NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance

Assessment report overview

XprESS multi-sinus dilation system for treating chronic sinusitis

This assessment report overview has been prepared by the Medical Technologies Evaluation Programme team to highlight the significant findings of the External Assessment Centre (EAC) report. It includes key features of the evidence base and the cost analysis, any additional analysis carried out, and additional information, uncertainties and key issues the Committee may wish to discuss. It should be read along with the sponsor's submission of evidence and with the EAC report. The overview forms part of the information received by the Medical Technologies Advisory Committee when it develops its recommendations on the technology.

Key issues for consideration by the Committee are described in section 6, following the summaries of the clinical and cost evidence.

This report contains information that has been supplied in confidence and will be redacted before publication. This information is highlighted in yellow. This overview also contains:

- Appendix A: Sources of evidence
- Appendix B: Comments from professional bodies
- Appendix C: Comments from patient organisations
- Appendix D: Additional analyses carried out by External Assessment Centre

1 The technology

The XprESS multi-sinus dilation system (MSDS, Entellus Medical) is a single-use device for treating chronic sinusitis. The system comprises a balloon-tipped device with a reshapeable end that is inserted through the nose into the maxillary, frontal or sphenoidal sinuses. XprESS MSDS also includes an inflation syringe, bending tool and 2 extension lines to provide irrigation. The balloon is moved into the bony sinus outflow tracts (ostia) and inflated with saline. This reshapes the ostia by displacing adjacent bone and paranasal sinus structures, allowing the sinuses to drain more effectively.

XprESS MSDS comes in 3 variants, XprESS Ultra, LoProfile and Pro, which differ in the dimensions of the suction tip and the balloon diameter and length. Selection is based on clinician preference and patient anatomy. The XprESS device, inflation syringe and bending tool are included in all variants. The Ultra and LoProfile (the version sold in the UK) systems also include an integrated PathAssist LED light fibre, which is available as an add-on for the Pro. The XprESS procedure can be done under local anaesthetic, once the surgeon has had sufficient experience of using the device.

2 Proposed use of the technology

2.1 Disease or condition

Sinusitis (also known as rhinosinusitis and sinus infection) occurs when the lining of the sinuses gets infected or irritated, becomes swollen, and creates extra mucus. The swollen lining may also interfere with mucus drainage.

Acute sinusitis refers to a temporary condition that is resolved within 12 weeks, which often occurs following colds.

Chronic sinusitis refers to sinusitis that lasts at least 12 weeks despite being treated and causes at least 2 of the following symptoms: nasal congestion; mucus discharge from the nose or mucus that drips down the back of the

throat; facial pain, pressure, or a feeling of ‘fullness’; or a decreased sense of smell. It can also be characterised by the presence of nasal polyps.

Recurrent acute sinusitis is a type of chronic sinusitis defined as 4 or more acute sinusitis episodes in a single year.

Chronic sinusitis can be uncomfortable or painful and may severely affect quality of life. If symptoms are moderate or severe and persistent despite medical therapy, surgical intervention may be needed. Complications from chronic sinusitis are rare but can be acute, often involving the spread of infection to other areas in the head, and include:

- adenoiditis, dacryocystitis and laryngitis in children
- orbital complications (cellulitis, orbital abscess and cavernous sinus thrombosis)
- intracranial complications (meningitis or abscess formation)
- osteomyelitis
- mucocele formation.

2.2 Patient group

Chronic sinusitis is a common condition that is estimated to affect 10% of the UK adult population. Chronic sinusitis occurs in all ages, genders and ethnic groups, and is reported to be increasing in prevalence. Acute sinusitis is more common in adults than in children, whose sinuses are not fully developed. People with allergies, diabetes and who have had sinusitis before are at greater risk of sinusitis.

2.3 Current management

Current treatment options for chronic sinusitis include nasal saline irrigation, intranasal corticosteroids, systemic antibiotics or topical drops, and functional endoscopic sinus surgery (FESS).

NICE's clinical knowledge summary on chronic sinusitis describes measures to relieve symptoms, particularly for acute episodes, that include analgesics for pain or fever, occasional intranasal decongestants and intranasal saline irrigation, and warm face packs. Patients should be offered advice about managing associated conditions (such as allergic rhinitis, asthma and dental infections), along with advice on smoking cessation and dental hygiene where appropriate. A short course of antibiotics may be prescribed for acute episodes, but longer-term courses are not recommended without seeking specialist advice. A course of intranasal corticosteroids of up to 3-months may be considered, especially if there is a suspicion of an allergic cause (such as concomitant allergic rhinitis).

A patient should be admitted to hospital if sinusitis is associated with a severe systemic infection, or a serious complication such as orbital or intracranial infection or inflammation.

Referral to an ear, nose, and throat (ENT) specialist should be considered for people with frequent recurrent episodes of acute sinusitis (for example more than 3 episodes requiring antibiotics in a year), unremitting or progressive facial pain (urgent referral for suspected malignancy), or nasal polyps that are causing significant nasal obstruction. Referral to an ENT specialist should also be considered if a person has taken intranasal corticosteroids for 3 months without effect.

FESS is currently the most common ENT surgery done for persistent and severe cases of chronic sinusitis[1]. During FESS, the surgeon uses a magnifying endoscope inserted through the nostrils to identify and remove affected sinus tissue and bone. The aim is to clear the obstructed ostia and flush out infected material, but retain enough healthy tissue for normal nose and sinus function. FESS is usually done under general anaesthetic, but can

[1] Lawrence, K et al. (2012) Management of chronic rhinosinusitis. BMJ 345:e7054

also be done under local anaesthetic in selected cases[2]. Scarring and adhesions can occur as a result of FESS, which may require post-operative removal of tissue, blood and bone (debridement). Other more serious risks occasionally associated with FESS include intraorbital and intracranial complications

NICE interventional procedure guidance on balloon catheter dilation of paranasal sinus ostia for chronic sinusitis concluded that the current evidence on the procedure's short-term efficacy is adequate and raised no major safety concerns..

2.4 Proposed management with new technology

The company proposes that XprESS would be used in people with chronic sinusitis or recurrent acute sinusitis when maximum medical management has failed. It would replace FESS in the current treatment pathway for patients with uncomplicated chronic or recurrent acute sinusitis who meet the criteria for medically necessary FESS. XprESS could be used in a day-case or outpatient setting under local anaesthetic, whereas FESS is an inpatient procedure done under general anaesthetic. The company has indicated that balloon dilation with XprESS may be unsuitable for patients with ciliary dysfunction, cystic fibrosis, sinonasal tumours or obstructive lesions, a history of facial trauma, severe or gross polypoid disease, and severe fungal sinusitis; these patients will still require FESS. The company has also stated that FESS may also still be considered for patients with more advanced chronic sinusitis.

2.5 Equality issues

No equality issues were identified during selection and routing, scoping or by the company. The EAC identified 1 potential equality issue. People with chronic sinusitis or recurrent acute sinusitis who cannot have FESS because of comorbidities may be eligible for XprESS under local anaesthetic.

[2] ENT UK (2015) – About Functional Endoscopic Sinus Surgery (FESS)

3 Company's claimed benefits

The benefits to patients claimed by the company are as follows:

- A minimally invasive alternative to FESS with equivalent efficacy but greater preservation of sinus tissue and mucosa with minimal acute inflammation.
- Reduction in risks associated with general anaesthetic, because the procedure can be done under local anaesthetic.
- Faster recovery time with less nasal bleeding and shorter duration of analgesic medication compared with FESS.
- Improved patient comfort and tolerance compared with other balloon technologies, since XprESS allows more control of device placement, has a smaller profile, a malleable tip, and does not include a guidewire.
- More accurate cannulation of the maxillary ostium compared with other balloon technologies.

The benefits to the health system claimed by the company are as follows:

- Reduction in theatre time compared with FESS.
- Reduction in staff numbers, because XprESS can be used in a day-case setting under local anaesthetic.
- Reduction in length of stay.
- Reduction in duration of analgesic medication.
- Reduction in post-operative nasal bleeding visits.
- Reduction in hospital readmissions.
- Ease of use compared with other balloon technologies because no guidewire is needed.

The sustainability benefits claimed by the company are as follows:

- Improved resource utilisation because of a shorter procedure time and fewer complications.

- Reduction in components and packaging waste because XprESS can be used to treat all sinus types.

4 Decision problem

Table 1 Summary of the decision problem

Population	People with chronic sinusitis, including recurrent acute sinusitis, in whom all medical therapy has failed
Intervention	The XprESS Multi-Sinus Dilation System
Comparator(s)	• Functional endoscopic sinus surgery (FESS) • Other balloon sinus dilation systems available in the NHS
Outcomes	The outcome measures to consider include: *Patient outcomes:* • Change in sinusitis symptoms (Sinus nasal outcome test [SNOT version 20 or 22] or sinusitis symptom inventory [RSI]) • Number of post-procedure sinusitis episodes requiring medication • Number of post-operative debridements • Change in ostial patency (assessment of sinus drainage pathway patency by endoscopy or CT scan) • Duration of analgesic medication • Patient-reported tolerance of the procedure and/or patient reported severity of pain scale • Number and types of sinus treated *Health care system outcomes:* • Length of hospital stay • Procedure time and theatre/outpatient treatment room time • Success rates of maxillary sinus ostial cannulation • Rate of revision surgery • Number of sinus-related follow-up appointments • Rate of readmission • Numbers and grade of staff required *Adverse effects* • Rate, and severity, of nasal bleeding • Device-related adverse events
Cost analysis	Comparator(s): Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be sufficiently long to reflect any differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different staff, treatment facilities (hospital theatre vs. day-case), and methods of anaesthetic are needed.

Special considerations, including issues related to equality	No equality issues have been identified. The XprESS MSDS may be a suitable alternative to FESS for patients who are unable or unwilling to tolerate general anaesthetic

5 The evidence

5.1 Summary of evidence of clinical benefit

The company conducted a literature search for evidence on XprESS and its predecessor device FinESS, through which it identified 11 published studies and 2 unpublished studies. The company did a meta-analysis of 6 of the 11 published studies (see pages 15 to 17 and pages 37 to 40 of the company's clinical submission).

The EAC judged the company's search terms to be appropriate, but could not fully reproduce them because the search strategies for the Cochrane database of systematic reviews were not fully reported. The EAC nevertheless reran the company's searches and conducted its own search, which identified no further evidence.

The EAC considered that 1 included study, Eloy et al. (2012), should be excluded from further assessment because the population (that is, patients who had previously had a failed frontal sinustomy) was not consistent with the scope. The EAC considered the 2 unpublished studies (FINESS registry study and Soler et al. 2016) to be technically within the scope but of very limited value, so did not consider them further. The EAC considered Brodner et al (2012) to be of limited relevance because it included both patients who had XprESS alone and patients who had a hybrid procedure involving FESS and XprESS, and results for the 2 groups could not be disaggregated. The EAC therefore assessed 12 publications, comprising 3 randomised clinical trials and 9 observational studies, 2 of which were unpublished.

Three studies reported on the REMODEL study (Cutler 2013, Bikhazi 2014, Chandra at al. 2016) a prospective, multicentre, non-inferiority, parallel randomised clinical trial (the methodology is most comprehensively reported in Cutler 2013). The trial compared FESS with balloon dilation systems (FinESS and XprESS) in adult patients with uncomplicated chronic sinusitis or recurrent acute sinusitis. The split between XprESS and FinESS was not reported in the papers but the company has indicated it was approximately 50:50. Patients and clinicians were blinded to their allocation. Blinding could not be maintained after treatment allocation, but some post-surgical assessments were done or audited by independent physicians. Following withdrawals after randomisation, there were 50 patients in the balloon arm and 42 in the FESS arm. A per-protocol analysis was done. The primary outcome measure was change in Sino-Nasal Outcome Test-20 (SNOT-20) scores at 6 months from baseline (pre-procedure).

Cutler (2013) reported outcomes up to 6 months after the procedure. At 1 week, the average change in SNOT-20 scores in the balloon arm was −1.49 (standard deviation [SD]±0.87), compared with −0.96 (SD±1.12) in the FESS arm. At 1 month, the average change was −1.70 (SD±0.98) for the balloon arm and −1.62 (SD±0.95) for FESS. At 6 months, the change was −1.67 (SD±1.10) for the balloon arm and −1.60 (SD±0.96) for FESS. The changes from baseline were significant ($p<0.001$) in both groups at all time points, and because the changes exceeded 0.8 the differences were judged to be clinically meaningful. With the exception of the results at 1 week ($p=0.014$), there was no statistically significant difference between the SNOT-20 scores in the balloon dilation and FESS arms. This indicated non-inferiority of the balloon procedures in terms of symptom improvement, with a potentially significant short-term effect (at 1 week). The authors also reported significant ($p<0.0001$) and clinically meaningful improvements in each of the subscales of the SNOT-20 at 6 months, with no statistically significant differences between the 2 arms. The same results were reported at 6 months for the subgroups that were considered: maxillary only or maxillary and anterior

ethmoid, presence or absence of accessory ostia, presence or absence of septal deviation, and sinusitis diagnosis (chronic or recurrent acute). In the balloon arm, 92.0% (46/50) of patients did not need a postoperative debridement compared with 26.2% (11/42) of patients in the FESS arm. There was a mean of 0.1±0.6 postoperative debridements per patient in the balloon arm compared with 1.2 ±1.0 in the FESS arm ($p<0.0001$). No statistically significant differences were found between balloon dilation and FESS in terms of post-discharge nausea and duration of over-the-counter pain medication. One patient in each arm had revision surgery.

Bikhazi (2014) described 12-month results for 89 of the 92 patients reported by Cutler (2013) who completed 1 year follow-up (48 balloon, 41 FESS). Changes in SNOT-20 scores from baseline remained significant (balloon arm: −1.64±1.06, FESS arm: −1.65±0.94; $p<0.0001$) and clinically meaningful in both groups, and confirmed non-inferiority at 12 months between the 2 interventions on this measure. In both arms patients reported significant reductions ($p<0.0001$) in sinusitis episodes at 12 months following surgery compared with the year before (4.2 in the balloon arm, 3.5 in the FESS arm), although the comparison was not significant. Overall patency (maximillary ostia) in those with an evaluable CT scan at 12 months was 96.7% in the balloon arm and 98.7% in the FESS arm but this was not statistically significant. Both treatments had positive effects in all the domains of the Work Productivity and Activity Impairment (WPAI) survey, except that FESS did not significantly improve the absenteeism domain ($p=0.169$).

Chandra et al. (2016) reported longer-term outcomes for patients from the original cohort who were not lost to follow-up, specifically at 18 months (n=66) and 24 months (n=25). The study also included an additional cohort of patients who had been subsequently randomised. This meant there was a total of 135 patients included at baseline, with results reported for 133 patients at 6 months and 130 patients at 12 months. Mean changes in SNOT-20 scores at 6 and 12 months were statistically significantly lower than baseline

and clinically meaningful in both arms in this enlarged cohort (6 months, balloon arm −1.56, FESS arm −1.60; 12 months, balloon arm −1.59, FESS arm −1.60). Mean changes in SNOT-20 scores were also significantly lower than baseline and clinically meaningful in the patients from the original cohort followed up at 24 months, balloon arm −1.65, FESS arm −1.45. There were no statistically significant differences between the 2 arms. Overall revision rates at 18 months were 2.7% in the balloon arm and 6.9% in the FESS arm; a non- statistically significant difference between the two arms.

The company and EAC identified a number of observational studies which compared balloon dilation (XprESS or FinESS) with baseline data. The EAC considered them to be of more limited relevance to the decision problem. Symptom improvement data from these studies were pooled in a meta-analysis reported in Chandra et al. (2016). The results from each study are reported in detail in the company's clinical submission (tables B7-24 to B7-30, pages 31 to 35) and were cross checked for accuracy by the EAC.

The XprESS Multi-Sinus Study (Gould et al. 2016) was a single-arm, prospective observational study. The study enrolled 82 adults with chronic sinusitis or acute recurrent sinusitis; the method of recruitment was not reported. Patients had to have maxillary sinus disease as a minimum, although patients with additionally affected sinuses (frontal, sphenoid or ethmoid) were also included. The study found a significant and clinically meaningful improvement in the primary outcome, change in mean SNOT-20 score at 12 months, compared with baseline (−1.57, $p<0.0001$). At 12 months there were also statistically significant reductions in RSI major symptoms score, medication use, absenteeism, and acute sinus infection and sinus-related physician visits. The authors reported that the procedure was a technical success in 307 of 313 sinuses operated on (98.1%), with only 1 patient needing revision at 12 months (1.3%), with no serious device or procedural adverse events. The procedure appeared to be well tolerated

(mean pain VAS 2.8±2.2) with a high degree of patient elicited satisfaction (87.8%).

The XprESS registry (Brodner et al. 2013) was the first full clinical study of the XprESS device. This was a single-arm, observational study that enrolled 175 patients needing treatment of the frontal recess and sphenoid sinus ostium, who had previously been scheduled for FESS. The primary outcome was safety, although effectiveness outcomes were also prespecified. Most (448 of 497) sinuses were treated using a hybrid procedure of FESS and XprESS (448/497); 31 had XprESS-only surgery, in 4 the balloon did not inflate, and in 10 the ostia could not be accessed using XprESS so FESS was used instead. Because these results were not disaggregated, they were not included in the Chandra (2016) meta-analysis. Results were similar to the other observational studies employing standalone balloon dilation only, including statistically significant reductions at 3 months in SNOT-20 score (−1.1), medication use, work or school days missed and sinus-related physician visits. There was no statistically significant reduction in acute sinus infections reported after the procedure, and no serious adverse events reported

The XprESS Maxillary Pilot Study (Gould et al. 2012) was a single-arm, prospective observational study involving 21 adult patients with uncomplicated refractory chronic sinusitis or recurrent acute sinusitis of the maxillary or anterior ethmoid sinuses. All patients had the XprESS procedure under local anaesthetic, and the main outcome was change in SNOT-20 score from pre-procedure to up to 6-months post-procedure. The study was not peer reviewed.

The RELIEF study (Levine et al. 2013) was a single-arm, prospective observational study involving 74 adult patients with refractory chronic sinusitis or recurrent acute sinusitis of the maxillary and anterior ethmoid sinuses. The primary outcome was quality of life as measured by SNOT-20; this and most other outcomes were reported at 12 months. All patients had the procedure with FinESS, the predecessor device to XprESS. There was a statistically

significant and clinically meaningful reduction in SNOT-20 score (−1.2) compared with baseline. Statistically significant reductions were also reported in RSI major symptoms, medication use (intranasal corticosteroids, antihistamines, antibiotics), absenteeism, sinus-related physician visits, and acute sinus infections. The procedure was reported as a technical success in 91.9% of sinuses operated on (124 of 135) with a revision surgery rate of 5.8% (4 of 69 patients). No serious adverse events were reported.

This BREATHE study was published in 3 papers: Stankiewicz (2011 and 2012) and Cutler (2011). This was the first published study of an Entellus balloon product (FinESS) involving 71 patients with chronic sinusitis of the maxillary or ethmoid sinuses. The study was a single-arm, prospective study. Follow-up was 2 years with the primary outcome of quality of life improvement measured using SNOT-20. There was a statistically significant and clinically meaningful improvement compared with baseline in SNOT-20 at 1 year (−1.80) and 2 year (−1.86) follow up. At 1 year there was also a statistically significant reduction in WPAI survey score and on the Work Limitation Questionnaire (WLQ) compared with baseline. The technical success rate was reported as 97.7% (129 of 132 sinuses). Procedures were well tolerated with a mean pain VAS of 2.7, and 88% of patients were reported to have recovered within 2 days. Patient satisfaction rates were 89% after 1 year and 91.5% after 2 years. After 2 years, 4 of 59 patients (6.8%) needed revision surgery. One patient was reported as having suffered a serious procedure-related adverse event following balloon dilation (subcutaneous emphysema).

The FinESS registry study was published as a protocol on ClinicalTrials.gov. However, it has not been subsequently published or peer reviewed, and was provided to the EAC in abstract form only. Because the EAC could not appraise this study, and only limited outcomes were reported, it did not consider it further. Data from the FinESS registry did contribute to the meta-analysis by Chandra et al. (2016).

Soler et al. (2016) is a single-arm, prospective observational study (n=50) expected to be published in 2016. It was provided to the EAC as an abstract that did not allow for critical appraisal, and only limited results were reported as academic in confidence. This was the only study that was reported in children. Although children were included the scope of the decision problem as a subgroup, the EAC understands through discussion with clinical experts that sinus surgery is rarely done in children in England. Because of this, the EAC did not consider the study any further.

Meta-analysis

Chandra et al. (2016) did a meta-analysis of the observational studies to compare their results on SNOT-20, RSI scores and short-term outcomes with those reported in the REMODEL study. These are reported in detail on pages 37 to 39 of the company's submission, and critiqued on pages 81 to 84 of the assessment report. The authors had access to individual patient data so the EAC could not replicate the meta-analyses. The authors reported that there was no statistical difference in SNOT-20 outcomes between studies (REMODEL FESS, REMODEL balloon dilation) or pooled observational studies), measured at 6, 12 and 24 months. There were significant reductions ($p<0.0001$) from baseline compared with 12 months in the standalone balloon studies in work/school missed due to nasal problems 5.0 days (± 9.5); homebound due to nasal problems 6.3 days (± 11.3); number of physician/nurse visits due to nasal problems 4.5 (± 11.5); number of infections of nose/sinuses 3.9 episodes (± 4.5); and number of antibiotic courses 2.9 (± 3.1).

Changes in WLQ score over 1 week, 1 month, 3 months, 6 months, 12 months, 18 months and 24 months compared with baseline were presented as a longitudinal graph. There were statistically significant and immediate reductions in several domains, which appeared maximal at 1 month before plateauing over 2 years.

Revision rates at 12 months were 1.7% for the FESS arm of the REMODEL trial, 1.4% for the balloon dilation arm of the REMODEL trial and 3.2% for the pooled analysis (p=0.628). However, this analysis was based on very low event numbers (a single patient in each of the REMODEL arms).

Adverse events

The company did a limited search for adverse events and identified 5 case reports of adverse events in a different balloon technology and 3 that did not specify which device was used (see page 36 of the company's clinical submission). The EAC searched the FDA MAUDE database for Entellus and identified 12 reports, of which 8 involved XprESS. Of the reports, 6 described cerebral spinal fluid leak in balloon-only procedures (n=2), balloon with septoplasty (n=2), or hybrid endoscopic sinus surgery (ESS) procedures (n=2). None noted any long-term adverse health effects as a consequence. One report was the case of orbital wall damage identified by the company in its clinical evidence submission, which was reported to have had no long-term adverse effect on the patient's vision. The eighth reported case was a death from massive intracranial bleed, shortly after successful completion of a bilateral maxillary balloon procedure. This was reported by the clinicians involved as unrelated to the device or procedure.

EAC conclusions on clinical evidence

The EAC considered the best evidence on the technology to be the papers arising from the REMODEL trial. This study design was assessed as being of high methodological quality, and internal validity was generally good. However, the EAC noted concerns about the high initial attrition rates in the FESS arm immediately following randomisation, and the subsequent need for per-protocol rather than intention-to-treat analysis. The EAC was satisfied that the evidence showed balloon dilation to be non-inferior to FESS in terms of the primary outcome (SNOT-20) for up to 2 years post-procedure. The EAC also judged that the evidence demonstrated that balloon dilation was equivalent to FESS over this time frame in terms of the secondary outcomes

measured, such as maintaining ostia patency, reducing future episodes of sinusitis, and improving work and productivity. However, it noted that long-term outcomes were based on small patient numbers. The EAC considered that there was evidence that balloon dilation with XprESS offers advantages over conventional FESS by speeding recovery, reducing post-operative pain and reducing the need for nasal debridement.

The observational studies supplemented the evidence from REMODEL and were supportive of its results. However, the EAC noted a number of methodological weaknesses in all the observational studies which led it to consider all the evidence from these studies to be of limited use to the decision problem. Although the studies matched the scope, the EAC was concerned about generalising the results from selected patients enrolled in trials in the US to the general population in the NHS. The EAC assumed equivalence between the FinESS and XprESS systems but considered there was only weak, indirect evidence to substantiate this assumption.

Table 2: Literature identified by the EAC

Abbreviations used RSI = Rhinosinusitis symptom inventory; FESS- Functional endoscopic sinus surgery; SNOT= sinus nasal outcome test; CRS= Chronic sinusitis; RARS= recurrent acute sinusitis; MSDS= multi-sinus dilation system					
Study	Study design (country)	Population	Intervention (I) versus comparator (C)	Outcomes considered	EAC comments on study
Full, peer-reviewed articles					
REMODEL study: Cutler et al. (2013) Bikhazi et al. (2014) Chandra et al. (2016)	Prospective, multi-centre, non-inferiority, parallel RCT (USA)	Adult patients with CRS or RARS Maxillary and/or anterior ethmoid sinuses.	I: Standalone XprESS or FinESS balloon dilation Data not disaggregated but reported by company to be proportionately equal. C: FESS	Changes in SNOT-20 (primary) Debridement frequency Technical success Nasal bleeding Recovery time Analgesic use Ostia patency Activity impairment, work impairment, productivity loss Patient satisfaction Revision rate Safety (adverse events)	KEY STUDY REMODEL RCT was the only comparative study and is therefore considered the key source of evidence. Patient recruitment was increased in the paper by Chandra et al. (2016) meaning results from individual published papers differ. This paper also reported a meta-analysis
Gould et al. (2014)	Observational (USA)	Adult patients with CRS or RARS All patients had maxillary sinus disease as minimum. Some patients with frontal, sphenoid, and/or ethmoid	I: Standalone XprESS balloon dilation C: None (baseline)	Changes in SNOT-20 (primary) Sinusitis symptom inventory (RSI) score Medication use Productivity/reinfection Revision rate Subject satisfaction Safety (adverse events)	USEFUL STUDY This was the only study that investigated the use of standalone XprESS MSDS in multiple sinuses (including the frontal and sphenoid sinuses)

Abbreviations used RSI = Rhinosinusitis symptom inventory; FESS- Functional endoscopic sinus surgery; SNOT= sinus nasal outcome test; CRS= Chronic sinusitis; RARS= recurrent acute sinusitis; MSDS= multi-sinus dilation system					
Study	Study design (country)	Population	Intervention (I) versus comparator (C)	Outcomes considered	EAC comments on study
		disease			
XprESS registry Brodner et al. (2013)	Observational (USA)	Adult patients with CRS Primarily patients treated for frontal sinus disease. Smaller numbers of patients treated sphenoid and maxillary disease	I: Standalone XprESS balloon dilation Hybrid surgery using XprESS MSDS C: None (baseline)	Changes in SNOT-20 (primary) Patency Medication use Productivity/reinfection Revision rate Serious adverse effects	VERY LIMITED USE Not possible to disaggregate patients receiving standalone or hybrid treatment. Excluded from meta-analysis
XprESS Maxillary Pilot Study Gould et al. (2012)	Observational (USA)	Adult patients with CRS or RARS Maxillary sinus (all) Anterior ethmoid sinus (some)	I: Standalone XprESS balloon dilation C: None (baseline)	Changes in SNOT-20 (primary) Technical success Medication use Recovery time Revision rate Serious adverse effects	LIMITED USE Small case series published in white paper (not peer reviewed)
RELIEF study Levine et	Observational (USA)	Adult patients with CRS or RARS	I: Standalone FinESS balloon dilation C: None (baseline)	Changes in SNOT-20 (primary) Technical success	LIMITED USE XprESS MSDS not used. Patients excluded if they had

Abbreviations used RSI = Rhinosinusitis symptom inventory; FESS- Functional endoscopic sinus surgery; SNOT= sinus nasal outcome test; CRS= Chronic sinusitis; RARS= recurrent acute sinusitis; MSDS= multi-sinus dilation system					
Study	Study design (country)	Population	Intervention (I) versus comparator (C)	Outcomes considered	EAC comments on study
al. (2013)		Maxillary and anterior ethmoid disease.		Tolerance Debridements RSI Medication use Productivity/reinfection Revision rate Serious adverse effects	any other sinuses affected.
BREATHE study: Cutler et al. (2011) Stankiewicz et al. (2011 and 2012)	Observational (USA)	Adult patients with CRS Maxillary sinus	I: Standalone FinESS balloon dilation C: None (baseline)	Changes in SNOT-20 Technical success Recovery time Revision rate Work Limitation Questionnaire (WLQ) Work Productivity and Activity Impairment (WPAI) Subject satisfaction Serious adverse effects	LIMITED USE Patients were excluded if they had disease of the frontal, posterior ethmoid, or sphenoid sinuses
Abstracts					
FinESS registry	Observational (USA)	Adults with CRS Maxillary and ethmoid sinuses	I: Standalone FinESS balloon dilation C: None (baseline)	Change in SNOT-20 Technical success Productivity/reinfection RSI score Revision rate Serious adverse effects	VERY LIMITED USE Unpublished abstract Data used in meta-analysis
Soler et al. (2016)	Observational (USA)	Paediatric patients with	I: Standalone XprESS balloon dilation	Change in SNOT-22 Technical success	VERY LIMITED USE Unpublished abstract

Abbreviations used RSI = Rhinosinusitis symptom inventory; FESS- Functional endoscopic sinus surgery; SNOT= sinus nasal outcome test; CRS= Chronic sinusitis; RARS= recurrent acute sinusitis; MSDS= multi-sinus dilation system					
Study	Study design (country)	Population	Intervention (I) versus comparator (C)	Outcomes considered	EAC comments on study
		CRS (2 to 21 years)	C: None (baseline)	RSI Change in SN-5 (Sinus and Nasal Quality of Life Survey	Only evidence reported in children, unknown generalisability

5.2 Summary of economic evidence

The company conducted a search of the health economics literature on balloon sinus dilation using XprESS or equivalent systems, and FESS. This identified 134 articles, 6 of which were included in the company's economic analysis (see pages 7 to 14 of the company's economic submission).

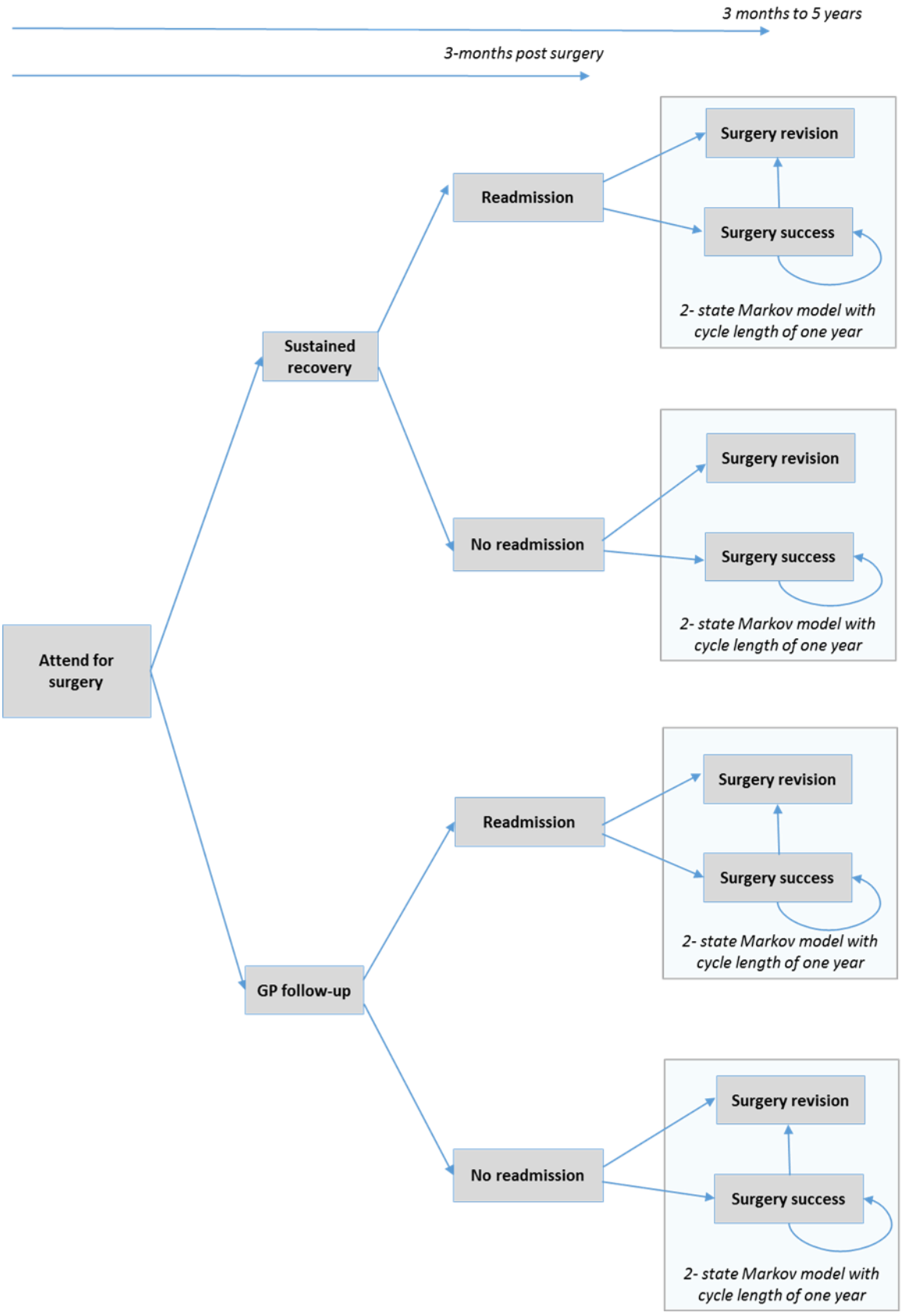
The EAC judged the company's search terms to be appropriate. However, it noted inconsistencies in the search terms across the databases searched; that the company's submissions did not provide search terms for its searches of the Cochrane database or the NHS Economic Evaluation Database; and that the company's searches would have benefited from the inclusion of a wider range of databases, such as the cost-effectiveness registry.

The EAC reran the company's searches where details were provided, and conducted additional searches. The EAC concluded that none of the economic studies identified by the company was relevant to the decision problem, and identified no additional relevant studies

De novo analysis

The company presented a decision tree model to capture costs and outcomes in the first year following sinus surgery and a Markov model to capture costs and outcomes out to 5 years after sinus surgery, applying a 1-year cycle length (see figure 1).

Figure 1 Structure of the company's economic model


3 months to 5 years
3-months post surgery
Attend for surgery
Sustained recovery
GP follow-up
Readmission
No readmission
Readmission
No readmission
Surgery revision
Surgery success
2- state Markov model with cycle length of one year
Surgery revision
Surgery success
2- state Markov model with cycle length of one year
Surgery revision
Surgery success
2- state Markov model with cycle length of one year
Surgery revision
Surgery success
2- state Markov model with cycle length of one year

Model parameters

Patients entered the model needing sinus surgery, and could be routed to either FESS or XprESS. The model base case used a theoretical patient who needed an average of 2.75 sinuses to be treated in 1 episode of care. The first phase of the decision tree captures differences in treatment costs. The next stage covers the first 3 months following surgery, during which patients either have a sustained recovery or need 1 or more GP visits, and in both scenarios could require a re-admission into secondary care. Surgical re-interventions and GP visits are also included from 3 months to 12 months. Irrespective of those outcomes, patients then enter a Markov model to capture outcomes out to 5 years using yearly cycle lengths. The Markov model consists of 2 mutually exclusive states, surgery revision or sustained recovery. Surgery revision is an absorbent state, meaning that patients cannot leave it, so it is assumed that patients could have only 1 revision surgery over the study period. Death, a common absorbent state in Markov models, is not included because it was expected to be a very rare outcome over the time horizon modelled.

Figures for clinical parameters were attained from public literature, expert opinion and UK audit data. The company relied heavily on UK audit data published by Brown et al. (2003) to determine the base values for FESS. It then used US data reported in Chandra et al. (2016) to determine the relative values for XprESS in relation to FESS.

Table 3: Clinical parameters used in the company's model

Variable	Base case value	Source
Probability of GP referral in first 3 months	XprESS = 0.24 FESS = 0.42	UK audit data, Brown (2003) on probability of a GP visits 3 months post-surgery with FESS and Chandra (2016) relative risk of nose bleed of XprESS compared with FESS (0.57).
Rate of GP visits in first 3 months	1.861	UK Audit (Brown 2003) Calculated based on the proportion reported to attend the GP,1 to 3 or more times within 3 months of chronic

		sinusitis surgery
Probability of readmission (in first 3 months)	XprESS = 0.023 FESS= 0.041	Brown (2003) probability of readmission within 3 month of FESS surgery and Chandra (2016) relative risk of nose bleed with XprESS
Monthly probability of GP visits in 5 years following surgery	XprESS = 0.10 FESS=0.12	Brown (2003) monthly rate of GP visits beyond 3 months for FESS and Chandra (2016) % difference in chronic sinusitis rates between FESS and XprESS
Revision surgery up to 12 months	XprESS = 3.6% FESS = 4.1%	Brown (2003) 1 year data on FESS, Chandra (2016) relative risk of revision
Revision surgery> 12 months	XprESS = 2.5% FESS = 2.9%	Brown (2003) 5 year follow up data on FESS, Chandra (2016) relative risk of revision
Proportion under local anaesthetic:	XprESS, 0% base, 2% scenario analysis FESS, 0% base, 60% scenario analysis	Expert advice

Costs and resource use

Sources used in calculating costs are provided in various tables on pages 43 to 49 of the company's submission.

The cost for FESS and XprESS surgery under general anaesthetic was based on staff costs for a nurse and surgeon, bed day costs, theatre time, device and surgical consumable costs. The total cost for a FESS surgery under general anaesthetic (including equipment costs of £300) was calculated to be £2,894. The total cost for XprESS surgery (including equipment costs of £900) was calculated to be £1,884. The equivalent costs under local anaesthetic were calculated by applying a ratio of 0.631 to the surgical costs under general anaesthetic reported in Zilvetti et al. (2009), providing costs for FESS of £2,536 and for XprESS of £,1524. These costs were also used in the model if the patient had a revision surgery.

Table 4: Costs used in the company's model

Variable	Cost	Source
Theatre time (per minute)	£20	NHS Institute for Innovation and Improvement (III, 2009)
Surgeon time (per minute)	£1.77	PSSRU 2015 (Curtis, 2015)
Nurse time (per minute)	£1.47	PSSRU 2015 (Curtis, 2015)
Unit cost of drapes and gowns per surgery:	£80	Cost of a drape and gown for a surgeon and nurse at £40 each (Medisave.co.uk)
Unit cost of tray /camera per surgery	£35	NHS Institute for Innovation and Improvement (III, 2009)
Hospital bed day cost	£400	Deltex Medical (2006)
XprESS equipment costs	£900	Company – Internal market data
FESS equipment costs	£300	Company – Internal market data
Costs of a readmission	£601	NHS Reference cost CZ12V – Minor Nose Procedures, 19 years and over with CC (2011/12)
GP visit	£94.43	PSSRU 2015, BNF (2016), Expert opinion.
Procedure Time (minutes)	XprESS = 30 FESS = 90	Expert opinion
Average length of stay in hospital (days)	XprESS = 0.43 FESS = 0.97	HES data (HSCIC)
Pain medication (days)	XprESS = 1 FESS = 2.8	REMODEL study
Cost of pain medication	£0.13	PSSRU 2015, BNF 2016

Results

The company reported a base-case per-patient cost of £2,679 for XprESS and £3,981 for FESS, representing an average saving of £1,302 per patient.

The company presented one-way deterministic sensitivity analyses varying the model parameters from their base-case level by 20%. The parameters with the biggest effect on the level of cost saving were equipment costs and procedure time for XprESS. The results of these analyses provided a range of cost savings, from £1,044 to £1,559.

Scenario analyses were done by changing parameter values to those reported in other sources. The parameters that were changed were type of anaesthetic

(from general only to include local), percentage with revisions each year, procedure time, length of hospital stay, percentage under local anaesthetic, and unit cost of theatre time (see pages 67 to 70 of the company's economic submission). None of these altered the direction of the cost saving for XprESS, and at worse reduced it to £367, when a unit cost for theatre time of £6.40 per minute was used.

Break-even analyses were conducted varying the procedure time with XprESS and FESS. The company reported that XprESS was cost neutral when the procedure time with XprESS was 80 minutes or cost saving when the procedure time with FESS was above 41 minutes

EAC critique of the company's model

The EAC noted the assumptions in the company's model and considered them to be largely appropriate, despite none of the included studies being relevant to the decision problem. It did note some important omissions in the model tornado diagram, such as the unit cost of a FESS procedure. The EAC was also unable to replicate results in the tornado diagram for the monthly rate of GP visits beyond 3 months with FESS. The EAC considered the company's analyses of the structural uncertainties to be limited. It judged that it would have been appropriate to run the model assuming that there was no difference in GP visits and readmission in the first 3 months following surgery, given that it was assumed that nasal bleeding at discharge was an indicator of each of these events.

EAC revisions to the company's model

The EAC made changes to a number of the clinical and cost parameters used in the company's model (see table 5).

Table 5 EAC revisions to the company's model, adapted from Table 4.16 in the assessment report

Variable	Company input	EAC input
Cost of procedure: FESS (general anaesthetic)	£2,594	£657
Cost of procedure: XprESS (general anaesthetic)	£984	£428
Cost of procedure: FESS (local anaesthetic)	£1,636	£456
Cost of procedure: XprESS (local anaesthetic)	£620	£466
Cost of training on XprESS	£0	£5.50
Proportion under local anaesthetic: FESS	0.0%	2.0%
Proportion under local anaesthetic: XprESS	0.0%	10%
Cost of GP visit	£95	£46
Cost of readmission	£601	£902
Revision surgery up to 12 months: FESS	4.1%	1.7%
Revision surgery up to 12 months: XprESS	3.6%	1.4%
Revision surgery between 12 months and 5 years: FESS	2.9%	1.0%
Revision surgery between 12 months and 5 years: XprESS	2.5%	1.0%
Cost of revision surgery: FESS	£2,594	£653
Cost of revision surgery: XprESS	£984	£432

The EAC revised the company's relative risk estimates for revision surgery, based on their limited numbers in the REMODEL study. It consulted experts and considered published evidence. It judged the estimates for the values up to 12 months provided in the REMODEL trial to be more appropriate. Based on expert opinion and Philpott et al. (2015), the EAC considered that the evidence did not show any difference in revision surgery rates between FESS and XprESS beyond 12 months.

Based on expert opinion, the EAC judged the company's base-case estimate of 0% for the proportion of XprESS procedures done under local anaesthetic to be conservative, and revised it to 10%. It also revised the estimate for FESS procedures done under local anaesthetic to 2%, noting that this was consistent with the company's scenario analysis.

The EAC conducted a bottom-up approach to determine the costs of FESS and XprESS surgery. In the absence of published data, the EAC consulted experts to determine the duration of surgery for FESS in the patient population eligible for XprESS. Based on the average of their responses the EAC

estimated procedure times for FESS of 42.5 minutes and for XprESS of 26.7 minutes. The figure for FESS was consistent with figures quoted in a national audit and a health technology assessment report. The EAC revised the cost of operating time to £13.65 per minute based on hourly data for ENT surgery (2014/15) as reported by the Information Services Division Scotland. It also revised the length of stay in hospital following FESS to under 5 hours (0.208 days), and for XprESS to 4.17 hours (0.174 days) based on expert responses. The EAC revised the cost per day in hospital to £370 using a weighted average of 2014/15 NHS reference costs for elective inpatient excess bed days for minor sinus procedures (CA29Z), intermediate sinus procedures (CA28Z), major sinus procedures (CA23Z) and complex sinus procedures (CA26Z). Based on these figures the EAC revised the cost of FESS under general anaesthetic to £657, and the cost of XprESS under general anaesthetic to £428 (see pages 124 to 126 of the assessment report). None of these figures includes equipment costs.

The EAC also revised the cost of FESS and XprESS under local anaesthetic using the same bottom-up approach. Using averages based on expert advice, it estimated procedure lengths of 30 minutes for FESS and 31.7 minutes for XprESS, and stay in hospital of 3.00 hours for FESS and 2.17 hours for XprESS. Information Services Division Scotland operating theatre costs of £13.65 a minute were used to calculate operation costs. The hospital bed cost of FESS was calculated using the same methodology.

The EAC revised the cost of revision surgery for FESS and XprESS, using weighted averages for procedures done under local and general anaesthesia. Using the cost per procedure figures, the cost of revision surgery with FESS was calculated by applying a 98% weighting for general anaesthetic and 2% weighting for local anaesthetic. The weightings applied for XprESS were 90% general anaesthetic and 10% local anaesthetic. This provided a cost per revision surgery for FESS of £653 and for XprESS of £432.

The EAC revised the cost of a GP visit based on expert advice, the British National Formulary and data from the Personal Social Services Research Unit. It used a value of £37 for a GP visit, and added drug prescription costs which differed according to the type of visit to calculate a value for a GP visit involving a blocked nose (£48.91), infection (£38.97 to £39.64), and blocked nose and infection (£50.00), taking the mean value of these figures to produce an estimate of £46.00.

The company did not include any training costs for XprESS because the company provides training at no extra cost, but the EAC judged that the costs for the staff time spent on training should be included in the model. It concluded that this amounted to 7 hours of a surgeon time at a cost of £106 an hour, £742 per surgeon. Over the duration of the economic model this was estimated to add £5.50 to the cost of each procedure.

The EAC conducted a bottom up costing for unit cost of an XprESS in an office setting. Based on responses from experts it used a length of a procedure in an office setting of 31.7 minutes, and a length of stay in hospital of 2.17 hours. It used NHS reference costs of £370 for a hospital bed day, PSSRU for the costs of surgeon time and a nurse time, and applied £115 for the costs of gown and a tray to produce an estimate of £251.

Results from the EAC's revisions to the model

The EAC's base-case analysis found that XprESS was cost incurring by £330 compared with FESS (average per-patient costs: XprESS £1,694, FESS £1,364). The EAC conducted univariate analyses on all the model parameters, varying their value by 20% (see figure 4.6, page 149 of the assessment report). None of the analyses changed the direction of the results, and XprESS remained cost incurring. The key drivers were the equipment cost of XprESS and the unit costs of a FESS and XprESS procedure under general anaesthetic. This was consistent with the company's analysis.

The EAC conducted a series of univariate sensitivity analyses on the main model parameters (see pages 152 to 164 of the assessment report). Sensitivity analysis on the length of FESS procedure done under general anaesthetic demonstrated that XprESS became cost saving when the duration of FESS exceeded 66.0 minutes, compared with the EAC base case of 42.5 minutes. Analysis on the length of stay in hospital after FESS found that XprESS became cost saving when hospital stay was longer than 1 day. Further analyses showed that length of XprESS procedure done under general anaesthetic had to be as low as 0 before XprESS became cost saving, and that no value for length of stay in hospital after XprESS under general anaesthetic changed the direction of the result. Analysis on the unit cost of theatre time demonstrated that XprESS became cost incurring when the unit cost exceeded £34 per minute (£2,040 per hour). Varying the unit cost of hospital stay had very little effect on the results, and the cost would have to reach an unreasonably high level for XprESS to become cost saving.

The EAC did a number of scenario analyses (see pages 157 to 171 of the assessment report). In the first of these, the EAC used hospital episode statistics data on length of stay, as per the company's model. In this scenario XprESS remained cost incurring but by a smaller magnitude of £136 per patient. The EAC considered a scenario in which XprESS was done in an office setting, so there were no theatre costs. This provided a total procedure cost of £251 (see table 4.20, page 158 of the assessment report). The proportion of procedures done in an office setting using local anaesthetic was varied between 0% and 100%, and the results showed that XprESS remained cost incurring even at 100%. The EAC also conducted scenario analyses in which:

- it used a cost ratio of 0.631 between general and local anaesthetic (as used in the company's submission)
- it used an annual revision rate of 3.5% between years 2 and 5, based on figures reported by Hopkins et al. (2009)

- the cost of a hospital appointment for debridement of £162 (NHS reference cost, 2014/15) was added to each FESS procedure
- It used a consistent proportion of 42% for patients visiting the GP in the first 90 days after the procedure for both treatments
- it varied the rate of revision surgery for XprESS at 2 to 5 years after surgery.

In all cases, XprESS remained cost incurring. The EAC considered a scenario that included an additional appointment for debridement after FESS, and in which the rate of XprESS procedures done in an office setting using local anaesthetic was varied. In this scenario, XprESS was cost saving when over 80% of procedures were done in an office setting under local anaesthetic and only assuming that every FESS procedure requires an additional hospital appointment for debridement (see figure 4.14, page 163 of the assessment report).

6 Ongoing research

The company identified 1 ongoing study, Soler et al. (2016), which was reported in abstract form in section 7.2 of the company's submission. The EAC's searches identified no other ongoing studies.

7 Issues for consideration by the Committee

Clinical evidence

Applicability of the evidence to the decision problem

All of the published evidence was from the US. With the exception of the REMODEL trial, the EAC judged the evidence on XprESS to have methodological, reproducibility and applicability issues that limited their usefulness to the decision problem.

The EAC considered that the REMODEL trial had shown XprESS to be equivalent to FESS in an array of outcomes and offered advantages in terms of speeding recovery, reducing post-operative pain and bleeding and reducing the need for debridement.

There remained some uncertainty over several clinical parameters which were important to the cost case:

- The importance of post-operative debridement after FESS. Post-operative debridement was common in the US REMODEL trial but most experts said it was not routine in UK NHS practice.
- The lack of data on patients with nasal polyps, which experts state can be present in UK patients who would be considered for FESS.
- Uncertainty in follow-up procedures, including the need for debridement, GP visits and the need for revision surgery.

Cost evidence

Economic evidence for the use of balloon dilation

The EAC and the company agreed that there were no relevant published economic studies and the cost evidence relied on the de novo model. There were a number of important parameters in the model that were subject to uncertainty and relied on differing expert opinion:

- Length of a FESS procedure (under general anaesthetic): experts consulted by the EAC produced a different estimate for the length of a FESS procedure (42.5 minutes) compared with the company (90 minutes). The EAC's scenario analyses found that XprESS became cost saving when a FESS procedure took longer than 66 minutes.
- The cost of theatre time: there was uncertainty in which factors were included in different estimates used for the cost of theatre time. There were large variations in the company's and the EAC's estimates.

- The plausibility of the cost-saving scenario for XprESS: XprESS is only cost saving when over 80% of procedures are done in an office setting under local anaesthetic and only assuming that every FESS procedure requires an additional hospital appointment for debridement. This scenario may not be representative of current NHS practice.
- The cost of the device: the cost of the XprESS device was a dominant factor in the cost model. It is not clear if discounts or price variation are available in the NHS.

8 Authors

Neil Hewitt, Technical Analyst

Paul Dimmock, Technical analyst (evaluations)

NICE Medical Technologies Evaluation Programme

May 2016

Appendix A: Sources of evidence considered in the preparation of the overview

A Details of assessment report:

- Jenks M, Willits I, EatonTurner E, The XprESS Multi-Sinus Dilation System for the treatment of chronic rhinosinusitis, April 2016

B Submissions from the following sponsors:

- Entellus Medical

C Related NICE guidance

- Respiratory tract infections – antibiotic prescribing: Prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care. (2008) NICE guideline CG69
- Balloon catheter dilation of paranasal sinus ostia for chronic sinusitis. (2008) NICE interventional procedures guidance 273
- Powered microdebrider turbinoplasty for inferior turbinate hypertrophy (2014) NICE interventional procedures guidance 498
- Radiofrequency tissue reduction for turbinate hypertrophy (2014) NICE interventional procedures guidance 495
- Insertion of customised titanium implants, with soft tissue cover, for orofacial reconstruction (2013) NICE interventional procedures guidance 449
- Suction diathermy adenoidectomy (2009) NICE interventional procedures guidance 328
- Ear, nose and throat conditions overview (2015) NICE pathway
- NICE clinical knowledge summary (2013) Sinusitis

D References

Bikhazi N, Light J, Truitt T, et al. (2014) Standalone balloon dilation versus sinus surgery for chronic rhinosinusitis: a prospective, multicenter, randomized, controlled trial with 1-year follow-up, Am J Rhinol Allergy; 28(4):323-9

Brodner D, Nachlas N, et al. (2013). Safety and outcomes following hybrid balloon and balloon-only procedures using a multifunction, multisinus balloon dilation tool. Int Forum Allergy Rhinol.; 3(8):652-8. doi: 10.1002/alr.21156. Epub 2013 Feb 19.

Chandra R, Kern R, Cutler J, et al. (2015) REMODEL Larger Cohort With Long-term Outcomes and Meta-Analysis of Standalone Balloon Dilation Studies. The Laryngoscope; 126(1):44-50

Cutler J, Bikhazi N, Light J, et al. (2013) Standalone balloon dilation versus sinus surgery for chronic rhinosinusitis: a prospective, multicenter, randomized, controlled trial. Am J Rhinol Allergy;27(5):416-22

Gould J; Alexander I; Tomkin E, et al., (2014) In-office, multisinus balloon dilation: 1-Year outcomes from a prospective, multicenter, open label trial; American Journal of Rhinology & Allergy, Volume 28, Number 2, pp. 156-163

Cutler J, Truitt T, Atkins J, et al. (2011) First clinic experience: patient selection and outcomes for ostial dilation for chronic rhinosinusitis. Int Forum Allergy Rhinol;1(6):460-5.

Stankiewicz J, Tami T, Truitt T, Atkins J, Winegar B, Cink P, et al. Impact of chronic rhinosinusitis on work productivity through one-year follow-up after balloon dilation of the ethmoid infundibulum. Int Forum Allergy Rhinol. 2011;1(1):38-45

Stankiewicz J, Truitt T, Atkins J, et al. (2012) Two-year results: transantral balloon dilation of the ethmoid infundibulum. Int Forum Allergy Rhinol. 2012;2(3):199-206.

Browne J, Hopkins C, Slack R, et al. (2003) The National Comparative Audit of Surgery for Nasal Polposis and Chronic Rhinosinusitis. London: Clinical Effectiveness Unit, Royal College of Surgeons of England; 2003. [cited 2016 4th April]. Available from: https://www.rcseng.ac.uk/surgeons/research/surgical-research/docs/the-national-comparative-audit-of-surgery-for-nasal-polyposis-and-chronic-rhinosinusitis.

Philpott C, Hopkins C, Erskine S. The burden of revision sinonasal surgery in the UK—data from the Chronic Rhinosinusitis Epidemiology Study (CRES): a cross-sectional study. BMJ Open. 2016;5(:e006680)

ISD Scotland. Theatres: Costs - detailed tables. 2015. Available from: http://www.isdscotland.org/Health-Topics/Finance/Costs/Detailed-Tables/Theatres.asp.

Appendix B: Comments from professional bodies

Expert advice was sought from experts who have been nominated or ratified by their Specialist Society, Royal College or Professional Body. The advice received is their individual opinion and does not represent the view of the society.

Mr Andrew Swift
Consultant ENT Surgeon and Rhinologist, British Rhinological Society

Mr Paul Chatrah
Consultant ENT surgeon, British Association of Otorhinolaryngologists, Head and Neck Surgeons (ENT UK)

Professor Valerie Lund
Professor of Rhinology, British Association of Otorhinolaryngologists, Head and Neck Surgeons (ENT UK)

Mr Carl Philpott
Consultant ENT Surgeon and Rhinologist, British Association of Otorhinolaryngologists, Head and Neck Surgeons (ENT UK)

Dr Hesham Saleh
Consultant Rhinologist and Facial Plastic Surgeon, British Society for Allergy & Clinical Immunology

Mr Rajiv Bhalla Consultant
ENT Surgeon and Rhinologist, British Rhinological Society

Mr Atef El Kholy
Consultant ENT Surgeon, British Association of Otorhinolaryngologists, Head and Neck Surgeons (ENT UK)

- Four of the expert advisers had direct involvement with the technology. Two had experience of using similar technologies, one of which manages patients on whom it is used in another part of their care pathway. The remaining expert indicated that they would like to use it but it is not currently available to them
- Four experts described XprESS as a minor variation on existing technologies, with little potential for impact, but one of these considered it to be a significant modification when considered from the context of surgical teams, as it is easier for the nurse assistants. Two experts described it as a significant modification of an existing technology, one of which expanded on their response and identified a finer balloon, re-shapeable tip, and the ability to treat multiple sinuses with a signal balloon, as the factors that made it so. The remaining expert did not consider it to be a minor variation but did not specify whether they considered it a significant modification or thoroughly novel.
- Five of the experts identified chronic sinusitis as the most appropriate indication for use. Acute frontal sinusitis and recurrent acute sinusitis was identified by the remaining experts, and acute sinusitis and/or acute recurrent sinusitis was identified by a further three experts. One expert was of the opinion that while the technology was advertised for use in the sphenoid and maxillary sinuses, there is rarely a need for these indications
- FESS was identified as a comparator by all bar one of the experts. The remaining expert identified navigated balloon technology (Medtronic). One expert also identified medical therapy alone and competing balloon dilation as an appropriate comparator
- A number of competing systems were identified produced by companies including Medtronic and Smith and Nephew. Acclarent was identified as a long standing comparator; however two experts note that Acclarent is being withdrawn from the UK
- Shorter procedures that can be undertaken ‘in office’ under local anaesthetic, by non-subspecialist ENT surgeons, with less trauma to the

patient, and a quicker recovery, were identified as possible benefits to patients from the use of this technology

- The possible benefits were similar to those cited for patients: fewer hospital admissions and reduced surgery time, arising from the potential to undertake the procedure ‘in office’ using local anaesthetic. The potential to reduce the waiting list for surgery was also identified
- One expert identified a dedicated outpatient clinic with nursing assistance as a necessary facility needed for the effective use of this technology, but generally these were considered to be minimal
- Five experts were of the opinion that specialist training would be required. The remaining two felt that training requirements would be minimal for those with experience of balloon sinuplasty systems or endoscopic interventions
- Controversies in the current pathway were identified but not always detailed. One expert noted that the technology is unlikely to replace the need for FESS, and that its effectiveness and place in the management of chronic sinusitis is unknown. A further expert noted a lack of confidence in balloon dilation among some surgeons
- All of the experts were of the opinion that NICE guidance could be useful, however 3 had caveats
- One was of the opinion that it should be considered as a further sinus tool, rather than a distinct procedure if guidance were developed. A second expert considered that for guidance to be useful it should look at patients with mild to moderate sinusitis. A third expressed reservations and considered that the support for similar technology in IPG273, was set against a backdrop of aggressive marketing by the company concerned

Appendix C: Comments from patient organisations

The following patient organisations were contacted and no response was received

- Action Against Allergy (AAA)
- Allergy Alliance
- Allergy UK
- Asthma Relief Charity
- Asthma UK
- Asthma, Allergy and Inflammation Research Trust
- British Lung Foundation
- Fungal Infection Trust

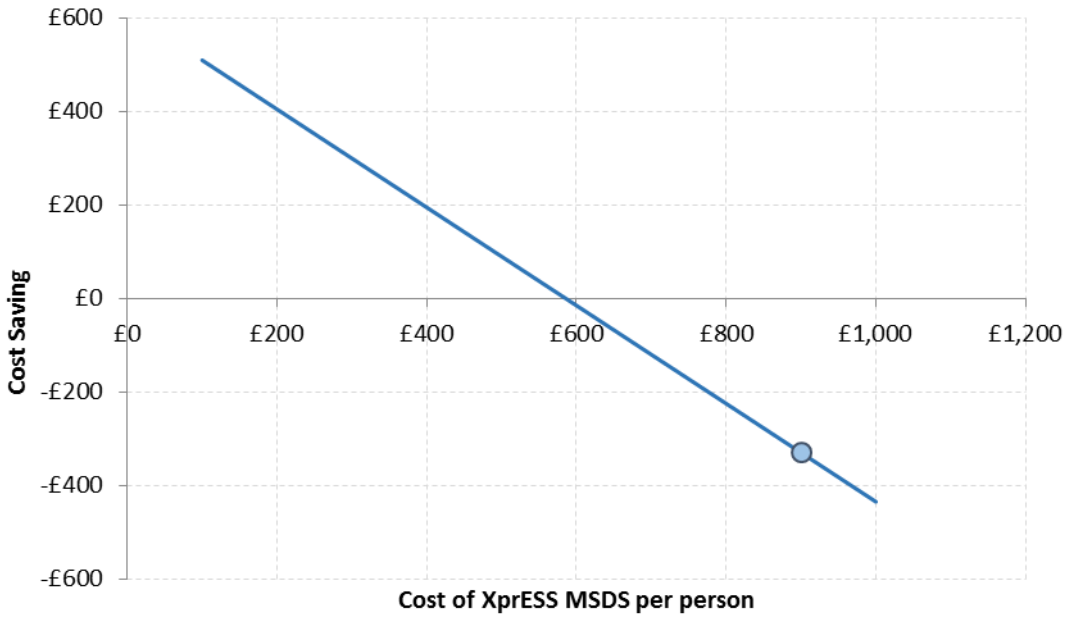
Appendix D: Additional analyses carried out by the External Assessment Centre

Following submission of the External Assessment Centre (EAC) assessment report NICE requested that the EAC conduct further sensitivity analyses around the cost of the XprESS Multi-Sinus Dilation System (MSDS) and the cost of comparator technologies. The analyses conducted are described in the subsequent sections of this document.

1. Price of XprESS MSDS

The EAC were asked to determine the price at which XprESS MSDS becomes cost saving. Univariate deterministic sensitivity analysis was conducted around the price of XprESS MSDS as shown in Figure 1.1. The device is currently priced at £900 per person. In order for XprESS MSDS to generate cost savings, it must be priced at less than £586 per person.

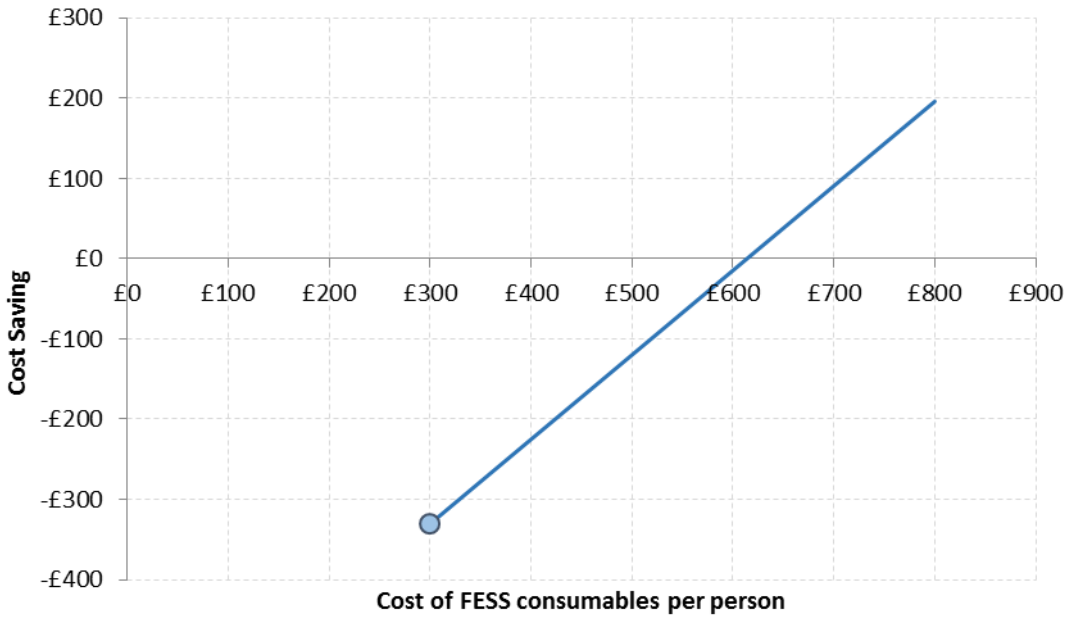
Figure 1.1: Univariate sensitivity analysis around the cost of XprESS MSDS per person



2. Price of functional endoscopic sinus surgery (FESS) consumables

The EAC were also asked to undertake sensitivity analysis around the cost of consumables used during FESS. The analysis conducted is displayed in Figure 2.1. In order for XprESS MSDS to be cost saving, the consumables must cost more than £614 per person (compared with £300 per person in the base case).

Figure 2.1: Univariate sensitivity analysis around the cost of FESS consumables per person



3. Two-way sensitivity analysis around the price of XprESS MSDS and the duration of the procedure

Within the EAC's assessment report the duration of FESS surgery under general anaesthetic was identified as a key driver of the analysis. The EAC's best estimate of this input of 42.5 minutes was based on expert advice whereby the experts were explicitly asked to provide an estimation of the duration of FESS in patients who would be eligible for treatment with XprESS MSDS. The EAC's best estimate did not reconcile with the company's input of 90 minutes; also based upon expert advice. Within the assessment report the EAC identified 66 minutes as the value over which XprESS MSDS generates cost savings. Two-way sensitivity analysis has been conducted whereby the price of XprESS MSDS and the duration of FESS surgery have been varied simultaneously. This analysis has been carried out in case of use

to the Medical Technologies Appraisal Committee (MTAC) in their discussions, were the company to set a new price for XprESS MSDS.

Figure 3.1 shows that as the procedure time with FESS and the cost of XprESS MSDS increase, XprESS MSDS becomes increasingly cost incurring. At a price of £800 or above the duration of FESS required for cost savings with XprESS MSDS to be generated becomes increasingly implausible.

Figure 3.1: Two-way sensitivity analysis

		Cost of XprESS MSDS									
	-£330	£100	£200	£300	£400	£500	£600	£700	£800	£900	£1,000
Duration of FESS (minutes)	30	£333	£229	£124	£19	-£86	-£191	-£296	-£401	-£506	-£611
	35	£404	£299	£194	£89	-£16	-£121	-£226	-£331	-£436	-£541
	40	£474	£369	£264	£159	£54	-£51	-£156	-£261	-£366	-£471
	45	£544	£440	£335	£230	£125	£20	-£85	-£190	-£295	-£400
	50	£615	£510	£405	£300	£195	£90	-£15	-£120	-£225	-£330
	55	£685	£580	£475	£370	£265	£160	£55	-£50	-£155	-£260
	60	£755	£651	£546	£441	£336	£231	£126	£21	-£84	-£189
	65	£826	£721	£616	£511	£406	£301	£196	£91	-£14	-£119
	70	£896	£791	£686	£581	£476	£371	£266	£161	£56	-£49
	75	£966	£861	£757	£652	£547	£442	£337	£232	£127	£22
	80	£1,037	£932	£827	£722	£617	£512	£407	£302	£197	£92