

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## INTERVENTIONAL PROCEDURES PROGRAMME

### Interventional procedure overview of insertion of a collagen plug to close an abdominal wall enterocutaneous fistula

An enterocutaneous fistula is an abnormal opening between the bowel and the surface of the skin of the abdomen. It allows bowel contents to leak out and can be difficult to treat. This procedure uses a plug made of polyurethane and animal tissue (such as pig intestine) that is inserted through the fistula, with the aim of helping it to heal.

#### 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 March 2014.

#### Procedure name

Insertion of a collagen plug to close an abdominal wall enterocutaneous fistula

#### Specialist societies

- Association of Coloproctology of Great Britain and Ireland
- Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland (AUGIS)
- British Society of Gastroenterology (BSG)

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- British Society of Interventional Radiology (BSIR).

## Description

### *Indications and current treatment*

An enterocutaneous fistula is an abnormal opening between the small or large bowel and the skin of the abdomen, which allows the contents of the bowel to leak. A fistula can arise from any part of the bowel (duodenum, jejunum, ileum, colon, or rectum). The most common predisposing conditions are inflammatory bowel disease and a history of bowel surgery or trauma.

Management options include total parenteral nutrition, and measures to prevent intestinal contents from passing through the bowel, so decreasing fistula output and encouraging healing. Surgical options include primary repair with resection of the fistula track, with or without bowel diversion (creating a stoma).

### *What the procedure involves*

A variety of techniques have been described for insertion of a collagen plug to close an enterocutaneous fistula, most being carried out with the patient under sedation. The fistula track is visualised using fluoroscopy and may need dilatation to allow passage of the plug. The track is then debrided to improve incorporation of the plug. A guide wire is inserted from the skin surface through the track into the bowel lumen and a delivery sheath is put in place. Once the delivery sheath is in position, the collagen plug is passed through the track, under fluoroscopic guidance. The delivery sheath is then taken out. The collagen plug is secured in place with absorbable sutures and a Molnar disk (disk used to retain the device in place). A radiopaque flange (or device footplate) attached to the internal end of the plug helps stop enteric fluids from entering the fistula track, and allows visualisation of the plug during placement. The collagen plug fills the fistula track and acts as a scaffold for tissue growth, allowing the fistula to become filled with tissue and to heal. The patient is usually kept in hospital for a few days of strict bed rest, to prevent displacement of the plug and to encourage its incorporation. Various plugs are available for use in this procedure.

## Literature review

### *Rapid review of literature*

The medical literature was searched to identify studies and reviews relevant to insertion of a collagen plug to close an abdominal wall enterocutaneous fistula. Searches were conducted of the following databases, covering the period from their commencement to 26 March 2014: 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 an abdominal wall enterocutaneous fistula.
Intervention/test	Insertion of a collagen plug to close an abdominal wall enterocutaneous fistula.
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 19 patients from 3 case series <sup>1,2,3</sup> and 2 case reports <sup>4,5</sup>.

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 insertion of a collagen plug to close an abdominal wall enterocutaneous fistula****Study 1 Lyon JW (2013)****Details**

Study type	<b>Case series (of individual reports)</b>
Country	US
Recruitment period	Jul 2010 – Sept 2012
Study population and number	N=6 patients with intraperitoneal abscess and associated chronic bowel fistula.
Age and sex	Mean 65.7 years (calculated by IP analyst from evidence table); 50% (3/6) female
Patient selection criteria	Enterocutaneous fistulas persistent beyond 6–8 weeks of treatment. All patients presented with an associated intraperitoneal abscess drained percutaneously with a pigtail catheter.
Technique	Closure of fistula using Biodesign collagen plugs via delivery sheath under radiologic guidance. All performed with the patient under moderate sedation (intravenous midazolam and fentanyl). Contrast agent was injected through the sheath to define the anatomy of the tract and the size and position of the bowel wall. The lining of the track was then debrided by passing an over-the-wire bronchoscopic brush up and down its full length. Then, the track was dilated by an angioplasty balloon. The track was irrigated with undiluted 1% hydrogen peroxide and a delivery sheath was passed over a guide wire until it was well within the target bowel. The device was implanted through the delivery sheath and positioned with its footplate within the bowel lumen. The device was sutured in place with absorbable suture and further secured with a Molnar disk (removed after 2 weeks).
Follow-up	<b>Mean: 15 months</b> (calculated by IP analyst from evidence table); (range: 3–32 months)
Conflict of interest/source of funding	One of the authors is a paid consultant for the manufacturer and the other 3 are paid employees of the manufacturer.

**Analysis****Follow-up issues:** None**Study design issues:** One patient was treated with an enterocutaneous fistula plug (EFP) device on 2 separate occasions.**Study population issues:** None**Other issues:** Reports the author's first use of the Biodesign plug.**Key efficacy and safety findings**

Efficacy							Safety
Number of patients analysed: 6							<ul style="list-style-type: none"> <li>33.3% (2/6) of patients experienced device migration:</li> <li>- Patient 4 presented a recurrent pelvic abscess 7 weeks after the procedure that revealed an underlying</li> </ul>
<b>Fistula closure</b>							
100% (6/6) fistulas were closed at 2 weeks' follow-up.							
	Age	Sex	Location	Follow-up (months)	Recurrence	Other	
1	76	Male	Rectum / Hartmann pouch	32	None	Patient underwent reversal of colostomy at 2 months.	
2	77	Female	Terminal	28	None	Patent had Crohn's disease.	

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			ileum				
3	73	Male	Jejunum	3	None	Patient was diagnosed with recurrence of tumour and hepatic metastatic disease at 3 months and subsequently died (timing not reported).	colonic fistula and a small pericolic abscess, which contained the silicon footplate of the EFP device. The colonic fistula was the recurrence of a separate defect previously closed with fibrin glue. The footplate was removed percutaneously and the abscess and fistula closed with 6 weeks of catheter drainage. - Patient 5: CT scan at 4 months showed that the EFP silicone footplate migrated out of the bowel lumen, causing presacral fluid collection. The footplate was removed percutaneously and a catheter left for drainage.
4	51	Female	Sigmoid colon	3.5	None	Patient subsequently underwent reversal of colostomy and an ischaemic stricture of sigmoid colon was resected (included fistulised area) at 3.5 months after the procedure.	
5	65	Female	Rectum / Hartmann pouch	9	Fistula reopened at 9 months	Patient died at 9 months from postoperative complications following additional surgical repairs when the fistula reopened (no further details provided).	
6	52	Male	Rectum / Hartmann pouch	16	Fistula reopened at 9 months. Presacral abscess also recurred with spontaneous purulent eruption from the site of earlier draining / EFP. After a short period of drainage the procedure was repeated without any recurrence at further 6 months.	At 10 weeks the patient underwent reversal of colostomy with reanastomosis.	
Abbreviations used: EFP, enterocutaneous fistula plug; FP, fistula plug; IP, interventional procedures; RYGBP, roux-en-y gastric bypass; SEMS, self-expanding metal stents; SEPS, self-expanding plastic stents							

## Study 2 Toussaint E (2009)

### Details

Study type	<b>Case series (of individual reports)</b>
Country	Belgium
Recruitment period	April 2006 to March 2007
Study population and number	<b>n=5 patients with enterocutaneous fistula</b>
Age and sex	Mean: 40 years; 80%(4/5) female
Patient selection criteria	Patients presenting with enterocutaneous fistulas following bariatric surgery that were refractory to other treatments (3 <sup>rd</sup> line treatment). Fistulas were defined by an outflow $\geq 50$ ml/day for more than 2 weeks, and occurrence following bariatric surgery. Median interval between fistula onset and treatment >20 weeks (4–44 weeks).
Technique	Closure of fistula using Surgisis collagen plug under endoscopic and fluoroscopic guidance. All performed with the patient under general anaesthesia. Three of the 5 patients also received a self-expanding metal stent (SEMS) or a self-expanding plastic stent (SEPS) in addition to the plug to close the fistula.
Follow-up	<b>Median: 18 months</b> (range: 8–29 months)
Conflict of interest/source of funding	Not reported

### Analysis

**Follow-up issues:** None

**Study design issues:** None

**Study population issues:** 60% (3/5) of patients had undergone sleeve gastrectomy, 40% (2/5) of patients had undergone Roux-en-Y gastric bypass (RYGBP).

**Other issues:** Fistula recurrence after 2<sup>nd</sup> treatment in a patient with a short fistula track did not allow implantation of the whole plug.

### Key efficacy and safety findings

Efficacy								Safety
Number of patients analysed: 5								No complications were observed and no mortality was associated with the procedure.
<b><i>Fistula closure and recurrence at follow-up (8-29 months)</i></b>								
	Age	Gender	Location	1 <sup>st</sup> procedure	Outcome after 1 <sup>st</sup> procedure	2 <sup>nd</sup> procedure	Outcome after 2 <sup>nd</sup> procedure	
1	40	Female	Gastrojejunal anastomosis	2FP+SEMS	complete closure	N/A	N/A	
2	43	Female	Sleeve	1FP+SEMS	recurrence	2FP+1SEMS	complete closure	
3	45	Female	Sleeve	1FP+SEPS	recurrence	1FP+2SEMS	recurrence	
4	34	Male	Sleeve	1FP	complete closure	N/A	N/A	
5	40	Female	Gastrojejunal anastomosis	1FP	recurrence	3FP+1SEMS	complete closure	

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Abbreviations used: EFP, enterocutaneous fistula plug; FP, fistula plug; IP, interventional procedures; RYGBP, roux-en-y gastric bypass; SEMS, self-expanding metal stents; SEPS, self-expanding plastic stents

## Study 3 Lomis NNT (2000)

### Details

Study type	<b>Case series (of individual reports)</b>
Country	US
Recruitment period	Not reported
Study population and number	n=5 patients with fistula or leak after percutaneous drainage of abdominal pelvic fluid collections.
Age and sex	Mean: 31.6 years (calculated by IP analyst from evidence table); 60% (3/5) female
Patient selection criteria	Consecutive patients with persistent leaks from the gastrointestinal tract to the skin refractory to conservative therapy. All patients had low to moderate volume of drainage (15–500 mL in 24 hours).
Technique	Closure of fistula using Vasoseal collagen plugs delivered via catheter directed techniques guided by fluoroscopy. All performed with the patient under local analgesia and sedation.
Follow-up	<b>Mean: 80 days</b> (calculated by IP analyst from evidence table) (range: 30–120 days, 4 patients)
Conflict of interest/source of funding	None

### Analysis

**Follow-up issues:** Patient 1 lost to follow-up at 120 days.

**Study design issues:** Imaging was only conducted for 2 patients (1 and 3).

**Study population issues:** The paper included 2 other patients who are not reported here because they did not have an enterocutaneous fistula; 1 patient with an anasthetic leak after paracentesis and 1 patient with a subhepatic leak.

**Other issues:** The paper does not describe the precise type of fistulas studied.

### Key efficacy and safety findings

Efficacy							Safety
Number of patients analysed: 5							No complications
	Gender	Age	Follow-up (days)	Location	Outcome	Other	
1	Male	30	120	Presacral	Full closure. CT at 3 days normal. Asymptomatic at 1 week.	Lost to follow up at 120 days	
2	Male	78	30	Pelvic abscess (2 tracks)	Full closure. Multiple other chest and abdominal abscesses. Died at 1 month.	Patient had multisystem illness from coccidioidomycosis. Patient had a fever at the time of the procedure.	
3	Female	27	90	Pelvic abscess	Full closure. Sinogram normal at 72 hours.	Patient had ulcerative colitis. Ileostomy takedown.	
4	Female	25	80	Intra-abdominal abscess	Full closure.	Patient has Crohn's disease	
5	Female	23	N/A	Abdominal wall	Plug failed (2 separate attempts made 1 week apart).	Authors report that patient had hypercortisolemia while indwelling tube was in place	

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					Required surgical closure of percutaneous endoscopic gastrostomy site.	which may have contributed to the failure of the plug (fistula track was of large calibre and short length).	
No fistula or abscess recurrence within the follow-up period.							
Abbreviations used: EFP, enterocutaneous fistula plug; FP, fistula plug; IP, interventional procedures; RYGBP, roux-en-y gastric bypass; SEMS, self-expanding metal stents; SEPS, self-expanding plastic stents							

## Study 4 Schultz DJ (2002)

### Details

Study type	<b>Case reports</b>
Country	US
Recruitment period	Not reported
Study population and number	n=2 <b>patients with enterocutaneous fistula</b>
Age and sex	Mean: 57.5 years; 50% (1/2) female
Patient selection criteria	Patients presenting enterocutaneous fistulas that have been refractory to non-operative management.
Technique	Closure of fistula using porcine small intestine submucosa under fluoroscopic guidance (patient 1) and without fluoroscopic guidance (patient 2). Sepsis prior to the procedure was controlled with percutaneous drainage and antibiotics
Follow-up	<b>Patient 1: 7 months; Patient 2: 12 months</b>
Conflict of interest/source of funding	Not reported

### Analysis

**Follow-up issues:** None

**Study design issues:** None

**Study population issues:** The technique was attempted on a 3<sup>rd</sup> patient but was aborted because the tract could not be cannulated.

**Other issues:** The device used was 'home-made'.

### Key efficacy and safety findings

Efficacy							Safety
Number of patients analysed: 2							Patient 1 was admitted on day 2 for 24 hours with fever to 102.4°F for which no cause was found (no further details given). This patient also reported several complaints of abdominal pain, nausea and vomiting with 1 admission for small bowel obstruction that resolved within 2 days of nasogastric suction.
<b><i>Fistula closure and recurrence</i></b>							
	<b>Age</b>	<b>Gender</b>	<b>Location</b>	<b>Follow-up (months)</b>	<b>Outcome</b>	<b>Comment</b>	
1	51	Female	pelvis	7	No fistula recurrence at follow-up.	See safety section.	Patient 2: no complications.
2	64	Male	Left upper quadrant of the abdomen	12	Continued to have fistula output at 1 day. Treated by removing the existing porcine submucosa and replacing with a new sheet of submucosa.  No fistula recurrence at follow-up.	Eating well and gaining weight at 1 year follow-up	
Abbreviations used: EFP, enterocutaneous fistula plug; FP, fistula plug; RYGBP, roux-en-y gastric bypass; SEMS, self-expanding metal stents; SEPS, self-expanding plastic stents							

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## Study 5 Wood J (2010)

### Details

Study type	<b>Case report</b>
Country	US
Recruitment period	Not reported
Study population and number	n=1 <b>patient with persistent gastrocutaneous fistula</b>
Age and sex	84-year-old male
Patient selection criteria	Patient with persistent gastrocutaneous fistula who had been managing the fistula with regular dressing changes, dietary modifications and proton pump inhibitors.
Technique	Closure of fistula using Surgisis collagen plug under endoscopic guidance. The patient was under general anaesthesia.
Follow-up	<b>19 months</b>
Conflict of interest/source of funding	None

### Analysis

**Follow-up issues:** None

**Study design issues:** None

**Study population issues:** None

**Other issues:** None

### Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: <b>1</b> The procedure took 15 minutes and the patient was discharged home the same day. He had good wound healing at 4-month follow-up. Patient remained on proton pump inhibitors but no longer restricted his diet. No evidence of fistula recurrence at 19-month follow-up.	No intra- or post-operative complications.
Abbreviations used: EFP, enterocutaneous fistula plug; FP, fistula plug; RYGBP, roux-en-y gastric bypass; SEMS, self-expanding metal stents; SEPS, self-expanding plastic stents	

## ***Efficacy***

### **Fistula closure and recurrence**

In a case series of 6 patients, fistula closure was achieved for 100% (6/6) of fistulas at 2 weeks but the fistula recurred in 33% (2/6) of patients. In both patients, the fistulas recurred at 9 months. The first patient died from postoperative complications after additional surgical repairs (no further details provided). For the second patient, after a short period of drainage, the procedure was repeated without any further recurrence at 6 months<sup>1</sup>.

In a case series of 5 patients, fistula closure was achieved for 40% (2/5) of fistulas after a few days. When closure did not occur, 67% (2/3) were closed by further treatment (timing not reported) without any further recurrence at 18-month median follow-up (range 8 to 29 months)<sup>2</sup>.

In a second case series of 5 patients, fistula closure was achieved for 80% (4/5) of fistulas at 80-day mean follow-up (range 30 to 120 days). In the remaining patient 2 separate procedures were done, 1 week apart, but closure was not achieved<sup>3</sup>.

## ***Safety***

Death was reported in 1 patient, 1 month after the procedure from coccidioidomycosis with multiple other chest and abdominal abscesses in a case series of 5 patients<sup>3</sup>. Death was reported in 1 patient 9 months after the procedure, as a result of postoperative complications after additional surgical repairs when the fistula reopened (no further details provided) in a case series of 6 patients<sup>1</sup>. Device migration was reported in 2 patients (both from the case series of 6 patients). One patient presented with a recurrent pelvic abscess 7 weeks after the procedure. A colonic fistula and a small pericolic abscess, which contained the silicon footplate of the device, were identified. The colonic fistula was the recurrence of a separate defect previously closed with fibrin glue. The footplate was removed percutaneously and the abscess and fistula closed after 6 weeks of catheter drainage. In the other patient, a CT scan at 4 months showed that the device footplate had migrated out of the bowel lumen, causing a pre-sacral fluid collection. The footplate was removed percutaneously and a catheter left in for drainage. The fistula recurred 9 months after the enterocutaneous fistula plug placement and the patient died from the postoperative complications following the additional surgical repairs (death reported in the previous section)<sup>1</sup>. One patient was admitted to hospital 2 days after the procedure because of pyrexia (102.4°F) in a case series of 2 patients: no cause was found and no further details were given. This patient had a further admission for small bowel obstruction that resolved within 2 days of nasogastric suction (timing not reported)<sup>4</sup>.

## ***Validity and generalisability of the studies***

- Very limited evidence base – only includes case reports with no long-term follow-up.

## ***Existing assessments of this procedure***

There were no published assessments from other organisations identified at the time of the literature search.

## ***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**

- Negative pressure wound therapy for the open abdomen. NICE interventional procedure guidance 467 (2013). Available from <http://guidance.nice.org.uk/IPG467>
- Closure of anal fistula using a suturable bioprosthetic plug. NICE interventional procedure guidance 410 (2011). Available from <http://guidance.nice.org.uk/IPG410>

## **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 does not represent the view of the society.

Dr Arcot. K. Venkatasubramaniam (Association of Coloproctology of Great Britain and Ireland), Dr Richard Owen and Dr Tarak Ramadan (British Society of Interventional Radiology).

- Two specialist advisers have never performed the procedure and 1 specialist adviser has performed the procedure at least once. All 3 advisers stated that the procedure is definitely novel and of uncertain safety and efficacy.
- One specialist adviser suggested an alternative shorter title for the procedure: 'Collagen plug for closure of abdominal wall enterocutaneous fistulas'.
- The comparator would be conservative measures (dietary modification, bowel rest [total parenteral nutrition], medications to decrease bowel fluid secretions) for 3–6 months, surgical repair (standard practice when conservative treatment fails), or fistula ablation with glue (NBCA) or Tisseal. In patients with Crohn's disease, the comparator would be infliximab infusions and subsequently surgery, which usually involves laparotomy.

- Theoretical adverse events: allergic reaction, increase in diameter or output of the fistula, peritonitis and bowel contents leaking into the abdominal cavity, bowel injury, vascular injury and bleeding.
- Anecdotal adverse event: 1 specialist adviser reported severe pain during the procedure requiring conversion to general anesthesia in 1 patient.
- Key efficacy outcome: permanent fistula closure and avoidance of need for surgical repair.
- Uncertainties: recurrence of fistula is a significant concern. The efficacy has to be assessed on a long-term basis. The specialist adviser who has performed the procedure reported that, while the closure success rate appears poor (somewhere between 20% and 80%, likely 50%, the surgical treatment of these fistulas also has a high recurrence rate. This group of patients often has some malnutrition and wound healing issues. This type of fistula is very difficult to treat.
- Training and facilities: healthcare staff should be trained on catheter and wire manipulation. There would need to be a fluoroscopy unit with a rotating C-arm. The manufacturer usually provides a model and product cards outlining the procedure in detail.
- Good team working between the colorectal surgeon and intervention radiologist is paramount in selecting patients and performing the procedure. The patients may need to be monitored for recurrence of the fistula and its consequences.
- Not many centres perform this procedure. Careful evaluation of the procedure is essential because there is insufficient evidence to promote it in a non-trial setting.
- One adviser stated that the speed of diffusion of the procedure may be fast if it proved to be effective and safe.
- Specialist advisers disagreed about how technically demanding the procedure is. One adviser who has never performed the procedure stated that it is not technically demanding and could be performed in most district hospitals that have a gastrointestinal interventional radiologist. The specialist adviser who has performed the procedure at least once stated that 'this is an uncommon and somewhat complex procedure and should only be attempted if other measures have failed. These fistulas are from bowel to the skin surface and a significant period of conservative management

such as dietary modification and/or total parenteral nutrition should have been tried; the majority of patients will either have had a failed surgical repair or are not surgical candidates due to co-morbidities’.

- Collagen-based products are widely used in managing complex abdominal wall hernias. There is evidence that collagen can disintegrate in the presence of small bowel contents. Long-term efficacy of collagen-based plugs in treating fistulas has to be evaluated in a trial setting.
- One adviser stated that the potential impact of this procedure on the NHS in terms of numbers of patients eligible for treatment and use of resources was moderate and the other 2 advisers stated that it was minor.
- One adviser stated that if the procedure is ‘effective and safe, it could potentially be extended to include other sets of patients such as patients with Crohn’s disease-related fistula, urinary bladder fistula, post-cholecystostomy and patients who had loop ileostomy/colostomy’.

## **Patient commentators’ opinions**

NICE’s Public Involvement Programme was unable to gather patient commentary for this procedure.

## **Issues for consideration by IPAC**

- The studies in the overview cover a range of techniques.
- NICE is not aware of any ongoing studies.

## References

1. Lyon JW, Hodde JP, Hucks D et al. (2013) First experience with the use of a collagen fistula plug to treat enterocutaneous fistulas. *Journal of Vascular & Interventional Radiology* 24:1559-1565.
2. Toussaint E, Eisendrath P, Kwan V et al. (2009) Endoscopic treatment of postoperative enterocutaneous fistulas after bariatric surgery with the use of a fistula plug: report of five cases. *Endoscopy* 41:560-563.
3. Lomis NN, Miller FJ, Loftus TJ et al. (2000) Refractory abdominal-cutaneous fistulas or leaks: percutaneous management with a collagen plug. *Journal of the American College of Surgeons* 190:588-592.
4. Schultz DJ, Brasel KJ, Spinelli KS et al. (2002) Porcine small intestine submucosa as a treatment for enterocutaneous fistulas. *Journal of the American College of Surgeons* 194:541-543.
5. Wood J, Leong S, McCarter M et al. (2010) Endoscopic-assisted closure of persistent gastrocutaneous fistula with a porcine fistula plug: report of a new technique. *Surgical Innovation* 17:53-56.

## **Appendix A: Additional papers on inserting a collagen plug device to close an enterocutaneous fistula on the abdominal wall**

There were no additional papers identified.

## Appendix B: Related NICE guidance for insertion of a collagen plug to close an abdominal wall enterocutaneous fistula

Guidance	Recommendations
Interventional procedures	<p><b>Negative pressure wound therapy for the open abdomen. NICE interventional procedure guidance 467 (2013).</b></p> <p>This document replaces previous guidance on negative pressure wound therapy for the open abdomen (interventional procedure guidance 322).</p> <p>1.1 Current evidence on the safety and efficacy of negative pressure wound therapy (NPWT) for the open abdomen is adequate to support the use of this procedure provided that normal arrangements are in place for consent, audit and clinical governance.</p> <p>1.2 NPWT for the open abdomen should only be carried out by healthcare professionals with specific training in the procedure: it should be done in accordance with the manufacturer's instructions when commercial products are used.</p> <p>1.3 NICE encourages further research into the role of NPWT for the open abdomen. Patient selection should be documented and research should report on efficacy outcomes such as impact on wound care and healing rates, and duration of hospital stay.</p> <p><b>Closure of anal fistula using a suturable bioprosthetic plug. NICE interventional procedure guidance 410 (2011)</b></p> <p>This document replaces previous guidance on closure of anal fistula using a suturable bioprosthetic plug (interventional procedure guidance 221). For details see <a href="#">'About this guidance'</a>.</p> <p>1.1 Current evidence on closure of anal fistula using a suturable bioprosthetic plug raises no major safety concerns. The evidence on efficacy is inadequate in quantity and quality. Therefore this procedure should only be used with special arrangements for clinical governance, consent and audit or research.</p> <p>1.2 Clinicians wishing to undertake closure of anal fistula using a suturable bioprosthetic plug are encouraged to enter patients into the Fistula-In-Ano Trial (FIAT) (<a href="http://www.hta.ac.uk/project/1998.asp">www.hta.ac.uk/project/1998.asp</a> or <a href="http://www.controlled-trials.com/ISRCTN78352529">www.controlled-trials.com/ISRCTN78352529</a>). Clinicians wishing to undertake closure of anal fistula using a suturable bioprosthetic plug outside a clinical trial should take the following actions.</p> <ul style="list-style-type: none"> <li>• Inform the clinical governance leads in their Trusts.</li> <li>• Ensure that patients understand the uncertainty about</li> </ul>

	<p>the procedure's efficacy and provide them with clear written information. In addition, use of NICE's information for patients (<a href="#">Understanding NICE guidance</a>) is recommended.</p> <ul style="list-style-type: none"><li>• Audit and review clinical outcomes of all patients having closure of anal fistula using a suturable bioprosthesis plug (see <a href="#">section 3.1</a>).</li></ul> <p>1.3 Closure of anal fistula using a suturable bioprosthesis plug should only be carried out by surgeons with specific training in the procedure. The methods agreed for the FIAT trial provide a useful source of information on technical aspects of the procedure.</p> <p>1.4 NICE may review the procedure upon publication of further evidence.</p>
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## Appendix C: Literature search for insertion of a collagen plug to close an abdominal wall enterocutaneous fistula

Database	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	26/03/2014	Issue 3 of 12, March 2014
Database of Abstracts of Reviews of Effects – DARE (CRD website)	26/03/2014	Issue 1 of 4, January 2014
HTA database (CRD website)	26/03/2014	Issue 1 of 4, January 2014
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	26/03/2014	Issue 1 of 12, January 2014
MEDLINE (Ovid)	26/03/2014	1946 to March Week 2 2014
MEDLINE In-Process (Ovid)	26/03/2014	March 25, 2014
PubMed	26/03/2014	n/a
EMBASE (Ovid)	26/03/2014	1974 to 2014 Week 12
BLIC	26/03/2014	n/a

Trial sources searched on 21/03/2014:

- National Institute for Health Research Clinical Research Network Coordinating Centre (NIHR CRN CC) Portfolio Database
- Current Controlled Trials *meta*Register of Controlled Trials – *m*RCT
- Clinicaltrials.gov

Websites searched on 21/03/2014:

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- French Health Authority (FHA)
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- Conference websites <<add details>>
- 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 Intestinal Fistula/
2	((enterocutaneous* or intestin* or external* or jejun* or rect* or bowel* or colon* or gastro* or duoden* or ileal* or ileum*) adj4 fistula*).tw.
3	ECF.tw.
4	Crohn Disease/
5	(Crohn* adj4 (diseas* or syndrom*)).tw.
6	(regional* adj4 enteritis).tw.
7	or/1-6
8	"Prostheses and Implants"/
9	Collagen/tu
10	((collagen* or bioprosthetic* or biosynthetic* or biomaterial*) adj4 (plug* or graft* or repair* or fix* or clos* or implant* or block*)).tw.
11	((porcine* or pig* or animal*) adj4 (collagen* or plug* or graft* or repair* or fix* or clos* or implant* or block*)).tw.
12	(porcine* adj4 intestin* submucosa*).tw.
13	"enterocutaneous fistula plug".tw.
14	EFP.tw.
15	or/8-14
16	7 and 15
17	Biodesign.tw.
18	16 or 17
19	animals/ not humans/
20	18 not 19