National Institute for Health and Care Excellence

IP986 – Implantation of a duodenal-jejunal bypass sleeve for managing obesity

Consultation Comments table

IPAC date: 14th June 2013

Com. no.	Consultee name and organization	Sec. no	Comments	Response Please respond to all comments
1	Consultee 1 Clinical Senior Lecturer	1	1.1 It is important to note that the DJBS is a treatment for diabetes and that the weight loss is merely a positive side effect of the device. Further research is vital to decide whether the DJBS is better than existing medical treatments such as injectable GLP-1 analogue therapy, but for many patients with progressive type 2 diabetes which is not adequately controlled with best medical therapy and who do not want to undergo bariatric surgery the DJBS can significantly improve glycaemia while also reducing body weight. 1.2 The DJBS is not comparable with bariatric surgery as the primary goal is not weight loss. The DJBS is much more akin to injectable GLP-1 analogues as the primary goal is glycaemic control and a side effect is weight loss. Inclusion of data on the GLP-1 audits such as those run by Dr Bob Ryder of the Association of British Clinical Diabetologist would be far more advantageous. 1.3 It would be a mistake to focus on weight loss as the primary outcome of the DJBS as the focus should be glycaemic control. The documentation of complications and technical problems are however vital and should be systematically collected (national GLP-1 audit).	Thank you for your comment. The Committee found the published evidence on the use of the procedure is in patients with obesity and before bariatric surgery and the evidence includes use of the procedure for treatment of obese patients with type 2 diabetes (T2DM). The published evidence includes 4RCTs, of which only 1 (in 2009) focused on the treatment of patients with T2DM and obesity (n=18) with a primary efficacy end point 'improvement in glycemic control'. The other 3 RCTs (published between 2009-10) and 2 further case series were in obese patients with primary endpoints 'weight loss and/or safety of the procedure'. A further 4 studies (all case series) were published (between 2011-13) in obese T2DM patients with primary outcomes glycemic control, changes in HbA1C, insulin levels, reduction of cardiovascular risk. The available evidence was for use primarily for bariatric management, not for patients who have diabetes only and who are not otherwise obese (BMI>30 kg/m^2). There is a lack of well-designed RCTs to determine the effect upon diabetes outcomes and T2DM as indication for this procedure. Therefore the Committee considered the principal focus for the guidance should be 'Obesity'. In section 6 of the guidance the Committee made some comments about the quality of studies and indications for this procedure (see 6.1-6.3 in the guidance).

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2	Consultee 2 - Manufacturer	1	Based on the results of the clinical trials, DJBS received CE Mark approval in October 2010 with an indication to treat patients with type 2 diabetes (T2D) and/or obesity who are not adequately controlled with medication and lifestyle intervention. DJBS stimulates the secretion of GLP-1, which mediates glucose dependent insulin secretion, and PYY, which suppresses appetite and food intake, in the GI tract leading primarily to significant improvements in glycemic control and the additional benefit of significant weight loss. Upon considering the efficacy and safety results of prior clinical trials (using the first generation device) all further trails are focusing on Diabetes management. Please see comments section 4. The capture of DJBS clinical data is only meaningful if the NBSR adequately captures associated glycemic control and cardiometabolic endpoints. Initial clinical trials were conducted with a focus on safety and weight loss in obese patients. We observed rapid glycemic control in T2D patients enrolled in these trials so we changed the intended indication for DJBS therapy. The DJBS is not indicated for short term weight loss so RCTs are not planned with these endpoints.	Thank you for your comment. Please see response to comment 1. The team is in correspondence with the NBSR leads and has shared your comments with them.

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3	Consultee 2 Manufacturer	**1 and title**	The headline for the IPAC process (IP986) was at the beginning: Implantation of a DJBS for the management of obesity and / or T2D. Our CE mark contains also T2D and/or obesity. Now it was changed only to obesity. Does it means that the IPAC committee has selected the indication for DJBS only to obesity or is the process divided in two independent processes for obesity and T2D? Will T2D reviewed separately?	Thank you for your comment. The Committee has considered all the evidence on this topic and decided to amend the scope of the guidance as reflected in the change to the title. The committee considered that at present there is not enough body of evidence to publish separate guidance with respect to type 2 diabetes.
4	Consultee 2 Manufacturer	**1**	We kindly ask you to expand our draft IPAC guidance for DJBS to allow the use of DJBS in clinical settings for Diabetes treatment (classification: e.g. Special or Other) and not to limit the usage of DJBS only in research.	Thank you for your comment. The Committee considered your comment and chose not to amend the guidance recommendations.
5	Consultee 2 Manufacturer	**1**	DJBS should be done in specialized centers which have participated in a DJBS multidisciplinary training. Initial procedures are done with an expert mentor. DJBS patients should be administrated by a multidisciplinary team and should be led (follow up) by a Diabetologist / Endocrinologist. Furthermore clinicians are able to enter the data into the DJBS registry, managed by the University Medical Center in Hamburg-Eppendorf (UKE).	Thank you for your comment MDTs are not usually recommended in the context of 'research only' recommendations. Such considerations are more correctly covered by research governance and management committees and are outside the remit of the NICE IP Programme. As this is a Research recommendation – referral to a register is not normally made. However the Guidance does include a suggestion that data be referred to UK based register, the National Bariatric Surgery Register in 1.2 of the guidance.

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6	Consultee 3 Health care professional Private practice	1	Whilst there may be a lack of health economic data to support widespread adoption by the NHS, there are still selected patients in high risk groups who we can safely say WOULD benefit from Endobarrier treatment so the blanket statement about research only is too strong	Thank you for your comment. The guidance is based on safety and efficacy data. Health economic considerations are out with the remit of the IP programme. The Committee reached its 'research only' based on the safety and efficacy data.
7	Consultee 4 NHS Professional	1	The main target for the device is for those patients with type 2 diabetes associated with obesity not for those with obesity alone. I have completed a study in 45 patients from 3 centres which will be published shortly and two further trials are underway. The NIHR EME (efficacy and mechanism evaluation) board has funded a study Reference: 12/10/04 A randomized controlled trial of a duodenal sleeve bypass device (Endobarrier) compared with standard medical therapy for the management of obese subjects with type 2 diabetes which I shall be leading from autumn 2013. There is a further industry funded trial in the US underway. I have undertaken a clinical study on the Endobarrier and have a further study funded by the NIHR.	Thank you for your comments and information about further ongoing trials. Please see response to comment 1.

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8	Consultee 5 NHS Professional	1	Agree completely with **1.1.** For **1.2** there is no page yet on the NBSR for this device. If this is your recommendation please can this be formally communicated to the NBSR committee via jtreglohan@alsgbi.org, as there is currently no funding in place to make this happen - it can't simply be added. If funding isn't forthcoming all patients should be recorded electronically with a dataset appropriately agreed by all who are doing this. Obviously every study on this would have thought-out datasets to which the clinicians must adhere. There is a clear need for well designed longer term studies and it probably should not be done out with such a study.	Thank you for your comments The IP team has consulted with officers for the NBSR who now confirm that it will be developed in order to accommodate data on this procedure. Paragraph 1.2 of the Guidance will not be changed.
9	Consultee 1 Clinical Senior Lecturer	2.1	Obesity without comorbidities is a much weaker risk factor than when type 2 diabetes is associated with obesity. Reducing weight by approximately 20% with bariatric surgery and sustaining it for 15 years also has no impact on mortality, but it is only those patients with type 2 diabetes or with prediabetes that appear to benefit (Bariatric surgery and long-term cardiovascular events. Sjstrm L et al). Thus the benefit of the DJBS may be primarily in reducing glycaemia and secondary having some reduction in weight.	Thank you for your comment. Section 2 is designed to be a concise summary of indications and current treatments for the management of the indication. See also the response to comment 1.

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10	Consultee 2 Manufacturer	2.1	Apparently the focus of the DJBS assessment has focused on obesity. The main indication of DJBS is the treatment of patients' type 2 diabetes (T2D) and/or obesity who are not adequately controlled with medication and lifestyle intervention. In addition DJBS has shown significant improvements in patients with T2D and BMI <30kg/m2. (Cohen R. et al., A Pilot Study of the Duodenal-Jejunal Bypass Liner in Low Body Mass Index Type 2 Diabetes) DJBS is a revolutionary approach to treating patients with T2D and/or obesity.	Thank you for your comment. See response to comment 1. Section 2 is designed to be a concise summary of indication and current treatments for management and not specific to DJBS. This study by Cohen RV (2013) has been found in our updated search and included in the Overview.
11	Consultee 2 Manufacturer	2.3	Unlike some bariatric procedures, DJBS is not a malabsorptive procedure. The effects of DJBS are based on gut hormonal signaling changes which lead to normalization of glycemic control. (Aguirre V. et al., An Endoluminal Sleeve Induces Substantial Weight Loss and Normalizes Glucose Homeostasis in Rats with Diet-Induced Obesity) Additional information concerning the change of gut hormones of DJBS are available under the following link: http://easd.conference2web.com/content/1304 Based on the clinical experiences of DJBS we would kindly recommend expanding the NICE IPAC guidance for DJBS to Special or Other and not to limit the usage of DJBS only in research.	The additional information in the link provided are findings from de Jonge (2013) study. This is an e-publication which will not have been covered by the NICE search strategy. It is a smaller study than those already presented in the Overview but provides some evidence on the mechanism of action. . The Committee considered your comment and removed the following text in the Overview under issues for consideration section: "The device's mechanism of action is unclear". The Committee considered your comment but decided not to change the guidance.

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12	Consultee 1 Clinical Senior Lecturer	2.3	Bariatric surgery does not work through restriction or by calorie malabsorption, but rather through reduction in calorie intake secondary to reduction in appetite (Progressive rise in gut hormone levels after Roux-en-Y gastric bypass suggests gut adaptation and explains altered satiety. Borg CM, le Roux CW et al; Laparoscopic adjustable gastric banding induces prolonged satiety, Dixon AF et al.) Equally the DBJS does not cause mechanical problems with absorption as there are no steatorhoea, but rather patient report similar changes in appetite than what is observed after GLP-1 analogue therapy.	Thank you for your comment. See response to comment 10.
13	Consultee 4 NHS Professional	2	The primary target for therapy is patients with type 2 diabetes with obesity. The initial studies also included the obese but the best outcomes have been observed in diabetes so this is the main indication. The device does not cause malabsorption but probably works through changes in gut hormones and changing insulin sensitivity through bile resorption.	Thank you for your comment. Please see response to comment 1. The committee noted you comment and decided not to change the guidance. The Committee considered your comment and removed the following text in the Overview under issues for consideration section: “The device’s mechanism of action is unclear”.

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14	Consultee 6 NHS Professional	2	Given the efficacy in reducing Hba1c and associated comorbidities I would recommend that this procedure is considered only in those patients with type 2 diabetes and at risk of significant complications where other modalities of treatment are exhausted and where other bariatric surgery procedures are not appropriate given high degree of risk. It should be used as an option in the treatment of diabetes with a positive effect on weight rather than a treatment for weight alone. It could also be considered as a bridging procedure for patients with diabetes and extreme weight where weight loss and improved diabetes control would allow a definitive procedure to occur where it otherwise may not.	Thank you for your comment. Please see response to comment 1. The committee noted you comment and decided not to change the guidance.

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15	Consultee 1 Clinical Senior Lecturer	3	**3.1** It would be a mistake to compare the DJBS with bariatric surgery or to see it as a bridge to bariatric surgery as the aim is to improve glycaemia and is much closer to GLP-1 analogue therapy in this regard. **3.2** There is no evidence of calorie malabsorption or any clinical suspicion of steathorea. In fact many patients may develop mild constipation which is not dissimilar to that observed with GLP-1 therapy. The mechanism is thought to be reduced small bowel transit. It is thus very difficult to imagine how a patient with mild constipation can be malabsorbing calories at the same time. The improvement in glycaemia may have to do with the increased bile acid signaling to the liver which reduces hepatic glucose output. This is currently the topic of intense study with the use of euglycaemic hyperinsulinaemic clamps. The reduction in appetite may relate to the increase in endogenous GLP-1 similar to what will be seen after GLP-1 analogue therapy.	Thank you for your comment. Please see response to comment 1 Section 3.2 has been amended.

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16	Consultee 2 Manufacturer	3.1	Endoscopic implantation of a DJBS is a minimally invasive procedure that is designed to treat patients with type 2 diabetes and/or obesity who are not adequately controlled with medication (oral and/or insulin) and lifestyle intervention. The use of DJBS for pre-surgical weight loss with the aim of improving outcomes and reducing the risk of postoperative complications could be another field of operation, but it is not the primary intended use. Additional studies and experiences are required in this setting.	Thank you for your comment. The device description of at least one device states bariatric and weight loss as lead use. Also see response to comment 1.
17	Consultee 2 Manufacturer	3.2	The effects of DJBS are based on gut hormonal signaling changes which lead to normalization of glycemic control. Additional information concerning the change of gut hormones of DJBS are available under the following link: http://easd.conference2web.com/content/1304	The Committee considered your comment and removed the following text from the Overview under “issues for consideration” section: “The device’s mechanism of action is unclear”.
18	Consultee 7 Patient	3	I am a patient who had the endobarrier in December 2011 and removed 2012. I used vast sways of info regarding what method I could safely and swiftly reduce my diabetic medication and weight. After going through information on gastro bypass, balloon, and band I chose the endobarrier. it has done more than help me control my diabetes, weight etc. it gave me the time to re train my brain into food control using real food ..in fact I was upset it had to come out at all. I would highly recommend everybody to this simple easy procedure.in and out same day. I found it suppressed hunger and when removed was expecting that to come back. it didn't ..and I'm still losing weight	Thank you for your comment.

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19	Consultee 3 Health care professional Private practice	3.3	patients avoid solid for for 2 weeks, not several weeks	Thank you for your comment. The Committee considered your comment and amended 3.3 in the guidance 3.3 states that 'after the procedure, patients are placed on a diet that typically involves progression from fluids to semi-solids, **before returning to solid foods'**.
20	Consultee 2 Manufacturer	3.3	Fluid or semi-solid food is recommended for the first two weeks. Thereafter, patients can return to a normal diet of solid food. It is recommended that patients should drink sufficient quantities of drink liquids regularly. Clinical trials and commercial experiences to date involve more than 800 patients. DJBS is utilized in the UK and other European countries within specialized centers of excellence	Thank you for your comment. The Committee considered your comment and amended 3.3 in the Guidance See response to comment 19
21	Consultee 4 NHS Professional	3	The procedure is straightforward for most competent endoscopists and will thus would be widely available if initial success is confirmed by the subsequent trials.	Thank you for your comment.

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22	Consultee 8 Carer	4	We conducted a study at Pontificia Universidad CatÃ³lica de Chile, Santiago, Chile that demonstrated safety and efficacy of Endobarrier therapy in 27 obese patients (average weight 110.7kg, BMI 45.3kg/m2). The Endobarrier demonstrated clinically significant impact on health issues such as hypertension, dyslipidemia and metabolic syndrome. At 12 months of treatment, patients achieved mean absolute weight loss of 22.6 kg (49.7 lbs), or 20.0% (p = <0.0001), and mean EWL of 47.0% (p<0.0001) and the improvements in CV risk factors (reduction in total cholesterol levels from 196.5 mg/dL at baseline to 161.0 mg/dL (p = <0.0001) and in diastolic BP from 84.8 mmHg at baseline to 71.2 mmHg (p= <0.0001). A subset of 6 patients with T2DM (mean baseline HbA1c of 7.9%) achieved a mean HbA1c reduction of 1.4% (p=0.05). EndoBarrier is a breakthrough therapy with potential to change the treatment paradigm for obese patients who want to regain control of their T2DM while also potentially improving other cardiovascular risk factors. We have been providing EndoBarrier therapy since 2010 to treat subjects who are obese and/or diabetic and are seeing remarkable results superior to non-surgical options.	Thank you for your comment. This study Escalona L (2012) has been included in the Overview.

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23	Consultee 9 Carer	4	We conducted a study with the EndoBarrier in patients at Hospital Oswaldo Cruz, Sao Paulo, Brazil to access glycemic control in patients with T2DM and BMI between 23 and 36 kg/m2. 16 patients with T2DM and average BMI =30.8 kg/m2 were implanted for 1 year to evaluate its effects on insulin sensitivity and glucose control. Key results included:• HbA1c ; 8.6% at baseline to 7.5% at 1 year (p<0.001)• HbA1c ≤ 7% in 62.5% of patients at 1 year• Decrease in total body weight loss of 9.4% (p<0.05)• Reduction in total cholesterol (218mg/dL at baseline to 189 mg/dL, p<0.05) and LDL (135 mg/dL at baseline to 111 mg/dL, p<0.05) • Improvement in insulin sensitivity within the first week (p<0.001) without relation to weight loss (1.2 kg) that persisted for the 12 months. EndoBarrier improves HbA1c early in treatment and our results showed the effects of EndoBarrier on insulin sensitivity and glucose metabolism, similar to that of gastric bypass, but without surgery. These findings support EndoBarrier as a viable treatment for patients with T2DM who are overweight and obese.	Thank you for your comment. This study Cohen RV (2013) has been found in our update search and included in the Overview.

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24	Consultee 1 Manufacturer	4	Many of the RCTs described above utilized an earlier stage device design, which has since been enhanced. There have been associated procedure and clinical staff training updates which resulted in marked improvement in clinician's knowledge and procedure technique. In a multicenter post market study conducted in the UK (in press) the implantation success rate was 100% (45/45); bleeding and migration rate was 2.2% (1/45). Recently published papers and a clinical efficacy and safety summary will be sent via email. RCTs are underway/in planning in the Netherlands (publication expected in 2013/14); UK (EME MRC 12/10/04; France (STIC funding *PENDING CONFIRMATION*) and United States of America (FDA: clinicaltrials.gov NCT01728116). These studies have endpoints related to diabetes control, cardiometabolic and safety. These studies capture data during both the implant period as well in the long term follow-up period.	Thank you for your comments. See comment 3 and 28 The current UK Imperial trial referred to is: NCT01114438 – a post marketing open label single group study in 45 obese type 2 diabetes patients (in 3 centres). Primary outcome: HbA1c at 12 months. As the study has been completed in January 2013 but is yet to be published the data cannot be included. UK EME MRC 12/10/04 is a RCT comparing endobarrier with standard medical therapy for obese subjects with diabetes. Estimated enrolment: 140 patients. It will start in autumn 2013. NICE only presents published efficacy data to the Committee for consideration. NICE also reviews Guidance when a substantive new body of peer-reviewed evidence becomes available.

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25	Consultee 10 Patient	4	I had the device inserted on the 11th May, 2011, I had no problems what so ever with its implant or with its removal. Not even a sore throat. I was in and out on the day of implant within 5 hours and on the day when it was removed 3 hours. My obesity was reduced by 3.5 stones from 19.stone 2 lbs. Within three days my tablets were reduced and now I no longer take any tablets for diabetes or blood pressure or cholesterol As I have stated above the implantation was achieved within a time scale of 5 hours, from entry to the clinic till discharge. The whole time of the implantation was 3/4 hour and the removal was 3 hours overall, and the actual process was less than 1/2 hour. It was very easy. I would recommend it to anyone.	Thank you for your comments.
26	Consultee 7 Patient	4	No weight gain.still weight loss	Thank you for your comment.
27	Consultee 3 Health care professional Private practice	4	UK post marketing surveillance study has been completed and data is being analysed I have previously done Endobarrier research supported by manufacturer	Thank you for your comment. The current UK Imperial trial referred to is: NCT01114438 – a post marketing open label single group study in 45 obese type 2 diabetes patients (in 3 centres). Primary outcome: HbA1c at 12 months. As the study has been completed in January 2013 but is yet to be published the data cannot be included. NICE only presents published efficacy data to the Committee for consideration. NICE also reviews Guidance when a substantive new body of peer-reviewed evidence becomes available.

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28	Consultee 4 NHS Professional	4	To add to these data the Imperial trial included another 45 patients with the device in place for a year. (abstract submitted to EASD for the September meeting) All 45 were successfully implanted, 32 have completed the year. 3 were removed either for pain, device migration or GI bleeding. 10 were removed for non-device reasons such as patient preference due to lack of efficacy, a requirement for anticoagulation for new atrial fibrillation. In those completing the study the average weight loss was 26lb (baseline 219) with a 1% drop in HbA1c (baseline 7.5%). In a 6 month dutch trial (personal communication Dr JW Greve) of the device versus diet in obese type 2 diabetics comparing 34 with the device and 39 controls. After six months, just prior to device explantation, the device group had lost 35.5Â±3.6% (10.3kg) of their excess weight vs. 19.6Â±3.6% (6.7kg) in the control group (p<0.01). HbA1c had improved from 8.4Â±0.1% to 7.0Â±0.2% in the device group and to 7.6Â±0.2% in the control group (p<0.05). Only one device was explanted for obstruction.	Thank you for your comments. IPAC only considers new safety events from unpublished literature. The current UK Imperial trial referred to is: NCT01114438 – a post marketing open label single group study in 45 obese type 2 diabetes patients (in 3 centres). Primary outcome: HbA1c at 12 months. As the study has been completed in January 2013 but is yet to be published the data cannot be included. These adverse events have already been covered in the Guidance. NICE only presents published efficacy data to the Committee for consideration. NICE also reviews Guidance when a substantive new body of peer-reviewed evidence becomes available. New atrial fibrillation has not been included as it is unlikely to be due to DJBS.

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29	Consultee 11 Carer	4	Our trial conducted at Hospital Dipreca, Santiago, Chile, evaluated the EndoBarrier for the treatment of T2DM; the study was conducted in 18 patients who were randomized to receive either the EndoBarrier (12) or a sham endoscopy (6). The primary endpoint was the reduction of HbA1c in patients with a mean baseline HbA1c of 9.1% and BMI of 38.9 kg/m2. Patients achieved the following over a 24-week period: Mean reduction of 2.4% in HbA1c in the treatment arm versus 0.8% for sham arm. Patients treated with EndoBarrier achieved a 20% decrease in the area under the glucose curve during a Week 1 meal tolerance test at compared to a 17% increase in sham. Our patients experienced immediate resolution of T2DM and continued resolution after the device was removed, as well as weight loss. The EndoBarrier is implanted endoscopically during an incision-less, outpatient procedure, with fewer risks than a surgical procedure. We are treating patients with T2DM in a commercial setting and are seeing results similar to our study. We see the EndoBarrier as a non-surgical therapy that may affect key metabolic pathways resulting in improvement in T2DM and significant weight loss.	Thank you for your comment. This study Rodriguez L (2009) has been included in the Overview. NICE only presents published efficacy data to the Committee for consideration. NICE also reviews Guidance when a substantive new body of peer-reviewed evidence becomes available.

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30	Consultee 12 Carer	4	Our research at University of Sao Paulo, Brazil over a 12 month period was an important milestone in the clinical development of the Endobarrier for the treatment for patients with T2DM who were obese. The trial included 22 patients and the primary endpoints were improvement in type 2 diabetes and excess weight loss. In patients that were implanted for 12 months, the average baseline HbA1c was 8.9% with an average weight of 121.8 kg. Observed results are detailed below: Average HbA1c decrease of 2.3% ($p<0.0001$), Weight loss of 20.2 kg; excess weight loss of 39% ($p<0.0001$), Normalization of insulin ($p=0.02$) and C-peptide ($p=0.015$), cholesterol ($p=0.001$), LDL ($p=0.01$), and triglycerides ($p=0.006$) levels. The EndoBarrier is a clinically important achievement and a promising indicator that this device may offer patients an innovative new solution to combat both type 2 diabetes and obesity. We believe that EndoBarrier can provide an option to pharmaceutical and surgical methods for treating type 2 diabetes and obesity and look forward to utilization of the EndoBarrier for these disease states when it receives regulatory approval in Brazil.	Thank you for your comment. This study Cohen RV (2013) has been found in our updated search and included in the Overview. Please see response to comment 1.

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31	Consultee 2 Manufacturer	**2, 4 and 5**	Please find attached some additional documents which are referenced in our comments: 1)Evidence summary documents 2) Cohen RV, Neto MG et al (2013). A pilot study of the duodenal-jejunal bypass liner in low body mass index type 2 diabetes. J clin Endocrinol Metab 98 (2): E279-82 3) Aguirre V, Stylopoulos N et al (2008) An endoluminal sleeve induces substantial weight loss and normalizes glucose homeostasis in rats with diet-induced obesity. Obesity Dec16(12):2585-92	Thank you for your comments. 1) The team investigated the summary documents and informed the Committee of the new evidence presented. The Committee considered the new safety evidence (oesophageal perforation in 1 patient) from 1 unpublished study (07-1) and agreed to include this severe adverse event in the guidance. 2) This study was identified in our recent update search. The Committee considered adding this to table 2 in the Overview because the population is slightly different from studies already in Table 2 (mean BMI of 30kg/m^2). 3) This study is not a clinical study therefore cannot be included in the Overview.

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32	Consultee 2 Manufacturer	**4 and 5**	Please find attached a table of the published literature for DJBS (a list of 23 studies were presented in the table).	Thank you for your comment. Eight studies are included in table 2 of in the Overview (Rodriguez L 2008, Tarnoff 2008, Rodriguez 2009, Schouten 2010, Gresin 2010, Moura 2011, Moura 2012, Escalona 2012). Four studies are included in Appendix A in the Overview (Montana 2012, Escalona 2010, Levine 2009, Gresin 2007). Five of the listed studies are not clinical studies and cannot be included in the Overview (Milone 2006, Tarnoff 2008, Tarnoff 2008, Aguirre 2008 and Munoz 2012). One study (Cohen 2013) found in our update searchwas added to table 2 in the Overview. Three studies (Patel 2013, a nonsystematic review; Malik 2006, a review, de Jonge 2013, an epublication) were added to appendix A in the Overview. One Study (Greve and Bouvy 2011) is a multiple publication of de Jonge 2013 and substitute unobtainable. One final study (Hakim 2012) has not been found.

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33	Consultee 1 Manufacturer	5	Given the bleeding rate seen in earlier clinical trials (using the first generation device), the recommendation to concomitantly treat with higher doses of proton pump inhibitors was made. A marked improvement in the bleeding rate has since been established. In a multicenter post market study conducted in the UK (in press) the bleeding rate was 2.2% (1/45). A detailed analysis of the safety experience will be sent via email. DJBS migration events typically are manifested in a tilting of the anchor component (<3cm movement) and still allows for a normal endoscopic removal. Most migration events occur after 9 months when metabolic normalization is well established. Endoscopic removal of the DJBS leads to resolution of complications or related events. In a multicenter post market study conducted in the UK (in press) the migration rate was 2.2% (1/45). Gastrointestinal events are the most common adverse events experienced with the DJBS. The majority of these events are mild to moderate and typically resolve soon after the initial implant period. Pseudopolyps are a normal physiological reaction to the DJBS and do not lead to complications.	Thank you for your comment. These adverse events have already been covered in the Guidance. The current UK Imperial trial referred to is: NCT01114438 – a post marketing open label single group study in 45 obese type 2 diabetes patients (in 3 centres). Primary outcome: HbA1c at 12 months. As the study has been completed in January 2013 but is yet to be published the data cannot be included.

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34	Consultee 10 Patient	5	As reported above, I remain within the tolerances so that I am not on any medication. Now some 9 months after the removal of the device I have put on 3/4 of a stone and I am now working to remove this. I had no problems. The diet is harsh in the first 20 days, but this is to be expected. I had no problems at all except bad smelling breath which was cured by drinking pineapple juice. Much more use should be made of this easy procedure to help many others who suffer.	Thank you for your comments.
35	Consultee 7 Patient	5	No problems at all .highly recommend it.	Thank you for your comment.
36	Consultee 3 Health care professional Private practice	5	31 cases at my centre. Only 1 device migration and 1 early removal because of side effects. No significant complications. The data quoted above does not ring true in the real world.	Thank you for your comment. The data quoted is from published literature.

Com. no.	Consultee name and organization	Sec. no	Comments	Response Please respond to all comments
37	Consultee 4 NHS Professional	5	In addition to these data from the Dutch study, (personal communication and abstract - Koehestanie Diabetes 2012 A305) 9 serious adverse events occurred. Six out of the nine events were device-related. One patient presented with melena however no bleeding was found during endoscopic evaluation and complaints disappeared with conservative treatment. In one patient the DJBL got obstructed, making early explantation necessary. One patient suffered from symptomatic gallstones during the course of the study and was treated with a cholecystectomy. All device-related serious adverse events resolved without sequelae. Only one procedure-related serious adverse event occurred, an esophageal perforation during a scheduled device explantation at month six. A longitudinal, partially transmural tear of the esophagus from probably one of the barbs was treated successfully by placement of a temporary stent. More safety data will emerge from the current Imperial trial on completion and the next NIHR study. Using higher doses of omeprazole in the Imperial study bleeding was seen in one patient only. The data above come from trials using an earlier stage design so complication rates are now lower.	Thank you for your comments. Safety events reported have been included in the Overview except 'oesophageal perforation'. The Committee agreed to include this procedure related serious adverse event in the guidance but the Consultee did not give permission to publish this unpublished data. The current UK Imperial trial referred to is: NCT01114438 – a post marketing open label single group study in 45 obese type 2 diabetes patients (in 3 centres). Primary outcome: HbA1c at 12 months. As the study has been completed in January 2013 but is yet to be published the data cannot be included. NICE reviews Guidance when a substantive new body of peer-reviewed evidence becomes available.

Com. no.	Consultee name and organization	Sec. no	Comments	Response Please respond to all comments
38	Consultee 2 Manufacturer	**General**	DJBS stimulates the secretion of GLP-1, which mediates glucose dependent insulin secretion, and PYY, which suppresses appetite and food intake, in the GI tract leading primarily to significant improvements in glycemic control and the additional benefit of significant weight loss. The metabolic impact of the DJBS has been presented at the EASD conference in 2011 and can be visualized under the following link: http://easd.conference2web.com/content/1304 The metabolic impact of DJBS on low BMI patients has been presented at the EASD conference in 2012 and can be visualized under the following link: http://www.easdvirtualmeeting.org/resources/2498	Thank you for your comment These are findings from de Jonge (2013) study. This is a smaller study than those already presented in the Overview but provides some evidence on the mechanism of action. It has been added to appendix A in the Overview. The Committee considered your comment and removed the following text in the Overview under issues for consideration section: “The device’s mechanism of action is unclear”.
39	Consultee 13 Conversion Specialist (CTO)	Notes	Over the last week, Diabetes.co.uk conducted a survey of our members to determine public interest in the duodenal-jejunal bypass sleeve. 1,005 people with uncontrolled type 2 diabetes and obesity responded to the survey. These people were educated with content about the duodenal-jejunal bypass sleeve and asked questions which are included in the following webpage (http://www.diabetes.co.uk/diabetes-directory/endobarrier-gastrointestinal-liner.html). Our survey found that 88% of people “Definitely would request”, 8% of people “Probably would request” and 4% of people “May request” the duodenal-jejunal bypass sleeve if it was offered and reimbursed by their NHS hospital.	Thank you for your comment.

"Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees."