NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of implantation of a duodenal–jejunal bypass sleeve for managing obesity

Inserting a plastic sleeve into the bowel for managing obesity

In this procedure a plastic tube-like sleeve or liner is inserted through the mouth into the bowel to line the upper part of the bowel. This is usually removed through the mouth after a year. It forms a barrier between food and the bowel and slows digestion.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this 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 overview was prepared in October 2012.

Procedure name

- Implantation of a duodenal-jejunal bypass sleeve for managing obesity

Specialist societies

- British Obesity and Metabolic Surgery Society
- British Society of Gastroenterology
- Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland
- Diabetes UK.

Description

Indications and current treatment

Obesity is defined as a body mass index (BMI) of 30 kg/m^2 or more. It is a risk factor for comorbidities such as type 2 diabetes, coronary heart disease and

hypertension. Weight loss reduces the risks of comorbidities and improves long-term survival.

Obesity is managed by dietary advice, exercise, lifestyle changes and medication. Bariatric surgery is considered as a treatment option in selected patients whose BMI is over 40 kg/m^2, or over 35 kg/m^2 for patients with other significant comorbidities, if they have not lost enough weight using non-surgical measures.

Surgical procedures aim to help patients lose weight by restricting the size of the stomach (for example, gastric banding or sleeve gastrectomy) and/or by decreasing the patient's capacity to absorb food (for example, Roux-en-Y gastric bypass or biliopancreatic diversion).

What the procedure involves

Endoscopic implantation of a duodenal-jejunal bypass sleeve (DJBS) is a minimally invasive procedure that has been used to promote weight loss in patients with obesity and with a view to improving comorbidities, including diabetes.

The procedure is done with the patient under general anaesthesia or sedation, using image guidance. The sleeve is positioned endoscopically (via the mouth). Using a delivery catheter, a capsule containing a single-use impermeable DJBS is positioned in the duodenal bulb just distal to the pylorus and is secured there using an integral spring metal anchor. The sleeve is advanced distally into the jejunum with the aid of a tension wire which is part of the introducer device. It extends approximately 60 cm down the small intestine and forms a barrier between food and the intestinal wall, delaying the mixing of digestive enzymes with the food.

After the procedure, patients are placed on a diet that typically involves progression from fluids to semi-solid foods, before returning to solid foods.

After a maximum of a year, the sleeve is removed under sedation, using endoscopy and image guidance. The anchor incorporates a drawstring mechanism that enables it to be collapsed and partly withdrawn into a plastic hood fitted to the endoscope. The entire device is then withdrawn.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to implantation of a duodenal-jejunal bypass sleeve for managing obesity. Searches were conducted of the following databases, covering the period from their commencement to 30 October 2012: 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 obesity and with or without type 2 diabetes.
Intervention/test	Implantation of a duodenal-jejunal bypass sleeve.
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 overview

This overview is based on approximately 335 patients from 4 RCTs[1–4] and 5 case series[5–9].

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 implantation of a duodenal-jejunal bypass sleeve for managing obesity

Abbreviations used: BMI: body mass index; DJBS: duodenal-jejunal bypass sleeve; EWL: excess weight loss; FPG: fasting plasma glucose; GA: general anaesthesia; GI: gastrointestinal; HbA1c: glycated haemoglobin; HDL: high-density lipoprotein; ITT: intention to treat; KUB: kidneys, ureters and bladder; LOCF: last observation carried forward; NIH: National Institutes of Health; PPI: proton pump inhibitors; SD: standard deviation; T2DM: Type 2 diabetes mellitus; TG/HDL ratio: triglyceride to high-density lipoprotein ratio.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Gersin K (2010)[1]
RCT
USA (4 centres)
Recruitment period: 2007–8
Study population: obese patients needing to lose weight before bariatric surgery
n=56 (27 DJBS vs 29 sham endoscopy) patients
Age: DJBS: 45years, sham: 43 years
Sex: 81% female (DJBS 71% female, sham 89% female)
Mean BMI: 46 kg/m^2
Patient selection criteria: age 18-55 years, baseline BMI 40kg/m^2 to 60 kg/m^2, or 35 kg/m^2 or more for patients with comorbidities.
Technique: DJBS (EndoBarrier) implanted and explanted under fluoroscopy and endoscopy. PPI prescribed for duration of study period.</td>
<td>Number of patients analysed: 25 DJBS vs 26 sham endoscopy (ITT)
Implantation outcomes
<table>
<tr><td>Implantation success</td><td>21/25</td></tr>
<tr><td>Implantation failure
(1 due to combination of difficult anatomy and investigator inexperience)
(3 due to short duodenal bulb)</td><td>(4/25)</td></tr>
</table>
Weight loss at 12 weeks (mean±SD)
<table>
<tr><th></th><th>DJBS (n=13)</th><th>Sham endoscopy (n=24)</th><th>p value</th></tr>
<tr><td>Mean % EWL</td><td>11.9±1.4</td><td>2.7±2.0</td><td>0.001</td></tr>
<tr><td>Mean % of patients with >10% EWL</td><td>62
(8/13)</td><td>17
(4/24)</td><td>0.01</td></tr>
<tr><td>Total weight change (kg)</td><td>−8±1.3</td><td>−2.1±1.1</td><td>0.002</td></tr>
<tr><td>Weight decrease (%)</td><td>5.8 ±0.7</td><td>1.5 ±0.9</td><td>0.002</td></tr>
</table>
</td>
<td>Early explantations
<table>
<tr><th>Total explants</th><th>38% (8/21)</th></tr>
<tr><td>GI bleeding with haematemesis at 11, 25 and 43 days post implantation. (severe in 2 patients, treated with sclerotherapy and endoscopic clips in 1, no further treatment needed in the other 2).</td><td>3</td></tr>
<tr><td>Abdominal pain, nausea and/or vomiting at 3, 9, 30 and 36 days (resolved with no treatment)</td><td>4</td></tr>
<tr><td>unrelated illness (breast carcinoma)</td><td>1</td></tr>
</table>
No symptoms of biliary obstruction, pancreatic duct obstruction or obstruction or migration of the device.
Adverse events in DJBS arm with more than 1% frequency (n=27, total events-108)
<table>
<tr><th>Adverse event</th><th>% (n)</th></tr>
<tr><td>Upper abdominal pain</td><td>13 (14)</td></tr>
<tr><td>Procedural nausea</td><td>9.3 (10)</td></tr>
<tr><td>Procedural</td><td>5.6 (6)</td></tr>
</table>
</td>
<td>Follow-up issues:
6 patients in the DJBS arm (2 who withdrew prior to implantation, 4 who had unsuccessful procedures) and 3 patients in the sham arm (who all withdrew prior to implantation) were lost to follow-up at the beginning of the study. A further 10 patients (8 in the DJBS arm and 2 in the sham arm) were lost to follow-up before 12 weeks.
Study design issues:
Patients were blinded but study personnel were not.
Study population issues:</td>
</tr>
</table>

Abbreviations used: BMI: body mass index; DJBS: duodenal-jejunal bypass sleeve; EWL: excess weight loss; FPG: fasting plasma glucose; GA: general anaesthesia; GI: gastrointestinal; HbA1c: glycated haemoglobin; HDL: high-density lipoprotein; ITT: intention to treat; KUB: kidneys, ureters and bladder; LOCF: last observation carried forward; NIH: National Institutes of Health; PPI: proton pump inhibitors; SD: standard deviation; T2DM: Type 2 diabetes mellitus; TG/HDL ratio: triglyceride to high-density lipoprotein ratio.

Study details	Key efficacy findings	Key safety findings	Comments
Sham arm; endoscopy and mock implantation Nutritional counselling at baseline. Follow-up: **12 weeks** Conflict of interest/source of funding: the study was funded by GI Dynamics (manufacturer). The first author is a consultant and shareholder in GI Dynamics.		vomiting Nausea 5.6 (6) Vomiting 3.7 (4) Constipation 2.8 (3) GI bleeding (with decrease in haemoglobin and haematocrit) 2.7 (3) Haematemesis 2.7 (3) Abdominal pain 1.9 (2) Dyspepsia 1.9 (2) Anaemia 1.9 (2) Pyrexia 1.9 (2) The majority of adverse events were mild or moderate. GI bleeding presented in this table might overlap with those presented above (not clear why these are reported separately). Comparative data for the sham arm were not reported.	• The DJBS patients had more comorbidities than patients in the sham endoscopy group. **Other issues**: • Lack of data on calorie intake.

Abbreviations used: BMI: body mass index; DJBS: duodenal-jejunal bypass sleeve; EWL: excess weight loss; FPG: fasting plasma glucose; GA: general anaesthesia; GI: gastrointestinal; HbA1c: glycated haemoglobin; HDL: high-density lipoprotein; ITT: intention to treat; KUB: kidneys, ureters and bladder; LOCF: last observation carried forward; NIH: National Institutes of Health; PPI: proton pump inhibitors; SD: standard deviation; T2DM: Type 2 diabetes mellitus; TG/HDL ratio: triglyceride to high-density lipoprotein ratio.

Study details

Rodriguez L (2009)[2]

RCT

Chile (single centre)

Recruitment period: 2007–8

Study population: patients with type 2 diabetes and obesity.

n=**18 (12 DJBS vs 6 sham endoscopy)**

Mean age: DJBS arm 45 years, sham arm 51 years

Sex: DJBS arm 67% female, sham arm 50% female

Mean BMI: DJBS arm 38.9 kg/m^2, sham arm 39.0 kg/m^{2}Mean HbA_{1c}: 9.1%

Patient selection criteria: aged 18–55 years with type 2 diabetes for more than 10 years and an HbA_{1c} 7–10%, fasting plasma glucose under 240 mg/dL and BMI 30–50 kg/m2.

Technique: DJBS (EndoBarrier) procedures used fluoroscopy and

Key efficacy findings

Number of patients analysed: **12 DJBS vs 6 sham endoscopy**

Change in glycaemic control measured by HbA_{1c} (ITT population) (mean±SD)

Mean HbA_{1c} %	**DJBS arm (n=12)**	**Sham arm (n=6)**	**p value**
Baseline	9.2	9.0	>0.05
12 weeks	−1.3±0.9	0.8±0.3	>0.05
24 weeks	−2.4±0.7	−0.8± 0.4	>0.05

HbA_{1c} change in population completing treatment is more than 0.05 at all time points between both arms.

Mean weight loss (ITT population) (mean±SD)

Mean weight change (kg)	**DJBS arm (n=12)**	**Sham arm (n=6)**
Week 1	−4.0±0.4	−4.0±0.6
Week 20	−10.2±1.3	−7.3±4.3

For the first 12 weeks mean weight loss was comparable (p>0.05) for both treatment arms for both ITT and completer groups. At week 24, there were only 3 sham patients remaining.

Change in FPG concentration (ITT population) (mean ±SD)

Mean FPG mg/dl	**DJBS arm (n=12)**	**Sham arm (n=6)**	**p value**
Baseline	193±24	140±38	<0.05
Week 1	−50±18	+25±29	0.042
12 weeks	−45±26	−8±35	>0.05
24 weeks	−83±39	+16±42	>0.05

Both arms had equivalent baseline FPG concentrations.

Key safety findings

Explants during 12 weeks' follow-up % (n)

Anchor migration (1 turned or migrated)	42 (5/12)
Migration with symptoms (moderate pain (n=1), nausea and moderate vomiting (n=1) and mild abdominal pain and vomiting (n=1)	60 (3/5)
Migration with no symptoms (noted at removal (n=1) and at scheduled endoscopy (n=1).	40 (2/5)

Adverse events (total 64)

Adverse events	**DJBS % (n=episodes)**
Upper abdominal pain (in 12 patients)	30.8 (20)
Vomiting (in 4 patients)	10.8 (7)
Abdominal pain	4.6 (3)
Nausea	7.7 (5)
Symptoms of hypoglycaemia (blood glucose more than 100 mg/dl)	7.7 (5)
Decreased blood iron	6.2 (4)

Comments

Follow-up issues:

- 42% (5/12) of patients in the device arm (with explanted devices) and 24% (2/6) of patients in the sham ITT arm were lost to follow-up at 12 weeks.

Study design issues:

- The method of randomisation was not reported. There was no allocation concealment.
- There was no significant difference between groups at baseline.
- Diabetic medications used were metformin and/or sulfonylurea. Patients in DJBS arm were taken off metformin more than sham group.

Abbreviations used: BMI: body mass index; DJBS: duodenal-jejunal bypass sleeve; EWL: excess weight loss; FPG: fasting plasma glucose; GA: general anaesthesia; GI: gastrointestinal; HbA1c: glycated haemoglobin; HDL: high-density lipoprotein; ITT: intention to treat; KUB: kidneys, ureters and bladder; LOCF: last observation carried forward; NIH: National Institutes of Health; PPI: proton pump inhibitors; SD: standard deviation; T2DM: Type 2 diabetes mellitus; TG/HDL ratio: triglyceride to high-density lipoprotein ratio.

Study details

endoscopy. Endoscopy 3 days and 4 weeks after explantation.

Sham procedure; upper GI endoscopy.

Liquid diet for the first week, pureed food during the second week and solids thereafter. Recommended intake 1200 calories per day for women and 1500 calories per day for men. 2.

Follow-up: **24 weeks**

Conflict of interest/source of funding: study funded by manufacturer. Authors are consultants/ shareholder for GI Dynamics.

Key efficacy findings

Oral antidiabetic medication use

	Follow-up	DJBS arm %	Sham arm %
Ceased drug use (ITT group)*	Week 12	42	17
Ceased drug use (group who completed treatment)**	Week 12	50	25
Ceased drug use (remaining patients)***	Week 24	40	25

*All treated patients. **All patients who completed at least 24 weeks.

***Patients remaining on the study.

Postprandial 7-point blood glucose profile

Mean postprandial plasma glucose AUC*	DJBS arm (n=12)	Sham arm (n=6)	p value
Baseline mg/dL	31,226± 11,570	27,558± 11,480	>0.05
Week 1	22% decrease	16% increase	0.016

*Area under the curve.

There was no change in postprandial insulin concentrations in either arm.

Key safety findings

Serum ferritin (not clear why it is reported separately from the one above)	1.5 (1)
Flatulence	4.6 (3)
Procedural vomiting	4.6 (3)
increased blood cholesterol	3.1 (2)
Erosive duodenitis	1.5 (1)
Constipation	1.5 (1)
Diarrhoea	1.5 (1)
Gastritis	1.5 (1)
Headache	1.5 (1)
Decreased HDL cholesterol	1.5 (1)
Esophagitis	1.5 (1)
Pain	1.5 (1)

All events were mild or moderate.

Comments

Abbreviations used: BMI: body mass index; DJBS: duodenal-jejunal bypass sleeve; EWL: excess weight loss; FPG: fasting plasma glucose; GA: general anaesthesia; GI: gastrointestinal; HbA1c: glycated haemoglobin; HDL: high-density lipoprotein; ITT: intention to treat; KUB: kidneys, ureters and bladder; LOCF: last observation carried forward; NIH: National Institutes of Health; PPI: proton pump inhibitors; SD: standard deviation; T2DM: Type 2 diabetes mellitus; TG/HDL ratio: triglyceride to high-density lipoprotein ratio.

Study details

Schouten R (2010)[3]

RCT

Netherlands (2 centres)

Recruitment period: not reported

Study population: patients with obesity who needed to lose weight before bariatric surgery

n = **41 (30 DJBS vs 11 diet alone)**

Mean age: device group 40.9 years, control group 41.2 years

Sex: DJBS arm 73% female, control arm 81% female

Mean BMI: DJBS arm 48.9 kg/m^2; control arm 47.4 kg/m^2

Patients with diabetes: DJBS arm 8, control arm 2

Patient selection criteria: aged 18– 55 years, BMI 40 –60 kg/m^2, or over 35kg/m^2 with related comorbidities. Patients were screened by a dietician and a psychologist and on a

Key efficacy findings

Number of patients analysed: **41 [30 DJBS vs 11 diet alone]**

Procedure outcomes % (n)

Implantation success	88 (26/30)
Implantation failure due to difficult anatomy at the beginning of the study (sharp curve between pylorus and duodenal bulb)	12 (4/30)
Explantation success	100

Weight loss after 12 and 24 weeks

	Follow-up	DJBS arm	Diet alone	p value
Mean % EWL	12 weeks	19% (n=24)	6.9% (n=11)	<0.002
Mean % of patients with >10% EWL	12 weeks	88%	27.3%	<0.05
Decrease in BMI (kg/m^2)	12 weeks	5.5 kg/m^2	1.9 kg/m^2	-
Mean % EWL	24 weeks	24.3 (n=3)	-	-

Type 2 diabetes at 12 weeks (mean±SD)

	Follow-up	DJBS arm (n=8)	Control arm (n=2)	p value
Fasting glucose	Baseline	11.1±4.3	7.6±2.4	0.23

Key safety findings

Explants prior to study completion % (n)

Total early explants	27% (8/26)
Migration (30 cm device migration at 4 months=1, at 24 weeks=4)	5
Dislocation of the anchor (after 3 months with epigastric pain*)	1
Sleeve obstruction (after 1 week with nausea and vomiting*)	1
Continuous epigastric pain (removed at 3 months*)	1

*Resolved after explantation.

Device in situ adverse events

	DJBS arm % (n=26)	Control arm % (n=11)
Patients with at least 1 adverse event	100	27.3 (3/11)
Nausea (first week)	76.9 (20/26)	9.1 (1/11)
Upper abdominal pain (first week)	50 (13/26)	
Pseudopolyp formation (noted at endoscopy or during device explantation)	50 (13/26)	

Comments

Follow-up issues:

- Overall, 69% (18/26) of patients completed the study.

Study design issues:

- There was no allocation concealment and the outcome assessors were not blinded.

Study population issues:

- DJBS group patients had more obesity-related complications than the diet control group.
- 10 patients (8 in DJBS arm and 2 in control arm) had type 2 diabetes for a mean period of 3 years.

Other issues:

Abbreviations used: BMI: body mass index; DJBS: duodenal-jejunal bypass sleeve; EWL: excess weight loss; FPG: fasting plasma glucose; GA: general anaesthesia; GI: gastrointestinal; HbA1c: glycated haemoglobin; HDL: high-density lipoprotein; ITT: intention to treat; KUB: kidneys, ureters and bladder; LOCF: last observation carried forward; NIH: National Institutes of Health; PPI: proton pump inhibitors; SD: standard deviation; T2DM: Type 2 diabetes mellitus; TG/HDL ratio: triglyceride to high-density lipoprotein ratio.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>waiting list for laparoscopic gastric bypass.

Technique: DJBS (EndoBarrier) implanted under GA and direct endoscopic guidance. Fluoroscopic guidance used after the first 8 implantations.

All patients followed low-calorie diet under supervision by a dietician. Patients also received PPI and multivitamin supplements during the study.

Follow-up: 3 months

Conflict of interest/source of funding: the study was supported by GI Dynamics (manufacturer of the device).</td>
<td>
<table>
<tr><td>(mmol/L)</td><td>12 weeks</td><td>9.3±3.8</td><td>6.7±1.1</td><td>0.13</td></tr>
<tr><td rowspan="2">HbA_{1c} %</td><td>Baseline</td><td>8.8±1.7</td><td>7.3±0.1</td><td>0.04</td></tr>
<tr><td>12 weeks</td><td>7.7±1.8</td><td>6.9±0.6</td><td>0.32</td></tr>
</table>
Diabetic status improved in 6 out of 8 patients in the device arm after 1 week (lower glucose levels, HbA_{1c}, and reduction in medication use).
</td>
<td>
<table>
<tr><td>Implant site inflammation (noted at endoscopy or during device explantation)</td><td>38.5 (10/26)</td><td></td></tr>
<tr><td>Vomiting (first week)</td><td>23 (6/26)</td><td></td></tr>
<tr><td>Adverse drug reaction</td><td>7.7 (2/26)</td><td></td></tr>
<tr><td>HbA_{1c} increase</td><td></td><td>9.1 (1/11)</td></tr>
<tr><td>Hypercholesterolaemia</td><td></td><td>9.1 (1/11)</td></tr>
<tr><td>Other (such as transient pyrosis, perioperative hypoxia or chest pain)</td><td>73.1 (19/26)</td><td>9.1 (1/11)</td></tr>
</table>
None of the events were severe, 61.3% were mild, and 38.7% were moderate. All minor events resolved after temporary medication.
</td>
<td>

Investigators took less time with the procedure as they gained experience and modified the technique with fluoroscopy guidance.

</td>
</tr>
</table>

Abbreviations used: BMI: body mass index; DJBS: duodenal-jejunal bypass sleeve; EWL: excess weight loss; FPG: fasting plasma glucose; GA: general anaesthesia; GI: gastrointestinal; HbA1c: glycated haemoglobin; HDL: high-density lipoprotein; ITT: intention to treat; KUB: kidneys, ureters and bladder; LOCF: last observation carried forward; NIH: National Institutes of Health; PPI: proton pump inhibitors; SD: standard deviation; T2DM: Type 2 diabetes mellitus; TG/HDL ratio: triglyceride to high-density lipoprotein ratio.

Study details

Tarnoff M (2009)[4]

RCT (multicentre pilot trial)

Chile

Recruitment period: not reported

Study population: patients with obesity who needed to lose weight before bariatric surgery

n=**40 (26 DJBS and low-calorie diet vs 14 low-calorie diet alone)**

Mean age: DJBS arm 38 years; control arm 43 years

Sex: DJBS arm- 60% female, control arm 57% female

Mean BMI: DJBS arm 42 kg/m^2, control arm 40 kg/m^2

Diabetes: DJBS arm 3, Control arm 1

Patient selection criteria: reflected current NIH guidelines for bariatric surgery :18–55 years old, BMI over 35 kg/m^2 with significant comorbidities or BMI 40-60 kg/m^2 with

Key efficacy findings

Number of patients analysed: **39 (25 DJBS and low-calorie diet vs 14 low-calorie diet alone)**

Procedural outcomes

Implantation success % (5 patients needed multiple implantation attempts due to difficulty advancing the catheter or positioning the anchor in the duodenal bulb)	100
Explantation success %	100

Weight loss at 12 weeks (mean±SD)

	DJBS arm	**Diet alone**	**p value**
% EWL	22.1±8 (n=19)	5.3±6.6 (n=4)	0.02
Absolute weight reduction	10.3±3.2 kg (n=19)	2.6±3.5 kg (n=4)	
% of patients who achieved at least 10% EWL	92 (23/25)	21 (3/14)	0.0001

Improvement in type 2 diabetes status

	DJBS arm (n=3)	**Diet alone (n=1)**
Diabetic status (week 1)	Improved	Improved
Diabetic status (12 weeks)	Improved* in 2 and resolved**	Improved

Key safety findings

Device in situ related events

Adverse events	**Device arm % (n=25)**
At least 1 adverse event	64 (16/25) (56 events)
Severe adverse events	**20 (5/25)** **5 events**
Upper gastrointestinal bleeding at mean of 14 days (n=3),	**12 (3/25)**
Anchor migration 2 cm from original position on day 47 with abdominal pain and several episodes of haematemesis (n=1; blood transfusion given),	**4 (1/25)**
Sleeve obstruction presented with abdominal pain and vomiting on day 30 (n=1)	**4 (1/25)**
(all devices were explanted, symptoms resolved, endoscopic examination showed no defined bleeding source and no further intervention was needed)	

Comments

Follow-up issues:

- The device was not implanted in 1 patient because of difficulties with their duodenal anatomy.
- 20% (5/25) of patients in the device group (who had their devices explanted early) and 71% (10/14) of patients in the control group were lost to follow-up at 12 weeks.

Study design issues:

- Outcome assessors were not blinded.

Study population issues:

- Four patients had type 2 diabetes (3 in the DJBS arm, 1 in the control arm).
- 5 explanted

Abbreviations used: BMI: body mass index; DJBS: duodenal-jejunal bypass sleeve; EWL: excess weight loss; FPG: fasting plasma glucose; GA: general anaesthesia; GI: gastrointestinal; HbA1c: glycated haemoglobin; HDL: high-density lipoprotein; ITT: intention to treat; KUB: kidneys, ureters and bladder; LOCF: last observation carried forward; NIH: National Institutes of Health; PPI: proton pump inhibitors; SD: standard deviation; T2DM: Type 2 diabetes mellitus; TG/HDL ratio: triglyceride to high-density lipoprotein ratio.

Study details

or without a comorbid condition, a history of failure with nonsurgical weight loss methods, candidates for Roux-en-Y gastric bypass.

Technique: DJBS (EndoBarrier) implanted under GA, with fluoroscopy and endoscopy guidance. PPI used throughout the study period. Liquid diet for 1 week and pureed diet for the second week.

All patients counselled on diet, exercise, and lifestyle change. at baseline. .

Follow-up: **12 week**

Conflict of interest/source of funding: none reported.

Key efficacy findings

	in 1	
% EWL (12 weeks)	19± 13.6	+0.8

*defined as reduction in HbA_{1c} and/or reduction of medications.

**elimination of diabetic medications with normal fasting plasma glucose and glycosylated haemoglobin.

Satiety assessment at 12 weeks

	DJBS arm % (n=19)	**Diet alone % (n=4)**
Greater satiety	89 (17/19)	0
Less satiety	5 (1/19)	100
Same satiety	5 (1/19)	0

Key safety findings

Mild to moderate adverse events	**80 (20/25) (51 events)**
Device related	86% (48 events)
Abdominal pain	100 (16/16)
Nausea	43 (7/16)
Vomiting	50 (8/16)
Abdominal distension	68 (11/16)
Gastrointestinal haemorrhage and drop in haemoglobin and haematocrit.	25 (4/16)
Constipation	6 (1/16)
Epigastric discomfort	6 (1/16)
Mild degrees of residual duodenal inflammation at 4 weeks post explant EGD	32% (8/25)

No signs or symptoms of biliary or pancreatic duct obstruction.

Implant procedure related adverse events

Non-cardiac chest pain (due to inadvertently placed endoscope and catheter in the oesophagus causing distension of the oesophagus and manifesting as significant chest pain) (1/25)

Comments

patients had gastric bypass surgery within weeks of explantation.

Other issues:

- Several technical limitations such as modification of the anchor barb design, which caused bleeding or haematemesis, migration and early learning curve issues such as the multiple implantation attempts in 5 patients and patency of the device were identified by the authors.

Abbreviations used: BMI: body mass index; DJBS: duodenal-jejunal bypass sleeve; EWL: excess weight loss; FPG: fasting plasma glucose; GA: general anaesthesia; GI: gastrointestinal; HbA1c: glycated haemoglobin; HDL: high-density lipoprotein; ITT: intention to treat; KUB: kidneys, ureters and bladder; LOCF: last observation carried forward; NIH: National Institutes of Health; PPI: proton pump inhibitors; SD: standard deviation; T2DM: Type 2 diabetes mellitus; TG/HDL ratio: triglyceride to high-density lipoprotein ratio.

Study details

de Moura (2011)[5]

Case series

Brazil

Recruitment period: not reported

Study population: morbidly obese and type 2 diabetes patients

n=**81**

Age: mean 50.8 years

Sex: 84.4% female

Mean BMI: 43.8 kg/m^2

Patient selection criteria: aged 18- 65 years with a BMI over 35 kg/m^2, T2DM with or without comorbidities, TG/HDL ratio ≥3.5,

Technique: DJBS (EndoBarrier)procedures used fluoroscopy and endoscopy. PPI used in entire study. Liquid diet initially, solid diet in 3rd week.

Follow-up: **6 months**

Conflict of interest/source of funding: 2 authors independent consultants of GI Dynamics.

Key efficacy findings

Number of patients analysed: **54**

Procedural outcomes % (n)

Implantation success	96 (78/81)
Implantation failure (due to short duodenal bulb)	4 (3/81)

Improvement in insulin resistance and metabolic syndrome at 6 months

	Patients N*	**Initial average TG/HDL ratio**	**Final average TG/HDL ratio**	**p value**
Controlled TG/HDL	23	5.15	2.85	<0.001
Not controlled TG/HDL ratio	31	6.2	5.47	0.1641
Total	54	5.75	4.36	<0.001

*Patients presented with insulin resistance and metabolic syndrome

Control of diabetes (HbA1c improvement) at 6 months

All patients implanted with the device achieved reductions in HbA1c (p<0.001).

Weight loss

Average weight loss of 12.6% of their initial weight.

Relationship between TG/HDL ratio control and weight loss

Comparing the patients who lost weight with the patients who controlled their TG/HDL ratio, an association can be observed between a weight loss greater than 10% of initial weight and control of TG/HDL ratio (p|<0.01) with an odds ratio of 5.06.

Key safety findings

Early explantations

Total explants	**16**
Migration	9
Observation of a free device anchor during endoscopy	4
Bleeding without migration	1
Patient request	1
Investigator decision	1

12 devices were removed at 16 weeks, 2 at 12 weeks and 2 at 4 weeks.

Comments

Follow-up issues:

- 38/54 patients completed the study (26 completed 24 weeks, 12 completed 20 weeks).

Study design issues:

- 70% (54/77) of the patients had an initial TG/HDL ratio greater than or equal to 3.5 indicating insulin resistance and metabolic syndrome.

Study population Comorbidities: 86% had hypertension, 36.7% had hyperlipidaemia.

Abbreviations used: BMI: body mass index; DJBS: duodenal-jejunal bypass sleeve; EWL: excess weight loss; FPG: fasting plasma glucose; GA: general anaesthesia; GI: gastrointestinal; HbA1c: glycated haemoglobin; HDL: high-density lipoprotein; ITT: intention to treat; KUB: kidneys, ureters and bladder; LOCF: last observation carried forward; NIH: National Institutes of Health; PPI: proton pump inhibitors; SD: standard deviation; T2DM: Type 2 diabetes mellitus; TG/HDL ratio: triglyceride to high-density lipoprotein ratio.

Study details

Escalona L (2012)[6]

Case series

Chile

Recruitment period: 2009–10

Study population: morbidly obese patients

n=**42**

Age: mean 36 years

Sex: 80% female

Mean BMI: 43.7 kg/m^2

Patients with type 2 diabetes: 6

Patient selection criteria: between 18 and 55 years with a BMI greater than 35 kg/m^2 if presenting with comorbidities such as hypertension, diabetes, and/or dyslipidaemia; otherwise with a BMI 40–60 kg/m^2.

Technique: DJBS (EndoBarrier) was implanted and explanted using fluoroscopy and endoscopy. Patients were advised at baseline to

Key efficacy findings

Number of patients analysed: **42**

Procedural outcomes % (n)

Implantation success	93 (39/42)
Implantation failure (due to short duodenal bulb)	7 (3/42)
Explantation success	100

Clinical parameters (n=24) (mean±SD)

	Baseline	**24 weeks**	**52 weeks**
Total weight (kg)	110.6±3.4	93.9±2.9 (p<0.0001)	88.2±2.8 (p<0.0001)
Total weight change (%)			−22.1±2.1 (p<0.0001) (19.9±1.8)
BMI change kg/m^2			−9.1±0.9 (p<0.0001)
Mean EWL%			47.0±4.4 (p<0.0001)
Diastolic BP (mm Hg)	85±1	81±3 (p=0.17)	71±2 (p<0.0001)
Total cholesterol (mg/dL)	197±7	164±8 (p<0.0001)	161±8 (p<0.0001)
Triglycerides (mg/dL)	160±16	133±12 (p=0.07)	115±11 (p=0.002)
HbA_{1c} (%)	6.3±0.3	5.8±0.1 (p=0.03)	6.0±0.2 (p=0.09)

Key safety findings

Device in situ adverse events % (n=39)

Gastrointestinal events (mild to moderate)	**%**
Upper abdominal pain	81
Nausea	41
Vomiting	33
Gastroenteritis	4.8
Early explantation	**38 (15/39)**
Anchor movement leading to device migration (<5 cm) at week 12-24 (n=1), week 24-36 (n=2), after week 36 (n=5)	53 (8/15)
Device obstruction (at weeks 1, 8 and 10)	20 (3/15)
Abdominal pain (at weeks 1 and 11)	13 (2/15)
Acute cholecystitis (at week 12) resolved after explantation	7 (1/15)
Patient request (at week 24, had Roux-en-Y gastric bypass)	7 (1/15)

Comments

Follow-up issues:

- 38% (15/42) of patients were lost to follow-up at 24 weeks.

Study design issues:

- Efficacy outcomes for patients in whom the device was explanted were not evaluated.
- % EWL is the amount of weight in kg that exceeded a BMI of 25 kg/m^2.
- Device migration of more than 2 cm with or without symptoms mandated removal.

Other issues:

- A new anchoring design was used in this study.

Abbreviations used: BMI: body mass index; DJBS: duodenal-jejunal bypass sleeve; EWL: excess weight loss; FPG: fasting plasma glucose; GA: general anaesthesia; GI: gastrointestinal; HbA1c: glycated haemoglobin; HDL: high-density lipoprotein; ITT: intention to treat; KUB: kidneys, ureters and bladder; LOCF: last observation carried forward; NIH: National Institutes of Health; PPI: proton pump inhibitors; SD: standard deviation; T2DM: Type 2 diabetes mellitus; TG/HDL ratio: triglyceride to high-density lipoprotein ratio.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>take a liquid and pureed diet for 2 weeks, followed by normal diet and moderate physical therapy for the rest of the study period. PPI, multivitamins and iron supplements were used during the study period. Surveillance endoscopies were performed at 12, 24 and 36 weeks.

Follow-up: 52 weeks

Conflict of interest/source of funding: study was funded by GI Dynamics (manufacturer). Two authors disclosed a financial relationship with the manufacturer.</td>
<td>Prevalence of metabolic syndrome (according to the adult treatment panel III criteria) was reduced from 83.3% to 41.6% of patients (p=0.012).

Change from baseline (at 52 weeks) in diabetic and non-diabetic patients
<table>
<tr><th></th><th>Diabetes patients (n=6)</th><th>Obese patients (n=18)</th></tr>
<tr><td>Total weight change (kg)</td><td>−17.1±4.3 (p=0.01)</td><td>−24.1±2.4 (p<0.0001)</td></tr>
<tr><td>BMI (kg/m^2)</td><td>−7.3±1.8 (p=0.01)</td><td>−9.8±0.9 (p<0.0001)</td></tr>
<tr><td>Diastolic blood pressure (mm Hg)</td><td>−16±2 (p=0.0003)</td><td>−13±2 (p<0.0001)</td></tr>
<tr><td>Total cholesterol (mg/dL)</td><td></td><td>−40±7 (p<0.0001)</td></tr>
<tr><td>Triglycerides (mg/dL)</td><td></td><td>−49±14 (p=0.003)</td></tr>
<tr><td>HbA$_{1c}$ (%)</td><td>−1.4±0.6 (p=0.052)</td><td></td></tr>
</table>
Patients who completed 52 weeks' follow-up regained a mean of 4.4 kg after 6 months, following removal of the DJBS without any kind of maintenance programme (giving a weight change of −17.7 kg from baseline to 18 months).</td>
<td></td>
<td></td>
</tr>
</table>

Abbreviations used: BMI: body mass index; DJBS: duodenal-jejunal bypass sleeve; EWL: excess weight loss; FPG: fasting plasma glucose; GA: general anaesthesia; GI: gastrointestinal; HbA1c: glycated haemoglobin; HDL: high-density lipoprotein; ITT: intention to treat; KUB: kidneys, ureters and bladder; LOCF: last observation carried forward; NIH: National Institutes of Health; PPI: proton pump inhibitors; SD: standard deviation; T2DM: Type 2 diabetes mellitus; TG/HDL ratio: triglyceride to high-density lipoprotein ratio.

Study details

de Moura E (2012)[7]

Case series

Brazil

Recruitment period: not reported

Study population: obese patients with type 2 diabetes

n=**22**

Age: mean 46.2 years

Sex: 86.4% female

Mean BMI: 44.8kg/m^2

Patient selection criteria: patients with type 2 diabetes between 18 and 65 years with a BMI over 40 kg/m^2 and below 60 kg/m^2.

Technique: DJBS (EndoBarrier) was implanted and explanted after 52 weeks using fluoroscopy and endoscopy. PPI were used until 2 weeks after explantation. Follow-up examinations were done at 1, 3 and 6 months after explantation.

Key efficacy findings

Number of patients analysed: **22**

Implantation success: 100%

Effect on metabolic parameters (Mean ±SD values)

	Base-line (n=22)	24 weeks (n=16)	52 weeks (n=13)	LCOF* (n=22)
Fasting glucose mg/dL	179.4± 68.8	−33.4± 9.2 (p<0.01)	−37.1±11.8 (p<0.01)	−30.3± 10.2 (p<0.01)
HbA1c %	8.9± 1.7	−1.5±0.4 (p<0.001)	−2.3±0.3 (p<0.0001)	−2.1±0.3 (p<0.0001)
Fasting insulin U/mL	19.5± 14.7	−5.2±2.8	−10.1±4.2 (p<0.05)	−7.3±2.6 (p<0.05)
Total cholesterol mg/dL	201± 37	−16.7±6.9 (p<0.05)	−28.1±5.6 (p<0.01)	−19.7±5.9 (p<0.01)
Triglycerides mg/dL	213± 89	−56.8±25 (p=0.05)	−62.4±18.3 (p=0.01)	−44.8± 17.4 (p<0.05)
Diastolic blood pressure (mm Hg)	79±10			−1.6±3.5 (p=0.65)

*last observation carried forward on or before explantation

Improvement in glycaemic control

Improvements in HbA_{1c} were reported regardless of baseline values. At the end of the study 73% (16/22) of patients had an

Key safety findings

Early device explantations % (n)

Total explantations	**40 (9/22)**
Device related (median 31 weeks)	**27 (6/22)**
Device migration or rotation (48 weeks after implant)	14 (3/22)
Gastrointestinal bleeding (4 weeks after implant)	4 (1/22)
Abdominal pain (24 and 30 weeks after implant)	9 (2/22)
Non-device related	**14 (3/22)**
Investigator request (at weeks 20 and 32 due to patients non-compliance with follow-up)	9 (2/22)
Unrelated malignancy (at 17 weeks due to metastatic ovarian cancer)	4 (1/22)

Adverse events that occurred in more than 10% of patients

Adverse event	% (n)	Device or procedure related (n)
Gastrointestinal disorders	95 (21/22)	12
Upper	91	11

Comments

Follow-up issues:

- 18/22 patients completed 24 weeks' follow-up. Only 13/22 patients completed 52 weeks' follow-up.

Study design issues:

- The study was small.
- The drug treatment for type 2 diabetes was not specified or standardised.

Study population issues:

- 77% (17/22) of patients had drugs for diabetes.

Other issues:

- Only 1 patient needed GA for explantation.
- Improvement in glycaemic control was also seen in

Abbreviations used: BMI: body mass index; DJBS: duodenal-jejunal bypass sleeve; EWL: excess weight loss; FPG: fasting plasma glucose; GA: general anaesthesia; GI: gastrointestinal; HbA1c: glycated haemoglobin; HDL: high-density lipoprotein; ITT: intention to treat; KUB: kidneys, ureters and bladder; LOCF: last observation carried forward; NIH: National Institutes of Health; PPI: proton pump inhibitors; SD: standard deviation; T2DM: Type 2 diabetes mellitus; TG/HDL ratio: triglyceride to high-density lipoprotein ratio.

Study details

Patients received 30 minutes' nutritional counselling (on diet, lifestyle and behaviour) at baseline and monthly follow-up visits. Liquid diet for 2 weeks. Daily vitamin and iron supplements were recommended.

Follow-up: **52 weeks**

Conflict of interest/source of funding: study sponsored by GI Dynamics (manufacturer).

Key efficacy findings

HbA_{1c} under 7% compared with only 4.5% (1/22) at baseline.

Weight loss (Mean ±SD values)

Mean % EWL at 52 weeks (n=13)	39.0±3.9 (p<0.0001)
Mean % of EWL (LOCF, n=22)	35.5±3.1 (p<0.0001)
Decrease in mean BMI (kg/m^2) (LOCF, n=22)	−6.7±0.7
Mean reduction in waist circumference (cm) (LOCF, n=22)	−13.0±1.7

Glycaemic control after device removal (at 6 months)

HbA_{1c} response continued for up to 6 months after device removal in 11 patients (−1.7±0.7%).

Key safety findings

abdominal pain	(20/22)	
Nausea	50 (11/22)	7
Vomiting	63 (14/22)	7
Diarrhoea	13 (3/22)	1
Procedural and other complications		
Procedural nausea	45 (10/22)	4
Procedural vomiting	32 (7/22)	3
Back pain	59 (13/22)	5

All events were mild or moderate, except 1 severe event caused by an unrelated malignancy.

Comments

patients with early explants.

- Authors suggest that changes in antidiabetic drug treatment regimens may have influenced the results.

Abbreviations used: BMI: body mass index; DJBS: duodenal-jejunal bypass sleeve; EWL: excess weight loss; FPG: fasting plasma glucose; GA: general anaesthesia; GI: gastrointestinal; HbA1c: glycated haemoglobin; HDL: high-density lipoprotein; ITT: intention to treat; KUB: kidneys, ureters and bladder; LOCF: last observation carried forward; NIH: National Institutes of Health; PPI: proton pump inhibitors; SD: standard deviation; T2DM: Type 2 diabetes mellitus; TG/HDL ratio: triglyceride to high-density lipoprotein ratio.

Study details

Rodriguez-Grunert L (2008)[8]

Case series

Country not reported

Recruitment period: not reported

Study population: patients awaiting gastric bypass surgery.

n=**12**

Age: mean 41 years

Sex: 58.3% female

Mean BMI: 43 kg/m^2

Patients with diabetes: 4

Patient selection criteria: candidates for gastric bypass by 1991 NIH guidelines.

Technique: DJBS (EndoBarrier) procedures used fluoroscopy and endoscopy. Weight loss counselling at each follow-up visit : 1000-calorie low-fat diet.

Follow-up: **12 weeks**

Conflict of interest/source of funding: study was funded by GI Dynamics (manufacturer).

Key efficacy findings

Number of patients analysed: **12**

Implantation success: 100%

Explantation success: 100%

Weight loss at 12 weeks (n=10)

Mean % EWL	23.6
Mean % of patients with >10% EWL	100
Average total weight loss (kg)	10.2
Average decrease in mean BMI (kg/m^2)	3.8

All patients reported greater satiety and reduced food volume intake after implantation.

Change in comorbid status at 12 weeks

	Hyper-lipidaemia (n=3)	**Hypertension (n=4)**	**Diabetes (n=4)**
Improvement*	2/3	1/4	-
Resolved**	-	1/4	3/4
No improvement	1/3	2/4	1/4

*reduction in FPG or HbA_{1c}, systolic or diastolic components, lab values and decrease in medication use.

**FPG and HbA_{1c}, systolic or diastolic components and/or lab values normalised, and no medication use.

Key safety findings

Early explantations

Excessive abdominal pain and discomfort related to device placement (at 9 days)	2/12

Adverse events (procedure and device related)

Total adverse events	**71 (n=12)**
Device related (possible and definite)	**78% (55/71)**
Abdominal pain (week 1)	6
Diarrhoea	1
Anchor site inflammation (noted on endoscopy)	12
Nausea (week 1)	18
Vomiting (week 1)	16
Inflammatory pseudopolyps (noted on 72-hour surveillance endoscopy)	'frequent'
Procedure related	**2/12**
Oral pharyngeal mucosal tear (at device removal)	1
GI mucosal disorder and oesophageal mucosal tear (at device removal)	1

All events were mild or moderate and were self-limited.

Comments

Follow-up issues:

- No patients were lost to follow-up.

Other issues:

- Three different physicians with distinct skill sets performed the procedures.
- Early explantations took longer than the later ones because of difficulty in dislodging the anchor, and caused mucosal tears.

Abbreviations used: BMI: body mass index; DJBS: duodenal-jejunal bypass sleeve; EWL: excess weight loss; FPG: fasting plasma glucose; GA: general anaesthesia; GI: gastrointestinal; HbA1c: glycated haemoglobin; HDL: high-density lipoprotein; ITT: intention to treat; KUB: kidneys, ureters and bladder; LOCF: last observation carried forward; NIH: National Institutes of Health; PPI: proton pump inhibitors; SD: standard deviation; T2DM: Type 2 diabetes mellitus; TG/HDL ratio: triglyceride to high-density lipoprotein ratio.

Study details

Cohen RV (2013)[9]

Case series

Brazil (single centre)

Recruitment period: not reported

Study population: patients with lower BMI and T2DM

n=**23**

Age: mean 49.8 years

Sex: 58.3% female

Mean BMI: 30 kg/m^2, T2DM duration: 6.6 years

Patient selection criteria: aged 18 and 55 years with T2DM of <10 years, with oral glucose lowering medications, HbA1c 7.5 - 10%, BMI 26-50 kg/m^2.

Technique: EndoBarrier deployed and removed under GA. Nutritional counselling, PPIs before implantation and 2 weeks after explantation. Liquid diet in first week and 1200-1500 calories intake thereafter.

Follow-up: **52 weeks**

Conflict of interest/source of funding: study was funded by GI Dynamics

Key efficacy findings

Number of patients analysed: **23**

Procedural outcomes % (n)

Implantation success	87 (20/23)
Implantation failure (due to unfavourable anatomy)	13 (3/23)
Mean implantation duration	348 days

Body weight glucose metabolism and plasma lipids during treatment with DJBS

	Baseline (n=20)	**Week 12 (n=19)**	**Week 52 (n=16)**	**p value**
Body weight(kg)	84.0±16.6	79.0±16.8	77.2±17.6	<0.0001
BMI (kg/m^2)	30.0±3.6	28.3±3.7	28.5±3.3	<0.0001
FPG (mg/dl)	207±61	132±41	155±52	.012
HbA1c (%)	8.7±0.9	7.0±0.9	7.5±1.6	.004
Total cholesterol	221±50	167±38	188±32	NR
Low density lipoprotein	135±40	95±33	108±31	NR
HDL	42±11	39±7	40±10	NR

62.5% (10/16) patients who completed the study had HbA1c levels <7% at week 52. 4/5 patients with HbA1c >9% at baseline did not show any reduction in HbA1c.

Diabetic medications: 7 patients decreased and 4 increased the number of drugs or the doses of antidiabetic drugs.

No significant correlation between change in body weight and change in FPG or HbA1c was observed (data not reported in paper).

Key safety findings

	% (n)
At least 1 adverse event (mild or moderate)	96% (22/23)
Most common device or procedure related adverse events	
Gastrointestinal disorders (including abdominal pain, nausea and vomiting)	13/23
Metabolism and nutritional disorders, including hypoglycaemia and iron deficiency	14/23
Early device removals (In 1 patient at 10 weeks due to noncompliance with follow-up, in 1 at 7 months due to recurring abdominal pain, in 2 due to device rotation and/or migration at 6 and 10 months)	**80% (4/20)**

Comments

Follow-up issues:

- Only 16 patients completed 1 year treatment.

Study design issues

- Patients with type 1 diabetes, insulin use, autoimmune disease, weight loss of >4.5 kg within 12 weeks, previous gastrointestinal surgeries, active Helicobacter pylori, on non-inflammatory drugs, weight loss medication, uncontrolled reflux disease were excluded.
- Women either postmenopausal, sterile or on oral contraceptives were included.
- Sulfonylurea dosage reduced to avoid hypoglycaemic events.

Efficacy

Weight loss

Excess weight loss

A randomised controlled trial (RCT) of 56 patients with obesity comparing duodenal–jejunal bypass sleeve (DJBS) (n=27) against sham endoscopy (n=29) reported a significantly higher percentage of excess weight loss (EWL) at 12-week follow-up for the DJBS group (n=13) than for the sham endoscopy group (n=24) (11.9%±1.4% and 2.7%±2.0% respectively, p=0.001). In the DJBS group, 62% (8/13) of patients achieved at least 10% EWL compared with 17% (4/24) in the sham endoscopy group (p=0.01)[1].

An RCT of 40 patients with obesity compared DJBS plus low-calorie diet (n=25) against low-calorie diet alone (n=14). The DJBS group achieved a greater mean percentage EWL than the diet group (22% compared with 5%; p=0.02) at 12 weeks' follow-up. An EWL of greater than 10% was achieved by 92% (23/25) of the patients in the DJBS group and 21% (3/14) of patients in the diet group (p=0.0001) at 12-week follow-up[4].

A case series of 42 patients with obesity treated by DJBS reported excess weight loss of 47.0±4.4% (p<0.0001) at 52-week follow-up[6].

Mean weight loss

In an RCT of 18 patients with obesity and type 2 diabetes, the mean weight loss in the DJBS (n=12) and sham endoscopy (n=6) groups was comparable (p>0.05) for both the patients who completed treatment and the intent to treat (ITT). At week 20, the mean ITT weight reduction was 10.2±1.3 kg for the DJBS group compared with 7.3±4.3 kg for the sham group[2].

Diabetic control

The RCT of 18 patients with obesity and type 2 diabetes comparing DJBS (n=12) against sham endoscopy (n=6) reported that ITT HbA_{1c} values decreased by 1.3±0.9% for the DJBS group and by 0.8±0.3% in the sham endoscopy group (p>0.05) at 12-week follow-up. At 24-week follow-up, the HbA1c had decreased by -2.4±0.7% –in the DJBS group and by 0.8±0.4% in the sham endoscopy group (p>0.05). These differences were not statistically significant. Mean postprandial glucose area under the curve was reduced in the DJBS arm by 22% from baseline, compared with a 16% increase in the sham endoscopy group (p=0.016)[2].

The RCT of 41 patients with obesity comparing DJBS plus diet (n=30) against diet alone (n=11) reported a reduction in fasting plasma glucose (FPG) and HbA1c levels in both groups at 12 weeks, with no significant difference in change

between groups (FPG p=0.13; HbA1c p=0.32). Diabetic control, defined as a decrease in glucose levels, HbA1c and medications, had improved in 75% (6/8) of patients in DJBS group at 12-week follow-up [3].

Lipid profile

The case series of 42 patients treated by DJBS reported a significant reduction in total cholesterol (from 197±7 mg/dL at baseline to 161±8 mg/dL at 52 weeks; p<0.0001) and triglycerides (from 160±16 mg/dL at baseline to 115±11 mg/dL at 52 weeks; p=0.002)[6].

The case series of 22 patients treated by a DJBS reported significant reductions in total cholesterol (19.7±5.9 mg/dL; p<0.01) and triglycerides (44.8±17.4 mg/dL; p<0.05) at last observation carried forward (LCOF) on or before explantation[7].

Blood pressure

The case series of 42 patients reported significant reduction from baseline in systolic (from 134±3 mm Hg to 125±2 mm Hg; p=0.01) and diastolic (from 85±1 mm Hg to 71±2 mm Hg; p<0.0001) blood pressure at 52-week follow-up. In this group, 6 patients with type 2 diabetes also reported significant reductions in blood pressure[6].

The case series of 22 patients reported non-significant decreases in mean systolic (from 134±14 mm Hg at baseline to 6.6±4.4 mm Hg at LCOF; p=0.15) and diastolic (from 79±10 mm Hg at baseline to −1.6±3.5 mm Hg at LCOF, p=0.65) blood pressure on or before explantation[7].

Implantation failure or difficulties

In the RCT of 56 patients the DJBS could not be implanted in 20% (4/25) of patients because of a short duodenal bulb (n=3) or a combination of patient anatomy and investigator inexperience (n=1)[1].

In the RCT of 40 patients, 19% (5/26) of patients in the DJBS group needed multiple implantation attempts because of difficulties advancing the catheter or positioning the anchor in the duodenal bulb[4].

Weight regain after removal of device

The case series of 42 patients with obesity reported that, without any kind of maintenance programme, patients who completed 52-week follow-up had regained a mean of 4.4 kg at 6 months after removal of the DJBS[6].

Glycaemic control after removal of device

The case series of 22 patients with obesity and type 2 diabetes reported that HbA_{1c} response continued for up to 6 months after device removal in 11 patients (mean percentage decrease 1.7±0.7%)[7].

Safety

Gastrointestinal haemorrhage

Gastrointestinal bleeding with haematemesis was reported in 14% (3/21) patients at 11, 25 and 43 days post implant respectively in the DJBS group of the RCT of 56 patients. The devices were removed. One patient needed sclerotherapy and endoscopic clips and 2 did not need further interventions to stop the bleeding[1].

Gastrointestinal bleeding was reported at a mean of 14 days in 3 patients in the DJBS group of the RCT of 40 patients. The devices were explanted and endoscopic examination showed no defined bleeding source that needed further intervention. In the same study, several episodes of haematemesis and abdominal pain were reported in 1 patient, caused by an anchor migrating 2 cm from its original position on day 47. Symptoms resolved after explantation of the device and a blood transfusion was given[4].

Early explantation

In the RCT of 18 patients 41% (5/18) of devices were explanted early, because of device migration with symptoms such as pain, nausea and vomiting (2 were asymptomatic)[2].

The RCT of 41 patients reported that 27% (8/26) of the devices were removed early because of severe nausea and vomiting (caused by sleeve obstruction, n=1), epigastric pain (n=2) and device migration (n=5)[3].

Chest pain during implantation

Non-cardiac chest pain was reported in 1 patient during DJBS implantation (because of an inadvertently placed endoscope and catheter causing distension of the oesophagus) in the RCT of 40 patients[4].

Pharyngeal tears

One pharyngeal mucosal tear and 1 oesophageal mucosal tear occurred during device removal in a case series of 12 patients. Further intervention was not needed[8].

Device migration

Device migration was reported in 41% (4/12) of patients in the DJBS group (4 because of anchor migration and 1 because of ‘device turning or migration’) during 12 weeks of follow-up in the RCT of 18 patients. All the devices were removed. Three patients presented with symptoms (1 with moderate pain, 1 with nausea, and 1 with vomiting and abdominal pain). Two patients had no symptoms, but device migration was noted at follow-up endoscopy (n=1) and at the time of device removal (n=1).

The RCT of 41 patients reported 30 cm device migration at 4 months in 1 patient and dislocation of the anchor after 3 months with epigastric pain in another patient. Symptoms resolved after explantation of the devices[3].

Sleeve obstruction

Sleeve obstruction with severe nausea and vomiting on day 30 was reported in 1 patient in the RCT of 40 patients[4]. The RCT of 41 patients reported 1 patient with sleeve obstruction, severe nausea and vomiting after 1 week. Symptoms resolved after removal of the devices[3].

Acute cholecystitis

Acute cholecystitis was reported in 1 patient 12 weeks after implantation in the case series of 42 patients. This resolved after device explantation[6].

Non-specific mild or moderate upper abdominal symptoms including pain and nausea

Procedural nausea and vomiting were reported in 10 and 6 patients in the DJBS arm of the RCT of 56 patients[1].

Nausea and upper abdominal pain were reported in 77% (20/26) and 50% (13/26) of patients respectively (mainly in the first week after the procedure) in the DJBS group of the RCT of 41 patients. All events resolved with medication[3].

Continuous epigastric pain was reported in 1 patient in the RCT of 41 patients. This resolved following explantation of the device at 3 months[3].

Pseudopolyp formation and implant site inflammation

Pseudopolyp formation and implant site inflammation were noted during explantation or at follow-up endoscopy in 50% (13/26) and 38% (10/26) of DJBS patients in the RCT of 41 patients[3].

Validity and generalisability of the studies

- Most of the studies published were small and implanted the device for a period of 3, 6 or 12 months only.
- The evidence is mainly from studies in South America and Europe (none from the UK).
- There is a lack of data on management after explantation.
- There is lack of long term data on how long any beneficial effect may last after removal of the device.

- There is a lack of patient reported outcomes data.
- The majority of the studies are sponsored by the manufacturer.

Existing assessments of this procedure

A Horizon Scanning Prioritising Summary Report conducted for Australia and New Zealand in 2010 concluded that 'EndoBarrier appears to have the potential to induce significant weight loss and improve diabetic symptoms'. It is mainly based on evidence from 4 RCTs[1-4]. In addition, it concludes that 'additional comparative studies with appropriate controls are necessary as the evidence base for this device is limited and lacks long-term follow-up results'[10].

The American College of Surgeons' report on endoluminal treatments for obesity in 2010 assessed the DJBS procedure using EndoBarrier. It concluded that 'the early evidence on the effectiveness of the EndoBarrier was encouraging. In comparison to diet control alone, patient who received the EndoBarrier lost significantly more weight and also experienced considerable improvements in their diabetic symptoms. However, when compared to patients who received sham endoscopy, those who underwent EndoBarrier treatment did not lose significantly more weight compared to the sham controls at 20 weeks' follow up'. Self-limiting nausea (up to 77%) and upper abdominal pain (up to 30%) were common in patients who received the EndoBarrier and some serious complications were evident, with early removal being required in 20% to 40% of patients'. It considered that 'additional long-term comparative studies (with appropriate controls) are necessary before any firm conclusions can be made regarding the safety and efficacy of the emerging procedures and devices. Until then these procedures and devices should only be used in a clinical trial setting'. In addition, it concluded that 'future research is necessary to determine if there are any particular patients' subgroups that may particularly benefit from certain procedures'. It also recommends that 'these procedures and devices are new and are undergoing active development and should be monitored as refinements will alter their safety and efficacy profiles'[11].

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

- Laparoscopic gastric plication for the treatment of severe obesity. NICE interventional procedures guidance 432 (2012). Available from www.nice.org.uk/guidance/IPG432

Clinical guidelines

- Obesity: guidance on the prevention, identification, assessment and management of overweight and obesity in adults and children. NICE clinical guideline 43 (2006). Available from www.nice.org.uk/guidance/CG43

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.

Mr James Byrne, Mr Alberic Fiennes, Mr Sean Woodcock (British Obesity & Metabolic Surgery Society); Professor McLaughlin, Dr J P Teare (British Society of Gastroenterology).

- One specialist adviser performs this procedure regularly, 2 specialist advisers have performed it at least once and 2 specialist advisers have never performed this procedure.

- Four specialist advisers considered the procedure to be novel and of uncertain safety and efficacy and 1 specialist adviser considered this to be a first in a new class of procedure.

- One specialist adviser listed the relevant comparators as best medical treatment of type 2 diabetes, intensive weight management in tandem with the above or laparoscopic proximal gastric bypass Roux-en-Y or laparoscopic sleeve gastrectomy in patients who meet the criteria in NICE clinical guideline 43. Two advisers stated that there is no accepted comparator to this procedure. They suggested that close diet supervision and gastric balloon may be considered as the closest comparators. A gastric balloon is placed freely in the stomach whereas a DJBS is placed in the duodenum/proximal jejunum and is secured in position with tissue anchors. Two advisers stated that standard weight loss surgical procedures such as gastric bands and bypasses are well established permanent procedures that are not comparable with a DJBS, as it is a temporary intervention.

- Four specialist advisers stated that the procedure is likely to be performed by less than 10% of specialists and 1 stated that an estimate could not be given but suspects it could be less than 1%.

- One adviser suggested that the title should be 'obesity with diabetes' as patients are often confused by the wording, thinking they could be treated for just obesity or just type 2 diabetes.

- Two advisers state there may be interspecialty controversy over the procedure between bariatric surgeons and gastroenterologists. They suggested that the

procedure may not be suitable for use in gastroenterology departments that lack standard bariatric or diabetological multidisciplinary support.

- The specialist advisers stated that key efficacy outcomes were glycaemic control in type 2 diabetes, reduction in HbA1c over time, reduction in type 2 diabetes medication use, weight loss or percentage EWL, improved plasma lipid profile, reduction in arterial blood pressure, patient reported outcomes such as quality of life, maintenance of benefit after device removal.

- One specialist adviser stated that the main uncertainties relate to the extent of clinical benefit during implant, the durability of the intervention's effect after explantation and how patient or other factors that may affect this, the identification of subgroups of patients most likely to derive benefit and patients for whom this intervention is likely to be cost effective. One specialist adviser noted that there was uncertainty about the mechanism of action of DJBS, as the device does not mimic gastric bypass or sleeve gastrectomy. He also states that efficacy depends on accurate placement and good diabetic care and/or weight management with lifestyle and dietary support. The same adviser suggests that DJBS should not be seen as a substitute for gastric bypass or sleeve gastrectomy and will need to demonstrate added sustained efficacy. Another specialist adviser noted that there was uncertainty about what percentage of people benefit, the durability of effect after device removal, and any medical therapies needed to maintain or enhance the benefit from the procedure. One specialist adviser noted that current results were still early and long-term results are needed.

- The specialist advisers stated that adverse events reported in the literature were bleeding, oesophageal laceration, device displacement, pain, nausea, vomiting, pharyngeal tears on removal, obstruction, migration and inflammation at the site of the sleeve.

- The specialist advisers listed anecdotal adverse events as bleeding, bolus obstruction needing removal, twisted or folded sleeve needing removal, migration with pain needing removal, multiple linear ulcerated areas with perforation in the proximal jejunum (repaired at laparotomy), erosion of the duodenal wall, device malplacement, device intolerance with abdominal pain and discomfort, misplacement of endoscope hood in pharynx during endoscopic removal of device, and inability to remove an obstructed and migrated device endoscopically (needing a laparotomy for removal).

- The specialist advisers listed theoretical adverse events as implantation failure; bleeding; perforation of the oesophagus, stomach, duodenum or proximal jejunum and consequent laparotomy; laceration of the oesophagus, stomach or duodenum; device malplacement during implantation or explantation; discomfort; duodenal ulceration; reduced absorption of dietary calcium and iron; loss of the hood positioned on the tip of the endoscope into the pharynx or larynx during device removal.

- Training: the specialist advisers stated that good interventional and upper gastrointestinal endoscopic skills are needed to perform the procedure. Practical training on live animal models followed by placement and retrieval of devices under supervision by an experienced proctor is needed. 2 advisers also stated that radiation protection training and good knowledge of patient selection and management at all stages (implantation and explantation, device in situ and post explantation) is essential. advisers stated that the multidisciplinary team structure should be comparable to that for type 2 diabetes care and/or bariatric surgery, and that endoscopic facilities with suitable equipment and ready access to emergency units in the event of serious complications such as bleeding or obstruction are needed. One adviser also suggested that treatment-specific training for nurse/dietician/physician follow-up teams is needed. He also stated that provision of patient information and continuous long-term follow-up is needed.

- One adviser stated that this procedure needs to be part of a comprehensive bariatric service as opposed to a standalone procedure. One adviser states that this procedure would be within the ability of all advanced endoscopists and does not need facilities beyond those in current units.

- One adviser stated that the role of this procedure in obesity treatment is more controversial and unclear than its role in type 2 diabetes treatment. One adviser stated that there are hazards if the device is marketed or promoted to teams wholly contained within specialities that lack an established multidisciplinary team support structure, or private practitioners who function without a similar robust framework.

- Two advisers stated that the manufacturer has a registry of all implants and a post-market UK study is in progress.

- Two advisers stated that the likely speed of diffusion is slow, as the adverse event rates are high and the device is currently expensive. One adviser stated that with the currently available evidence the procedure should only be offered within the context of long-term trials. Two advisers stated that there will be rapid uptake of the procedure in the next 2–5 years, mainly in the private sector.

- Two advisers stated that the procedure is likely to be carried out in most district general hospitals in the UK, and 3 advisers stated that it is likely to be done in a minority of hospitals. One adviser stated that it is likely to be done in bariatric units that offer a comprehensive service. In terms of patient numbers and use of resources, 4 specialist advisers stated that the impact on the NHS would be moderate and 1 specialist adviser stated that it would be minor. One adviser stated that the device cost is too high for widespread adoption. One adviser stated that it has a place as a staging procedure in patients with super-morbid obesity, to help them lose weight and control metabolic comorbidities before surgery. One adviser stated that if the procedure is shown to be cost

effective in certain subgroups of patients with diabetes (such as patients on injection therapy and patients with quality of life significantly compromised by difficulties with glycaemic control) then it is likely to have an impact on resource use.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme sent 23 questionnaires to 2 trusts for distribution to patients who had the procedure (or their carers). NICE received 8 completed questionnaires.

The Patient Commentators' views on the procedure were consistent with the published evidence and the opinions of the specialist advisers.

Issues for consideration by IPAC

- It is currently used only in post-marketing studies in NHS hospitals (in London, Manchester and Southampton) for specific patients in whom standard treatments are ineffective or inappropriate (standard treatments in the context of this guidance are the therapies which clinicians might recommend for the management of weight loss).
- The device has not yet received US Food and Drug Administration (FDA) approval.
- Ongoing trials:
  - NCT01114438: Post Marketing Study in Subjects Who Have Type 2 Diabetes Using the EndoBarrier™ Gastrointestinal Liner; type: open-label single-group assignment; location: United Kingdom (Imperial College/St. Mary's Hospital, London; Trafford General Hospital/NOSC, Manchester; Southampton General Hospital, Southampton); estimated enrolment: 45 patients; inclusion criteria: subjects with type 2 diabetes for more than 1 and up to 10 years who are on oral diabetic medications and/or insulin, with an Hb A_{1c} level over 7.5 and up to 10.0 and a BMI over 30 and under 50; primary outcome: HbA_{1c} at 12 months; estimated primary completion date: January 2013.

- NCT00985491: Study for Short Term Weight Loss in Candidates for Bariatric Surgery: type: open label single group assignment; location: Chile; estimated enrolment: 180 patients; inclusion criteria: BMI over 35 with co-morbidities, or BMI over 40 and under 60 without comorbidities, candidate for Roux-en-Y gastric bypass, failed on non-surgical weight loss methods; primary outcome: percentage of excess weight loss at 36 months; estimated study completion date: July 2016.
- NTC01372501: Study of obese subjects previously implanted with the Endobarrier Gastrointestinal Liner, type: open label single group assignment; location: Chile; estimated enrolment: 24 patients; inclusion criteria: previously implanted with Endobarrier, aged over 18 years and under 55 years; primary outcome: percentage of EWL at 52 weeks; estimated study completion date: April 2012.
- NCT00985114: Safety and efficacy study of Endobarrier in subjects with type II diabetes and obesity; type: multicentre RCT with crossover (after 12-month washout); location: Netherlands; estimated enrolment: 70 patients; inclusion criteria: type 2 diabetes treated for under 10 years, BMI over 30 and under 50, with an HbA_{1c} level over 7.5 and under 10%; primary end point: percentage of patients who achieve a greater than 0.5% reduction in HbA_{1c} at 24 weeks or last visit from baseline; study completion date: January 2012.
- NCT01728116: Safety and efficacy of Endobarrier in subjects with type 2 diabetes who are obese (ENDO); type: RCT; location: USA; estimated enrolment: 500; inclusion criteria: HbA_{1c} over 8.0% and under 10%, BMI over 30 and under 50; primary outcome: improvement in HbA_{1c} at 12 months; estimated study completion date: June 2015.
- NCT01718457: Endobarrier treatment in obese subjects with type 2 diabetes; type: interventional, single group assignment; location: Israel; estimated enrolment: 45; estimated study completion date: January 2018.

- NCT01724060: Effects of obesity on food preferences and metabolism (FPS); type: Observational case control study; location: UK; estimated enrolment: 400; estimated study completion date: October 2014.
- EME MRC study: location: United Kingdom; type: RCT; estimated enrolment: 140 patients; A grant application was submitted to the EME (Efficacy and Mechanism) programme with the Medical Research Council. Decision for approval expected in quarter 4 2012.

References

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11. Endoluminal treatments for obesity (2010). Horizon scanning in surgery: application to surgical practice and education. Prepared by Australian Safety and Efficacy Register of New Interventional Procedures – Surgical for the American College of Surgeons

Appendix A: Additional papers on implantation of a duodenal-jejunal bypass sleeve for managing obesity

The following table outlines the studies that are considered potentially relevant to the 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
de Moura et al (2012). Six month results of the duodenal-jejunal bypass liner for the treatment of obesity and type 2 diabetes. J Gastroint Dig Syst S2:003.doi:10.4172/2161-069X.S2-003	Case series n=22 Obese and T2DM patients for bariatric surgery EndoBarrier implanted. Follow-up=24 weeks	100% technical success. At week 24 mean weight loss was 14kg ($p<0.001$). BMI dropped on average 5.4 points and excess weight loss was 22.2%. Fasting blood glucose significantly reduced (baseline 171.8 mg/dl, wk 24=141.5mg/dl). Glycosated haemoglobin level significantly reduced from 8.8% to 7.3%. Anti-diabetic medication use reduced except metformin.	Study with longer follow-up included in table 2.
de Jonge C, Rensen SS et al. (2013) Endoscopic Duodenal-Jejunal Bypass Liner Rapidly Improves Type 2 Diabetes. Obes Surg. Mar 23. [Epub ahead of print]	Case series n=17 Obese patients (BMI 30-50 kg/m^2) with type 2 diabetes DJBL for 24 weeks Follow-up:24 weeks	At 24 weeks patients lost 12.7 ± 1.3 kg ($p < 0.01$), while HbA_{1c} had improved from 8.4 ± 0.2 to 7.0 ± 0.2 % ($p < 0.01$). Both fasting glucose levels and the postprandial glucose response were decreased at 1 week and remained decreased at 24 weeks (both $p < 0.01$). In parallel, the glucagon response decreased (23,762 ± 4,732 vs. 15,989 ± 3,193 vs. 13,1207 ± 1,946 pg/mL/min, $p < 0.05$) and the GLP-1 response increased (4,440 ± 249 vs. 6,407 ± 480 vs. 6,008 ± 429 pmol/L/min, $p < 0.01$). The GIP response was decreased at week 24 (baseline-115,272 ± 10,971 vs. week 24-88,499 ± 10,971 pg/mL/min, $p < 0.05$). Insulin levels did not change significantly. Glycemic control was still improved 1 week after	Larger studies included in table 2. Reports changes in gut peptides.

		explantation.	
Escalona A, Yanez R et al (2010). Initial human experience with restrictive duodenal-jejunal bypass liner for treatment of morbid obesity.Surgery for Obesity & Related Diseases 6 (2) 126-131.	Case series n=10 BMI: 40.8kg/m^2 DJBS combined with a restrictor orifice (flow restrictor). Follow-up: 12 weeks	Devices implanted and removed after 12 weeks. The % EWL and TWL at explantation was 40% +/- 3% and 16.7 +/- 1.4 kg. The 4-hour GE was 98% +/- 1% at baseline, 72% +/- 6% at 4 weeks (P = 0.001 versus baseline), and 84% +/- 5% at 12 weeks (P <.05 versus baseline). After explantation, the rate of GE returned to normal in 7 of 8 subjects, but remained slightly delayed in 1 subject (84% at 4 hours). Episodes of nausea, vomiting, and abdominal pain required endoscopic dilation of the restrictor orifice with a 6-mm through-the-scope balloon in 7 patients and a 10-mm balloon in 1, with no clinically significant adverse events.	Implantation of a flow restrictor with DJBS to induce weight loss (adjunct procedure).
Gagner, M (2011). Intragastric balloons appear safer and better than the endoscopic duodenojejunal bypass liners (DJBL) for preoperative weight loss in bariatric surgery. Gastrointestinal Endoscopy 73 (4): 850-851.			Letter to editor.
Gersin KS, Keller JE, et al (2007). Duodenal- jejunal bypass sleeve: a totally endoscopic device for the treatment of morbid obesity. Surgical Innovation 14 (4) 275-278.	Case report n=1 36 year old woman BMI: 45.2kg/m^2 follow-up= 3 months	Device placed with no complications. Device removed after 3 months. Total weight lost was 9.09 kg.	Larger studies with longer follow-up included in table 2.
Levine A, Ramos A, et al (2009). Radiographic appearance of endoscopic duodenal-jejunal bypass liner for treatment of obesity and type 2 diabetes. Surgery for Obesity & Related Diseases 5 (3): 371-374.	Case series n=8 (from 3 studies, 3 centres) DJBS (Endobarrier) Radiographic appearance of the device in	The anchor on the device provides a good seal that remains intact for <197 days. 1 leak from a tear in the proximal end of liner material was observed at removal (occurred in vivo as a result of inadequate fabrication techniques that	Study reports radiographic appearance of device in vivo. Larger studies with longer follow-up included in table 2.

	vivo by contrast swallow or direct injection of water soluble contrast media.	have subsequently improved. Considerable variability in the position and orientation of anchor in images.	
Malik A, Mellinger JD et al. (2006) Endoluminal and transluminal surgery current status and future possibilities. Surgical Endoscopy, 20: 1179-92	Review		Literature review, no new data.
Montana R, Slako M, and Escalona A (2012). Implantation of the duodenal-jejunal bypass sleeve under conscious sedation: A case series. Surgery for Obesity and Related Diseases.8 (5): pp e63-e65.	Case series n=3 BMI: 36 to 48 kg/m^2 DJBS under conscious sedation.	Mean procedure time -23 minutes. Patients remained stable during recovery phase. No adverse effects were observed. Discharged next day tolerating a liquid diet.	Larger studies with longer follow-up included in table 2.
Patel SR, Hakim D et al. (2013) The dueodenal-jejunal bypass sleeve (Endobarrier Gastrointestinal Liner) for weight loss and treatment of type 2 diabetes. Surgery for Obesity Related Disorders Feb 4. pii: S1550-7289(13)00034-8. doi: 10.1016/j.soard.2013.01.015. [Epub ahead of print]	Non-systematic review DJBS	Most studies used 12-week excess weight loss (EWL) as a primary outcome measure with results ranging from 11.9%–23.6%. One study to date used 52-week EWL as its primary measure with a significant outcome of 47%. Our group has seen this technology cause significant weight loss, resolution of type 2 diabetes mellitus, and improvement in cardiovascular risk factor profile.	Non-systematic review
Sandler BJ, Rumbaut, R, Swain CP et al (2011). Human experience with an endoluminal, endoscopic, gastrojejunal bypass sleeve. Surgical Endoscopy 25 (9) 3028-3033.	Case ceries n= 24 Device: GDJBS (ValenTX) Mean BMI: $42kg/m^2$ 7 patients with diabetes. Follow-up: 12 weeks	22 patients implanted with device. 17 maintained it for 12 weeks. 39.7% excess weight loss noted at 12 weeks. Device was explanted early because of early postoperative dysphagia. All patients with diabetes mellitus had normal blood glucose levels and none required antihyperglycemic medications. All four patients with elevated hemoglobin A1c levels preoperatively showed improvement .	Different device (gastroduodenojejunal bypass sleeve-ValenTX) of longer length (120cm) secured at the esophagogastric junction with endoscopic and laparoscopic techniques.

Appendix B: Related NICE guidance for implantation of a duodenal-jejunal bypass sleeve for managing obesity

Guidance	Recommendations
Interventional procedures	**Laparoscopic gastric plication for the treatment of severe obesity. NICE interventional procedures guidance 432 (2012)** 1.1 The evidence on laparoscopic gastric plication for severe obesity raises no major safety concerns in the short term. There is inadequate evidence about safety in the long term, specifically with regard to the reversibility of the procedure and how it affects the safety of any further gastric surgery that may be necessary. There is limited evidence of efficacy in the short and medium term but more evidence is needed about the long-term efficacy of the procedure. Therefore, laparoscopic gastric plication for the treatment of severe obesity should only be used with special arrangements for clinical governance, consent and audit or research. 1.2 Clinicians wishing to undertake laparoscopic gastric plication for the treatment of severe obesity should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients understand the uncertainties about the procedure's long-term efficacy and about how the procedure may affect the safety of any further gastric surgery that they may need. Clinicians should provide patients with clear written information. In addition, the use of NICE's information for the public is recommended. 1.3 Laparoscopic gastric plication for severe obesity should only be carried out in units specialising in bariatric surgery that can offer the procedure as one of a range of treatment options. This recommendation is consistent with Obesity: guidance on the prevention, identification, assessment and management of overweight and obesity in adults and children (NICE clinical guideline 43; see section 1.2.6 of the guideline for details on surgical interventions). 1.4 Clinicians should submit data on all patients undergoing laparoscopic gastric plication for severe obesity to the National Bariatric Surgery Registry. Data should be entered into the register under the 'other' procedure category. Clinicians should also collect and review these data as part of local audit. 1.5 NICE encourages further research on laparoscopic gastric plication for severe obesity, which should include information about long-term efficacy and safety, and specifically how the procedure influences further gastric surgery. Comparison with alternative procedures would be useful.
Clinical guidelines	Obesity: guidance on the prevention, identification, assessment and management of overweight and obesity in adults and children. NICE clinical guideline 43 (2006). Available from www.nice.org.uk/CG43 **1.2.6 Surgical interventions** **Adults and children** 1.2.6.1 Bariatric surgery is recommended as a treatment option for

	people with obesity if all of the following criteria are fulfilled: • they have a BMI of 40 kg/m^2 or more, or between 35 kg/m^2 and 40 kg/m^2 and other significant disease (for example, type 2 diabetes or high blood pressure) that could be improved if they lost weight • all appropriate non-surgical measures have been tried but have failed to achieve or maintain adequate, clinically beneficial weight loss for at least 6 months • the person has been receiving or will receive intensive management in a specialist obesity service • the person is generally fit for anaesthesia and surgery • the person commits to the need for long-term follow-up. See recommendations 1.2.6.12 and 1.2.6.13 for additional criteria to use when assessing children, and recommendation 1.2.6.7 for additional criteria for adults. 1.2.6.2 Severely obese people who are considering surgery to aid weight reduction (and their families as appropriate) should discuss in detail with the clinician responsible for their treatment (that is, the hospital specialist and/or bariatric surgeon) the potential benefits and longer-term implications of surgery, as well as the associated risks, including complications and perioperative mortality. 1.2.6.3 The choice of surgical intervention should be made jointly by the person and the clinician, and taking into account: • the degree of obesity • comorbidities • the best available evidence on effectiveness and long-term effects • the facilities and equipment available • the experience of the surgeon who would perform the operation. 1.2.6.4 Regular, specialist postoperative dietetic monitoring should be provided, and should include: • information on the appropriate diet for the bariatric procedure • monitoring of the person's micronutrient status • information on patient support groups • individualised nutritional supplementation, support and guidance to achieve long-term weight loss and weight maintenance. 1.2.6.5 Arrangements for prospective audit should be made, so that the outcomes and complications of different procedures, the impact on quality of life and nutritional status, and the effect on comorbidities can be monitored in both the short and the long term. 1.2.6.6 The surgeon in the multidisciplinary team should: • have undertaken a relevant supervised training programme • have specialist experience in bariatric surgery • be willing to submit data for a national clinical audit scheme.

Appendix C: Literature search for implantation of a duodenal-jejunal bypass sleeve for managing obesity

Database	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	27/03/13	Issue 2 Feb 2013
Database of Abstracts of Reviews of Effects – DARE (CRD website)	27/03/13	Issue 2 Feb 2013
HTA database (CRD website)	27/03/13	Issue 2 Feb 2013
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	27/03/13	Issue 2 Feb 2013
MEDLINE (Ovid)	27/03/13	1946 to March Week 2 2013
MEDLINE In-Process (Ovid)	27/03/13	March 26, 2013
EMBASE (Ovid)	26/03/13	1974 to 2013 Week 12
CINAHL (NLH Search 2.0/EBSCOhost)	27/03/13	1981-present

Trial sources searched on 31 October 2012

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

Websites searched 31 October 2012

- National Institute for Health and Clinical Excellence (NICE)
- 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 search
- Evidence Updates (NHS Evidence)
- 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 Duodenum/su [Surgery]

2 (Duoden* adj3 surg*).tw.
3 ((bypass or gasterointest*) adj3 (sleeve* or line*)).tw.
4 ((Bypass or gastero-intest*) adj3 (sleeve* or line*)).tw.
5 (Duoden* adj3 (sleeve or line*)).tw.
6 (jejun* adj3 (sleeve* or line*)).tw.
7 Endobarrier*.tw.
8 DJBL.tw.
9 DJBS.tw.
10 or/1-9
11 obesity/ or obesity, morbid/
12 obesit*.tw.
13 Diabetes Mellitus, Type 2/
14 (Type 2 adj diabetes*).tw.
15 non-insulin-dependent-diabetes mellit*.tw.
16 ((adult or matur* or late*) adj onset adj diabete* mellit*).tw.
17 or/11-16
18 10 and 17
19 Animals/ not Humans/
20 18 not 19
21 limit 20 to ed=20121031-20130331