NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of corticosteroid-eluting bioabsorbable stent or spacer insertion during endoscopic sinus surgery to treat chronic rhinosinusitis

Rhinosinusitis is when the air-filled cavities of the face (the sinuses) become infected and inflamed. It can cause facial pain and tenderness, a blocked or runny nose, fever, and headache. In this procedure, a stent (short tube) or spacer is inserted through the nose using an endoscope (a thin tube with a camera on the end) and placed in the drainage system of a sinus. The stent or spacer holds the drainage system open, and slowly releases corticosteroid medication into the sinus. The aim is to reduce inflammation. After several weeks the stent dissolves.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This IP overview was prepared in August 2015.

Procedure name

- Corticosteroid-eluting bioabsorbable stent or spacer insertion during endoscopic sinus surgery to treat chronic rhinosinusitis

Specialist societies

- ENT UK (British Association of Otorhinolaryngology - Head and Neck Surgery).

Description

Indications and current treatment

The paranasal sinuses are air-filled cavities, located in the bony structures of the face, which communicate with the nasal space via small openings (ostia). Rhinosinusitis occurs when the mucosal lining of the paranasal sinuses becomes inflamed and infected. Typical symptoms include fever, pain and tenderness over the infected area, together with a blocked or runny nose. Acute rhinosinusitis frequently resolves spontaneously with little or no treatment, but in some cases it becomes chronic.

The symptoms of chronic rhinosinusitis are usually managed with analgesics, antibiotics, topical corticosteroids or nasal irrigation. If these interventions fail, surgical procedures may be needed to enhance drainage from the sinuses. However, adhesions and scarring may develop after surgery, compromising drainage. Scarring occurs less frequently if the mucosa remains intact. Foam dressings, nasal packing and middle meatal spacers are sometimes used after surgery to try and maintain sinus patency.

What the procedure involves

Inserting a corticosteroid-eluting bioabsorbable stent or spacer for paranasal sinus disease aims to deliver topical corticosteroid after surgery and to maintain patency of the newly created drainage system. It is done with the patient under general anaesthesia, during functional endoscopic sinus surgery, which may include balloon sinuplasty. At the end of the surgery, the corticosteroid-eluting stent is inserted into the relevant ostium under endoscopic guidance. The stent dissolves over several weeks.

Outcome measures

The Sino-Nasal Outcome Test (SNOT)-20 and SNOT-22 scales determine patients' disease-specific health status by evaluating the severity of distinct parameters specifically related to physical problems, functional limitations and emotional consequences of rhinosinusitis. Scores for each parameter are rated from 0 to 5, with higher scores indicating more severe symptoms.

The Lund-MacKay staging system measures the degree of sinus disease seen as opacification. Each sinus is scored from 0 (no opacification) to 2 (complete opacification). The total score ranges from 0 (completely clear) to 24 (completely opacified) for each patient.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to corticosteroid-eluting bioabsorbable stent or spacer insertion during endoscopic sinus surgery to treat chronic rhinosinusitis. The following databases were searched, covering the period from their start to 19 June 2015: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with chronic rhinosinusitis.
Intervention/test	Corticosteroid-eluting bioabsorbable stent or spacer insertion during endoscopic sinus surgery.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 290 patients from 5 randomised controlled trials, 1 case series and 1 case report [1–8].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on corticosteroid-eluting bioabsorbable stent or spacer insertion during endoscopic sinus surgery to treat chronic rhinosinusitis

Study 1 Marple BF (2011)

Details

Study type	**Randomised controlled trial (Advance II)**
Country	USA (11 centres)
Recruitment period	2009–10
Study population and number	**n=105 (210 ethmoid sinuses; 105 corticosteroid-releasing stents versus 105 non-corticosteroid-releasing stents)** Patients with chronic rhinosinusitis, with or without nasal polyps, scheduled to undergo endoscopic sinus surgery with bilateral ethmoidectomy
Age and sex	Mean 47 years; 57% (60/105) male
Patient selection criteria	Diagnosis of chronic rhinosinusitis defined as inflammation of the mucosa of the nose and paranasal sinuses of at least 8 weeks' duration. Presence of bilateral ethmoid disease and candidacy for endoscopic sinus surgery were confirmed by CT scan with a minimum Lund-MacKay stage of 6. Patients were excluded for a known history of immune deficiency, insulin-dependent diabetes, allergy or intolerance to corticosteroids, oral corticosteroid-dependent condition, clinical evidence of acute bacterial sinusitis, or clinical evidence of invasive fungal sinusitis, history or diagnosis of glaucoma or ocular hypertension, closed angle, presence of cataracts grade +3 or higher, or presence of posterior subcapsular cataract.
Technique	Bioabsorbable self-expanding corticosteroid (mometasone furoate)-releasing Propel sinus implant (Intersect ENT, USA) was used in the treatment group. A non-drug-releasing implant with an identical structure and appearance was used for the control sinuses. Implants were placed bilaterally in the ethmoid sinuses. Patients were given a 14-day course of antibiotics starting 1 day before surgery.
Follow-up	**90 days**
Conflict of interest/source of funding	Study was sponsored by Intersect ENT, USA. Three authors are consultants for Intersect ENT, 1 author is an Intersect ENT employee and vice president of clinical affairs. One author is a consultant for Alcon, Teva, and Sunovion.

Analysis

Follow-up issues:

- Of the 105 patients who were enrolled, 102 (97%) completed the ear, nose and throat follow-up visits over 90 days and 103 (98%) completed the ocular follow-up visits over the 90-day follow-up.

Study design issues:

- Double-blind study with a within-patient control. An independent panel of 3 sinus surgeons graded the day 30 endoscopies for assessment of the efficacy endpoint. The panel was kept blinded to treatment assignment.
- The primary efficacy endpoint was the reduction in need for postoperative interventions at day 30.
- The primary safety endpoint was defined as the absence of clinically significant intraocular pressure elevation over the 90-day follow-up.
- A sample size of 105 (allowing for 5 lost to follow-up) was determined to provide >90% power. Sinus randomisation was done after completion of successful endoscopic sinus surgery, before opening either implant package.
- A standardised concomitant medications regimen was used to avoid confounding the efficacy assessment. During the initial 30-day follow-up, no oral or topical corticosteroid sprays were permitted. Debridement was permitted during the follow-up visits.

Study population issues:

- 30% (31/105) of patients had had 1 or more previous sinus procedures, and 59% presented with polyps at baseline. 15 patients from 8 centres received oral corticosteroids before surgery.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **105 (105 treatment sides versus 105 control sides)**

Main efficacy results at day 30

Outcome	n	Corticosteroid-eluting stent	control stent	Relative reduction	p value
Postoperative intervention needed (either surgery to separate an adhesion or oral corticosteroids to resolve recurrent inflammation)					
- panel judgement	96	33.3% (32/96)	46.9% (45/96)	-29.0%	0.028
- clinical investigators	105	21.9% (23/105)	31.4% (33/105)	-30.3%	0.068
Frank polyposis					
- panel judgement	85	18.8% (16/85)	34.1% (29/85)	-44.9%	0.002
- clinical investigators	104	3.8% (4/104)	7.7% (8/104)	-50.6%	0.344
Additional efficacy measures					
Middle turbinate lateralisation	105	1.9% (2/105)	6.7% (7/105)	-71.6%	0.125
Significant adhesion (graded as dense or severe)	104	4.8% (5/104)	12.5% (13/104)	-61.6%	0.039

Relative reduction was calculated as:

(Rate in treatment group)–(rate in control group)/(rate in control group)

9 patients could not be assessed by the panel for postoperative intervention because of suboptimal video quality or inadequate imaging of the relevant anatomy.

According to the panel, the need for adhesion lysis was reduced by 52.0% (p=0.005) and the need for oral corticosteroids was reduced by 29.0% (p=0.088).

According to clinical investigators' judgements, the need for adhesion lysis was reduced by 43.0% (p=0.033) and the need for oral corticosteroids was reduced by 25.0% (p=0.388).

Safety

There were no clinically significant intraocular pressure increases (defined as an increase of ≥10 mmHg persisting for 2 weeks on the sinus side adjacent to the drug-releasing implant but not on the control side).

There were no clinically significant changes from baseline in lens opacities.

One patient with a family history of glaucoma entered the study with moderately elevated intraocular pressure and later had a +12 mmHg increase in 1 eye (adjacent to treated sinus) at day 90 that the ophthalmologist believed to be secondary to an acute exacerbation of rhinosinusitis. The patient was treated with topical corticosteroids, oral corticosteroids and antibiotics. Pressures returned to baseline within 1 week after treatment with a pressure-lowering medication.

Adverse events considered to be related to implant

- 1 patient needed adhesion lysis bilaterally at day 14, with concurrent implant removal, because of crusting, granulation and scarring of the middle turbinate that had begun at an earlier 1-week visit. The patient was treated with nasal irrigation, debridement, and prednisone taper, and the event resolved without sequelae.
- In 1 patient, the control implant was removed 1 week postoperatively, and at 2 weeks there was frank pus in the contralateral sinus. The patient was treated with a prednisone taper and amoxicillin. A relationship between the event and the study implant could not be ruled out. The event resolved without sequelae.

Study 2 Murr AH (2011)

Details

Study type	Randomised controlled trial
Country	USA (4 centres)
Recruitment period	2008–9
Study population and number	**n=43** (38 patients were enrolled in a randomised cohort, with corticosteroid-eluting stent in 1 sinus and non-corticosteroid-eluting stent in the other sinus; 5 patients were enrolled in a non-randomised cohort, each with bilateral corticosteroid-eluting stents) Adult patients with chronic rhinosinusitis, with or without nasal polyps, scheduled to have primary or revision functional endoscopic sinus surgery.
Age and sex	Mean 48 years; 58% (25/43) male
Patient selection criteria	Diagnosis of chronic rhinosinusitis defined as symptomatic inflammation of sinuses of at least 12 consecutive weeks' duration. Presence of bilateral ethmoid disease and candidacy for endoscopic sinus surgery were confirmed by CT scan with a minimum Lund-MacKay stage of 6 before study entry. Patients were excluded if they had a known history of intolerance to corticosteroids, an oral corticosteroid-dependent condition, a history of immune deficiency, insulin-dependent diabetes, or fungal rhinosinusitis.
Technique	Bioabsorbable self-expanding corticosteroid (mometasone furoate)-releasing sinus implant (Intersect ENT, USA) was used in the treatment group. A non-drug-releasing implant with an identical structure and appearance was used for the control sinuses. Implants were placed bilaterally. The planned surgical intervention was bilateral ethmoidectomy with middle meatal antrostomy. Concurrent septoplasty and surgical treatment of the other paranasal sinuses was permitted. Patients were given a 14-day course of antibiotics starting 1 day before surgery.
Follow-up	**60 days**
Conflict of interest/source of funding	Funding was provided by Intersect ENT, USA; 4 authors are consultants for Intersect ENT, 1 author is a consultant for Intersect ENT and Entrigue Inc., 1 author is a consultant for Intersect ENT and Entellus Inc., 1 author is Vice President, Clinical and Regulatory Affairs for Intersect ENT.

Analysis

Study design issues:

- Oral corticosteroids were not permitted during the 14 days before surgery. Intranasal corticosteroid sprays were permitted up to the day before surgery. Oral and topical intranasal corticosteroid sprays were not allowed during the study follow-up period.
- Patients, physicians and research staff were kept blinded to the stent version being placed in each sinus.
- Debridement was permitted during the follow-up visits.
- The primary efficacy hypothesis was that the corticosteroid-eluting sinus stent would reduce inflammation in the ethmoid cavity at day 21 compared to the control side using a 100 mm visual analogue scale. A minimally important clinical difference was defined to be half of the standard deviation. Power to detect an effect size of 0.5 standard deviations was 85%.
- Systemic safety was assessed by enrolment of a separate and distinct cohort of 5 patients who had bilateral corticosteroid-releasing stents.

Study population issues:

- 37% (31/43) of patients had prior functional endoscopic sinus surgery; 72% (31/43) of patients had polyps. The mean total Lund Mackay CT stage was 13.4.
- Right and left sides were well balanced with regard to mean CT stage.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>Number of patients analysed: 43

The stents were successfully deployed in all sinuses. By day 30, an average of <10% of the stent material remained and was completely eliminated at the later time points.

Endoscopic scores of ethmoid sinus inflammation (100 mm visual analogue scale, 0 represents no inflammation and 100 represents significant presence of severe inflammation)
<table>
<tr><th>Follow-up</th><th>Corticosteroid-eluting stent
Mean (SD)</th><th>Control stent
Mean (SD)</th><th>p value</th></tr>
<tr><td>Day 7</td><td>29.6 (21.8)</td><td>29.4 (22.7)</td><td>0.6038</td></tr>
<tr><td>Day 14</td><td>24.7 (20.0)</td><td>31.2 (22.0)</td><td>0.0780</td></tr>
<tr><td>Day 21</td><td>23.2 (17.7)</td><td>35.3 (21.8)</td><td>0.0032</td></tr>
<tr><td>Day 30</td><td>20.2 (18.5)</td><td>30.1 (22.4)</td><td>0.0011</td></tr>
<tr><td>Day 45</td><td>15.9 (16.1)</td><td>24.0 (23.0)</td><td>0.0022</td></tr>
<tr><td>Day 60</td><td>12.0 (17.3)</td><td>17.5 (22.5)</td><td>0.0855</td></tr>
</table>
Polypoid mucosal changes (any grade of +1 or higher)
• Corticosteroid-eluting stent=18.4% (7/38)
• Control stent=36.8% (14/38), p=0.0391

Significant adhesions
• Corticosteroid-eluting stent=5.3% (2/38)
• Control stent=21.1% (8/38), p=0.0313

Middle turbinate lateralisation
• Corticosteroid-eluting stent=5.3% (2/38)
• Control stent=15.8% (6/38), p=0.2188</td><td>‘No device-related adverse events occurred.’

In the cohort of 5 patients treated by bilateral corticosteroid-eluting stents, plasma corticosteroid concentrations were below the quantification limit at all follow-up time points. The mean cortisol concentrations at baseline and at follow-up time points were within normal limits and indicated no evidence of adrenal suppression.</td></tr>
<tr><td colspan="2">Abbreviations used: SD, standard deviation</td></tr>
</table>

Study 3 Forwith KD (2011)

Details

Study type	**Prospective case series (Advance)**
Country	USA (7 centres)
Recruitment period	2009
Study population and number	**n=50 (90 treated sinuses)** Adult patients, with or without nasal polyps, scheduled to have primary or revision functional endoscopic sinus surgery
Age and sex	Mean 44 years; 52% (26/50) male
Patient selection criteria	Diagnosis of chronic rhinosinusitis, defined as symptomatic inflammation of the mucosa of the paranasal sinuses of at least 8 consecutive weeks' duration. The diagnosis, presence of ethmoid sinus disease, and candidacy for surgery were confirmed by CT scan before study entry. Patients were excluded if they had a known history of intolerance to corticosteroids, an oral corticosteroid-dependent condition, a history of immune deficiency, insulin-dependent diabetes, history or diagnosis of glaucoma or ocular hypertension, or clinical evidence of either acute bacterial rhinosinusitis or invasive fungal rhinosinusitis.
Technique	Bioabsorbable self-expanding corticosteroid (mometasone furoate)-releasing sinus implant (Intersect ENT, USA) was used. The planned surgical intervention was bilateral or unilateral ethmoidectomy. Concurrent septoplasty and surgical treatment of the other paranasal sinuses was permitted. There was no specific perioperative antibiotic regimen.
Follow-up	**6 months**
Conflict of interest/source of funding	The study was sponsored by Intersect ENT, which provided funding for the investigation. One author is a consultant for Johnson & Johnson, Medtronic and Olympus; 1 is a shareholder of Allergan Corporation, and a consultant for Transcend Endo-optics, Ivantis, and Intersect ENT; 1 author is a consultant for Intersect ENT.

Analysis

Follow-up issues:

- The overall follow-up rate was 98% to day 60 and 90% to 6 months. One patient withdrew after day 30 because of scheduling difficulties and 4 additional patients were lost to follow-up at 6 months.

Study design issues:

- Oral and topical intranasal corticosteroid sprays were not allowed during the study follow-up period to day 60. At day 30, clinicians were given the option to prescribe corticosteroids if deemed medically necessary.
- Endoscopic examination and grading of the sinuses was done during the follow-up visits to day 90.
- Debridement was permitted during the follow-up visits.
- Ethmoid sinus inflammation was measured on a 100 mm visual analogue scale, where 0 was defined as none, and 100 was defined as severe. Middle turbinate position was graded on a 4-point categorical scale (medialised, normal, partially lateralised, and lateralised). Adhesion formation was graded on a 5-point categorical scale (none, small/nonobstructing, obstructing/easily separated, dense/obstructing/difficult to separate, and severe/complete adhesion to middle turbinate to lateral nasal wall).
- Patients were asked to assess their symptoms using validated disease-specific symptom-scoring instruments, the Rhinosinusitis Disability Index (RSDI) and the Sino-Nasal Outcome Test-22 (SNOT-22).
- One of the patients with bilateral stent placement had an artificial eye, so a total of 99 eyes were evaluated for ocular safety.

Study population issues:

- 28% (14/50) of patients had prior sinus procedures; 66% (33/50) of patients had polyps. The mean total Lund-Mackay CT stage was 11.2.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>
Number of patients analysed: 50 (90 treated sinuses)

The stents were successfully deployed in all patients. By visual estimation, an average of 14.9% of the stent material was remained at day 30, and this was reduced to 0.2% at day 60.

The mean inflammation scores were described as ‘minimal’ at all time points. They declined from day 7 to day 14 (from approximately 28mm to approximately 21mm, estimated from graph) and from day 30 to 60 (from approximately 20mm to approximately 15mm, estimated from graph).
• Polypoid tissue formation at day 30 (any grade of +1 or higher)=10% (9/90)
• Frank polyposis (grade 2, there were no grade 3 or 4 changes)=2.2% (2/90)
• Significant adhesion=1.1% (1/90)
• Middle turbinate lateralisation=4.4% (4/90)
• Revision rate=2.2% (2/90) (1 patient needed surgical revision within 6 months)

Mean normalised SNOT-22 scores (scale 0–5, higher scores indicate worse symptoms):
• Baseline=2.8
• 30 days=1.1
• 60 days=0.8
• 6 months=1.0
All changes from baseline reflected statistically significant improvement (p<0.0001)

Mean Rhinosinusitis Disability Index (RSDI) scores (higher scores indicate worse symptoms)
• Baseline=48.5
• 30 days=23.4
• 60 days=12.6
• 6 months=18.2
All changes from baseline reflected statistically significant improvement (p<0.0001)

Intraocular pressures, mean (standard deviation)
<table>
<tr><th></th><th>Eyes on stented sides n=89</th><th>Eyes on non-stented sides, n=10</th></tr>
<tr><td>Baseline mean IOP (mmHg)</td><td>15.0 (3.1)</td><td>14.7 (2.4)</td></tr>
<tr><td>Day 30 mean IOP (mmHg)</td><td>14.3 (3.3)</td><td>14.3 (2.9)</td></tr>
<tr><td>Mean change from baseline</td><td>-0.7 (2.6)</td><td>-0.4 (3.6)</td></tr>
</table>
The authors described the changes from baseline as clinically and statistically insignificant.

There were no clinically significant changes from baseline in lens opacities.
</td><td>
There was 1 adverse event – headache with sensation of sinus pressure and irritation. This was determined to be primarily due to functional endoscopic sinus surgery but was exacerbated by presence of crusting adherent to the stent. The event occurred on day 21 and resolved without sequelae after stent removal.
</td></tr>
<tr><td colspan="2">Abbreviations used: IOP, intraocular pressure; SNOT, Sino-Nasal Outcomes Test</td></tr>
</table>

Study 4 Côté DWJ (2010)

Details

Study type	**Randomised controlled trial**
Country	Canada
Recruitment period	Not reported
Study population and number	**n=19 (38 nasal cavities; 19 corticosteroid (triamcinolone)-impregnated bioresorbable dressing versus 19 saline-impregnated dressing)** Adult patients with chronic rhinosinusitis with polyposis
Age and sex	Not reported
Patient selection criteria	Chronic rhinosinusitis with polyposis refractory to medical treatment needing bilateral sinus surgery. Patients were excluded if they were ineligible for informed consent, unwilling or unable to comply with the postoperative visits necessary for data collection, or history of intolerance to triamcinolone.
Technique	At the conclusion of endoscopic sinus surgery, the patient was randomised to either the left or right nasal cavity to receive 2 ml of a 40 mg/ml triamcinolone solution-impregnated bioresorbable dressing (Nasopore; Stryker, Canada). The contralateral sinus received an identical dressing soaked in saline. Nasal packing remained in situ until suctioned from middle meatus at the first postoperative visit 1 week later.
Follow-up	**6 months**
Conflict of interest/source of funding	Nasopore dressings were donated by Stryker Canada, which had no involvement in study design, protocol, methods or analysis. The authors declared no conflicts of interest.

Analysis

Follow-up issues:

- Some patients missed 1 or 2 of the postoperative clinic visits. At the 6-month follow-up, results from 84% (16/19) of patients were available.

Study design issues:

- Consecutive patients were recruited. Patients served as their own controls. Patients were randomised to receive corticosteroid-impregnated dressing in the left or right nasal cavity and saline-impregnated dressing in the contralateral nasal cavity. The method of randomisation is unclear. Randomisation allocation was placed in an envelope and remained sealed until all postoperative data was collected. The primary investigator, surgical staff and patient were unaware of treatment allocation.
- Patients resumed their nasal saline irrigation and intranasal corticosteroid sprays postoperatively per routine at the study centre.
- Postoperative healing assessments of oedema, crusting, secretions, and scarring were done at postoperative visits using validated Lund-Kennedy and Perioperative Sinus Endoscopy (POSE).
- Sample size was calculated to give a power of 80% to detect a difference in means between populations of 3.5 which was felt to be clinically relevant.

Study population issues:

- There were no significant differences between the nasal cavities with regard to preoperative POSE, Lund-Kennedy and Lund-Mckay scores.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>Number of patients analysed: 19 (38 sinus cavities)

Perioperative Sinus Endoscopy Scores, mean (range)
<table>
<tr><th>Follow-up</th><th>n</th><th>Corticosteroid-impregnated dressing</th><th>Control</th><th>p value</th></tr>
<tr><td>Baseline</td><td>19</td><td>13.2 (8–17)</td><td>13.1 (8–17)</td><td>0.83</td></tr>
<tr><td>7 days</td><td>15</td><td>5.3 (3–10)</td><td>6.8 (4–11)</td><td>0.0266</td></tr>
<tr><td>14 days</td><td>19</td><td>4.6 (1–8)</td><td>6.8 (3–11)</td><td>0.001</td></tr>
<tr><td>28 days</td><td>18</td><td>4.7 (1–11)</td><td>5.8 (1–10)</td><td>0.27</td></tr>
<tr><td>3 months</td><td>18</td><td>4.5 (0–11)</td><td>5.7 (0–11)</td><td>0.049</td></tr>
<tr><td>6 months</td><td>16</td><td>5.2 (0–13)</td><td>6.5 (0–13)</td><td>0.01172</td></tr>
</table>
Lund-Kennedy Scores, mean (range)
<table>
<tr><th>Follow-up</th><th>n</th><th>Corticosteroid-impregnated dressing</th><th>Control</th><th>p value</th></tr>
<tr><td>Baseline</td><td>19</td><td>5.3 (2–8)</td><td>5.2 (2–8)</td><td>0.375</td></tr>
<tr><td>7 days</td><td>14</td><td>2.4 (1–4)</td><td>3.1 (1–4)</td><td>0.039</td></tr>
<tr><td>14 days</td><td>17</td><td>2.7 (1–5)</td><td>3.6 (1–7)</td><td>0.027</td></tr>
<tr><td>28 days</td><td>17</td><td>2.4 (0–4)</td><td>3.1 (1–5)</td><td>0.129</td></tr>
<tr><td>3 months</td><td>16</td><td>2.0 (0–4)</td><td>2.9 (0–5)</td><td>0.007</td></tr>
<tr><td>6 months</td><td>16</td><td>2.3 (0–4)</td><td>2.9 (1–5)</td><td>0.02</td></tr>
</table>
Synechiae were rare in both the treatment and control groups; there was a trend to less synechia formation in the corticosteroid treatment group but the data lacked statistical significance (p<0.025).</td><td>There were no adverse side effects.</td></tr>
</table>

Study 5 Rudmik L (2012)

Details

Study type	**Randomised controlled trial**
Country	Canada
Recruitment period	2009–11
Study population and number	**n=36** (18 corticosteroid [dexamethasone] Sinu-Foam™ versus 18 Sinu-Foam™ alone) Adult patients with chronic rhinosinusitis without nasal polyposis.
Age and sex	Mean age 50 versus 49 years; 56% (20/36) male
Patient selection criteria	Age≥18 years; diagnosis of chronic rhinosinusitis with nasal polyposis according to the 2007 American Academy of Otolaryngology guidelines; persistent symptoms despite medical management, defined as nasal saline irrigations, topical nasal corticosteroids spray for 3 months, and a course of systemic corticosteroids with a broad-spectrum oral antibiotic; minimum bilateral endoscopic sinus surgery procedure consisting of maxillary antrostomy and ethmoidectomy; ability to adhere to the follow-up schedule. Exclusion criteria included: nasal polyposis; uncorrectable coagulopathy; emergency surgical procedures; systemic inflammatory disease.
Technique	Endoscopic sinus surgery included maxillary antrostomy and ethmoidectomy. All patients had Sinu-Foam™ mixed with either dexamethasone or sterile water (placebo) placed into each of the ethmoid cavities at the end of the procedure.
Follow-up	**3 months**
Conflict of interest/source of funding	None

Analysis

Follow-up issues:

- No patients were lost to follow-up.

Study design issues:

- Patients were randomised to either the intervention or placebo using a computer generated block-randomisation allocation. Patients and the principal investigator were blinded to the assigned group.
- All patients received a perioperative systemic corticosteroid taper (prednisone 30 mg daily starting 1 week before surgery, which was tapered off postoperatively over 10 days) and a perioperative course of an oral antibiotic starting 1 week before surgery and continuing for 1 week postoperatively.
- Postoperative care included nasal saline irrigations starting 1 day after endoscopic sinus surgery. All patients had a middle-meatal debridement at 1 week postoperatively.
- The primary outcome was postoperative endoscopic grading, using the Lund-Kennedy scoring system.
- A 25% improvement in mean Lund-Kennedy scores was assumed, to give a power of 90% and an alpha of 5% with sample size of 36.

Study population issues:

- There were no significant baseline differences between the patient groups with regard to demographics and CT stage.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>Number of patients analysed: 36

Endoscopy Grade (Lund-Kennedy score, higher scores indicate worse symptoms), mean (standard deviation)
<table>
<tr><th></th><th>Corticosteroid group</th><th>Placebo group</th><th>p value</th></tr>
<tr><td>1 week</td><td>6.7 (1.4)</td><td>7.3 (2.4)</td><td>0.489</td></tr>
<tr><td>4 weeks</td><td>5.3 (2.4)</td><td>5.0 (2.1)</td><td>0.816</td></tr>
<tr><td>3 months</td><td>3.3 (1.6)</td><td>3.1 (1.6)</td><td>0.631</td></tr>
</table>
Both groups had a significant improvement in endoscopy score at follow-up (p<0.001).</td><td>There were no postoperative complications or adverse events noted in either group.</td></tr>
</table>

Study 6 Dautremont JF (2014)

Details

Study type	**Randomised controlled trial (postoperative systemic corticosteroids versus postoperative placebo pill)**
Country	Canada
Recruitment period	2012–3
Study population and number	**n=36** (18 postoperative prednisone 30 mg daily for 7 days versus 18 postoperative placebo pill daily for 7 days) Adult patients with chronic rhinosinusitis and nasal polyposis refractory to medical therapy, scheduled to have endoscopic sinus surgery.
Age and sex	Mean age 46 versus 41 years; 50% (18/36) male
Patient selection criteria	Age>18 years; diagnosis of chronic rhinosinusitis with nasal polyposis according to the 2007 Adult Sinusitis Guidelines, and elected endoscopic sinus surgery for refractory chronic rhinosinusitis (defined as persistent symptoms despite a minimum of 3 months topical corticosteroid spray or irrigations, minimum of 2-week course of systemic corticosteroid and a minimum 2-week course of broad-spectrum antibiotic in the presence of mucopurulence). Exclusion criteria included patients with suspected systemic inflammatory disease, cystic fibrosis, and any contraindication to systemic corticosteroids. Patients having concurrent septoplasty were not excluded.
Technique	Endoscopic sinus surgery included bilateral maxillary antrostomy, total ethmoidectomy, sphenoidotomy, and frontal sinusotomy. All patients had 1 Nasopore^{TM} dissolvable spacer soaked with 2 ml of triamcinolone placed into each of the ethmoid cavities at the end of the procedure.
Follow-up	**2 months**
Conflict of interest/source of funding	None

Analysis

Follow-up issues:

- No patients were lost to follow-up.

Study design issues:

- Patients were randomised to either the intervention or placebo using a computer generated block-randomisation allocation. Patients and surgeons were blinded to the assigned group.
- All patients received 7 days of oral prednisone and oral antibiotic preoperatively.
- Postoperative care included high volume nasal saline irrigations 3 times a day starting 1 day after endoscopic sinus surgery, continuing the systemic antibiotic for 7 days postoperatively, and an endoscopic debridement at 1 and 3 weeks postoperatively. Topical nasal corticosteroid therapy was initiated at the 1-week postoperative visit. Topical corticosteroid therapy following the debridement consisted of high volume budesonide irrigation once daily, initiated after the first nasal cavity debridement.
- The primary outcome was endoscopic grading at postoperative month 2, using the 20-point Lund-Kennedy scoring system (assesses the presence of polyps, oedema, discharge, scarring and crusting).
- The secondary outcome was disease-specific quality-of-life at postoperative month 2, measured using the Sinonasal Outcome Test (SNOT-22) questionnaire.
- A 25% improvement in Lund-Kennedy scores was assumed, to give a power of 90% and an alpha of 5% with sample size of 36.

Study population issues:

- There were no significant differences between the patient groups with regard to demographics, chronic rhinosinusitis-related comorbidities, and preoperative measures of disease severity.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>Number of patients analysed: 36

Endoscopy Grade (Lund-Kennedy score, higher scores indicate worse symptoms), mean±standard deviation
<table>
<tr><th></th><th>Systemic corticosteroid group</th><th>Placebo group</th><th>p value (between groups)</th></tr>
<tr><td>Baseline</td><td>8.5±2.1</td><td>8.9±2.6</td><td>0.579</td></tr>
<tr><td>Month 2 postoperative</td><td>2.2±1.6</td><td>1.7±1.5</td><td>0.343</td></tr>
<tr><td>Mean absolute difference</td><td>6.2±2.3</td><td>7.2±3.1</td><td></td></tr>
<tr><td>p value</td><td><0.001</td><td><0.001</td><td></td></tr>
</table>
Quality of life score (SNOT-22, higher scores indicate worse symptoms), mean±standard deviation
<table>
<tr><th></th><th>Systemic corticosteroid group</th><th>Placebo group</th><th>p value (between groups)</th></tr>
<tr><td>Baseline</td><td>47.8±18.2</td><td>42.2±18.1</td><td>0.355</td></tr>
<tr><td>Month 2 postoperative</td><td>11.5±7.3</td><td>10.4±10.1</td><td>0.722</td></tr>
<tr><td>Mean absolute difference</td><td>36.4±20.3</td><td>31.8±18.7</td><td></td></tr>
<tr><td>p value</td><td><0.001</td><td><0.001</td><td></td></tr>
</table>
</td><td>No safety data were reported in the paper.</td></tr>
</table>

Study 7 Food and Drug Administration Manufacturer and user facility device experience (MAUDE) database

Details

Study type	**Case report**
Country	USA
Recruitment period	2012
Study population and number	**n=1**
Age and sex	Not reported
Patient selection criteria	Not reported
Technique	Propel corticosteroid-eluting sinus stent (Intersect ENT) was used.
Follow-up	**3 weeks**
Conflict of interest/source of funding	Event was reported by Intersect ENT.

Analysis

Key efficacy and safety findings

safety
Number of patients analysed: 1 **Peri-orbital cellulitis** A patient with insulin-dependent diabetes was treated by revision functional endoscopic sinus surgery, including bilateral ethmoidectomies, maxillary antrostomies and frontal sinusotomies. Drug-releasing stents were placed in the right and left ethmoid sinuses. A haemostatic agent was also used. Three weeks postoperatively, the patient experienced symptoms of rhinosinusitis and had developed peri-orbital cellulitis on the right side. Routine post-surgical debridement was done and antibiotics were prescribed to treat the infection. The patient's infection cleared and the patient was asymptomatic after taking the antibiotics.

Efficacy

Symptom relief

A case series of 50 patients reported the mean normalised SNOT-22 scores (scale 0 to 5, higher scores indicate worse symptoms) reduced from 2.8 at baseline to 1.0 at 6-month follow-up ($p<0.0001$). The mean Rhinosinusitis Disability Index (higher scores indicate worse symptoms) reduced from 48.5 at baseline to 18.2 at 6-month follow-up ($p<0.0001$)[3].

Endoscopic evaluation

A randomised controlled trial of 43 patients treated by a corticosteroid-eluting sinus stent in 1 side and a non-corticosteroid-eluting sinus stent in the other side reported a statistically significant reduction in inflammation, assessed at endoscopy, at days 21 to 45 for the corticosteroid-eluting stent compared with the control stent, but the difference was no longer statistically significant at day 60[2]. The scores, measured on a 100 mm visual analogue scale, reduced from 29.6 at day 7 to 12.0 at day 60 for the treatment group and from 29.4 to 17.5 in the control group.

A randomised controlled trial of 19 patients treated by a corticosteroid-impregnated or a saline impregnated bioresorbable dressing reported a significant improvement in endoscopy scores and Lund-Kennedy scores at 6-month follow-up (mean 5.2 and 2.3 versus 6.5 and 2.9, $p=0.012$ and 0.02)[4].

A randomised controlled trial of 36 patients treated by a foam mixed with corticosteroid or a foam mixed with saline (placebo) reported no difference in endoscopy score between the groups at 3-month follow-up (3.3 versus 3.1, $p=0.631$)[5].

Chronic rhinosinusitis with nasal polyps

A randomised controlled trial of 105 patients treated by a corticosteroid-releasing stent in 1 side and a non-corticosteroid-releasing stent in the other reported frank polyposis in 19% (16/85) versus 34% (29/85) of sinuses at day 30, according to a panel judgement ($p=0.002$)[1]. The randomised controlled trial of 43 patients reported polypoid mucosal changes in 18% (7/38) of sinuses treated by a corticosteroid-eluting stent and 37% (14/38) of sinuses treated by a control stent ($p=0.039$) at day 60[2]. The case series of 50 patients reported polypoid tissue formation at day 30 in 10% (9/90) of sinuses and frank polyposis in 2% (2/90) of sinuses[3].

Adhesions

The randomised controlled trial of 105 patients treated by a corticosteroid-releasing stent in 1 side and a non-corticosteroid-releasing stent in the other reported significant adhesion in 5% (5/104) versus 13% (13/104) of sinuses at day 30 ($p=0.039$)[1].The randomised controlled trial of 43 patients reported significant adhesions in 5% (2/38) of sinuses treated by a corticosteroid-eluting

stent and 21% (8/38) of sinuses treated by a control stent (p=0.031) at day 60[2]. The case series of 50 patients reported significant adhesions in 1% (1/90) of sinuses[3].

Middle turbinate lateralisation

The randomised controlled trial of 105 patients treated by a corticosteroid-releasing stent in 1 side and a non-corticosteroid-releasing stent in the other reported middle turbinate lateralisation in 2% (2/105) versus 7% (7/105) of sinuses at day 30 (p=0.125)[1].The randomised controlled trial of 43 patients reported middle turbinate lateralisation in 5% (2/38) of sinuses treated by a corticosteroid-eluting stent and 16% (6/38) of sinuses treated by a control stent (p=0.219)[2].

Revision rate

The case series of 50 patients reported a revision rate of 2% (2/90) (1 patient needed surgical revision within 6 months)[3]. The randomised controlled trial of 105 patients treated by a corticosteroid-releasing stent in 1 side and a non-corticosteroid-releasing stent in the other reported the need for postoperative intervention (either surgery to separate an adhesion or oral corticosteroids to resolve recurrent inflammation) in 33% (32/96) versus 47% (45/96) of sinuses at day 30, according to a panel judgement (p=0.028)[1].

Safety

Implant removal

Bilateral adhesion lysis with concurrent implant removal was reported in 1 patient in a randomised controlled trial of 105 patients; the implant was removed on day 14 because of crusting, granulation and scarring of the middle turbinate. The patient was treated with nasal irrigation, debridement, and prednisone taper, and the condition resolved without sequelae[1].

Infection

Peri-orbital cellulitis was reported in 1 patient on the Food and Drug Administration Manufacturer and user facility device experience (MAUDE) database. The patient, who had insulin-dependent diabetes, was treated by revision functional endoscopic sinus surgery, including bilateral ethmoidectomies, maxillary antrostomies and frontal sinusotomies. Drug-releasing stents were placed in the right and left ethmoid sinuses. Three weeks postoperatively, the patient experienced symptoms of rhinosinusitis and had developed peri-orbital cellulitis on the right side. Routine post-surgical debridement was done and antibiotics were prescribed to treat the infection. The patient's infection cleared and the patient was asymptomatic after taking the antibiotics [7].

Infection was reported in 1 sinus treated by a bioabsorbable corticosteroid-releasing stent in the randomised controlled trial of 105 patients; endoscopic examination at 2 weeks postoperatively revealed frank pus and the patient was

treated with prednisone taper and antibiotics. The infection resolved without sequelae[1].

Headache

Headache with sensation of sinus pressure and irritation was reported in 1 patient in a case series of 50 patients[3]. This was determined to be primarily due to functional endoscopic sinus surgery but was exacerbated by presence of crusting adherent to the stent. The event occurred on day 21 and resolved without sequelae after stent removal.

Validity and generalisability of the studies

- The comparative studies compared corticosteroid-eluting stents or spacers against non-corticosteroid-eluting stents or spacers. There were no studies comparing corticosteroid-eluting stents after endoscopic sinus surgery against no stents.
- Different kinds of stent or spacer were used between studies. The first 3 studies used a self-expanding bioabsorbable corticosteroid-releasing implant[1-3]. Other studies used dissolvable material, such as foam, mixed with corticosteroid. One study noted that this was an off-label use of the spacer[5].
- Three randomised controlled trials used within-patient rather than between-patient randomisation[1,2,4].
- Most of the studies included patients with or without polyps. One study excluded patients with nasal polyposis[5].
- Only 1 study included patient-reported outcomes to assess the impact of the procedure on patients' symptoms and quality of life[3].
- All of the studies were done in the USA or Canada.

Existing assessments of this procedure

A Cochrane review on 'Steroid-eluting sinus stents for improving symptoms in chronic rhinosinusitis patients undergoing functional endoscopic sinus surgery' was published in in 2015[6]. The review excluded studies that used a within-patient comparison. It concluded that 'there is currently no evidence from high-quality randomised controlled trials to demonstrate the benefits over those of surgery alone, of steroid-eluting sinus stents for patients with chronic rhinosinusitis (CRS) undergoing functional endoscopic sinus surgery (FESS), when compared to non-steroid-eluting sinus stents, nasal packing or no treatment. …Well–designed randomised controlled trials are required to evaluate the efficacy of steroid-

eluting sinus stents for CRS patients undergoing FESS in terms of improving sinonasal symptoms and quality of life. Study investigators should use between-patient rather than within-patient comparisons for future trials.'

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Balloon catheter dilation of paranasal sinus ostia for chronic sinusitis. NICE interventional procedure guidance 273 (2008). Available from http://www.nice.org.uk/guidance/ipg273

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to where comments are considered voluminous, or publication would be unlawful or inappropriate. Three Specialist Advisor Questionnaires for corticosteroid-eluting bioabsorbable stent or spacer insertion during endoscopic sinus surgery to treat chronic rhinosinusitis were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme sent 35 questionnaires to 2 NHS trusts for distribution to patients who had a stent inserted (or their carers). The questionnaires were prepared for patients who had been treated by inserting a drug eluting stent after endoscopic sinus surgery to treat chronic sinusitis. NICE subsequently refined the scope of this assessment to include only treatment with a corticosteroid eluting bioabsorbable stent. NICE received 16 completed questionnaires, but it was not possible to identify which ones specifically related to the use of a corticosteroid-eluting bioabsorbable stent or spacer.

Issues for consideration by IPAC

None other than those described above.

References

1. Marple BF, Smith TL, Han JK et al. (2012) Advance II: a prospective, randomized study assessing safety and efficacy of bioabsorbable steroid-releasing sinus implants. Otolaryngology - Head and Neck Surgery 146: 1004–11
2. Murr AH, Smith TL, Hwang PH et al. (2011) Safety and efficacy of a novel bioabsorbable, steroid-eluting sinus stent. International Forum of Allergy and Rhinology 1: 23–32
3. Forwith KD, Chandra RK, Yun PT et al. (2011) ADVANCE: a multisite trial of bioabsorbable steroid-eluting sinus implants. Laryngoscope 121: 2473-80
4. Côté DWJ, Wright ED. (2010) Triamcinolone-impregnated nasal dressing following endoscopic sinus surgery: a randomized, double-blind, placebo-controlled trial. Laryngoscope 120: 1269–73
5. Rudmik, L. Mace J, Mechor B. (2012) Effect of a dexamethasone Sinu-Foam™ middle meatal spacer on endoscopic sinus surgery outcomes: A randomized, double-blind, placebo-controlled trial. International Forum of Allergy and Rhinology 2: 248–51
6. Dautremont JF, Mechor B, Rudmik L. (2014) The role of immediate postoperative systemic corticosteroids when utilizing a steroid-eluting spacer following sinus surgery. Otolaryngology and Head and Neck Surgery 150: 689–95
7. Food and Drug Administration (FDA). Manufacturer and user facility device experience (MAUDE) database. Available from: www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/search.cfm [accessed September 2014]
8. Huang Z, Hwang P, Sun Y et al. (2015) Steroid-eluting sinus stents for improving symptoms in chronic rhinosinusitis patients undergoing functional endoscopic sinus surgery. Cochrane Database of Systematic Reviews issue 6: CD010436

Appendix A: Additional papers on corticosteroid-eluting bioabsorbable stent or spacer insertion during endoscopic sinus surgery to treat chronic sinusitis

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Campbell RG, Kennedy DW (2014) What is new and promising with drug-eluting stents in sinus surgery? Current Opinion in Otolaryngology & Head & Neck Surgery 22: 2-7	Review 2 RCTs, 1 prospective single-cohort study and a meta-analysis (of 2 studies)	Steroid-eluting implants are well tolerated and an effective addition to the armamentarium utilised in the management of chronic rhinosinusitis.	The studies are already included in table 2.
Han JK, Marple BF, Smith TL et al. (2012) Effect of steroid-releasing sinus implants on postoperative medical and surgical interventions: an efficacy meta-analysis. International Forum of Allergy & Rhinology 2: 271–9	Meta-analysis (2 studies) n=143	According to the grading done by a panel, drug-releasing implants reduced postoperative interventions by 35% (p=0.0008), lysis of adhesions by 51% (p=0.0016), and oral steroid need by 40% (p=0.0023), compared to controls. The relative reduction in frank polyposis was 46% (p<0.0001).	Pooled results from 2 studies that are already included in table 2.
Kennedy DW. (2012) The PROPEL steroid-releasing bioabsorbable implant to improve outcomes of sinus surgery. Expert Review of Respiratory Medicine 5: 493–8	Review	To date, 3 clinical trials have demonstrated that the implant is safe and maintains the results of sinus surgery by decreasing postoperative inflammation, polyposis, adhesions and middle turbinate lateralization. This implant reduces the need for oral steroids with their associated risks and reduces the need for uncomfortable postoperative debridement and removal of scarring.	Review of studies that are already included in table 2.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Rudmik L, Soler ZM, Orlandi RR et al. (2011) Early postoperative care following endoscopic sinus surgery: an evidence-based review with recommendations. International Forum of Allergy and Rhinology 6: 417– 30	Systematic review 3 studies on drug-eluting stents or spacers	An evidence-based postoperative treatment protocol after endoscopic sinus surgery would include the use of nasal saline irrigation, sinus cavity debridement, and initiation of standard topical nasal steroid spray. Due to a relative balance between possible therapeutic advantages and potential adverse effects, the use of postoperative antibiotics, systemic steroids, off-label topical steroid medications, and drug eluting materials are all options for postoperative care.	No meta-analysis.
Zhao X, Grewal A, Briel M et al. (2013) A systematic review of nonabsorbable, absorbable, and steroid-impregnated spacers following endoscopic sinus surgery. International Forum of Allergy and Rhinology 3: 896–904	Systematic review 11 RCTs (5 steroid versus plain spacer; 6 nonabsorbable versus absorbable)	Comparison between nonabsorbable spacers and absorbable spacers showed that there was no significant difference in adhesion rates if nonabsorbable spacers are used for at least 48 hours after surgery. Steroidal spacers may reduce adhesions, but more consistent data reporting is required for meta-analysis.	No relevant meta-analysis.

Appendix B: Related NICE guidance for corticosteroid-eluting biabsorbable stent or spacer insertion during endoscopic sinus surgery to treat chronic sinusitis

Guidance	Recommendations
Interventional procedures	**Balloon catheter dilation of paranasal sinus ostia for chronic sinusitis. NICE interventional procedure guidance 273 (2008).** 1.1 Current evidence on the short-term efficacy of balloon catheter dilation of paranasal sinus ostia for chronic sinusitis is adequate and raises no major safety concerns. Therefore, this procedure can be used provided that normal arrangements are in place for clinical governance, consent and audit. 1.2 This procedure should only be carried out by surgeons with experience of complex sinus surgery, and specific training in both the procedure and the use of fluoroscopy. 1.3 Publication of long-term outcomes will be helpful in guiding the future use of this technique. NICE may review the procedure upon publication of further evidence.

Appendix C: Literature search for corticosteroid-eluting bioabsorbable stent or spacer insertion during endoscopic sinus surgery to treat chronic sinusitis

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	19/06/2015	Issue 6 of 12, June 2015
HTA database (Cochrane Library)	19/06/2015	Issue 2 of 4, April 2015
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	19/06/2015	Issue 5 of 12, May 2015
MEDLINE (Ovid)	19/06/2015	1946 to June Week 2 2015
MEDLINE In-Process (Ovid)	19/06/2015	June 18, 2015
EMBASE (Ovid)	19/06/2015	1974 to 2015 Week 24
PubMed	19/06/2015	n/a
BLIC	19/06/2015	n/a

Trial sources searched on 22 October 2014

- Current Controlled Trials *meta*Register of Controlled Trials – *m*RCT
- Clinicaltrials.gov
- WHO International Clinical Trials Registry

Websites searched on 22 October 2014

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- EuroScan
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	exp Sinusitis/
2	(Sinusit* or rhinosinusit* or (sinus* adj4 (diseas* or infect*))).tw.
3	Natural Orifice Endoscopic Surgery/
4	Nasal Surgical Procedures/
5	((Sinus* or rhinosinus*) adj4 (surger* or surgic*)).tw.
6	FESS.tw.

7	or/1-6
8	Drug-Eluting Stents/
9	Drug Implants/
10	((drug-elut* or drug-coat* or (drug adj4 elut*) or (drug adj4 coat*)) adj4 (stent* or implant* or catheter* or spacer*)).tw.
11	DES.tw.
12	(steroid-releas* or drug-releas* or doxycycline-releas* or ((steroid* or doxycycline* or drug*) adj4 (releas* or elut* or deliver*))).tw.
13	mometasone furoate.tw.
14	or/8-13
15	Absorbable Implants/
16	(absorb* or bioabsorb* or biodegrad* or bioresorb*).tw.
17	15 or 16
18	7 and 14 and 17
19	(Propel adj4 (stent* or implant*)).tw.
20	18 or 19
21	animals/ not humans/
22	20 not 21