National Institute for Health and Care Excellence

IP1315/2 Biodegradable subacromial spacer insertion for rotator cuff tears

IPAC date: 14th September 2023

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 NHS professional	1.1-1.3, and 3.6	The guidance is well worded and provides solid and appropriate recommendations based on the current evidence base. The recommendations are clear and will benefit patients. This will protect patients from poor outcomes when this well-marketed product would otherwise be used widely (as demonstrated by the fact that around 30,000 people received the balloon in Europe prior to the recent evidence). Given the failure of case-series to identify the issues identified by our randomised trial, I would personally recommend that any further research should be in the form of a randomised trial only. In point 3.6 (and expanded on in the overview document), I do not believe there is such a clear conflict between the trials, one showed the balloon was inferior to debridement, the other showed that the balloon was non-inferior compared to partial repair, a technique that is rarely used in the UK because of poor reported results in previous case series. It is stated that "Patient selection may have contributed to these conflicting results". This has been widely stated by company-funded individuals to explain the difference but is based on no data or evidence, in fact the evidence presented in our paper was that cuff tear size had no influence on the result. In the correspondence in The Lancet associated with the paper, it was clear that baseline differences in movement was based on a mis-interpretation of how range of motion was measured (pain free-range of motion in our paper, and active range in the Verma et al paper, these would typically give very different results). Although the authors of the Mease paper have no conflicts, it makes the same error in interpretation and quotes a paper whose	Thank you for your comment. 'Randomised controlled trials' has been added to section 1.3. 'Conflicting findings' or 'conflicting results' has been removed from the overview, and section 3.6 has been changed in response to the consultee's comment.

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			authors are also conflicted. By retaining this line in the guideline, I believe NICE is propagating a critique from company-funded individuals based on no evidence, allowing enthusiasts an opportunity to argue for continued to use a device that is inferior to debridement. Our two year results (OSS, WORC and EQ5D) have been analysed and the paper is in preparation, they continue to support these guidelines. As ever, more research is welcome and the clarity of NICE guidelines on what research entails is also welcome, I fully support this. Personally, I think the only way in which future research will help is if further randomised trials are performed. Overall, the committee are to be congratulated on a good set of guidance which will benefit patients.	
2	Consultee 3 NHS Professional	1.1 to 1.3, and 3.7	I fully agree with draft recommendation 1.1 that the biodegradable subacromial spacer should not be used for the management of irreparable cuff tears The evidence to supprot its use when debridement is not an option is also very poor. I note the comments that in the other published RCT comparing its use to partial thickness cuff repairs that this is somehow a different patient population to the RCT comparing it to debridement i.e. it was a patient selection issue; the evidence does not support these comments and the patient populations are almost identical. Consequently, I am not convinced that further evidence is really needed; the conclusion should be that the biodegradable subacromial spacer has no place to play in the treatment of irreprable cuff tears. I also struggle with the comment that it somehow might have a role in patients wih irreparable cuff tears AND inflammatory arthritis; I can find no evidence to support this comment	Thank you for your comment. The consultee has considered this comment but decided not to change section 1.2 ‘research only’. The rationale is detailed in the section of ‘why the committee made these recommendations’. Section 3.7 of the draft guidance has been removed.
3	Consultee 2 Stryker UK Ltd	1.1	1.1 When debridement is a suitable option, biodegradable subacromial spacer insertion for rotator cuff tears should not be used.	Thank you for your comment.

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			Based on evaluation of the available data in its totality, the evidence continues to demonstrate that InSpace is an appropriate treatment option for patients with massive rotator cuff tears. Additionally, recent publications continue to support this conclusion, including a meta-analysis(see 'InSpace Meta-Analysis previously provided in Structured Information Request') which evaluated the clinically meaningful improvements after the implantation of InSpace for massive irreparable rotator cuff tears. A total of 10 articles were included in the analysis of minimal clinically important difference (MCID), patient acceptable symptomatic state (PASS) and substantial clinical benefit (SCB) achievement. This systematic review article included data on 379 patients. The most commonly reported outcome measure was the Constant score and the pooled rate of MCID achievement for this score was 83%. Similar proportions of MCID achievement were seen in the ASES score and Oxford Shoulder Score (83 to 87.5% and 78% respectively). PASS and SCB were reported at a lower rate: two articles for PASS and one for SCB. Achievement of PASS for the Constant score was 98% from one study and 51% for ASES. The authors concluded that patients who had undergone isolated subacromial balloon spacer implantation achieved high rates of clinically significant improvements at a short to midterm follow-up. Further, as noted in recommendation 1.3, longer term follow-up to demonstrate durability of outcomes is appropriate and should be considered when weighing the influence of the available evidence. At the present time, the only randomized controlled trial currently published with minimum of two-year follow-up is Verma et al2, which demonstrated that InSpace performed comparably to Partial Repair in a prospective, randomized, multicenter, blinded, controlled study. This study also demonstrated additional patient and surgeon valued benefits with InSpace, including reduced operative time, earlier recovery of outcomes compared to the control and no device-related complications through two years. Additionally, it is important to note that the available evidence does not indicate that InSpace introduces an unacceptable safety concern in the indicated population and is generally regarded as safe when used in accordance with the instructions for use. The two published randomized controlled trials demonstrate that patients treated	The committee has considered this comment but decided not to change the recommendations. InSpace meta-analysis (unpublished) provided by the company was considered when preparing the overview, with the key relevant publications included in the overview. Two RCTs (Melcalfe 2022; Verma 2022) were included in the main evidence of the overview. The rationale for the recommendations is detailed in the section of 'why the committee made these recommendations', and the committee's comments on the 2 trials are described in sections 3.5 and 3.6.

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			with InSpace realized a clinically meaningful improvement in patient reported outcomes, and there were no differences in safety outcomes between the InSpace and control arms in either study.2,3 As such, we believe a recommendation of 'research only' would be more appropriate and suggest the following revised recommendation: When debridement only as a surgical procedure is a suitable option, biodegradable subacromial spacer insertion for rotator cuff tears should be used only in research. Furthermore, we are requesting a clarification to the description of the debridement procedure to be consistent with the description of the control procedure in the STARTS:REACTS study, if this recommendation is based on the findings from this clinical study, to the following revised recommendation: - When debridement only is a suitable option, biodegradable subacromial spacer insertion for rotator cuff tears should be used only in research.	
4	Consultee 2 Stryker UK Ltd	1.3	Results from the START:REACTS study demonstrate that patient selection is a 'Key Consideration' for use of InSpace and that product labeling should be consulted for patient selection considerations to support clinical success with InSpace. In this study, both the InSpace and the debridement only groups showed improvement at the 12-month endpoint, however the results from the Oxford Shoulder Score favored the debridement group (34.3 points vs. 30.3 points). The authors claimed that the use of InSpace could be harmful, however they reported no differences between the two groups in adverse events reported. Three serious adverse events were reported to be related to surgery: one in the debridement group and two in the debridement with device group. Finally, analgesia use (i.e., number of patients taking pain medication for their shoulder) was similar between both groups at the final follow-up (49% in the debridement group and 49% in the debridement with device group). 14 Although the study favored debridement only, there was no evidence in the study to show that the use of InSpace exposed patients to any undue risks. Additionally, improvements in the Oxford Shoulder Score and all secondary endpoints (i.e, flexion angle, CS, and Western Ontario Rotator Cuff (WORC) score) which achieved a threshold of meaningful clinical improvement difference (MCID) (i.e., 275 for WORC,	Thank you for your comment. Two RCTs (Metcalfe et al., 2022 [the START:REACTS study]; Verma et al., 2022) were included in the main evidence of the overview. The committee has made a comment relating to people with a missing or non-intact coracoacromial ligament (section 3.7 of the final guidance). Section 1.4 specifies the importance of patient selection, "patient selection should be done by a multidisciplinary team experienced in managing the condition, including clinicians with specific training in the procedure."

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			10 for CS, and 6 for OSS) was demonstrated in the InSpace group despite having a smaller improvement than those treated with debridement only. 3,4 Additionally, it should be noted that this study did include patients with a missing or non intact coracoacromial ligament. A missing or non-intact coracoacromial ligament is listed as a 'Warning' in the product labelling, and as such, the risks and benefits of using InSpace to treat patients with this pathology should be carefully considered. In the START:REACTS study, the coracoacromial ligament was not retained in 11% of participants in the debridement only group and 5% of participants in the debridement plus InSpace group. A second randomized controlled trial was published by Verma et al. In this trial, 229 patients were assessed for eligibility with a final 184 subjects ultimately randomized and treated (93 to the InSpace group and 91 to the partial repair group).2 In contrast to the STARTS:REACTs study, the patient population was limited to those patients with confirmed massive rotator cuff tears, in the absence of a subscapularis repair and with an intact coracoacromial ligament. This study followed subjects for 24 months and reported on the change in baseline for the ASES score with secondary outcomes reported for the Western Ontario Rotator Cuff (WORC) score, Constant-Murley score, Visual Analog Scale (VAS) for pain and finally the EuroQol-5 Dimensions-5 Level (EQ-5D-5L) quality of life score. Significant improvement from baseline to Month 24 in the ASES score was demonstrated for both groups with a mean difference from baseline to the final follow-up at 24 months of 46.22 ± 20.89 in the InSpace group and 42.53 ± 20.54 points in the partial repair group. Significant differences between groups were observed in the Constant score at Week 6 and Month 24 and the WORC score at Day 10 in favor of the InSpace group. Forward elevation improvement favored the InSpace group at several timepoints (Day 10, Week 6, Month 12 and Month 24). Additionally, the mean operative time for the InSpace group was significantly shorter than the partial repair group (InSpace: 44.6 minutes; partial repair: 71.2 minutes). Notably, at Month 24, 10% of the InSpace subjects realized a forward elevation range of motion improvement greater than that of the greatest range-of-motion responder in the partial repair group. No device-related surgical complications or device-related serious adverse events were reported. Reoperation was reported in seven total subjects (3 or 3.3% in partial	The rationale for the draft recommendations is detailed in the section of 'why the committee made these recommendations'. In terms of "Overview of level I randomized controlled trials" provided by the consultee, it compared 2 RCTs (Metcalfe et al., 2022; Verma et al., 2022). Both trials were included in the overview and considered by the committee.

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			repair and 4 or 4.3% in InSpace) Please refer to the attached "Overview of level I randomized controlled trials" resource for further comparisons.	
5	Consultee 2 Stryker UK Ltd	3.7	The company is not able to provide guidance on the use of the device in the patient population with inflammatory arthritis due to the lack of evidence-based clinical trials on this population of patients. Users should consult the product labeling prior to use of the InSpace system. It should be noted, as described in the product labeling, that the risks and benefits of implanting the InSpace Implant in patients with the following conditions should be carefully considered: • Blood coagulation disorders, compromised immune systems, severe chronic diseases such as heart failure, cirrhosis and/or severe liver dysfunction, chronic renal failure or any other conditions that would compromise healing. • Deltoid palsy. • Evidence of significant osteoarthritis or cartilage damage in the shoulder. • Evidence of significant gleno-humeral instability. • Missing or not-intact coracoacormial ligament. The complete product labeling should be consulted for important safety information prior to the use of the InSpace system.	Thank you for your comment. Section 3.7 of the draft guidance has been removed.

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