNF, 2022
Naproxen (500mg)	56 / £1.14 / £0.04	NHS Indicative price, BNF 2017	28 / £1.36 / £0.05	Drug Tariff cost, BNF, 2022
Omeprzole (20mg	28 / £0.87 / £0.03	NHS Indicative price, BNF 2017	28 / £0.89 / £0.03	Drug Tariff cost, BNF, 2022
Tapentadol (200mg)	56 / £99.64 / £1.78	NHS Indicative price, BNF 2017	56 / £99.64 / £1.78	Drug Tariff cost, BNF, 2022
Low medication cost	£27.38	BNF Formulary (cocodamol 4 x 8/500 mg + naproxen 2 x 500 mg + Omeprazole 20 mg)	£51.27	
High medication cost	£669.78	BNF Formulary (tapentadol 200 mg + naproxen 2 x 500 mg + Omeprazole 20 mg)	£672.97	
Unit cost of GP visit	£31	PSSRU 2016 (middle cost of GP visits)	£31.19	PSSRU 2021 (GP unit cost per patient contact lasting 9.22 minutes, including direct care staff, excluding qualifications)
Unit cost of preassessment visit	£177.27	NHS reference cost 2015-16 (WF01B: Non-Admitted Face to Face Attendance, First; Service code 191; Pain Management)	£192.45	NHS reference cost 2019-20 (WF01B: Non-Admitted Face to Face Attendance, First; Service code 191; Pain Management)
Unit cost of outpatient visit	£131.21	NHS reference cost 2015-16 (WF01A - Non-Admitted Face to Face Attendance, Follow up; Service code 191; Pain Management)	£228.59	NHS reference cost 2019-20 (WF01A - Non-Admitted Face to Face Attendance, Follow up; Service code 191; Pain Management)
Total Pain Management	£445.19		£489.53	
# total value is a mean of (low medication cost + GP visit) or (high medication cost + GP visit + outpatient visit)				

Table 4: Staff and Hospital Costs

Parameter	iFUSE (2008)	iFUSE (2022)	Source
Procedure time (iFuse)	59	59	Heiney 2015
Unit cost of theatre time (all)	£17.03	£19.03	Information Services Division (ISD) Scotland (Average cost per minute for Orthopaedics surgery). Updated with 2019-20 data
Length of Stay (iFuse)	0.8	0.8	Heiney 2015
Unit cost of hospital stay (iFuse)	£380.99	£415.44	NHS Reference Costs (weighted average cost of elective, excess bed days for back pain interventions HC53, 54, 60, 61, 62, 63, 64). Inflated using PSSRU inflation calculator to 2020/21.

11. Results from updated model

In 2018, the cost savings reported with iFuse were an estimated £129 per patient over an 8-year time horizon with cost savings increasing year by year to a 30-year time horizon. The EAC used updated costs to assess whether and to what extent these cost savings may have changed.

That EAC has not updated the sensitivity analysis at this time as this would require a full update of the economic model, including the clinical parameters which is not within the scope of this review. However, as there was uncertainty around what the surgical accessories costs in the model related to, the EAC conducted a sensitivity analysis on this input only. Varying the cost of the surgical accessories ±20% did not alter the point at which iFuse became cost saving (year 9 for standard implants and year 10 for 3D printed implants).

Once the updated costs have been incorporated into the model, iFuse is cost incurring up to 8 years (-£323) however it becomes cost saving from year 9 (£230.37) onwards. When using the cost of the iFuse-3D implant, it only becomes cost saving from year 10 (£172.31) onwards (table 5).

Table 5: Results from updated costs

					Cost saving compared to Stepped pathway	
Model	Time Horizon	iFuse (standard implant)	iFuse (3D implant)	Stepped Pathway	For iFuse standard implant	For iFuse 3D implant
Company base case (2018)	7 years	£7,319	N/A	£7,644	£325.07	N/A
EAC base case (2018)	8 years	£7,345	N/A	£7,474	£129	N/A

					Cost saving compared to Stepped pathway	
Model	**Time Horizon**	**iFuse (standard implant)**	**iFuse (3D implant)**	**Stepped Pathway**	**For iFuse standard implant**	**For iFuse 3D implant**
EAC base case (costs/resources updated 2022)	8 years	£8,082	£8,662	£7,759	-£323*	-£903*
EAC base case (costs/resources updated 2022)	9 years	£8,284	£8,868	£8,515	£230	-£353
EAC base case (costs/resources updated 2022)	10 years	£8,482	£9,068	£9,241	£759	£172
**Negative values indicate cost incurring*						

12. Conclusion

The EAC did not identify anything to suggest that there have been any changes to the clinical pathway. No new guidelines were identified and, in particular, there was no evidence to suggest that open surgery, a comparator excluded by clinical experts in the original assessment, should now be included. The EAC did contact clinical experts to request their input however none commented.

The results indicate that iFuse is now cost incurring (-£323 per patient) at an 8-year time horizon however it becomes cost saving at 9 years (£230 per patient).

The company identified an additional iFuse-3D printed implant which is more expensive (£1,395 compared with £1,212 for a standard implant). The company claims that the iFuse-3D implant makes up the majority of sales however, so the EAC also investigated the impact of using the cost of the 3D implant and found it to be cost incurring until year 10 when iFuse-3D becomes cost saving (£172 per patient).

The EAC consider the current model to be valid however this is based on the assumption that the iFuse-3D implant is clinically equivalent to the iFuse implant.

As in the original cost modelling, savings mainly come from fewer steroid joint injections and less pain relief medication with iFuse compared with non-surgical management. iFuse is likely to be cost saving over time, although it may take longer for it to become cost saving, particularly if there has been a shift to using iFuse-3D.

The EAC considers that recommendation 1.3 may need to be updated as it is possible that iFuse is no longer cost saving at 8 years as currently stated. Reasons for this may include increases in costs of the iFuse technology as well as a move to the use of the more costly iFuse 3D implant however the full impact of these changes cannot be stated without first assessing all other model inputs, including clinical inputs, for any changes.

13. References

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Appendix 2. Background documents for this review

Hyperlinks for the background documents for this review report:

1. Medical technologies guidance document
2. Assessment report
3. Scope of assessment
4. A copy of the company information request regarding the technology
5. A list of expert advisers and their completed questionnaires on the MTG review
6. Executable cost model which aligns with the base case described in the MTG documents
7. If there is new evidence which is relevant to any of the clinical parameters in the model, the analyst should send the updated values.
8. Any relevant other documents which are not available on the NICE website.

Appendix C – Details of studies and ongoing trials

Tables 5-7: Study Details

Table 5: Long Term Outcomes from INSITE and SIFI (LOIS, NCT02270203)

Aim: to evaluate the long-term safety and effectiveness of SI joint fusion using the iFuse Implant System in patients with degenerative sacroiliitis (DS) and/or sacroiliac joint disruptions (SD). **Outcomes**: SIJ pain score, ODI score, Quality of Life, Adverse Events, Patient Satisfaction					
Study ID	**Study Design**	**Population**	**Intervention & Comparator**	**Results**	**Comments**
Whang 2019 5 Year Follow Up	Extended follow-up from two ongoing multicentre prospective US clinical trials (12 centres) N=103 participants enrolled in the study All participants have already undergone the surgical procedure of interest (SI joint fusion with iFuse Implant System). The two ongoing trials are: • SIFI:(Sacroiliac Joint Fusion with iFuse Implant System) a single-arm trial of	N=93	iFuse (type not reported however Patel et al 2019 reports that a prior version of the device was used in INSITE and SIFI) No Comparator	Mean SIJ pain score decreased from 81.5 (SD 12.7) to 27.1 (29.4) Mean SIJ pain score change from baseline of 54.1 (32.3) points ($p<0.0001$) 82% (n=77) participants had SIJ pain score improvements of at least 20 points Oswestry Disability Index: decreased from 56.3 (12.1) pre-operatively to 29.9 (21.2) at 5 years. Improvement of 26.2 (21.6) points ($p<0.0001$) 68.8% (n=64) of participants had improved ODI score of at least 15 points from pre-op score	3-year reporting is unclear in that detailed results are not presented in Darr 2018b Whang et al (2019) does include the results for 3 and 4 year as well as the 5-year outcomes

Aim: to evaluate the long-term safety and effectiveness of SI joint fusion using the iFuse Implant System in patients with degenerative sacroiliitis (DS) and/or sacroiliac joint disruptions (SD). **Outcomes**: SIJ pain score, ODI score, Quality of Life, Adverse Events, Patient Satisfaction					
Study ID	**Study Design**	**Population**	**Intervention & Comparator**	**Results**	**Comments**
	patients with degenerative sacroiliitis or sacroiliac joint disruption who underwent iFuse placement, and • INSITE (Investigation of Sacroiliac Fusion Treatment): a randomized clinical trial of the same patient population who underwent either non-surgical treatment or iFuse placement			EuroQOL-5D time trade off index score improved from 0.45 (0.17) at baseline to 0.75 (0.22) at 5 years; improvement of 0.29 (0.26) points ($p<0.0001$) Proportion of patients stating they would definitely undergo procedure again was 75% (85% at 2 years)	
Darr 2018a 4 Year Follow Up		N=93 patients who underwent sacroiliac joint fusion		Improvements in pain and ODI were maintained at 4-year follow-up Decrease from baseline for mean SIJ pain score was 54 points Decrease from baseline for mean ODI score was 26 points Increase from baseline for mean quality of life score was 0.3 points	

Aim: to evaluate the long-term safety and effectiveness of SI joint fusion using the iFuse Implant System in patients with degenerative sacroiliitis (DS) and/or sacroiliac joint disruptions (SD). **Outcomes**: SIJ pain score, ODI score, Quality of Life, Adverse Events, Patient Satisfaction					
Study ID	**Study Design**	**Population**	**Intervention & Comparator**	**Results**	**Comments**
				Daily opioid use reduced from 77% immediately prior to surgery to 43% at 4 year follow up N=114 adverse events reported between years 3 and 4 (none were considered device related). There was one surgical revision of the target SIJ between years 3 and 4	
Darr 2018b 3 Year Follow Up		N=96 (n=103 eligible patients, loss to follow-up n=5; death from other causes n=2 and withdrawal of consent n=1)		2-year responses were slightly larger in participants at LOIS sites compared with participants not at taking part (improvement in VAS SIJ pain of 62.3 vs. 48.0 points, p<0.0001; improvement in ODI of 28.8 vs. 23.9 points, p=0.0776) Mean SIJ pain score decreased to 26.2 (mean preoperative score was 55 points (p<0.0001))	

Aim: to evaluate the long-term safety and effectiveness of SI joint fusion using the iFuse Implant System in patients with degenerative sacroiliitis (DS) and/or sacroiliac joint disruptions (SD). **Outcomes**: SIJ pain score, ODI score, Quality of Life, Adverse Events, Patient Satisfaction					
Study ID	**Study Design**	**Population**	**Intervention & Comparator**	**Results**	**Comments**
				Mean ODI score decreased to 28 points (56 pre-operatively, p<0.0001) 72.3% (n=60) had improved ODI scores of at least 15 points from pre-op 96% of subjects were very or somewhat satisfied at 3 years. 73% of participants would definitely undergo the procedure again (versus 87% at 2 years, p=0.003) N=168 adverse events reported in 75 subjects of which 22 were related to the pelvis. There were no device related or procedure related adverse events	
Abbreviations: ODI, Oswestry Disability Index, SIJ, sacroiliac joint; SIJF, sacroiliac joint fusion					

Table 6: Study of Bone Growth in the Sacroiliac Joint after Minimally Invasive Surgery with Titanium Implants (SALLY, NCT03122899)

Aim: To report clinical and functional outcomes of SIJF using 3D-printed triangular titanium implants (TTI) for patients with chronic SI joint dysfunction **Outcomes**: SIJ pain score, ODI score, Quality of Life, Adverse Events, Patient Satisfaction, Radiological Outcomes					
Study ID	**Study Design**	**Population**	**Intervention & Comparator**	**Results**	**Comments**
Patel 2021	Prospective multicentre, single arm clinical trial 24-month outcomes N=51 subjects enrolled in the study	N=43	Sacroiliac joint fusion using iFuse 3D printed implants No comparator	Mean SIJ pain rating improved from 78.5 at baseline to 21.5 at 24 months ($p<0.0001$) Mean ODI improved from 52.8 at baseline to 28.3 at 24 months ($p<0.0001$) Opioid use decreased from 59% at baseline to 18% at 24 months 30 adverse events in 18 subjects from month 12 to 24 2 were procedure related	All patients underwent sacroiliac joint fusion with iFuse 3D printed implants however clinicaltrials.gov reports this as a randomised study in which patients were randomised to 6 month or 12-month CT scan. Actual scores at 6 months are not reported in Patel 2019. Numbers for 6-month follow-up calculated based on the reported change in score of 51 points for SIJ pain and 23.6 for ODI.
Patel 2020	Prospective multicentre, single arm clinical trial 12-month follow-up	N=46 12-month follow-up available for 46 participants		Mean SIJ pain scores improved from 78.5 preoperatively to 21 at 12-month follow-up	

Aim: To report clinical and functional outcomes of SIJF using 3D-printed triangular titanium implants (TTI) for patients with chronic SI joint dysfunction **Outcomes**: SIJ pain score, ODI score, Quality of Life, Adverse Events, Patient Satisfaction, Radiological Outcomes					
Study ID	**Study Design**	**Population**	**Intervention & Comparator**	**Results**	**Comments**
				Mean ODI improvement from 52.8 at baseline to 27.9 at 12 months ($p<0.0001$) Opioid use decreased from 57% to 22% Quality of Life (EuroQOL-5D time trade-off index) improved from 0.47 at baseline to 0.74 at month 12 ($p<0.0001$) Physical Function Test: ASLR test improved for both the most painful and least painful side ($p<.0001$) Five times sit-to-stand mean times improved from 23.4 seconds at baseline to 17.8 seconds at 12 months ($p=0.0053$) Transitional up-and-go decreased from a mean of 22.6 seconds at baseline to 15.6 seconds at 12 months ($p<.0001$)	

Aim: To report clinical and functional outcomes of SIJF using 3D-printed triangular titanium implants (TTI) for patients with chronic SI joint dysfunction **Outcomes**: SIJ pain score, ODI score, Quality of Life, Adverse Events, Patient Satisfaction, Radiological Outcomes					
Study ID	**Study Design**	**Population**	**Intervention & Comparator**	**Results**	**Comments**
				Apposition of bone to at least 30%of the devices' surface area within the sacrum, occurred in 100% of participants Evidence of bridging bone was seen in 16 (70%) sides at 6 months and 17 (77%) sides at 12 months Satisfaction rates were high throughout 112 adverse events were reported in 43 participants, 1 was device related, and 6 were procedure related	
Patel 2019	Prospective multicentre, single arm clinical trial 6-month follow-up	N=28 (first 28 participants from a target sample size of 51) Follow-up available for 24 participants		Mean SIF pain scores decreased from 79.1 preoperatively to 78.1 at six months ($p<0.0001$) Mean ODI score decreased from 49.9 preoperatively to 26.6 at six months ($p<0.0001$) Opioid use decreased from 57% at baseline to 35% at 3 months and 21% at 6 months ($p=0.0077$)	

Aim: To report clinical and functional outcomes of SIJF using 3D-printed triangular titanium implants (TTI) for patients with chronic SI joint dysfunction **Outcomes**: SIJ pain score, ODI score, Quality of Life, Adverse Events, Patient Satisfaction, Radiological Outcomes					
Study ID	**Study Design**	**Population**	**Intervention & Comparator**	**Results**	**Comments**
				Physical function tests: Mean ASLR on the most painful side improved from 2.7 at baseline to 0.9 at 6 months ($p<0.0001$) Five times sit-to-stand mean times improved from 26 sec at baseline to 21 sec at 6 months ($p=0.0298$) Mean scores for timed transitional up and go improved from 24s at baseline to18s at 6 months ($p=0.0076$) 83% of participants were fully ambulatory at 6 months compared with 89% at baseline 46 adverse events were reported in 19 participants, none were device related and 4 were probably or definitely procedure related	
Abbreviations: ASLR, Active straight leg raise; CM, conservative management; ODI, Oswestry Disability Index, SIJ, sacroiliac joint; SIJF, sacroiliac joint fusion					

Table 7: Additional Studies

Study ID	Study Design	Population	Intervention & Comparator	Outcomes and Results	Comments
Dengler 2019 Dengler 2018 (abstract only)	Prospective, multicentre randomised controlled trial	N=103 adults with chronic sacroiliac joint pain	Sacroiliac joint arthrodesis (fusion) with iFuse Conservative Management	Low back pain improvement was significantly larger at 6 months in the SIJ fusion group: • iFuse 43.3 points compared with CM 5.7 points (p<0.0001) Improvement in lower back pain after SIJ fusion persisted at 24 months (mean improvement 45.3 points (95% CI 37 to 54) Improvements in leg pain: • 1.4 points at 6 months and 7.7 points at 24 months for CM • 30 points at 6 months and 32 points at 24 months for iFuse Mean ODI improvement: • 5.6 points at 6 months and 8 points at 24 months for CM • 26 points (95% CI 21 to 32 points) at 24 months for iFuse (6 month not reported) 79% of participants with reported low back pain improvement with iFUSE at 6	Results are reported from the full publication only

Study ID	Study Design	Population	Intervention & Comparator	Outcomes and Results	Comments
				months, maintained at 24 months by at least 20 VAS points compared with 22% at 6 months and 24% at 24 months with conservative management Quality of Life (EQ-5D time trade-off) improvements were: • 6 month: 0.37 point with iFuse vs. 0.09 with CM • 24 month: 0.39 point vs. 0.15 point ASLR showed significant improvement in the iFuse group from baseline ($p<0.0001$) and compared with conservative management ($p<0.0001$) Opioid use: • iFuse: Decrease from 56% at baseline to 33% at 24 months ($p=0.009$) • CM: no change from baseline ($p=1$) Adverse Events at 6 months: • iFuse: 20 adverse events in 16 subjects • CM: 17 adverse events in 15 subjects	

Study ID	Study Design	Population	Intervention & Comparator	Outcomes and Results	Comments
				Adverse Events at 24 months: • iFuse: 39 events rated severe (4 probably/definitely related to device or procedure) • CM: 27 severe adverse events (1 related to study procedure) Radiographic Analysis • No evidence of implant breakage or migration • Breaches (penetration of corticol margins) occurred in 17 of 198 implants • 5 implants showed radiolucency along a single side and 3 along all three sides	
Schmidt 2021	Retrospective Cohort Study	N=19 patients (24 SI fusions)	iFuse	Outcomes: VAS scores, quality of life using SF-36 Mean follow-up was 58 months Post-operative VAS scores were significantly improved compared with pre-operative scores (7 vs 3 p=0.0001)	

Study ID	Study Design	Population	Intervention & Comparator	Outcomes and Results	Comments
				Physical function scores improved significantly postoperatively (40 vs 55 p=0.016) Role limitations due to physical and emotional health were significantly improved at follow-up: • Physical Health: 0 vs. 50 (p=0.016) • Emotional Health: 0 vs. 67 (p=0.0078)	
Abbreviations: ASLR, Active straight leg raise; CM, Conservative Management; ODI, Oswestry Disability Index, SIJ, sacroiliac joint; SIJF, sacroiliac joint fusion					

Table 8: Ongoing Studies

Study ID	Aim	Study Design	Intervention	Comparator	Outcomes	Status
NCT03507049 Randers et al 2021 Multicentre (Norway and Sweden)	To examine whether there is a difference in pain reduction between patients treated with a minimally invasive fusion of the sacroiliac joint compared with patients undergoing a sham operation	Prospective, double blind, randomised controlled, multicentre trial	Sacroiliac Joint Fusion (iFuse)	Sham surgery	Primary Endpoint: Group difference in sacroiliac joint pain intensity on the operated side at 6 months postoperatively, measured by the Numeric Rating Scale	Recruiting Estimated study completion date: 2023
NCT04824534	To determine spatiotemporal parameters, pelvic obliquity, centre of gravity and load capacity in patients suffering from SIJ dysfunction before and after MISJF surgery. Movement parameters will also be determined in healthy individuals to compare with patients suffering from SIJ dysfunction	Prospective cohort study	Sacroiliac Joint Fusion (iFuse)	None		Recruiting however the estimated study completion was February 2022

Table 9: Studies relating to lumbar fusion

Published Study	Aim
CHANDRA VEMULA, V., PRASAD, B., JAGADEESH, M., VUTTARKAR, J. & AKULA, S. 2018. Minimally invasive transforaminal lumbar interbody fusion using bone cement-augmented pedicle screws for lumbar spondylolisthesis in patients with osteoporosis. Case series and review of literature. *Neurology India,* 66**,** 118-125.	Evaluate the clinical and radiological outcome of minimally invasive spine surgery transforaminal lumbar interbody fusion (MIS-TLIF) in patients with spondylolisthesis and poor bone quality, performed with rigid instrumentation using bone cement [poly(methylmethacrylate)]-augmented fenestrated pedicle screws.
Panico M, Chande RD, Lindsey DP, et al. The use of triangular implants to enhance sacropelvic fixation: a finite element investigation. Spine J Off J North Am Spine Soc. Epub ahead of print June 2, 2020. DOI: 10.1016/j.spinee.2020.05.552.	Explored the use of iFuse in different configurations in which the implants supplemented standard sacropelvic fixation with S2AI screws in order to further increase the stability of S2AI fixation. FEA model
San Miguel-Ruiz JE, Polly D, Albersheim M, et al. Is the Implant in Bone? The Accuracy of CT and Fluoroscopic Imaging for Detecting Malpositioned Pelvic Screw and SI Fusion Implants. *Iowa Orthop J* 2021;41:89–94.	The accuracy of CT and fluoroscopic imaging for detecting malpositioned pelvic screw (2SAI) and SI fusion implants (iFuse-3D) during lumbopelvic fixation.
de Andrada Pereira B, Lehrman JN, Sawa AGU, et al. Biomechanical effects of a novel posteriorly placed sacroiliac joint fusion device integrated with traditional lumbopelvic long-construct instrumentation. *J Neurosurg Spine* 2021;1–10.	Effect of SI joint fusion with iFuse placed posteriorly with traditional lumbopelvic long-construct instrumentation. Cadaver model
Martin CT, Holton KJ, Jones KE, et al. Bilateral open sacroiliac joint fusion during adult spinal deformity surgery using triangular titanium implants: technique description and presentation of 21 cases. *J Neurosurg Spine* 2021;1–	Bilateral open sacroiliac joint fusion during adult spinal deformity surgery with iFuse, technique and case series. n=21 patients
de Andrada Pereira B, Wangsawatwong P, Lehrman JN, et al. Biomechanics of a laterally placed sacroiliac joint fusion device supplemental to S2 alar-iliac fixation in a long-segment adult spinal deformity construct: a cadaveric	Biomechanics of a laterally placed sacroiliac joint fusion device supplemental to S2 alar-iliac fixation in a long-segment adult spinal deformity construct: a cadaveric study of stability and strain distribution. Cadaver model

study of stability and strain distribution. *J Neurosurg Spine* 2021;1–11.	
Panico M, Chande RD, Lindsey DP, et al. Innovative sacropelvic fixation using iliac screws and triangular titanium implants. *Eur Spine J Off Publ Eur Spine Soc Eur Spinal Deform Soc Eur Sect Cerv Spine Res Soc*. Epub ahead of print September 25, 2021. DOI: 10.1007/s00586-021-07006-9.	Innovative sacropelvic fixation using iliac screws and triangular titanium implants. Cadaver model
Berlin C, Patel P, Lieberman I, et al. Robotic Sacroiliac Fixation Technique for Triangular Titanium Implant in Adult Degenerative Scoliosis Surgery: 2-Dimensional Operative Video. *Oper Neurosurg Hagerstown Md* 2021;opab326.	Present a technique for placing triangular titanium sacroiliac implants (iFuse Bedrock™) alongside S2AI screws using a robotic platform (Mazor X).
Ongoing Studies	**Aim**
Evaluation of the iFuse Bedrock Technique in Association With Posterior Lumbosacral Fusion With Iliac Fixation (NCT05276024)	To describe the impact of the iFuse Bedrock technique to decrease post-operative pains in patients who underwent multilevel posterior lumbosacral fusion

Appendix D – Literature search strategy

Conducted by NICE gIS

Database searches:

Databases*	Date searched	No retrieved	Version/files
MEDLINE (Ovid)	09/11/2021	432	1946 to November 08, 2021
MEDLINE In-Process (Ovid)	09/11/2021	28	1946 to November 08, 2021
Medline ePub ahead of print (OVID)	09/11/2021	62	November 08, 2021
EMBASE (Ovid)	09/11/2021	909	1974 to 2021 November 08
Embase Conference (OVID)	09/11/2021	326	1974 to 2021 November 08
CDSR (Wiley)	09/11/2021	0	Issue 11 of 12, November 2021
CENTRAL (Wiley)	09/11/2021	425	Issue 10 of 12, October 2021
CENTRAL conferences	09/11/2021	31	Issue 10 of 12, October 2021
**Database of Abstracts of Reviews of Effects – DARE (CRD)	09/11/2021	0	n/a
HTA database (CRD)	09/11/2021	3	n/a
HTA database (INAHTA)	09/11/2021	2	n/a
Epistemonikos	09/11/2021	96	n/a
Total		***2314***	
Total after deduplication		**1809**	

From January 2015 no new records/commentaries will be added to DARE or NHS EED.

Database strategies: MEDLINE (Ovid)
Ovid MEDLINE(R) <1946 to November 08, 2021> 1 iFuse.af. 11 2 SI-Bone.af. 24 3 (NCT01741025 or NCT04062630 or NCT01640353 or NCT01681004 or NCT03122899 or NCT03507049 or NCT02270203 or NCT04824534).af. 3 4 or/1-3 33 5 Minimally Invasive Surgical Procedures/ 27775 6 Spinal Fusion/ 28229 7 Arthrodesis/ 9720 8 "Prostheses and Implants"/ 47950 9 Titanium/ 42343 10 or/6-9 123206 11 5 and 10 1588

12 ((mini* invasive* or MIS) adj4 (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil*)).tw. 28857
13 ((titanium* or triang*) adj4 (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil*)).tw. 10341
14 ((sacroiliac* or sacroiliac* or sacrum* or SI or SIJ) adj4 (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil* or arthrodes* or immobili*)).tw. 2700
15 or/11-14 42295
16 Sacroiliac Joint/ 4308
17 Sacroiliitis/ 619
18 Low Back Pain/ 24086
19 ((sacroiliac* or sacroiliac* or sacrum* or SI or SIJ) adj4 (joint* or pain* or dysfunct* or stabili* or instability* or unstable* or disrupt* or inflamm* or degenerat* or arthritis* or osteoarthritis* or injur* or hypermobil* or hyper-mobil* or syndrome* or fracture* or disease* or disorder* or motion*)).tw. 5901
20 (sacroiliitis or sacroileitis).tw. 1939
21 Pelvic Bone/ 10154
22 (pelvic adj4 (bone* or girdle* or ring* or joint* or pain* or dysfunct* or stabili* or instability* or unstable* or disrupt* or inflamm* or degenerat* or arthritis* or osteoarthritis* or injur* or hypermobil* or hyper-mobil* or syndrome* or fracture* or disease* or disorder* or motion*)).tw.28535
23 or/16-22 64675
24 15 and 23 1631
25 4 or 24 1640
26 Animals/ not Humans/4878281
27 25 not 26 1562
28 limit 27 to ed=20171101-20211109 485
29 limit 28 to english language 432

Database strategies: MEDLINE In-Process (Ovid)

Ovid MEDLINE(R) In-Process & In-Data-Review Citations <1946 to November 08, 2021>

1 iFuse.af. 0
2 SI-Bone.af. 0
3 (NCT01741025 or NCT04062630 or NCT01640353 or NCT01681004 or NCT03122899 or NCT03507049 or NCT02270203 or NCT04824534).af. 0
4 or/1-3 0
5 Minimally Invasive Surgical Procedures/ 0
6 Spinal Fusion/ 0
7 Arthrodesis/ 0
8 "Prostheses and Implants"/ 0
9 Titanium/ 0
10 or/6-9 0
11 5 and 10 0
12 ((mini* invasive* or MIS) adj4 (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil*)).tw. 443
13 ((titanium* or triang*) adj4 (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil*)).tw. 112
14 ((sacroiliac* or sacroiliac* or sacrum* or SI or SIJ) adj4 (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil* or arthrodes* or immobili*)).tw. 59
15 or/11-14 611
16 Sacroiliac Joint/ 0

17 Sacroiliitis/ 0
18 Low Back Pain/ 0
19 ((sacroiliac* or sacroiliac* or sacrum* or SI or SIJ) adj4 (joint* or pain* or dysfunct* or stabili* or instability* or unstable* or disrupt* or inflamm* or degenerat* or arthritis* or osteoarthritis* or injur* or hypermobil* or hyper-mobil* or syndrome* or fracture* or disease* or disorder* or motion*)).tw. 81
20 (sacroiliitis or sacroileitis).tw. 22
21 Pelvic Bone/ 0
22 (pelvic adj4 (bone* or girdle* or ring* or joint* or pain* or dysfunct* or stabili* or instability* or unstable* or disrupt* or inflamm* or degenerat* or arthritis* or osteoarthritis* or injur* or hypermobil* or hyper-mobil* or syndrome* or fracture* or disease* or disorder* or motion*)).tw.383
23 or/16-22 468
24 15 and 23 29
25 4 or 24 29
26 Animals/ not Humans/0
27 25 not 26 29
28 limit 27 to dt=20171101-20211109 29
29 limit 28 to english language 28

Database strategies: Medline ePub ahead of print (OVID)

Ovid MEDLINE(R) Epub Ahead of Print <November 08, 2021>

1 iFuse.af. 3
2 SI-Bone.af. 4
3 (NCT01741025 or NCT04062630 or NCT01640353 or NCT01681004 or NCT03122899 or NCT03507049 or NCT02270203 or NCT04824534).af. 0
4 or/1-3 6
5 Minimally Invasive Surgical Procedures/ 0
6 Spinal Fusion/ 0
7 Arthrodesis/ 0
8 "Prostheses and Implants"/ 0
9 Titanium/ 0
10 or/6-9 0
11 5 and 10 0
12 ((mini* invasive* or MIS) adj4 (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil*)).tw. 1023
13 ((titanium* or triang*) adj4 (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil*)).tw. 180
14 ((sacroiliac* or sacroiliac* or sacrum* or SI or SIJ) adj4 (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil* or arthrodes* or immobili*)).tw. 106
15 or/11-14 1289
16 Sacroiliac Joint/ 0
17 Sacroiliitis/ 0
18 Low Back Pain/ 0
19 ((sacroiliac* or sacroiliac* or sacrum* or SI or SIJ) adj4 (joint* or pain* or dysfunct* or stabili* or instability* or unstable* or disrupt* or inflamm* or degenerat* or arthritis* or osteoarthritis* or injur* or hypermobil* or hyper-mobil* or syndrome* or fracture* or disease* or disorder* or motion*)).tw. 202
20 (sacroiliitis or sacroileitis).tw. 37
21 Pelvic Bone/ 0
22 (pelvic adj4 (bone* or girdle* or ring* or joint* or pain* or dysfunct* or stabili* or instability* or unstable* or disrupt* or inflamm* or degenerat* or arthritis* or

osteoarthritis* or injur* or hypermobil* or hyper-mobil* or syndrome* or fracture* or disease* or disorder* or motion*)).tw.590
23 or/16-22 784
24 15 and 23 62
25 4 or 24 64
26 Animals/ not Humans/0
27 25 not 26 64
28 limit 27 to english language 62

Database strategies: EMBASE and Embase Conference (OVID)

Embase <1974 to 2021 November 08>

1 iFuse.af. 58
2 SI-Bone.af. 145
3 (NCT01741025 or NCT04062630 or NCT01640353 or NCT01681004 or NCT03122899 or NCT03507049 or NCT02270203 or NCT04824534).af. 32
4 or/1-3 168
5 minimally invasive surgery/ 46921
6 spine fusion/ 26861
7 arthrodesis/ 12981
8 prosthesis/ 32397
9 titanium/ 51400
10 or/6-9 120450
11 5 and 10 1724
12 ((mini* invasive* or MIS) adj4 (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil*)).tw. 54385
13 ((titanium* or triang*) adj4 (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil*)).tw. 13390
14 ((sacroiliac* or sacroiliac* or sacrum* or SI or SIJ) adj4 (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil* or arthrodes* or immobili*)).tw. 5053
15 or/11-14 72991
16 sacroiliac joint/ 7129
17 sacroiliitis/ 5206
18 low back pain/ 63329
19 ((sacroiliac* or sacroiliac* or sacrum* or SI or SIJ) adj4 (joint* or pain* or dysfunct* or stabili* or instability* or unstable* or disrupt* or inflamm* or degenerat* or arthritis* or osteoarthritis* or injur* or hypermobil* or hyper-mobil* or syndrome* or fracture* or disease* or disorder* or motion*)).tw. 11003
20 (sacroiliitis or sacroileitis).tw. 4090
21 pelvic girdle/ 6792
22 (pelvic adj4 (bone* or girdle* or ring* or joint* or pain* or dysfunct* or stabili* or instability* or unstable* or disrupt* or inflamm* or degenerat* or arthritis* or osteoarthritis* or injur* or hypermobil* or hyper-mobil* or syndrome* or fracture* or disease* or disorder* or motion*)).tw.48605
23 or/16-22 127240
24 15 and 23 3456
25 4 or 24 3519
26 Nonhuman/ not Human/ 4882884
27 25 not 26 3429
28 limit 27 to dc=20171101-20211109 1301
29 limit 28 to english language 1235

30 limit 29 to (conference abstract or conference paper or "conference review") 326
31 29 not 30 909

Database strategies: CDSR, CENTRAL and CENTRAL conferences (Wiley)

#1 iFuse 16
#2 SI-Bone 14
#3 (NCT01741025 or NCT04062630 or NCT01640353 or NCT01681004 or NCT03122899 or NCT03507049 or NCT02270203 or NCT04824534) 11
#4 {or #1-#3} 31
#5 MeSH descriptor: [Minimally Invasive Surgical Procedures] explode all trees 29903
#6 MeSH descriptor: [Spinal Fusion] explode all trees 1008
#7 MeSH descriptor: [Arthrodesis] explode all trees 1084
#8 MeSH descriptor: [Prostheses and Implants] explode all trees 18091
#9 MeSH descriptor: [Titanium] explode all trees 875
#10 {or #6-#9} 19201
#11 #5 and #10 3594
#12 ((mini* invasive* or MIS) near/4 (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil*)):ti,ab,kw 13003
#13 ((titanium* or triang*) near/4 (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil*)):ti,ab,kw 835
#14 ((sacroiliac* or sacroiliac* or sacrum* or SI or SIJ) near/4 (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil* or arthrodes* or immobili*)):ti,ab,kw 8327
#15 {or #11-#14} 25286
#16 MeSH descriptor: [Sacroiliac Joint] explode all trees 117
#17 MeSH descriptor: [Sacroiliitis] explode all trees 17
#18 MeSH descriptor: [Low Back Pain] explode all trees 4222
#19 ((sacroiliac* or sacroiliac* or sacrum* or SI or SIJ) near/4 (joint* or pain* or dysfunct* or stabili* or instability* or unstable* or disrupt* or inflamm* or degenerat* or arthritis* or osteoarthritis* or injur* or hypermobil* or hyper-mobil* or syndrome* or fracture* or disease* or disorder* or motion*)):ti,ab,kw 17211
#20 (sacroiliitis or sacroileitis):ti,ab,kw 223
#21 MeSH descriptor: [Pelvic Bones] explode all trees 560
#22 (pelvic near/4 (bone* or girdle* or ring* or joint* or pain* or dysfunct* or stabili* or instability* or unstable* or disrupt* or inflamm* or degenerat* or arthritis* or osteoarthritis* or injur* or hypermobil* or hyper-mobil* or syndrome* or fracture* or disease* or disorder* or motion*)):ti,ab,kw 4854
#23 {or #16-#22} 26448
#24 #15 and #23 5638
#25 #4 or #24 with Publication Year from 2017 to 2021, with Cochrane Library publication date Between Nov 2017 and Nov 2021, in Trials 500
#26 (clinicaltrials or trialsearch):so 381884
#27 #25 not #26 456
#28 "conference":pt 191399
#29 #27 and #28 31 – conference results
#30 #27 not #28 425

Database strategies: DARE and HTA (CRD)

Line	Search	Hits
1	(iFuse)	4
2	(SI-Bone)	4
3	((NCT01741025 or NCT04062630 or NCT01640353 or NCT01681004 or NCT03122899 or NCT03507049 or NCT02270203 or NCT04824534))	0
4	#1 OR #2 OR #3	4
5	MeSH DESCRIPTOR Minimally Invasive Surgical Procedures EXPLODE ALL TREES	4907
6	MeSH DESCRIPTOR Spinal Fusion EXPLODE ALL TREES	301
7	MeSH DESCRIPTOR Arthrodesis EXPLODE ALL TREES	330
8	MeSH DESCRIPTOR Prostheses and Implants EXPLODE ALL TREES	
9	MeSH DESCRIPTOR Titanium EXPLODE ALL TREES	26
10	#6 OR #7 OR #8 OR #9	3085
11	#5 AND #10	623
12	((mini* invasive* or MIS) near (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil*))	439
13	((titanium* or triang*) near (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil*))	27
14	((sacroiliac* or sacroiliac* or sacrum* or SI or SIJ) near (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil* or arthrodes* or immobili*))	29
15	#11 OR #12 OR #13 OR #14	1071
16	MeSH DESCRIPTOR Sacroiliac Joint EXPLODE ALL TREES	27
17	MeSH DESCRIPTOR Sacroiliitis EXPLODE ALL TREES	1
18	MeSH DESCRIPTOR Low Back Pain EXPLODE ALL TREES	531
19	((sacroiliac* or sacroiliac* or sacrum* or SI or SIJ) near (joint* or pain* or dysfunct* or stabili* or instability* or unstable* or disrupt* or inflamm* or degenerat* or arthritis* or osteoarthritis* or injur* or hypermobil* or hyper-mobil* or syndrome* or fracture* or disease* or disorder* or motion*))	45
20	((sacroiliitis or sacroileitis))	5
21	MeSH DESCRIPTOR Pelvic Bones EXPLODE ALL TREES	56
22	(pelvic near (bone* or girdle* or ring* or joint* or pain* or dysfunct* or stabili* or instability* or unstable* or disrupt* or inflamm* or degenerat* or arthritis* or osteoarthritis* or injur* or hypermobil* or hyper-mobil* or syndrome* or fracture* or disease* or disorder* or motion*))	279
23	#16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22	858
24	#15 AND #23	26
25	#4 OR #24	26
26	* FROM 2017 TO 2021	506
27	#25 AND #26	3

Database strategies: HTA database (INAHTA)

Search History [27 Results] Selected

Line	Query	Hits	Date
27	#26 OR #25 OR #1	2	
26	#24 AND #2	8	
25	#24 AND #15	2	
24	#23 OR #22 OR #21 OR #20 OR #19 OR #18 OR #17 OR #16	143	
23	((pelvic near (bone* or girdle* or ring* or joint* or pain* or dysfunct* or stabili* or instability* or unstable* or disrupt* or inflamm* or degenerat* or arthritis* or osteoarthritis* or injur* or hypermobil* or hyper-mobil* or syndrome* or fracture* or disease* or disorder* or motion*))	0	
22	"Pelvic Girdle Pain"[mh]	0	

21 "Pelvic Bones"[mh] 2
20 ((sacroiliitis or sacroileitis)) 2
19 ((sacroiliac* or sacroiliac* or sacrum* or SI or SIJ) near (joint* or pain* or dysfunct* or stabili* or instability* or unstable* or disrupt* or inflamm* or degenerat* or arthritis* or osteoarthritis* or injur* or hypermobil* or hyper-mobil* or syndrome* or fracture* or disease* or disorder* or motion*)) 1
18 "Low Back Pain"[mh] 137
17 "Sacroiliitis"[mh] 1
16 "Sacroiliac Joint"[mh] 17
15 #14 OR #13 OR #12 OR #11 3
14 ((sacroiliac* or sacroiliac* or sacrum* or SI or SIJ) near (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil* or arthrodes* or immobili*)) 1
13 ((titanium* or triang*) near (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil*)) 0
12 ((mini* invasive* or MIS) near (surg* or treat* or implant* or fuse* or fusion* or fixat* or stabil*)) 2
11 #10 AND #5 0
10 #9 OR #8 OR #7 OR #6 173
9 "Titanium"[mh]5
8 "Prostheses and Implants"[mh] 129
7 "Arthrodesis"[mh] 6
6 "Spinal Fusion"[mh] 44
5 "Minor Surgical Procedures"[mh] 1
4 #3 OR #2 OR #1 450
3 NCT01741025 or NCT04062630 or NCT01640353 or NCT01681004 or NCT03122899 or NCT03507049 or NCT02270203 or NCT04824534 0
2 SI-Bone 450
1 iFuse 4

Due to the amount of results being retrieved for SI-BONE, this line has been limited with the condition terms, line 24.

Database strategies: Epistemonikos

Title/Abstarct: iFuse OR abstract: iFuse

OR Title/Abstarct: SI-Bone

OR Title/Abstarct: (NCT01741025 OR NCT04062630 OR NCT01640353 OR NCT01681004 OR NCT03122899 OR NCT03507049 OR NCT02270203 OR NCT04824534)

OR Title/Abstarct: (((mini* invasive*) AND (surg* OR treat* OR implant* OR fuse* OR fusion* OR fixat* OR stabil*) AND (sacroiliac* OR sacroiliac* OR sacrum* OR SI OR SIJ OR pelvic)))

OR Title/Abstarct: (((titanium* OR triang*) AND (surg* OR treat* OR implant* OR fuse* OR fusion* OR fixat* OR stabil*) AND (sacroiliac* OR sacroiliac* OR sacrum* OR SI OR SIJ OR pelvic)))

AND Publication year 2017-2021