Intragastric balloons for the temporary management of morbid obesity

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Assessment report

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The Medical Services Advisory Committee (MSAC) is an independent committee which has been established to provide advice to the Minister for Health and Ageing on the strength of evidence available on new and existing medical technologies and procedures in terms of their safety, effectiveness and cost-effectiveness. This advice will help to inform government decisions about which medical services should attract funding under Medicare.

MSAC recommendations do not necessarily reflect the views of all individuals who participated in the MSAC evaluation.

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Executive summary

The procedure

Intragastric balloons (IGBs) are silicone elastomer devices filled with either saline solution or air which are endoscopically placed into the stomach. The devices are left in place for a maximum period of 6 months at a time. IGBs partially fill the stomach, inducing a sensation of satiety and thus reducing appetite and food intake. They are intended for use in morbidly obese patients as an adjunct to existing therapies that assist with weight reduction (ie diet, physical exercise, pharmacotherapy and behavioural therapy).

The current review has assessed the two devices currently available in Australia: The BioEnterics IGB and the Heliosphere IGB.

Medical Services Advisory Committee – role and approach

The Medical Services Advisory Committee (MSAC) was established by the Australian Government to strengthen the role of evidence in health financing decisions in Australia. The MSAC advises the Minister for Health and Ageing on the evidence relating to the safety, effectiveness and cost-effectiveness of new and existing medical technologies and procedures and under what circumstances public funding should be supported.

A rigorous assessment of evidence is thus the basis of decision making when funding is sought under Medicare. A team from Adelaide Health Technology Assessment, Discipline of Public Health, School of Population Health and Clinical Practice, The University of Adelaide, was engaged to conduct a systematic review of literature on the use of intragastric balloons for the temporary management of obesity. An advisory panel with expertise in this area then evaluated the evidence and provided advice to the MSAC.

MSAC's assessment of intragastric balloons for the temporary management of morbid obesity

This assessment examined two specific issues:

- What is the safety, effectiveness and cost-effectiveness of intragastric balloons ± conventional therapies (diet ± physical activity ± behavioural therapy ± drug therapy) compared to conventional therapies alone in the management of morbid obesity?

- What is the safety, effectiveness and cost-effectiveness of intragastric balloons followed by surgical treatment compared to surgical treatment alone in the management of morbid obesity in patients at increased surgical risk?

Clinical need

Obesity is associated with a number of serious health consequences. The prevalence of obesity among Australian adults has increased from 11 per cent in 1995 to 16 per cent in 2004–05. In parallel with these demographic changes, there is an increasing number

of Australians who require therapeutic interventions for obesity. It is estimated that between 4,903 and 8,000 patients would receive an IGB each year if its insertion and removal was publicly funded.

Safety

IGBs have been proposed for use in clinical practice *in addition* to conventional management. Because of the risks associated with the procedure, consideration needs to be given to the added health risks associated with the use of IGBs and any potential benefits that they may have on weight loss.

Intragastric balloons ± continued conventional obesity treatment

A total of 39 studies reported on the safety outcomes of 4,718 patients treated with BioEnterics IGBs. The studies reported major complications in a small proportion of patients. These included death (0.06%), migration of the balloon and subsequent gastrointestinal obstruction (0.6%), gastric perforation (0.2%), oesophageal ruptures (0.02%) and biliary pancreatitis (0.02%). Physical intolerance of the balloon requiring early balloon removal was also reported (1.8%).

In addition, there were minor complications such as nausea and vomiting; and technical failures of the device including balloon deflation (2.6%), rupture/bursting of the balloon (0.2%) and a defective valve (0.04%).

Two studies reported on the safety outcomes associated with Heliosphere IGBs in a total of 42 patients. Only minor complications (nausea and vomiting) and technical difficulties relating to the placement/removal of the balloon were reported.

Intragastric balloons followed by surgery

Two studies provided limited evidence that IGB treatment was associated with improved safety during subsequent laparoscopic surgery in super-obese patients. These studies reported that no patients required conversion to open surgery or had intra-operative complications.

Effectiveness

Intragastric balloons ± continued conventional obesity treatment

Evidence pertaining to the effectiveness of IGBs was identified in 29 studies. The majority of the studies were level IV intervention evidence, with only three studies being level II intervention evidence (randomised controlled trials).

The results from these small sample randomised controlled trials are contradictory. One study found BioEnterics IGBs and diet treatment to be more effective on weight loss when compared with a sham and diet treatment, while the other two studies found no significant difference. The evidence available at present on the effectiveness of IGBs in the temporary treatment of morbid obesity is therefore inconclusive.

Intragastric balloons followed by surgery

Four studies addressed the use of BioEnterics IGBs prior to bariatric surgical treatment (level III and level IV intervention evidence). The results were consistent in that pre-

surgical treatment with IGBs had no impact on long-term weight loss following bariatric surgery.

Cost considerations

There is a lack of evidence on which to perform an economic evaluation. However, a financial analysis of the expenditures associated with insertion and removal of IGBs for the temporary management of morbid obesity has been undertaken. This analysis shows that the unit cost for the placement and removal of IGBs is $3,827. Based on an estimated 4,903–8,000 procedures conducted per year (of which 96 per cent will be in the private sector), a total cost of $19,236,067 – $30,535,600 per year would potentially be incurred by the Australian healthcare system for IGB treatments. These costs would be in addition to the costs associated with providing conventional obesity management for morbidly obese patients.

Recommendation

The MSAC has considered the safety, and clinical effectiveness of intragastric balloons for the temporary management of morbid obesity in addition to conventional treatment such as diet, exercise and behaviour modification.

The MSAC finds that intragastric balloons used for the temporary management of morbid obesity pose additional risks to patients when compared to the standard treatment for morbid obesity and that they do not provide additional clinical benefits over standard treatment.

There may be a role for the temporary placement of intragastric balloons for the management of the super obese patient prior to bariatric surgery however, evidence to support this approach is limited.

The MSAC finds that the use of intragastric balloons for the temporary management of morbid obesity is less cost-effective than standard treatment for morbid obesity.

The MSAC recommends that public funding is not supported for this procedure.

The Minister for Health and Ageing endorsed this recommendation on the 20th May 2008.

Introduction

The Medical Services Advisory Committee (MSAC) has reviewed the use of intragastric balloons, which are therapeutic devices for the temporary management of morbid obesity. The MSAC evaluates new and existing health technologies and procedures for which funding is sought under the Medicare Benefits Scheme in terms of their safety, effectiveness and cost-effectiveness, while taking into account other issues such as access and equity. The MSAC adopts an evidence-based approach to its assessments, based on reviews of the scientific literature and other information sources, including clinical expertise.

The MSAC's terms of reference and membership are at Appendix A. The MSAC is a multidisciplinary expert body, comprising members drawn from such disciplines as diagnostic imaging, pathology, surgery, internal medicine and general practice, clinical epidemiology, health economics, consumer health and health administration.

This report summarises the assessment of current evidence for the use of intragastric balloons for the temporary management of morbid obesity.

Background

Obesity

The World Health Organization (WHO) defines overweight as a body mass index (BMI) of over 25 kg/m^2 and obesity as a BMI over 30 kg/m^2 (WHO 2003). Morbid obesity is characterised as a BMI of over 40 kg/m^2 or a BMI of over 35 kg/m^2 with concomitant co-morbidities. BMI is an acceptable measure of total body fat and can be used to estimate the relative risk of disease (NHMRC 2003).

A second internationally recognised means of classification is the measurement of the waist circumference. This correlates closely with the BMI and is used as an approximate index of intra-abdominal fat mass and total body fat (WHO 2007a). Waist circumference is a valid measure of abdominal fat mass and disease risk in individuals with BMI less than 35 kg/m^2. In those with BMI more than 35 kg/m^2, waist circumference adds little to the measure of risk provided by the measurement of BMI (NHMRC 2003).

The definitions of overweight and obese for each weight measurement are summarised in Table 1.

Table 1 Definition of overweight and obesity index (Cameron et al 2003)

Body mass index (kg/m^2)		Waist circumference (cm)		
Underweight	Less than 18.5	Males:	overweight	94–101
Normal weight	18.5 and less than 25		obese	≥102
Overweight	25 and less than 30	Females:	overweight	80–87
Obese	30 and above		obese	≥88
Morbidly obese	≥35 with co-morbidity or ≥40			
Super-obese	50 and above			

Source: WHO 2003

The cut-off points for overweight and obesity have been derived in populations that are predominantly Caucasian. They are therefore likely to be appropriate for Caucasian Australians, and may be less relevant for Indigenous, African and Asian Australians (NHMRC 2003).

Obesity has a multifactorial aetiology. The main factor is an energy imbalance due to a higher level of calorie intake than energy expenditure through physical activity over a considerable period of time (Department of Health and Ageing 2002). Genetic and environmental factors also play a role.

Gene-related differences may account for some of the disparities found in weight gain among populations (Marti & Martinez 2006). The number of genes that have been linked with human obesity phenotypes has been increasing (Perusse et al 1999). Some monogenetic forms of obesity are well investigated, and there is strong evidence that mutations in single genes like leptin, the leptin receptor and the melanocortin 4-receptor lead to severe obesity (Boutin & Froguel 2001). Genetic alterations only effect a small percentage of cases (less than 1%) (University of Washington 2004). Despite years of intensive research, it is not possible yet to explain the genetics of the most common forms of obesity (University of Washington 2004). There are also some rare syndromes,

such as Prader-Willi syndrome, the Bardet-Biedl syndrome and pseudohypoparathyroidism type 1 A, that are characterised by obesity (Bell et al 2005). Monogenetic and single syndromic forms of the condition cannot explain the worldwide increasing prevalence of obesity, and common forms are more likely a result of a complex interaction of polygenetic and environmental factors (Loos & Bouchard 2003).

The rising prevalence of obesity predominantly reflects lifestyle changes (Marti & Martinez 2006). Global increases to epidemic proportions are attributable to a number of factors including:

- a global shift in diet towards increased intake of energy-dense foods that are high in fat and sugars but low in vitamins, minerals and other micronutrients; and

- a trend towards decreased physical activity due to the increasingly sedentary nature of many forms of work, changing modes of transportation and increasing urbanisation (WHO 2007b).

Being overweight and obese is associated with a number of serious health consequences. The risk of suffering from weight associated diseases increases progressively as BMI increases. Diseases such as diabetes, coronary heart disease, stroke, musculoskeletal disorders, osteoarthritis and some cancers (of the breast, colon, kidney and gallbladder) are the main health consequences of being overweight and obese. Other associated quality of life issues are respiratory difficulties, chronic musculoskeletal problems, skin problems and infertility (WHO 2003; WHO 2006). Morbidly obese patients in general, and super-obese patients in particular (with BMI 50 kg/m^2 and above), represent a great challenge for the surgeon as well as the anaesthetist should they require a surgical intervention (Busetto et al 2004).

Social disadvantages and psychological consequences are experienced by obese people. Weight-based stigma and discrimination have been identified in key areas including employment, education, healthcare and social relationships (Puhl & Brownell 2003). Quality of life impairments increase proportionately with weight gain (Kolotkin et al 2001). Data provided by the Australian Society for the Study of Obesity suggests that being female and young are characteristics associated with a higher risk of being adversely psychologically affected by obesity (ASSO n.d.). The perception in the general population is that obesity results from a lack of self-discipline and from out-of-control eating impulses (Puhl & Brownell 2003).

The procedure

The BioEnterics intragastric balloon (BIB) is a soft silicone elastomer balloon which is endoscopically inserted, via the oesophagus, into the stomach, where it is inflated to its full size and spherical shape with 400–700 mL of sterile saline solution (Figure 1). Once the balloon is inflated, the filling tube is removed and the balloon is free to move within the stomach. It is suggested that the BIB acts as an artificial bezoar (ie a ball of food, mucus, vegetable fibre, hair or other material that cannot be digested in the stomach), leading to a sensation of satiety and thus reducing the desire for food intake (INAMED Health 2005; Fernandes et al 2007).

Figure 1 BioEnterics® intragastric balloon (source INAMED Health 2005)

The intragastric balloon (IGB) is designed to remain in place for a period of 6 months, at which time it must be endoscopically removed or replaced. The combination of a supervised diet and behavioural modification program is recommended, to assist with the maintenance of weight loss, following the placement and after the removal of the BIB.

A second available device used for the non-surgical treatment of obesity is the Heliosphere® IGB system manufactured by Helioscopie (France). Like the BioEnterics IGB, the Heliosphere® is inserted endoscopically into the stomach but filled with air after the placement. With a volume of 650–750 mL of air, the Heliosphere® weighs less than 30 g. The Heliosphere® must be removed or replaced after a maximum of 6 months (Allison 2006).

Intended purpose

IGBs are indicated for severely obese patients (BMI ≥40 kg/m^2 or a BMI ≥35 kg/m^2 with co-morbidities) who: (1) have to lose weight prior to bariatric or other surgery in order to reduce the surgical risk or (2) are not suitable for surgery. Obese patients with a BMI of 30–39 kg/m^2 with significant coexisting health risks and who are unable to achieve a persistent weight loss by participating in a supervised weight-control program also form part of the BIB treatment target group (INAMED Health 2005).

The main contraindications for the placement of IGBs are listed in Table 2.

Table 2 Contraindications for the placement of the BioEnterics® intragastric balloon

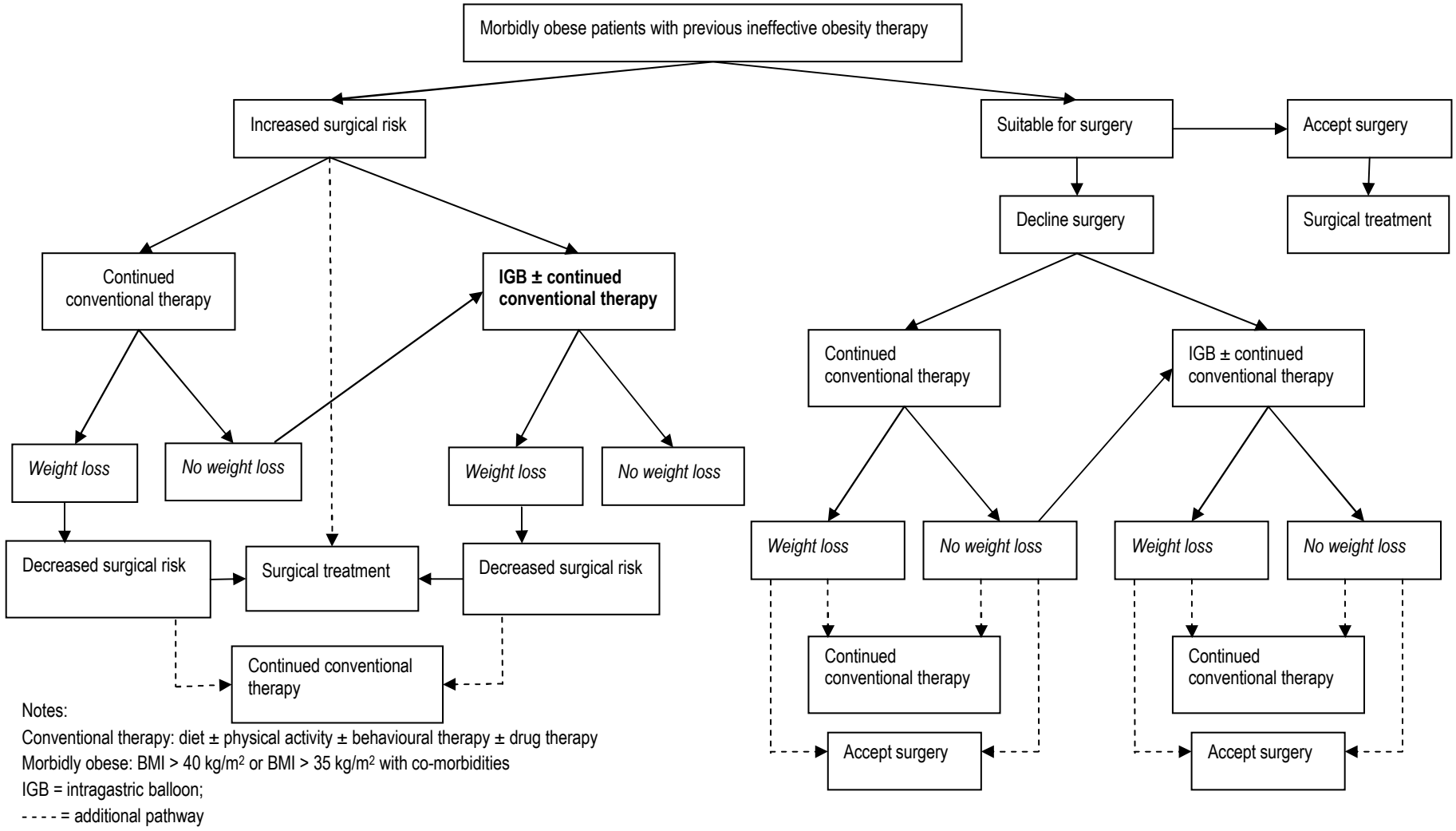
Physical contraindications	Previous gastric or intestinal surgery Any inflammatory disease of the gastrointestinal tract including oesophagitis, gastric ulceration, duodenal ulceration, cancer or specific inflammation such as Crohn's disease Potential upper gastrointestinal bleeding conditions such as oesophageal or gastric varices, congenital or acquired intestinal telangiectasis, or other congenital anomalies of the gastrointestinal tract such as atresias or stenosis Large hiatal hernia A structural abnormality in the oesophagus or pharynx such as stricture or diverticulum Any other medical condition which would not permit elective endoscopy Patients receiving aspirin, anti-inflammatory agents, anticoagulants or other gastric irritants who are not under medical supervision
Psychological contraindications	Major prior or present psychological disorder Alcoholism or drug addiction
Other contraindications	Pregnancy Breastfeeding Patients unwilling to participate in an established medically supervised diet and behaviour modification program, with routine medical follow-up

Adapted from INAMED Health 2005; Fernandes et al 2007

It should be noted that morbidly obese patients with co-morbidities like hypertension and coronary artery disease are at increased risk for hypoxemia and arrhythmia during the endoscopic procedure. This may require the adoption of specific safety measures while performing endoscopic procedures in this group of patients. Patients may require clinical observation for a longer period following the procedure (Fernandes et al 2007). The current MBS schedule specifies, in relation to endoscopic procedures performed in Australia, that when the patient is anaesthetised the anaesthetic equipment, administration and monitoring, and postoperative and resuscitation facilities should conform to the professional standards outlined by the Australian & New Zealand College of Anaesthetists, Gastroenterological Society of Australia and Royal Australian College of Surgeons (ANZCA 2004).

Clinical decision-making processes concerned with the use of IGBs in the management of morbid obesity are presented in Figure 2.

Figure 2 Clinical decision tree for placement of intragastric balloons for the temporary management of morbid obesity



Notes:
Conventional therapy: diet ± physical activity ± behavioural therapy ± drug therapy
Morbidly obese: BMI > 40 kg/m^2 or BMI > 35 kg/m^2 with co-morbidities
IGB = intragastric balloon;
- - - - = additional pathway

Existing treatment options

There is a wide range of obesity treatment programs available. These can be divided into non-surgical methods (eg diet, physical activity programs, behavioural therapy and pharmacotherapy) and surgical methods (ie bariatric surgery). Because of the multifactorial aetiology of obesity, a combination of treatment programs within a multidisciplinary management approach is considered to provide the best opportunity for treatment. The choice of treatment should be based on individual considerations including severity and co-morbidities (NHMRC 2003).

Dietary interventions aim at reducing the total energy intake. There are numerous diet programs, which can be divided into reduced-energy, low-energy and very low-energy diets. It is clear that diets combined with a physical activity program or behavioural therapies are more successful than calorie reduction alone. *The clinical practice guidelines for the management of overweight and obesity in adults* (NHMRC 2003) conclude that low-fat *ad libitum* diets combined with increased physical activity achieve the best results for long-term weight loss. Other diets have shown good short-term results but until recently there was little evidence of long-term effectiveness.

Physical activity as a single treatment program for obesity is not appropriate for achieving long-term weight loss. It should be noted, however, that physical activity in combination with any other treatment program is one of the key factors for improving the effectiveness of long-term maintenance and the state of health (NHMRC 2003).

Behavioural therapy may assist patients to identify and modify their eating and physical activity habits, and can improve the effectiveness of other treatment strategies. As a single treatment approach, behavioural therapy does not suffice for achieving long-term weight loss (NHMRC 2003; Lambert et al 2006).

Pharmacotherapy is only recommended for overweight patients with a BMI over 27 kg/m^2 with co-morbidities or for obese patients with a BMI over 30 kg/m^2. Medical therapy should only be used for patients who have not successfully lost weight through diet, physical activity and behavioural modification therapies. Phentermine, diethylpropion, orlistat and sibutramine are the four current pharmaceuticals that have been approved by the Therapeutic Goods Administration for the treatment of obesity in Australia (NHMRC 2003).

There are two general approaches used in the *surgical treatment of obesity* — bypass procedures and restrictive procedures. The most commonly performed procedures are laparoscopic gastric banding and laparoscopic gastric bypass (Sjostrom et al 2007). Other techniques less often performed are sleeve gastrectomy and biliopancreatic diversion. These methods restrict either the intake of food or its absorption, and are an effective approach for achieving a long-term weight loss. Surgical treatment is restricted to morbidly obese patients who have been unable to lose weight using other non-surgical methods, who have acceptable operative risks and who are likely to comply with a long-term treatment and follow-up (National Guideline Clearinghouse 2006). There are some complications associated with bariatric surgery including pulmonary embolism, respiratory failure, gastrointestinal leaks, bleeding, stomal obstruction and stenosis. There is an increasing level of risk related to the degree of obesity (Steinbrook 2004).

Comparators

1. IGBs with/without continued conventional therapy (diet ± physical activity ± behavioural therapy ± drug therapy) were compared with continued conventional therapy alone.

2. IGBs followed by obesity surgery were compared with obesity surgery alone.

Marketing status of the device

Two IGBs are registered on the Australian Register of Therapeutic Goods (ARTG) for use in Australia (Table 3).

Table 3 Intragastric balloons listed on ARTG (as at 17 October 2007)

Product name	ARTG no.	Product no.	Sponsor
BioEnterics intragastric balloon	106802	185345	Allergan Australia Pty Ltd
Heliosphere intragastric balloon device	133198	218960	Morton Surgical Pty Ltd T/A Matrix Surgical Company

Current reimbursement arrangement

Currently there are no items listed on the Medicare Benefits Schedule (MBS) covering the insertion or removal of IGBs. Surgical procedures used for the treatment of morbid obesity that are covered by MBS are listed in Table 4. The Pharmaceutical Benefits Scheme (PBS) includes orlistat (Xenical) (PBS item number 30511).

Table 4 MBS item numbers covering surgical treatment of morbid obesity

MBS Item numbers	Services
30511	MORBID OBESITY, gastric reduction or gastroplasty for, by any method (Anaes.) (Assist.) **Fee:** $750.70 **Benefit:** 75% = $563.05
30512	MORBID OBESITY, gastric bypass for, by any method including anastomosis (Anaes.) (Assist.) **Fee:** $923.80 **Benefit:** 75% = $692.85
30514	MORBID OBESITY, surgical reversal, by any method, of procedure to which item 30511 or 30512 applies (Anaes.) (Assist.) **Fee:** $1,360.05 **Benefit:** 75% = $1,020.05
31441	LONG-TERM IMPLANTED RESERVOIR associated with the adjustable gastric band, repair, revision or replacement of (Anaes.) **Fee:** $222.35 **Benefit:** 75% = $166.80 85% = $189.00
14215	LONG-TERM IMPLANTED RESERVOIR associated with the adjustable gastric band, accessing of to add or remove fluid **Fee:** $86.50 **Benefit:** 75% = $64.90 85% = $73.55

Approach to assessment

Objective

To determine whether there is sufficient evidence, in relation to clinical need, safety, effectiveness and cost-effectiveness, to have the use of IGBs for the temporary management of morbid obesity considered for public funding.

Research questions

1. What is the prevalence of morbid obesity among adult Australians? *(not assessed through systematic literature review)*

2. What is the safety, clinical effectiveness and cost-effectiveness of intragastric balloons ± conventional therapies (diet ± physical activity ± behavioural therapy ± drug therapy) compared to conventional interventions alone in the management of morbid obesity?

3. What is the safety, clinical effectiveness and cost-effectiveness of intragastric balloons followed by surgical treatment compared to surgical treatment alone in the management of morbid obesity in patients at increased surgical risk?

Expert advice

An advisory panel with expertise in endocrinology, gastroenterology, bariatric surgery, general practice and consumer issues was established to evaluate the evidence and provide advice to the MSAC from a clinical perspective. In selecting members for advisory panels, the MSAC's practice is to approach the appropriate medical colleges, specialist societies and associations, and consumer bodies for nominees. Membership of the advisory panel is provided in Appendix B.

Review of literature

Literature sources and search strategies

The medical literature was searched to identify relevant studies and reviews for the period spanning 1990 to June 2007. Appendix C describes the electronic databases that were used for this search and the other sources of evidence that were investigated. Grey literature (ie literature that is not available through the usual bibliographic sources such as databases or indexes and includes technical reports, working papers, committee reports, symposia, unpublished work etc) was included in the search strategy. Unpublished literature, however, was not canvassed as it is difficult to search for this literature exhaustively and systematically, and trials that are difficult to locate are often smaller and of lower methodological quality (Egger et al 2003). It is, however, possible that these unpublished data could impact on the results of this assessment.

The search terms used to identify literature in electronic databases on the safety and effectiveness of IGBs are also presented in Appendix C.

Inclusion/exclusion criteria

The criteria for including articles in this report varied depending on the type of research question being addressed. Often a study was assessed more than once because it addressed more than one research question. One researcher applied the inclusion criteria to the collated literature. If there was any doubt concerning inclusion of papers, this was resolved by group consensus to ensure that all potentially relevant studies were captured. In general, studies were excluded if they:

- did not address the research question;
- did not provide information on the pre-specified target population;
- did not include the pre-specified intervention;
- did not compare results to the pre-specified comparators;
- did not address one of the pre-specified outcomes and/or provided inadequate data on these outcomes (in some instances, a study was included to assess one or more outcomes but had to be excluded for other outcomes due to data inadequacies); or
- did not have the appropriate study design.

Where two or more papers reported on different aspects of the same study, they were treated as one study. Similarly, if the same data were duplicated in multiple articles, only results from the most comprehensive or most recent article were included.

The inclusion criteria relevant to each of the research questions posed in this assessment are provided in Appendix E and Appendix G. The research question concerning clinical need and burden of disease was not assessed by a systematic literature review as recent data regarding obesity are available from national or state/territory surveys.

Search results

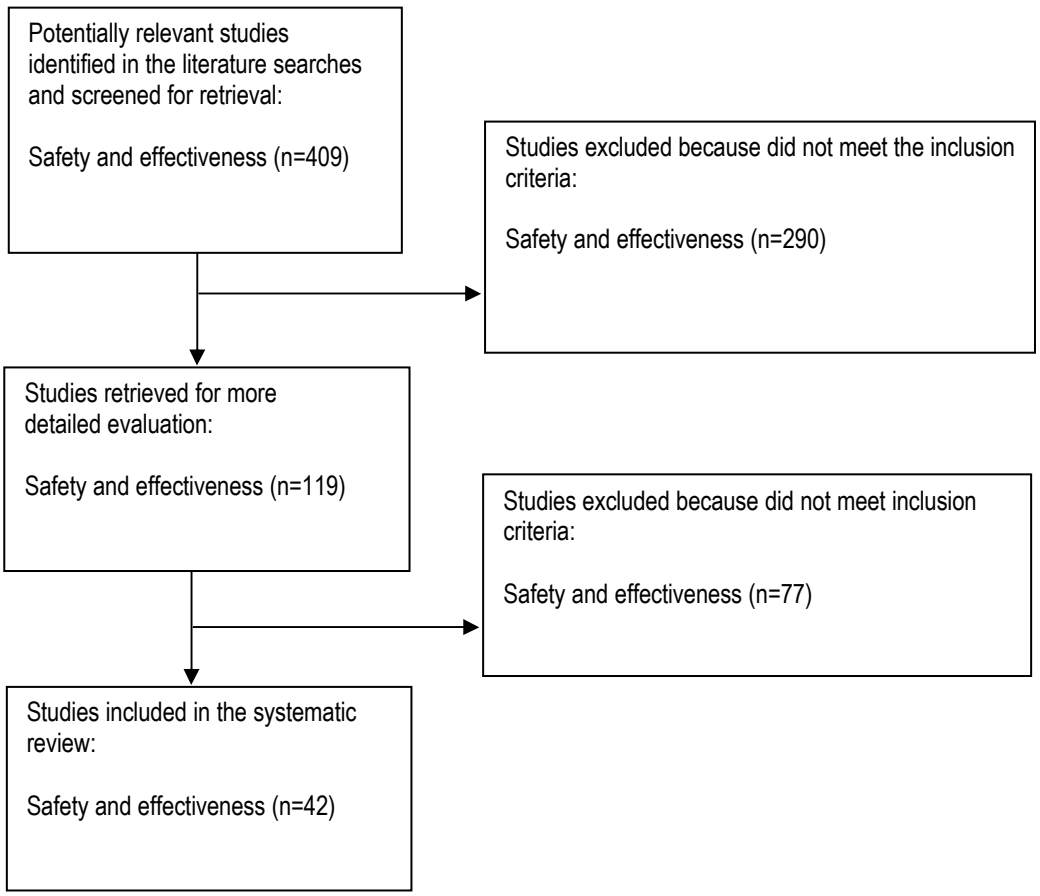
The process of study selection for this report went through six phases:

1. All reference citations from all literature sources were collated into an Endnote 8.0 database.
2. Duplicate references were removed.
3. Studies were excluded, on the basis of the citation information, if it was obvious that they did not meet the pre-specified inclusion criteria. Citations were assessed by one reviewer. Studies marked as requiring further evaluation by the reviewer were retrieved for full-text assessment.
4. Studies were included to address the research questions if they met the pre-specified criteria applied by one reviewer to the full-text articles. Those articles meeting the criteria formed part of the evidence-base. The remainder provided background information.
5. The reference lists of the included articles were pearled for additional relevant studies. These were retrieved and assessed according to phase 4.

6. The evidence-base consisted of articles from phases 4 and 5 that met the inclusion criteria.

Any doubt concerning inclusions at phase 4 was resolved by group consensus to ensure that all potentially relevant studies were captured. The results of the process of study selection are provided in Figure 3.

Figure 3 Study selection process



Data extraction and analysis

A profile of key characteristics was developed for each included study (Appendix E).

Burden of disease has been reported as the prevalence of obesity in Australia.

Descriptive statistics were extracted or calculated for all safety and effectiveness outcomes (defined in the assessment protocol) in the individual studies, including numerator and denominator information, means and standard deviations. A statistically significant difference was determined at $p<0.05$.

Assessment of effectiveness was largely concerned with determining whether there were improvements in weight loss from baseline. Differences between the intervention group and comparator at baseline have been considered to ensure that results reflect a real change due to the intervention rather than the result being affected by baseline differences between treatment groups. In instances where both baseline and follow-up data were provided for an outcome in intervention and comparator groups, the absolute difference between the pre- and post-intervention scores has been calculated.

The majority of studies in this report were uncontrolled pre-test/post-test case series. Effectiveness data from both pre- and post-intervention have been presented, as well as the absolute difference and the results of any statistical testing conducted by the authors.

Validity assessment of individual studies

The evidence presented in the selected studies was assessed and classified using the dimensions of evidence defined by the National Health and Medical Research Council (NHMRC 2000a).

These dimensions (Table 5) consider important aspects of the evidence supporting a particular intervention and include three main domains: strength of the evidence, size of the effect and relevance of the evidence. The first domain is derived directly from the literature identified as informing a particular intervention. Each of the last two requires expert clinical input as part of its determination.

Table 5 Evidence dimensions

Type of evidence	Definition
Strength of the evidence	
Level	The study design used, as an indicator of the degree to which bias has been eliminated by design. [a]
Quality	The methods used by investigators to minimise bias within a study design.
Statistical precision	The p-value or, alternatively, the precision of the estimate of the effect. It reflects the degree of certainty about the existence of a true effect.
Size of effect	The distance of the study estimate from the 'null' value and the inclusion of only clinically important effects in the confidence interval.
Relevance of evidence	The usefulness of the evidence in clinical practice, particularly the appropriateness of the outcome measures used.

[a] See Table 6

Strength of the evidence

The three sub-domains (level, quality and statistical precision) are collectively a measure of the strength of the evidence.

Level

The 'level of evidence' reflects the effectiveness of a study design to answer a particular research question. Effectiveness is based on the probability that the design of the study has reduced or eliminated the impact of bias on the results.

The new version of the NHMRC evidence hierarchy provides a ranking of various study designs ('levels of evidence') by the type of research question being addressed (NHMRC 2005). Table 6 is an abbreviated version of this evidence hierarchy relevant to an assessment of an intervention.

Table 6 Designations of intervention levels of evidence adapted from NHMRC (2005)

Level	Intervention [a]
I [b]	A systematic review of level II studies
II	A randomised controlled trial
III-1	A pseudorandomised controlled trial (ie alternate allocation or some other method)
III-2	A comparative study with concurrent controls: non-randomised, experimental trial [c] cohort study case-control study interrupted time series with a control group
III-3	A comparative study without concurrent controls: historical control study two or more single-arm studies [d] interrupted time series without a parallel control group
IV	Case series with either post-test or pre-test/post-test outcomes

Table notes

[a] Definitions of these study designs are provided in NHMRC (2000b; pp. 7–8); [b] a systematic review will only be assigned a level of evidence as high as the studies it contains, excepting where those studies are of level II evidence; [c] this also includes controlled before-and-after (pre-test/post-test) studies, as well as indirect comparisons (ie using A vs B and B vs C to determine A vs C); [d] comparing single-arm studies, ie case series from two studies.

Note 1: Assessment of comparative harms/safety should occur according to the hierarchy presented for each of the research questions, with the proviso that this assessment occurs within the context of the topic being assessed. Some harms are rare and cannot feasibly be captured within randomised controlled trials; physical harms and psychological harms may need to be addressed by different study designs; harms from diagnostic testing include the likelihood of false positive and false negative results; harms from screening include the likelihood of false alarm and false reassurance results.

Note 2: When a level of evidence is attributed in the text of a document, it should also be framed according to its corresponding research question, eg level II intervention evidence; level IV diagnostic evidence.

Quality

The appraisal of trials and cohort studies pertaining to treatment safety and effectiveness was undertaken using a checklist developed by NHMRC (Khan et al 2001; NHMRC 2000a). This checklist was used for trials and cohort studies. Uncontrolled before-and-after case series are a poorer level of evidence for the assessment of effectiveness. The quality of this type of study design was assessed according to a checklist developed by the York Centre for Reviews and Dissemination in the UK (Khan et al 2001).

Statistical precision

Statistical precision was determined using statistical principles. Small confidence intervals and p-values give an indication as to the probability that the reported effect is real and not attributable to chance (NHMRC 2000a)

Size of effect

For intervention studies on the placement of intragastric balloons it was important to assess whether statistically significant differences are also clinically important. It is considered that even a modest loss of 5–10 per cent of starting weight can result in significant health benefits (NHMRC 2003).

The size of the effect needed to be determined, as well as whether the 95% confidence interval includes only clinically important effects.

Relevance of evidence

Similarly, the outcome being measured should be appropriate and clinically relevant. Inadequately validated (predictive) surrogate measures of a clinically relevant outcome should be avoided (NHMRC 2000b).

Assessment of the body of evidence

Appraisal of the body of evidence was conducted along the lines suggested by the NHMRC in their guidance on clinical practice guideline development (NHMRC 2005). Five components are considered essential by the NHMRC when judging the body of evidence:

- the evidence base – which includes the number of studies sorted by their methodological quality and relevance to patients;
- the consistency of the study results – whether the better quality studies had results of a similar magnitude and in the same direction, ie homogenous or heterogenous findings;
- the potential clinical impact – appraisal of the precision, size and clinical importance or relevance of the primary outcomes used to determine the safety and effectiveness of the intervention;
- the generalisability of the evidence to the target population; and
- the applicability of the evidence – integration of this evidence for conclusions about the net clinical benefit of the intervention in the context of Australian clinical practice.

A matrix for assessing the body of evidence for each research question, according to the components above, was used for this assessment (Table 7)(NHMRC 2005).

Table 7 Body of evidence assessment matrix

Component	A Excellent	B Good	C Satisfactory	D Poor
Evidence-base	Several level I or II studies with low risk of bias	One or two level II studies with low risk of bias or a SR/multiple level III studies with low risk of bias	Level III studies with low risk of bias, or level I or II studies with moderate risk of bias	Level IV studies, or level I to III studies with high risk of bias
Consistency	All studies consistent	Most studies consistent and inconsistency may be explained	Some inconsistency reflecting genuine uncertainty around clinical question	Evidence is inconsistent
Clinical impact	Very large	Substantial	Moderate	Slight or restricted
Generalisability	Population(s) studied in body of evidence is/are the same as the target population	Population(s) studied in the body of evidence is/are similar to the target population	Population(s) studied in body of evidence is/are different to target population for guideline but it is clinically sensible to apply this evidence to target population	Population(s) studied in body of evidence is/are different to target population and it is hard to judge whether it is sensible to generalise to target population
Applicability	Directly applicable to Australian healthcare context	Applicable to Australian healthcare context with few caveats	Probably applicable to Australian healthcare context with some caveats	Not applicable to Australian healthcare context

Results of assessment

What is the clinical need / burden of disease?

The worldwide prevalence of obesity and overweight has reached epidemic proportions, with approximately 1.6 billion adults (aged 15+ years) being overweight and at least 400 million being clinically obese (WHO 2006). In Australia, similar trends are evident. The prevalence of obesity among Australian adults increased from 11 per cent in 1995 to 15 per cent in 2001 and reached 16 per cent in 2004–05 (AIHW 2006).

The most recent nationally collected measured height and weight data is derived from the 1999–2000 AusDiab study (Dunstan et al 2001). This study found 19 per cent of males and 22 per cent of females aged 25 years and over to be obese, and 48 per cent of males and 30 per cent of females to be overweight but not obese. The prevalence of obesity was highest in the 55–64 years age group (29%). Table 8 and Table 9 show the age- and gender-specific prevalence of overweight and obesity in Australia, calculated from measured weight and height data.

Table 8 Age-specific prevalence (%) of overweight (BMI ≥ 25 kg/m²) in Australia

	Age (years)						
	25–34	**35–44**	**45–54**	**55–64**	**65–74**	**> 75**	**Total**
Males	60.5	64.2	72.4	74.0	73.1	63.8	67.4
Females	35.1	44.5	58.1	67.6	68.9	52.2	52.0
Total	48.1	54.4	65.3	70.8	70.8	57.1	59.6

Adapted from Dunstan et al 2001

Table 9 Age-specific prevalence (%) of obesity (BMI ≥ 30 kg/m²) in Australia

	Age (years)						
	25–34	**35–44**	**45–54**	**55–64**	**65–74**	**> 75**	**Total**
Males	17.0	17.5	20.5	25.5	20.5	11.6	19.1
Females	12.2	19.4	26.0	31.9	29.7	14.9	21.8
Total	14.7	18.4	23.2	28.7	25.5	13.5	20.5

Adapted from Dunstan et al 2001

The AusDiab study also reported waist circumference data, which is an independent risk factor for Type 2 diabetes and coronary heart disease. Twenty-seven per cent of males and 34 per cent of females aged 25 years and over were classified as abdominally obese (Dunstan et al 2001).

The 2004–05 Australian National Health Survey represents the most recent national data; however, it is based on self-reported height and weight. This survey reported that 2,500,000 Australian adults were estimated as obese (with a BMI of 30 kg/m^2 or more), which represents 19 per cent of males and 17 per cent of females aged 18 years and over (ABS 2006). Males aged 45–54 years and females aged 55–64 years recorded the highest proportion of obesity (23.2% and 21.7% respectively). In addition, 4.9 million Australian adults were classified as overweight (with a BMI of more than 25 kg/m^2 but less than 30 kg/m^2), representing 41 per cent of males and 25 per cent of females. Overall, 62 per cent of males and 45 per cent of females were estimated to be overweight or obese. However, only 32 per cent of men and 37 per cent of women considered themselves as being overweight. The proportion of adults classified as overweight or obese has

increased over the last 10 years: for men from 52 per cent to 62 per cent and for women from 37 per cent to 45 per cent. The prevalence of self-reported overweight and obesity was similar across all states and territories (Table 10).

Data on self-reported height and weight collected by state and territory computer-assisted telephone interviews (CATI) has provided similar results to the Australian National Health Survey (AIHW 2006). The estimated obesity rates were 16.5 per cent for males and 16.3 per cent for females; and overweight rates were estimated at 42.1 per cent for males and 26.3 per cent for females. Similar rates were found across all states and territories (Table 10).

Table 10 Prevalence of self-reported overweight and obesity in adult Australians (%) (2004 CATI surveys)

	NSW	Vic [a]	Qld	WA	SA	Tas	ACT	NT	Aust [b]
Males									
Overweight	41.0	42.9	40.5	46.0	44.1	43.0	39.5	42.6	42.1
Obese	16.3	14.7	20.0	14.1	18.5	15.1	14.8	18.3	16.5
Overweight or obese	57.3	57.6	60.5	60.1	62.6	58.1	54.2	60.9	58.6
Females									
Overweight	26.0	25.3	26.5	27.2	28.9	25.8	26.2	24.0	26.3
Obese	15.4	16.0	16.5	17.0	19.4	17.5	15.9	15.9	16.3
Overweight or obese	41.4	41.3	43.1	44.2	48.3	43.3	42.1	39.9	42.5
Persons									
Overweight	33.7	34.1	33.6	36.3	36.4	34.2	32.9	34.3	34.2
Obese	15.8	15.3	18.3	15.5	18.9	16.3	15.3	17.2	16.4
Overweight or obese	49.5	49.4	51.8	51.8	55.3	50.6	48.2	51.5	50.6

Table 11 Prevalence of self-reported overweight and obesity in adult Australians (%) (2004–05 NHS)

	NSW	Vic [a]	Qld	WA	SA	Tas	ACT	NT	Aust [b]
Persons									
Overweight	35.8	36.3	34.2	35.4	35.8	36.2	34.6	n/a	35.5
Obese	18.0	17.0	18.7	17.3	19.6	19.5	18.2	n/a	18.0
Overweight or obese	53.8	53.3	52.9	52.8	55.4	55.7	52.8	n/a	53.6

[a] Results adjusted for missing values; [b] derived from a weighted average of the state and territory estimates for state CATI data
Source: AIHW 2006

The socioeconomically disadvantaged groups have higher rates of overweight and obesity. Among adults who were classified as most disadvantaged (first quintile), 50 per cent were overweight or obese compared with the least disadvantaged (fifth quintile) (AIHW 2006). Females in the most disadvantaged socioeconomic group had nearly double the rate of obesity (23%) of those in the most advantaged group (12%). Likewise, males in the most disadvantaged group were more likely to be obese than those in the most advantaged group (19% vs 13%).

Aboriginal and Torres Strait Islander people were almost twice as likely to be obese (27%) compared with non-Indigenous Australians (15%) (AIHW 2006).

Comparative data from the World Health Organization (WHO) shows that Australia has a similar prevalence of overweight and obesity to the United States, Canada and United Kingdom, but considerably higher than France and Japan (AIHW 2006).

According to Medicare statistics, 1,397 surgical procedures for morbid obesity (MBS items 30511 and 30512) were performed in 2001. The numbers have increased steadily to 6,319 procedures in 2005–06 and 7,772 in 2006–07 (Medicare Australia 2007). It is estimated that the use of surgical treatment for obesity in 2007–08 will be approximately 8,000.

IGBs would only be used in patients at increased surgical risk, or in those patients who initially refuse surgical treatment, rather than for routine use in patients who undergo surgery for obesity. In the absence of any better estimate, this population was determined by assessing the number of patients who were excluded from receiving laparoscopic adjustable gastric banding (LAGB) in a recent Australian study by Dixon et al (2008). From a total of 133 people screened, 73 were excluded from the study for various reasons (including absence of diabetes, which would not be a contraindication for surgery in Australia). When patients who had diabetes were included in the surgical group (rather than the excluded group), 51 (38% of those initially enrolled) were excluded and 82 (62%) were eligible for surgery.

It is therefore estimated that the 8,000 Australians who are predicted to undergo surgery for obesity each year come from a total screened population of 12,903, and that 4,903 of these patients (38%) would be unsuitable for surgery and potential candidates for IGBs.

Is it safe?

The inclusion criteria established a priori for identifying studies on the safety of intragastric balloons (IGBs) are provided in Appendix E and Appendix F.

Forty one studies, with a total of 4,760 patients, reported on the safety of IGBs. Of these, two were randomised controlled trials, one was a comparative study with historical controls, 29 were case series and seven were case reports. Data describing the relevant outcomes have been extracted and are presented in Appendix E and Appendix F. Data from studies have been entered in a hierarchical manner according to the study's level of evidence, quality assessment and publication data.

Only two studies refer to the safety of the Heliosphere IGB (Appendix F), with the remaining 39 assessing the BioEnterics IGB (BIB; Appendix E).

The primary safety outcomes described are related either to the placement/removal of the IGB or to potential complications during the IGB treatment. The secondary safety outcomes are related to technical failure of the IGB.

Intragastric balloon ± continued conventional obesity treatment

BioEnterics intragastric balloon

Primary safety outcomes

Deaths

Death was reported in three patients receiving BIB treatment. Two patients, with a history of gastric surgery, died from untreatable peritonitis following gastric perforation that occurred during IGB treatment (Genco et al 2005). Another patient, with multiple severe co-morbidities, died of complications occurring during IGB placement (ie respiratory arrest after massive aspiration) (Spyropoulos et al 2007).

Complications associated with balloon placement and removal

Two patients experienced acute gastric dilatation associated with the endoscopic placement of the IGB (Genco et al 2005).

Only one adverse event was reported in association with endoscopic removal of the IGB. This was a Mallory-Weiss laceration and minor gastric bleeding (Mathus-Vliegen & Tytgat 2005).

Complications occurring during balloon treatment

The adverse events possible during IGB treatment can occur early in the treatment (ie during the first days after the balloon placement) or later. It is generally expected that minor gastrointestinal symptoms will occur in the first days following the IGB placement (eg nausea, vomiting, gastro-oesophageal reflux, epigastric discomfort). These symptoms are usually controlled by symptomatic medication. In some patients the symptoms are more severe, cannot be controlled by medication or, in some instances, extend for longer periods of time. Only a few of the included studies have clearly distinguished between the early and later occurrence or persistence of symptoms associated with IGBs.

In a randomised controlled trial comparing the BIB with a sham procedure, the study reported that 32 patients suffered adverse events within 48 hours after the BIB placement. These included epigastric pain in 84 per cent of patients receiving the balloon, compared with 9 per cent receiving the sham (relative risk = 9.3), and nausea in 81 per cent compared with 25 per cent in the sham group (relative risk = 3.4) (Genco et al 2006). Symptoms were easily controlled with medical therapy in all cases.

Major complications reported during the IGB treatment in the 38 included studies on the BIB were:

- migration of the balloon and subsequent gastrointestinal obstruction in 26 patients (0.6%)
- gastric perforation in seven patients (0.2%)
- oesophageal rupture in one patient (0.02%)
- biliary pancreatitis in one patient (0.02%).

Severe nausea and vomiting was reported in 20 patients. Across all 38 included studies, physical intolerance of the balloon (manifested as gastrointestinal symptoms) and requiring early removal of the BIB was reported in 85 patients (1.8%). Psychological intolerance was described in 14 patients (0.3%).

Pulmonary insufficiency was reported in three patients, renal insufficiency in one patient, and atrial fibrillation in one patient.

Minor complications included the following: oesophageal erosion (10 patients, 0.2%), oesophagitis (34 patients, 0.7%), gastric erosion (8 patients, 0.2%), gastric ulceration (9 patients, 0.2%), gastro-oesophageal reflux (60 patients, 1.3%), gastric stasis (28 patients, 0.6%), chronic gastric dilatation (1 patient, 0.02%), hypokalemia (16 patients, 0.4%), dehydration (33 patients, 0.7%), and cutaneous allergic reaction (1 patient, 0.02%).

Secondary safety outcomes

Across all studies, from a total of 4,718 patients, deflation of the balloon was reported in 121 patients (2.6%), rupture/bursting in 11 (0.2%) and defective valve in two (0.04%).

One study comparing three IGB retrieval techniques found that the number of balloons lost during retrieval was associated with the retrieval technique used, after controlling for other variables such as the number of antispastic drug ampoules used, cumulative symptom and discomfort scores, age and gender. Galloro et al (2007) concluded that balloon retrieval by double-channel gastroscope and foreign body forceps plus the symmetrical polypectomy shark retrieval snare were more effective (no balloons lost) than the other two techniques. In comparison, the standard gastroscope with foreign body forceps and standard gastroscope with retrieval snare techniques both resulted in 7 per cent of balloons being lost (Galloro et al 2007).

Heliosphere intragastric balloon

Primary safety outcomes

Only two studies (case series), including a total of 42 patients, have reported on the safety outcomes related to the Heliosphere IGB (Appendix G). These case series

reported nausea and vomiting in 84–100 per cent of patients (Forestieri et al 2006; Mion et al 2007). Moderate to severe abdominal pain was reported in 13 patients (Mion et al 2007) and psychological intolerance was described in one patient (Mion et al 2007).

Secondary safety outcomes

Forestieri et al, in a good quality case series, reported IGB failure requiring insertion of a second balloon in 5 of the 10 patients (Forestieri et al 2006). The IGB was not found in the stomach at the time of removal in one patient.

Another case series reported several difficulties related to the following steps in placement and removal of the IGB: opening of the sheath, separation of the balloon from its catheter, insertion of the catheter needle in the balloon and grasping of the balloon with the removal catheter (Mion et al 2007).

Intragastric balloon followed by surgery

Several authors have proposed the pre-operative treatment of morbidly obese patients with IGBs and diet in order to reduce the risk of complications related to surgical procedures (Weiner et al 1999; Busetto et al 2004; Alfalah et al 2006).

Surgical complications increase with a higher BMI. It is considered that as little as a 10 per cent weight reduction may have dramatic effects on cardiopulmonary and metabolic function (Alfalah et al 2006; Weiner et al 1999).

Super-obese patients in particular (BMI > 50 kg/m^2) represent a great challenge for both the surgeon and the anaesthetist (Busetto et al 2004). The rate of intra-operative complications is higher in the super-obese patient group than the overall morbidly obese patient group. The extreme visceral obesity makes intubation and mechanical ventilation procedures difficult. The creation of pneumoperitoneum, which is required by the laparoscopic procedures, is technically difficult. Because the operation field is frequently poorly visualised, there is a high probability of conversion to open surgery (ie to a fully open surgical procedure) (Alfalah et al 2006).

The main factors responsible for difficulties associated with laparoscopic procedures in super-obese patients are:

- the thick abdominal wall which makes the manipulation of laparoscopic instruments difficult
- excessive intra-abdominal adipose tissue and shortened mesentery which limit adequate exposure of the operative area
- hepatomegaly and a fragile liver — the liver is difficult to retract, leading to poor exposure of the upper abdomen.

A good quality historical control study (level III-2 intervention evidence) investigated the impact of pre-operative BIB treatment on reducing both the rate of conversion to open surgery and the rate of intra-operative complications in super-obese patients undertaking laparoscopic gastric banding (LAGB) (Busetto et al 2005). Forty-three super-obese patients undergoing 6 months of BIB treatment followed by LAGB (balloon group) were compared with sex-, age- and BMI-matched historical controls undertaking LAGB only in the same institution. The operative time and overall hospital stay were shorter in the balloon group. No patient from the balloon group required conversion to open surgery or had intra-operative complications. The rate of conversion to open surgery was

3 per cent in the LAGB only group. The rate of intra-operative complications was slightly higher (although not statistically significant) in the LAGB only group.

A good quality case series (level IV intervention evidence) also reported no conversion to open surgery in a group of 15 morbidly obese patients undertaking 4–7 months of BIB treatment prior to LAGB (Weiner et al 1999).

Summary

Intragastric balloons ± continued conventional obesity treatment

A total of 39 studies reported on the safety outcomes of 4,718 patients undertaking BioEnterics intragastric balloon treatment.

Major complications reported were: death (3 patients, 0.06%), migration of the balloon and subsequent gastrointestinal obstruction (26 patients, 0.6%), gastric perforation (7 patients, 0.2%), oesophageal rupture (1 patient, 0.02%) and biliary pancreatitis (1 patient, 0.02%). Physical intolerance of the balloon requiring early balloon removal was reported in 85 patients (1.8%).

The most common minor complications reported were nausea and vomiting. Other minor complications recorded were: oesophageal and gastric erosion, gastric ulceration, gastro-oesophageal reflux, gastric stasis, chronic gastric dilatation, hypokalemia, dehydration and cutaneous allergic reaction.

Balloon deflation was reported in 121 patients (2.6%); rupture/bursting of the balloon in 11 patients (0.2%) and defective valve in 2 patients (0.04%).

Two studies reported on the safety outcomes within 42 patients receiving Heliosphere intragastric balloon treatment. Only minor complications (nausea and vomiting) and technical difficulties related to the placement/removal of the balloon were reported.

Intragastric balloons followed by surgery

Two studies reported on the safety outcomes of super-obese patients who underwent pre-surgical BioEnterics intragastric balloon treatment. This treatment was associated with improved safety during surgery, with no patient requiring conversion to open surgery or having intra-operative complications.

Is it clinically effective?

Studies were included in this assessment of the effectiveness of IGBs in the management of morbid obesity according to the inclusion criteria, defined a priori (Appendix G and Appendix H).

Thirty-three studies met the inclusion criteria. The results of these studies are presented in Appendix G and Appendix H). Data summarised in these tables describe the relevant clinical effectiveness outcomes. The studies have been listed in tables in a hierarchical manner according to each study's level of evidence, quality assessment, alphabetical order and recency of publication. A Cochrane review was identified, but could not be included as the majority of the included studies addressed other types of IGBs, many of which are no longer in use (Fernandes et al 2007).

Among the included 33 studies, only three randomised controlled trials (level II intervention evidence) were identified: two of good quality (Genco et al 2006; Mathus-Vliegen & Tytgat 2005) and one of fair quality (Martinez-Brocca et al 2007). All randomised controlled trials had small patient samples.

The majority of included studies (29) were case series (level IV intervention evidence) of good quality. Among them, one study also had a cohort study component on a smaller patient sample, which was of poor quality (Doldi et al 2004). One historically controlled study (level III-2 intervention evidence) of good quality was also included (Busetto et al 2004).

Only two studies used the Heliosphere IGB (Forestieri et al 2006; Mion et al 2007), with all the remaining studies using the BIB.

The study population for 13 studies consisted strictly of morbidly obese patients, with the rest including predominantly morbidly obese but also various proportions of obese and/or overweight patients.

Intragastric balloon ± continued conventional obesity treatment

Weight loss

All studies reported changes in body weight using one or more of the following measures: mean body weight, BMI, mean excess weight, mean waist circumference (before and after the balloon treatment), mean weight loss and mean excess weight loss (%EWL) (Appendix G and Appendix H).

A good quality randomised double-blind, crossover, sham-controlled trial (level II intervention evidence) investigated the effectiveness of the BIB (3 months of balloon treatment) (Genco et al 2006). Thirty-two patients were randomised as follows: one group with 3 months of balloon treatment followed by 3 months of sham treatment; and a second group receiving 3 months of sham treatment followed by 3 months of treatment with a BIB. All patients were also instructed to follow a 1,000 kcal/day diet. After 3 months the mean weight loss was 15 ± 6 kg in the BIB group compared with 3 ± 1 kg in the sham group ($p<0.001$). The mean BMI reduction was also significantly higher in the BIB group (5.8 ± 0.5 vs. 0.4 ± 0.2 kg/m^2; $p<0.001$). Mean EWL was significantly higher in the BIB group compared with the sham group (34.0 ± 4.8% vs. 2.1 ± 1%). At 3 months after the crossover, the mean weight loss was higher in the group receiving BIB treatment than in the group which had the BIBs removed

(13 ± 8 kg vs. 6 ± 3 kg $p<0.001$). Similarly, the BMI reduction was significantly higher in the BIB group (5.1 ± 0.5 vs. 1.1 ± 0.3 kg/m^2). Comparing the mean EWL during the sham period before and after the crossover, the study found it to be significantly higher in the group receiving the sham after the BIB treatment (4.6 ± 5.1% vs. 2.1 ± 1%; $p<0.05$). The study concluded that BIB is an effective adjuvant device, and that its effectiveness was not related to any placebo effect.

Another good quality randomised double-blind controlled trial conducted in the Netherlands (Mathus-Vliegen & Tytgat 2005) investigated the effectiveness at 3 months of IGB treatment compared with sham treatment, effectiveness of IGB treatment at 1 year, and weight maintenance at 1 year after IGB removal. The study included 43 patients who were randomised in two groups as follows: one group received sham balloon placement for the first 3 months followed by a BIB every 3 months for the remainder of the first year (3 balloons); and the second group were treated with BIB placement every 3 months for the first year (4 balloons). All patients were prescribed a restricted diet (1,000–1,500 kcal/day) and physical exercise. The patients in the BIB group were required to lose a minimum of 6.5 kg within the first 3 months, and 13 kg within 6 months, to continue the study. After 3 months of treatment, the mean weight loss in the BIB group was 12.9 kg (10.4% of initial body weight) while the sham group had a mean weight loss of 11.2 kg (9% of initial body weight). Mean weight loss difference between the BIB and the sham group at 3 months was 1.62 kg [95% CI –1.92, 5.16]. The study concluded that there was no independent benefit of the BIB beyond diet and physical exercise. Weight loss after 6, 9 and 12 months was similar for both groups. Patients who achieved a weight loss of 6.5 kg or greater at 3 months had greater weight loss at 6 and 12 months and were better able to maintain it after 2 years. In the second year of follow-up, patients gained weight but the weight remained 12.7 kg (9.9%) below the initial average body weight. A weight loss of 10 per cent or more was maintained by 47 per cent of patients.

A randomised controlled trial of fair quality enrolled 22 patients for 4 months BIB treatment compared with a sham procedure (Martinez-Brocca et al 2007). The mean weight loss in the BIB treated group was 12.7 ± 5.6 kg compared with 8.9 ± 9.2 kg in the sham group. No significant difference was found between weight loss in the BIB treatment group compared with the sham group.

Only one cohort study of poor quality compared BIB and diet treatment versus diet alone (Doldi et al 2004). The mean weight loss after 4 months of BIB plus diet was 15.5 kg in females and 21.0 kg in males; in the diet-only group it was 11.6 kg in females and 16.4 kg males. At 12 months of follow-up (ie at 9 months after balloon removal) the mean weight loss was 11.2 kg in females and 24.0 kg in males; in the diet-only group it was 15.1 kg in females and 18.7 kg in males.

The results of the two studies reporting outcomes of the effectiveness of the Heliosphere IGB are summarised in Table 29 (Appendix H).

The case series (level IV intervention evidence) meeting the inclusion criteria reported mean weight loss in the range 4–20 kg over a period of 6 months of BIB treatment. For the Heliosphere IGB, one study reported a mean weight loss of 17.5 kg (range 5–33 kg) at 6 months (Forestieri et al 2006) and another study a mean weight loss of 9.3 per cent (range 3–20%) at 4 months (Mion et al 2007).

A case series with a 1-year follow-up reported that most of the weight loss occurred in the first 2 months following placement of a BIB and diet treatment (Ganesh et al 2007). The majority of patients regained weight after BIB removal. Another case series reported that mean weight loss was 11.1 kg at 12 months after BIB removal (Herve et al 2005). For patients with baseline BMI > 40 kg/m^2, mean weight loss was 17.2 kg at BIB removal and 15.7 kg at 12 months after BIB removal. In a case series with a mean 18 months of follow-up after BIB removal, 71 per cent of patients had an EWL of 25 per cent or more at BIB removal; and at 6–30 months follow-up, 40 per cent of the patients maintained the same percentage of EWL (Melissas et al 2006).

Obesity related co-morbidities

Several studies have reported on the impact of BIB treatment on obesity-related co-morbidities (Appendix G).

A large good quality case series enrolled 2,515 patients, among whom 56.4 per cent had co-morbidities (eg hypertension, diabetes, respiratory disorders, osteo-arthropathy, dyslipidaemia) (Genco et al 2005). Following treatment consisting of BIB placement, diet and medical therapy, the co-morbidities were resolved in 44.3 per cent of the patients, improved in 44.8 per cent (requiring less pharmacological dosages or shift to other therapies) and unchanged in 10.9 per cent of patients.

One good quality case series (level IV intervention evidence) reported on the impact of BIB and diet treatment on a patient population with sleep apnoea (Busetto et al 2005). This study reported that weight loss was associated with clinically significant improvements in sleep-disordered breathing and the diurnal symptoms of the obstructive sleep apnoea syndrome.

Two other studies mentioned improvements in co-morbidities. The clinical trial conducted by Mathus-Vliegen and colleagues (Mathus-Vliegen & Tytgat 2005) reported a decrease in co-morbidities (hypertension, hyperlipidaemia) after 1 year of BIB treatment. Doldi and colleagues (2004) reported, in a case series, improvement in cardiovascular and respiratory function in all patients, and reduction of insulin dose and oral hypoglycaemic agents in diabetic patients after 4–6 months of BIB and diet treatment.

Quality of life and patient satisfaction

A case series reported that the scores of a specific quality of life questionnaire (IWQOL – Lite) improved significantly at 4 months of Heliosphere balloon treatment (Mion et al 2007).

A second study by Totte et al (2001) reported that, from 126 patients receiving 6 months of BIB and diet treatment, 15 per cent were very satisfied, 13 per cent satisfied, 22 per cent reasonably satisfied, 9 per cent poorly satisfied and 40 per cent totally unsatisfied with the achieved weight reduction. Another case series which evaluated 100 patients reported that 50 per cent of patients were satisfied with BIB treatment (Herve et al 2005). In another small study with 15 included patients, 10 were highly satisfied and 4 were satisfied with the BIB treatment (Mui et al 2006).

Intragastric balloon followed by surgery

From the 33 included studies, only four addressed the use of the BIB prior to surgical obesity treatment of morbidly obese patients. One study was a good quality historical

control (level III-2 intervention evidence), and there were three case series (level IV intervention evidence). The results are summarised in Appendix G.

The good quality historical control study compared a group of 43 patients undergoing BIB treatment followed by laparoscopic adjustable gastric banding (LAGB) with a group of sex-, age- and BMI-matched historical controls undergoing LAGB alone (Busetto et al 2004). The percentage of EWL at 6 months after banding was higher in the BIB followed by LAGB group compared with the control group. No significant difference was found between the groups at 1, 2 and 3 years after surgery.

Alfalah et al (2006), in a case series of 10 patients awaiting surgery, reported that patients achieved a 10 per cent EWL in the third month of the IGB treatment, after which it reached a plateau. There was an overall decrease of excess weight to 7 per cent in the sixth month of IGB treatment.

In one case series, which enrolled 196 patients undertaking LAGB, 15 received 4–7 months of BIB treatment prior to surgery (Weiner et al 1999). The mean weight loss was 18.1 kg (range 13–30 kg) at the time of balloon removal. There was no difference in the postoperative weight loss between patients with or without preoperative BIB treatment.

From a case series of 140 patients who initially refused bariatric surgery due to fear of complications and death, and who underwent IGB treatment instead, 32.1 per cent accepted surgical intervention during the follow-up period following IGB removal (Melissas et al 2006). Of these, 32.5 per cent were considered as failures at the time of IGB removal (ie they had lost between 0% and 22.7% of their excess weight), 63.6 per cent were considered successes (ie they had lost 25% or more of their excess weight) and 7.1 per cent were successes at the time of IGB removal but were unable to maintain satisfactory weight loss after the IGB removal.

Summary

Intragastric balloons ± continued conventional obesity treatment

From the 29 included studies, only three were randomised controlled trials (level II intervention evidence) and the remainder were case series (level IV intervention evidence).

The results from the randomised controlled trials are contradictory. One study found the BioEnterics intragastric balloon and diet treatment to be more effective on weight loss when compared with a sham and diet treatment, while two other studies found no significant difference.

Several studies have reported a decrease in co-morbidities in patients undertaking BioEnterics intragastric balloon and diet treatment for a period of 4–6 months.

Intragastric balloons followed by surgery

From the 33 included studies, only four addressed the use of BioEnterics intragastric balloons prior to bariatric surgical treatment. One study was a historical control (level III-2 intervention evidence) and three were pre-test/post-test case series (level IV intervention evidence).

The results were consistent in that the BioEnterics intragastric balloon pre-surgical treatment had no impact on long-term weight loss following bariatric surgery.

What are the economic considerations?

The evidence from the systematic review did not allow for any conclusions to be drawn regarding the safety and effectiveness of IGBs. Therefore, a cost-effectiveness analysis could not be performed. However, a financial analysis of the expenditures associated with insertion and removal of IGBs for the temporary management of morbid obesity has been conducted.

The financial evaluation proposed differs from the comparison used in the literature review, in which the service under evaluation is IGB *with or without* conventional obesity therapy. Rather, as IGBs are to be used as an addition to current practice, the financial evaluation compares the costs of IGBs plus conventional obesity therapy versus conventional obesity therapy alone.

Financial incidence analysis

In performing the financial incidence analysis, it has been assumed that patients receive only one IGB treatment. Costs associated with managing adverse events of IGBs were not included, as a consequence of the paucity of evidence.

Unit costs

The unit costs associated with IGBs for the treatment of morbid obesity are summarised in Table 12 and Table 13. It is assumed that the cost of implanting the IGB would be equivalent to the cost of removing a foreign body (MBS item 13506) plus half the cost of performing an endoscopy (MBS item 30473).

Based on this assumption, the unit cost for implanting the BioEnterics intragastric balloon (BIB) is estimated to be $2,498, and the unit cost for removing the BIB $1,329 (total = $3,827). The unit costs for implanting and removing the Heliosphere intragastric balloon are estimated to be $2,354 and $1,109 (total = $3,463). The costs relating to the BIB have been used for the subsequent analyses. The costs to the states and territories, and to patients or their health insurance companies, would be reduced if some patients received the Heliosphere rather than the BIB.

Table 12 Unit costs associated with insertion of an intragastric balloon in a private day hospital facility

Items	Cost estimate	Source of estimate
Devices		
BioEnterics® intragastric balloon	Balloon system $1,295 + GST = $1,424.50 Needle aspirator $195 + GST = $214.50	Allergan Australia Pty Ltd
Heliosphere® intragastric balloon	Balloon system $1,495.00 (introduction kit)	Morton Surgical Pty Ltd
Medical practitioner services		
Pre-operative assessment	MBS item 17610 = $38.80	
Initiation of anaesthesia	MBS item 20740 = $89.50	
Time units	MBS item 23022 or 23023 = $35.80	Expert opinion of Advisory Panel member indicates that the procedure takes 20–30 minutes
Placement of the balloon	MBS item 13506 plus 50% of MBS item 30473 $166.60 + 50% x $159.95 = $246.60	Allergan Australia Pty Ltd and expert opinion of an Advisory Panel member
Total	$410	
Accommodation fees		
Cost of day hospital facilities	Operating room, special procedure suites and hotel costs = $448.00	Total average charge per AR-DRG V5.0 Public Hospitals Data Bureau; G42B – other gastroscopy

MBS item 17610: ANAESTHETIST PRE- ANAESTHESIA CONSULTATION Fee: $38.80 Benefit: 75% = $29.10 85% = $33
MBS item 20740: INITIATION OF MANAGEMENT OF ANAESTHESIA for upper gastrointestinal endoscopic procedures (5 basic units) Fee: $89.50 Benefit: 75% = $67.15 85% = $76.10
MBS item 23022: 21 MINUTES TO 25 MINUTES (2 basic units) Fee: $35.80 Benefit: 75% = $26.85 85% = $30.45
MBS item 23023: 26 MINUTES TO 30 MINUTES (2 basic units) Fee: $35.80 Benefit: 75% = $26.85 85% = $30.45
MBS item 30473: OESOPHAGOSCOPY (not being a service to which item 41816 or 41822 applies), GASTROSCOPY, DUODENOSCOPY or PANENDOSCOPY (1 or more such procedures), with or without biopsy, not being a service associated with a service to which item 30476 or 30478 applies (Anaes.) Fee: $159.95 Benefit: 75% = $120.00; 85% = $136.00
MBS item 13506: GASTRO-OESOPHAGEAL balloon intubation, Minnesota, Sengstaken-Blakemore or similar, for control of bleeding from gastric oesophageal varices Fee: $163.00 Benefit: 75% = $122.25; 85% = $138.55

Table 13 Unit costs associated with removal of an intragastric balloon in a private day hospital facility

Items	Cost estimate	Source of estimate
Devices		
BioEnterics® intragastric balloon	Removal system: Grasper $255.00 + GST = $280.50 Needle aspirator $195.00 + GST = $214.50	Allergan Australia Pty Ltd
Heliosphere® intragastric balloon	Removal kit = $275.00	Morton Surgical Pty Ltd
Medical practitioner services		
Pre-operative assessment	MBS item 17610 = $38.80	
Initiation of anaesthesia	MBS item 20740 = $89.50	
Time units	MBS item 23022 or 23023 = $35.80	Expert opinion of Advisory Panel member indicates that the procedure takes 20–30 minutes
Removal of the balloon	MBS item 30478 = $221.75	Allergan Australia Pty Ltd and expert opinion of an Advisory Panel member
Total	$389	
Accommodation fees		
Cost of day hospital facilities	Operating room, special procedure suites and hotel costs = $448.00	Total average charge per AR-DRG V5.0 Public Hospitals Data Bureau; G42B – other gastroscopy

MBS item 17610: ANAESTHETIST PRE- ANAESTHESIA CONSULTATION Fee: $38.80 Benefit: 75% = $29.10 85% = $33

MBS item 20740: INITIATION OF MANAGEMENT OF ANAESTHESIA for upper gastrointestinal endoscopic procedures (5 basic units) Fee: $89.50 Benefit: 75% = $67.15 85% = $76.10
MBS item 23022: 21 MINUTES TO 25 MINUTES (2 basic units) Fee: $35.80 Benefit: 75% = $26.85 85% = $30.45
MBS item 23023: 26 MINUTES TO 30 MINUTES (2 basic units) Fee: $35.80 Benefit: 75% = $26.85 85% = $30.45
MBS item 30473: OESOPHAGOSCOPY (not being a service to which item 41816 or 41822 applies), GASTROSCOPY, DUODENOSCOPY or PANENDOSCOPY (1 or more such procedures), with or without biopsy, not being a service associated with a service to which item 30476 or 30478 applies. Fee: $156.50; Benefit: 75% = $117.40 85% = $133.05
MBS item 30478: OESOPHAGOSCOPY (not being a service to which item 41816, 41822 or 41825 applies), gastroscopy, duodenoscopy or panendoscopy (1 or more such procedures), with 1 or more of the following endoscopic procedures - polypectomy, removal of foreign body, diathermy, heater probe or laser coagulation, or sclerosing injection of bleeding upper gastrointestinal lesions, not being a service associated with a service to which item 30473 or 30476 applies (Anaes.) Fee: $221.75 Benefit: 75% = $166.35; 85% = $188.50

Clinical need

The intended use for intragastric balloons is in patients who are morbidly obese and have failed to lose weight following conventional obesity management. According to the 2004–05 Australian National Health Survey, 2.5 million Australian adults were estimated as obese (ABS 2006). No national data were available from this survey on the prevalence of *morbid* obesity in particular. Another survey found the prevalence of self-reported morbid obesity to be 3.6 per cent among adult South Australians (Department of Health 2003). The prevalence of morbid obesity would be a considerable overestimate of the clinical need for IGBs, as only those patients who have failed to lose weight following conventional obesity management are potential candidates for the procedure.

A better estimate of the number of patients who could potentially receive IGBs would be those who fail to lose weight following conventional treatments but who are unsuitable for surgical treatment. This estimate is based on the number of patients who undergo surgery for obesity and on an Australian study on the number of patients who are screened for surgery but are unsuitable for various reasons (see 'What is the clinical need / burden of disease?' section.

Based on this data, the potential use of IGBs is estimated to be 4,903 procedures per year (assuming no leakage). However, the rate of patients who initially refuse surgery may increase if IGBs become funded for this indication. An upper estimate of 8,000 IGB treatments per year is therefore used.

Cost to the Australian Government

The Australian Government is responsible for payment of the rebate on items from the Schedule of Medicare Benefits.

It is assumed that the uptake of IGBs would have a similar public/private patient split to the LAP-BAND®. Therefore, 96 per cent of IGB therapies would be eligible for MBS reimbursement, with the remaining 4 per cent falling under the Australian Healthcare Agreements between the states/territories and the Australian Government (LAP-BAND® data provided by the applicant). As it is estimated that there would be approximately 4,903 to 8,000 procedures performed annually, approximately 4,707 to 7,680 per year would be performed in the private sector and be eligible for MBS reimbursement. To calculate the financial implications to the Commonwealth of subsidising IGBs, the estimated cost per procedure is multiplied by the expected uptake of the procedure in private hospitals. Therefore, a total cost of $2,812,021 to $4,511,328 for IGB therapies per year would be incurred by the Commonwealth (Table 14).

Table 14 Expenditure borne by the Australian Government in one full year

Resource item	Cost estimate per patient	No of patients	Expenditure
Medical practitioner services	75% of $796.55	4,707–7,680	$2,812,021 – $4,511,328
		Total	$2,812,021 – $4,511,328

Cost to private health insurance or patient

Costs that would be incurred by private health insurance and/or the patient are that of the implantable device and the accommodation associated with the hospital stay in a private hospital, plus the co-payment for medical practitioner fees. Assuming 4,707 to 7,680 procedures are performed in private hospitals, the approximate cost to individual patients or health insurance companies for devices and accommodation would be $15,199,550 to $24,799,776 (Table 15).

Table 15 Expenditure borne by private health insurance or patients in one full year

Resource item	Cost estimate per patient	No of patients	Expenditure
Medical practitioner services	75% of $796.55	4,707–7,680	$937,340 – $1,529,376
Devices	$2,134	4,707–7,680	$10,044,738 – $16,389,120
Accommodation	$896	4,707–7,680	$4,217,472 – $6,881,280
		Total	$15,199,550 – $24,799,776

Total cost to the states and territories

Under the Australian Healthcare Agreements, the states and territories fund in-patient procedures on public patients in public hospitals, as well as public patients in an outpatient facility. By making two assumptions, that the unit costs of the procedure are the same for a public patient as they are for a private patient, and that 196 to 320 procedures will be performed annually, the total cost to the states and territories of providing IGB therapy is $750,004 to $1,224,496 (Table 16).

Table 16 Expenditure borne by the states and territories in one full year

Resource item	Cost estimate per patient	No of patients	Expenditure
Medical practitioner services	$796.55	196–320	$156,124 – $254,896
Devices	$2,134	196–320	$418,264 – $682,880
Accommodation	$896	196–320	$175,616 – $286,720
		Total	$750,004 – $1,224,496

Total cost to the Australian healthcare system overall

The total healthcare expenditure borne by society (including costs to the MBS, states and territories, patients, and private health insurance) of placing and removing 4,903 to 8,000 IGBs would be between $19,236,067 and $30,535,600 per year (Table 17).

Table 17 Expenditure borne by Australian healthcare system in one full year

Resource item	Cost estimate per patient	No of patients	Expenditure
Australian government			
Medical practitioner services	75% of $796.55	4,707–7,680	$2,812,021 – $4,511,328
States and territories			
Medical practitioner services	$796.55	196–320	$156,124 – $254,896
Devices	$2,134	196–320	$418,264 – $682,880
Accommodation	$896	196–320	$175,616 – $286,720
Private health insurance or patients			
Medical practitioner services	25% of $796.55	4,707–7,680	$937,340 – $1,529,376
Devices	$2,134	4,707–7,680	$10,044,738 – $16,389,120
Accommodation	$896	4,707–7,680	$4,217,472 – $6,881,280
		Total	$19,236,067 – $30,535,600

Discussion

Safety

Intragastric balloon ± continued conventional obesity treatment

The majority of the included studies reported on the safety of the BIB. Both major complications (including death) and minor complications were reported. Only two studies addressing the safety of the Heliosphere IGB were identified. They reported only minor adverse events and technical difficulties related to the placement/removal of the IGB.

Because IGBs are proposed for use in clinical practice *in addition* to conventional obesity management, they will carry additional risks. Inserting and removing the IGBs are invasive procedures with associated risks. Consideration needs to be given to the added health risks associated with IGB placement compared to any potential benefits the procedure may have on weight loss. An important aspect to be considered is the fact that the target population comprises patients with morbid and super-morbid obesity who have previously failed to lose weight based on conventional treatment alone, and that untreated obesity is associated with considerable associated health risks.

Complications relating to the placement of IGBs can either be associated with the endoscopic placement/removal of the balloon or can occur during the period of time the balloon is left in the stomach. The latter can be a consequence of prolonged contact with the mucous membrane (eg erosions, ulcerations, perforations), or migration of the balloon resulting in obstruction of the gastrointestinal tract at various levels (Fernandes et al 2007).

Not all studies have clearly distinguished between the symptoms occurring immediately after balloon placement and those occurring later during the treatment. The distinction is of importance, as it is generally accepted that, in the first days following balloon placement, minor gastrointestinal symptoms (eg nausea, vomiting, gastro-oesophageal reflux, epigastric discomfort) are expected but are usually controlled by medication. Symptomatic medication was administered to all patients in some studies and only when needed in others; and some studies have not provided clear information on this topic. It was therefore difficult to distinguish whether the reported adverse events occurred early or later in IGB treatment, and whether they occurred in the absence of symptomatic medication or if they persisted even after medication had been administered.

Intragastric balloon followed by surgery

In morbidly obese patients, and super-obese patients in particular, surgical treatment for obesity is recommended as it provides long-term weight loss. It is also recognised that surgical complications increase with higher BMI; therefore, in this group of patients weight loss prior to surgery is preferable in order to reduce the risks associated with the surgical procedures.

Weight loss is responsible for a reduction in risk of complications during bariatric surgery. The four studies included in the review reported increased safety (ie fewer conversions to open surgery and less intra-operative complications) in super-obese patients undergoing BIB treatment before laparoscopic surgery. This represents limited

evidence, suggesting reduced surgical risks in super-obese patients but no evidence for the overall morbidly obese patient population.

From the four studies reporting on BIB treatment before surgery, only one comparative study, with historical controls, mentioned that the pre-surgical patient management included diet in addition to BIB (Busetto et al 2004). In the remaining studies it is not clear whether patients were receiving any form of supervised obesity treatment during IGB placement. The data presented in these studies are insufficient to explain to what extent (ie the effectiveness, as detailed below) the IGBs are responsible for weight loss in this group of patients. Therefore, it is premature to draw conclusions about the impact of IGB treatment on the safety of subsequent laparoscopic obesity surgery.

If additional evidence becomes available in the future on the effectiveness of IGBs in weight loss, this may support their use as a means of ensuring increased safety in subsequent surgical procedures. Consideration will need to be given to the benefit to patient outcomes due to the pre-surgical use of IGBs versus the added risks to patient that are associated with the balloon treatment itself.

If future evidence demonstrates no added benefit from the IGB treatment compared with conventional obesity management, pre-surgical IGB treatment will merely add to the risks associated with surgery.

Effectiveness

Intragastric balloon ± continued conventional obesity treatment

The majority of studies meeting the inclusion criteria constitute a low level of intervention evidence (level IV). Only three of the included studies were of level II intervention evidence (ie randomised control trials). The majority of the studies referred to the BIB, with only a few reporting on the Heliosphere IGB.

Genco et al (2006), in a randomised controlled trial, reported a significant effect of BIB treatment on weight loss after 3 months compared with sham treatment. By contrast, two other trials found no independent benefit of the BIB treatment compared with sham treatment at 3 months and 4 months respectively (Mathus-Vliegen & Tytgat 2005; Martinez-Brocca et al 2007).

In all the above trials, patients with previously treatment-resistant obesity were enrolled, undertaking 3 months of IGB treatment supplemented by diet which resulted in weight loss. Mean weight loss reported in the IGB group was 15 ± 6 kg (Genco et al 2006) and 11.2 kg (Mathus-Vliegen & Tytgat 2005) after 3 months respectively, and 12.7 ± 5.6 kg after 4 months (Martinez-Brocca et al 2007). Although patients lost weight, only one study found a statistically significant difference between the IGB and sham groups, and concluded that weight loss could be attributed to BIB (Genco et al 2006). Further, the clinical significance of the results reported by these clinical trials is also difficult to interpret.

All included trials had small patient samples (n=32, 22 and 43); therefore, their results should be interpreted with caution. Often, the number of patients included in clinical trials is not adequate, as the required sample size may be difficult to achieve. As a result, the type II error is common in clinical research (Egger & Smith 1997). A type II error occurs when a trial shows no significant treatment effect when, in reality, such an effect

exists (Altman & Bland 1995). For example, the trial conducted in the Netherlands by Mathus-Vliegen and colleagues had been initially designed as a multicentre study involving 140 patients, but ended up as a single-centre study with only 43 patients. Based on the trial's results at 3 months, the sample size necessary to achieve 80 per cent power would have been 360 patients (Mathus-Vliegen & Tytgat 2005). A consequence of low statistical power is a wide confidence interval (Altman & Bland 1995). The above trial reported a mean weight loss difference at 3 months between the IGB and the sham group of 1.62 kg [95%CI: –1.92, 5.16].

Another aspect that needs consideration is the difference that might exist between a controlled trial environment and routine clinical practice. Being enrolled in a supervised program, with regular follow-up and assessment of dietary habits, might increase adherence to diet (Mathus-Vliegen & Tytgat 2005). Further, results that show no difference between balloon and sham groups may suggest that the effect of either treatment may be to promote increased adherence of enrolled patients to the recommended diet.

An attempt was made to summarise the data of the three trials by means of meta-analysis, but the heterogeneity between the studies was too large for a pooled analysis to be meaningful, even had the variance data been available for all three studies (one study provided only point estimates for mean weight loss in the IGB and sham groups, but no confidence intervals (Mathus-Vliegen & Tytgat 2005)).

Given the available evidence, it is uncertain, within IGB plus diet treatment, what role in the observed weight loss can be attributed to IGBs. In the identified evidence, only one poor quality comparative study reported on BIB plus diet treatment versus diet alone (Doldi et al 2004). Randomised clinical trials with adequate sample size that compare IGB plus diet treatment versus diet alone are required to elucidate this issue.

Another issue that requires consideration is the long-term impact on weight loss of IGB treatment after balloon removal. The randomised controlled trial by Genco and colleagues (2006) found that excess weight loss during the sham period was significantly higher in the group receiving the sham after the IGB treatment, which may suggest an effect of the IGB in maintaining weight loss after removal of the IGB. Another randomised controlled trial with a 1-year follow-up after IGB removal found that, although patients gained weight after removal of the IGB, a weight loss of 10 per cent or greater was maintained by 47 per cent of patients (intention-to-treat analysis) (Mathus-Vliegen & Tytgat 2005). In this study the patients were seen bi-weekly by a physician and dietician, and optionally by a behavioural therapist. A restricted diet (1,000–1,500 kcal) was recommended and self-help groups were organised for aerobic fitness and aqua jogging. Several uncontrolled studies have also reported maintained weight loss after IGB removal (Melissas et al 2006; Ganesh et al 2007; Herve et al 2005). Similarly to the short-term impact on weight loss, the role of IGBs in changing patient behaviour and adherence to a low calorie diet beyond removal of the IGB will require more controlled studies with adequate patient samples.

Several studies have reported a reduction in co-morbidities in patients undertaking IGB plus diet treatment. Weight loss has been associated with improvement in cardiovascular and respiratory function (Mathus-Vliegen & Tytgat 2005; Busetto et al 2005; Doldi et al 2004).

Intragastric balloon followed by surgery

A small number of studies (level III-2 and level IV intervention evidence) investigated the use of BIB prior to obesity surgery in morbidly obese patients. One study found that mean EWL was higher at 6 months after surgery in the group undertaking pre-surgical BIB treatment compared with patients undertaking surgery alone; nevertheless, no difference was observed in the long term at 1, 2 and 3 years follow-up (Busetto et al 2004). Based on the available evidence, the potential use of the BIB before obesity surgery may be justified — not by any added effectiveness, as no impact on overall long-term weight loss was demonstrated, but rather by increasing the safety of surgery in selected patients. This aspect is discussed in more detail in the safety section above.

It has also been proposed that BIB could be used as a means of testing adherence to restrictive procedures prior to preceding to surgical obesity intervention, but this role was not sufficiently covered in the available evidence (Weiner et al 1999; Galloro et al 1999).

One study reported that a considerable percentage of patients who had initially refused surgery accepted it after undergoing IGB treatment (Melissas et al 2006).

Another suggested the use of IGB treatment in patients awaiting surgery, eg in the case of long waiting lists for bariatric surgery (Weiner et al 1999).

An overall evaluation of the body of evidence for IGBs is presented in Table 18.

Table 18 Assessment of body of evidence

Component	A Excellent	B Good	C Satisfactory	D Poor
Evidence-base		Three level II studies with low risk of bias		
Consistency			Some inconsistency reflecting genuine uncertainty around clinical question	
Clinical impact			Moderate	
Generalisability		Population(s) studied in the body of evidence is/are similar to the target population		
Applicability		Applicable to Australian healthcare context with few caveats		

Economic considerations

The systematic review conducted found the evidence on the safety and clinical effectiveness of IGBs to be insufficient at the present time. Therefore, a cost-effectiveness analysis could not be performed. Only a financial analysis was undertaken of the expenditures associated with insertion and removal of IGBs.

While survey data shows that the prevalence of obesity among adult Australians has reached epidemic levels, insufficient data is currently available on the size of the morbidly obese subgroup. IGBs are intended for use in morbidly obese patients only after they have failed to lose weight by means of conventional obesity treatment. Based on available data, it is difficult to estimate the current number of patients who may be indicated for this intervention or future trends in this group. The financial incidence analysis performed has used an estimate of the number of patients who are evaluated for obesity surgery, but found unsuitable for surgical treatment, as the minimum expected number of patients likely to receive an IGB (n=4,903). There is potential for leakage if an increased number of patients initially refuse surgery in favour of first trying an IGB. An upper estimate of use is therefore 8,000 IGBs per year.

Per patient, the total cost of inserting and removing one IGB is estimated to be $3,827. The cost to the Australian government would be $597 per person. It is estimated that between 4,903 and 8,000 patients are likely to receive an IGB per year and that 4,707 to 7,680 patients would receive an IGB in the private health system. This would result in an expenditure increase between $2,812,021 and $4,511,328 to be borne by the Australian government.

IGBs are temporary devices which have to be removed after 6 months. If the weight loss is not satisfactory, additional IGB treatments may be recommended. The analysis assumed that only one IGB treatment would be used in each patient. If more than one treatment is needed per patient, this will increase the associated expenditures.

The insertion and removal of IGBs are invasive procedures with associated risks. The management of complications associated with the use of IGBs may increase expenditures associated with the procedure. Due to insufficient evidence, these costs were not included in the financial analysis.

Conclusions

Safety

IGBs are invasive procedures compared with conventional obesity therapies such as diet, exercise or behaviour modification, and therefore are associated with an increased risk of adverse events. Complications may occur either during the placement/removal of the IGB or during the IGB treatment. In evaluating the safety of the procedure, consideration has been given to the reduced safety associated with IGBs when compared with conventional obesity therapies, as well as any benefits of weight loss resulting from IGB treatment. Although rare, major complications (including death) associated with the procedure have been reported in the literature. Minor complications have also been associated with IGB treatment.

Effectiveness

IGBs in combination with conventional obesity therapies are effective in assisting weight loss in morbidly obese patients. However, it is unclear whether IGBs provide any additional benefit over conventional obesity therapies. Furthermore, there is little evidence regarding whether weight loss that could be attributed to IGBs is sustained in the long term. More evidence is needed to assess the impact of IGBs, in addition to diet, in both short- and long-term weight loss in morbidly obese patients.

The evidence available at present on the effectiveness of IGBs in the temporary treatment of morbid obesity is inconclusive.

Economic considerations

The available evidence on safety and effectiveness did not allow a formal economic analysis to be undertaken at this time. The financial evaluation undertaken was based on an assessment of expenditures associated with the placement/removal of IGBs and an estimate of the total cost to the Australian healthcare system. The overall financial impact of this procedure to the Australian health system is estimated to be between $19,236,067 and $30,535,600 per year, of which $2,812,021 to $4,511,328 would be borne by the Australian government.

Recommendations

The MSAC has considered the safety, and clinical effectiveness of intragastric balloons for the temporary management of morbid obesity in addition to conventional treatment such as diet, exercise and behaviour modification.

The MSAC finds that intragastric balloons used for the temporary management of morbid obesity pose additional risks to patients when compared to the standard treatment for morbid obesity and that they do not provide additional clinical benefits over standard treatment.

There may be a role for the temporary placement of intragastric balloons for the management of the super obese patient prior to bariatric surgery however, evidence to support this approach is limited.

The MSAC finds that the use of intragastric balloons for the temporary management of morbid obesity is less cost-effective than standard treatment for morbid obesity.

The MSAC recommends that public funding is not supported for this procedure.

The Minister for Health and Ageing endorsed this recommendation on the 20th May 2008.

Appendix A MSAC terms of reference and membership

MSAC's terms of reference are to:

- advise the Minister for Health and Ageing on the strength of evidence pertaining to new and emerging medical technologies and procedures in relation to their safety, effectiveness and cost-effectiveness and under what circumstances public funding should be supported;
- advise the Minister for Health and Ageing on which new medical technologies and procedures should be funded on an interim basis to allow data to be assembled to determine their safety, effectiveness and cost-effectiveness;
- advise the Minister for Health and Ageing on references related either to new and/or existing medical technologies and procedures; and
- undertake health technology assessment work referred by the Australian Health Ministers' Advisory Council (AHMAC) and report its findings to AHMAC.

The membership of MSAC comprises a mix of clinical expertise covering pathology, nuclear medicine, surgery, specialist medicine and general practice, plus clinical epidemiology and clinical trials, health economics, consumers, and health administration and planning:

Member	Expertise or affiliation
Dr Stephen Blamey (Chair)	general surgery
Associate Professor John Atherton	cardiology
Associate Professor Michael Cleary	emergency medicine
Associate Professor Paul Craft	clinical epidemiology and oncology
Professor Geoff Farrell	gastroenterology
Dr Kwun Fong	thoracic medicine
Professor Richard Fox	medical oncology
Dr Bill Glasson	ophthalmologist
Professor Jane Hall	health economics
Professor John Horvath	Chief Medical Officer, Department of Health and Ageing
Associate Professor Terri Jackson	health economics
Professor Brendon Kearney	health administration and planning
Associate Professor Frederick Khafagi	nuclear medicine
Dr Ray Kirk	health research
Dr Ewa Piejko	general practice
Dr Ian Prosser	haematology
Ms Sheila Rimmer	consumer health issues

Dr Judy Soper	radiology
Professor Ken Thomson	radiology
Dr Mary Turner	Australian Health Ministers' Advisory Council representative
Dr David Wood	orthopaedics
Mr Peter Woodley	Assistant Secretary, Medical Benefits Schedule (MBS) Policy Development Branch, Department of Health and Ageing

Appendix B Advisory panel and evaluators

Advisory panel for application 1112: Intragastric balloons for the temporary management of morbid obesity

A/Professor Michael Cleary (Chair) Emergency Medicine	Member of MSAC
Dr Blair Bowden Bariatric Surgery	Royal Australian College of Surgeons nominee
Dr Steven Kan General Practitioner	Royal Australian College of General Practitioners nominee
A/Professor Donald Perry-Keene Endocrinology	Former member of the MSAC
Professor Joe Proietto Endocrinology	Endocrine Society of Australia nominee
Mr Garett Smith General and Upper Gastrointestinal Surgery	Gastroenterological Society of Australia nominee
Ms Catherine M Thompson Registered Nurse	Consumers' Health Forum nominee

Evaluators

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Appendix C Search strategies

Bibliographic databases used to identify literature

Electronic database	Time period
Cochrane Library – including, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, the Cochrane Central Register of Controlled Trials (CENTRAL), the Health Technology Assessment Database, the NHS Economic Evaluation Database	1990 – 06/2007
Current Contents	1990 – 06/2007
Embase.com (including Embase and Medline)	1990 – 06/2007
Pre-Medline	1990 – 06/2007
ProceedingsFirst	1990 – 06/2007
Web of Science – Science Citation Index Expanded	1990 – 06/2007
EconLit	1990 – 06/2007

Additional sources of literature

Source	Location
Internet	
NHMRC- National Health and Medical Research Council (Medicare Australia)	http://www.health.gov.au/nhmrc/
US Department of Health and Human Services (reports and publications)	http://www.os.dhhs.gov/
New York Academy of Medicine Grey Literature Report	http://www.nyam.org/library/greylit/index.shtml
Trip database	http://www.tripdatabase.com
Current Controlled Trials metaRegister	http://controlled-trials.com/
National Library of Medicine Health Services/Technology Assessment Text	http://text.nlm.nih.gov/
U.K. National Research Register	http://www.update-software.com/National/
Google Scholar	http://scholar.google.com/
Hand Searching (Journals from 2006-2007)	
Diabetes, obesity & metabolism	Library or electronic access
International journal of obesity	Library or electronic access
International journal of obesity and related metabolic disorders: journal of the International Association for the Study of Obesity	Library or electronic access
Obesity	Library or electronic access
Obesity research	Library or electronic access
Study of obesity	Library or electronic access
Obesity surgery: the official journal of the American Society for Bariatric Surgery and of the Obesity Surgery Society of Australia and New Zealand	Library or electronic access
Surgery for obesity and related diseases: official journal of the American Society for Bariatric Surgery	Library or electronic access
Expert Clinicians	Library or electronic access
Studies other than those found in regular searches	MSAC Advisory Panel
Pearling	
All included articles will have their reference lists searched for additional relevant source material	

Search terms utilised

Element of clinical question	Suggested search terms
Population	**MeSH:** obesity OR obesity, morbid OR body mass index OR body weight changes **Text words:** obes* OR (morbid* AND obes*) OR ((BMI OR body mass index) AND (35 or 40))
Intervention/test	**MeSH:** gastric balloon **Text words:** (gastric OR intragastric) AND (balloon* OR bubble*) OR BioEnterics intragastric balloon OR BIB OR Heliosphere
Comparator (if applicable)	n/a
Outcomes (if applicable)	n/a

Appendix D Internet sites searched

Websites of health technology assessment groups

AUSTRALIA	
Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S)	http://www.surgeons.org/open/asernip-s.htm
Centre for Clinical Effectiveness, Monash University	http://www.med.monash.edu.au/healthservices/cce/evidence/
Centre for Health Economics, Monash University	http://chpe.buseco.monash.edu.au
AUSTRIA	
Institute of Technology Assessment / HTA unit	http://www.oeaw.ac.at/ita/e1-3.htm
CANADA	
Agence d'Evaluation des Technologies et des Modes d'Intervention en Santé (AETMIS)	http://www.aetmis.gouv.qc.ca/en/
Alberta Heritage Foundation for Medical Research (AHFMR)	http://www.ahfmr.ab.ca/publications.html
The Canadian Agency for Drugs And Technologies in Health (CADTH)	http://www.cadth.ca/index.php/en/
Canadian Health Economics Research Association (CHERA/ACRES) – Cabot database	http://www.mycabot.ca
Centre for Health Economics and Policy Analysis (CHEPA), McMaster University	http://www.chepa.org
Centre for Health Services and Policy Research (CHSPR), University of British Columbia	http://www.chspr.ubc.ca
Health Utilities Index (HUI)	http://www.fhs.mcmaster.ca/hug/index.htm
Institute for Clinical and Evaluative Studies (ICES)	http://www.ices.on.ca
Saskatchewan Health Quality Council (Canada)	http://www.hqc.sk.ca
DENMARK	
Danish Centre for Evaluation and Health Technology Assessment (DACEHTA)	www.sst.dk/Planlaegning_og_behandling/Medicinsk_teknologivurdering.aspx?lang=en
Danish Institute for Health Technology Assessment (DIHTA)	http://www.dihta.dk/publikationer/index_uk.asp
Danish Institute for Health Services Research (DSI)	http://www.dsi.dk/engelsk.html
FINLAND	
Finnish Office for Health Technology Assessment (FINOHTA)	http://www.stakes.fi/finohta/e/
FRANCE	
L'Agence Nationale d'Accréditation et d'Evaluation en Santé (ANAES)	http://www.anaes.fr/
GERMANY	
German Institute for Medical Documentation and Information (DIMDI) / HTA	http://www.dimdi.de/en/hta/index.html
THE NETHERLANDS	
Health Council of the Netherlands Gezondheidsraad	http://www.gr.nl/adviezen.php
Institute for Medical Technology Assessment (Netherlands)	http://www.imta.nl/
NEW ZEALAND	
New Zealand Health Technology Assessment (NZHTA)	http://nzhta.chmeds.ac.nz/
NORWAY	
Norwegian Centre for Health Technology Assessment (SMM)	http://www.oslo.sintef.no/smm/Publications/Engsmdrag/FramesetPublications.htm
SPAIN	
Agencia de Evaluación de Tecnologias Sanitarias, Instituto de Salud "Carlos III"I/Health Technology Assessment Agency (AETS)	http://www.isciii.es/aets/

Andalusian Agency for Health Technology Assessment (Spain)	http://www.juntadeandalucia.es/salud/orgdep/AETSA/default.asp?V=EN
Catalan Agency for Health Technology Assessment (CAHTA)	http://www.aatm.es/cgi-bin/frame.pl/ang/pu.html
SWEDEN	
Center for Medical Health Technology Assessment	http://www.cmt.liu.se/English/Engstartsida.html
Swedish Council on Technology Assessment in Health Care (SBU)	http://www.sbu.se/admin/index.asp
SWITZERLAND	
Swiss Network on Health Technology Assessment (SNHTA)	http://www.snhta.ch/
UNITED KINGDOM	
Health Technology Board for Scotland	http://www.htbs.org.uk/
National Health Service Health Technology Assessment (Vandenberghe et al) / National Coordinating Centre for Health Technology Assessment (NCCHTA)	http://www.hta.nhsweb.nhs.uk/
NHS Quality Improvement Scotland	http://www.nhshealthquality.org/
National Institute for Clinical Excellence (NICE)	http://www.nice.org.uk/index.htm
The European Information Network on New and Changing Health Technologies	http://www.euroscan.bham.ac.uk/
University of York NHS Centre for Reviews and Dissemination (NHS CRD)	http://www.york.ac.uk/inst/crd/
UNITED STATES	
Agency for Healthcare Research and Quality (AHRQ)	http://www.ahrq.gov/clinic/techix.htm
Harvard School of Public Health – Cost-Utility Analysis Registry	http://www.tufts-nemc.org/cearegistry/index.html
Institute for Clinical Systems Improvement (ICSI)	http://www.icsi.org
Minnesota Department of Health (US)	http://www.health.state.mn.us/htac/index.htm
National Information Centre of Health Services Research and Health Care Technology (US)	http://www.nlm.nih.gov/hsrph.html
Oregon Health Resources Commission (US)	http://egov.oregon.gov/DAS/OHPPR/HRC/about_us.shtml
Office of Health Technology Assessment Archive (US)	http://www.wws.princeton.edu/~ota
U.S. Blue Cross/ Blue Shield Association Technology Evaluation Center (Department of Science and Technology - Brazilian Health Technology Assessment General)	http://www.bcbs.com/consumertec/index.html
Veteran's Affairs Research and Development Technology Assessment Program (US)	http://www.va.gov/resdev

Specialty websites

Australasian Society for the Study of Obesity	http://www.asso.org.au/home
Association for Study of Obesity	http://www.aso.org.uk/portal.aspx?mlmenuid=1976&TargetPortal=35&ApplicationID=33
BioEnterics Corporation / Inamed Development Company (USA)	http://www.inamed.com
Dieticians Association of Australia	http://www.daa.asn.au/
European Association for the Study of Obesity	http://www.easoobesity.org/
European Federation of Endocrine Societies (EFES)	http://www.euro-endo.org/default.htm
The Endocrine Society of Australia	http://www.endocrinesociety.org.au/
Gastroenterological Society of Australia	http://www.gesa.org.au/
Helioscopie – France	http://www.helioscopie.fr
International Federation for the Surgery of Obesity (IFSO)	http://www.obesity-online.com/ifso/
International Society for the Study of Obesity	http://www.iaso.org/
North American Association for the Study of Obesity	http://www.naaso.org/

Appendix E Safety outcomes of the BioEnterics intragastric balloon

Table 19 Inclusion criteria for identification of studies relevant to an assessment of the safety of placement of intragastric balloons for the temporary management of morbid obesity

Characteristic	Criteria
Publication type	Randomised or non-randomised controlled trials, cohort studies, registers, case series, case reports or systematic reviews of these study designs. Non-systematic reviews, letters, editorials, animal, in vitro and laboratory studies were excluded
Patient	1. Morbidly obese patients who have received previous ineffective non-surgical obesity therapy and who are at increased surgical risk (and therefore need to lose weight before surgical treatment for obesity) or have refused surgical treatment
	2. Morbidly obese patients (BMI > 40 kg/m^2 or BMI > 35 kg/m^2 with co-morbidities) with previous ineffective non-surgical obesity therapy who are at increased surgical risk (and therefore should lose weight before surgical treatment for obesity)
Intervention/test	1. Placement of the intragastric balloon ± continued conventional obesity treatment
	2. Placement of the intragastric balloon followed by surgical obesity treatment
Comparator	1. Continued conventional obesity treatment (diet ± physical activity ± behavioural therapy ± drug therapy)
	2. Surgical obesity treatment
Outcome	Primary: major complications (migration, oesophageal/gastrointestinal obstruction or perforation); minor complications (gastric erosion, ulceration, nausea, electrolytic abnormalities) Secondary: technical failure, bursting of the balloon
Language	Non-English language articles were excluded unless they appeared to provide a higher level of evidence than the English language articles identified

IGB = intragastric balloon

Table 20 Comparative studies reporting safety outcomes associated with the BioEnterics intragastric balloon

Study	Study design and quality appraisal	Population	Intervention	Safety outcomes		
				Primary		Secondary
(Genco et al 2006)	Randomised controlled trial (crossover) Level II intervention evidence Quality: good	N = 32 (24 female, 8 male) Mean BMI = 43.7 kg/m^2 (range 40–45) Mean age = 36.2 years (range 25–50) Co-morbidities Not stated	Group A (N=16) BIB followed by sham procedure after 3 months (+1,000 kcal diet) Group B (N=16) Sham procedure followed by BIB after 3 months (+1,000 kcal diet)	Epigastric pain following BIB placement in 27 patients (84%) Nausea following BIB placement in 26 patients (81%) Vomiting following BIB placement in 27 patients (84%)	Epigastric pain following sham procedure in 3 patients (9%) Nausea following sham procedure in 8 patients (25%)	
				Balloon vs sham relative risk : Epigastric pain: 9.3 Nausea: 3.2 Overall: Gastro-oesophageal reflux (53.12%) All the above symptoms were well controlled by medication		
(Mathus-Vliegen & Tytgat 2005)	Randomised controlled trial Level II intervention evidence Quality: good	N = 43 (36 female, 7 male) Mean BMI = 43.3 kg/m^2 (range 33.9–61.3) Mean age = 41.4 years Co-morbidities n/a	BIB + 1,000–1,500 kcal diet + exercise Group 1 (N=23) sham balloon placement for the first 3 months; followed by a balloon every 3 months for the remainder of the first year (3 balloons) Group 2 (N=20) Balloon placement every 3 months for one year (4 balloons)	Overall: Severe nausea, vomiting and abdominal cramps in 3 patients requiring balloon removal (6.9%) Severe oesophagitis due to the prohibited use of NSAIDs in 2 patients (4.7%) Severe oesophagitis in 1 patient with a hiatal hernia after a substantial weight loss of 32.6 kg (2.3%) Oesophageal erosions in 10 patients (23.3%) Gastric erosions in 4 patients (9.3%) Mallory-Weiss laceration and minor gastric bleeding in 1 patient at balloon removal (2.3%)		3 balloon deflations
(Busetto et al 2004)	Historical control Level III-3 intervention evidence	N = 86 Case group (BIB pre-surgical) N = 43 Mean age = 43.3 years	BIB before undergoing LAGB Comparator LAGB without pre-operative treatment	Overall: Complication rate (7%) Elimination of the balloon by stool in 1 patient (1.2%) Severe vomiting with mild dehydration in 1 patient (1.2%)		

Study	Study design and quality appraisal	Population	Intervention	Safety outcomes	
				Primary	Secondary
	Quality: good	Mean BMI = 58.4 kg/m^2 (range 47.9–74.4) Control group (only LAGB) N = 43 Mean age = 42.8 years Mean BMI = 56.9 kg/m^2 (range 46.7–70.2) Co-morbidities case group (control group) (%) Type 2 diabetes 44.2 (18.6), hypertension 69.8 (53.5), dyslipidaemia 27.9 (27.9), hyperuricemia and/or gout 16.3 (25.6), obstructive sleep apnoea syndrome 67.4 (62.8), Osteoarthritis 69.8 (74.4), depression 14.0 (14.0), binge eating disorder 16.3 (18.6)		Cutaneous allergic reaction in 1 patient (1.2%)	

BIB = BioEnterics intragastric balloon; BMI = body mass index; LAGB = laparoscopic gastric banding; NSAIDs = non-steroidal anti-inflammatory drugs

Table 21 Case series reporting safety outcomes associated with the BioEnterics intragastric balloon

Study	Study design and quality appraisal	Population	Intervention	Safety outcomes	
				Primary	Secondary
(Alfalah et al 2006)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 10 (10 female) Mean BMI = 64 kg/m^2 (range 59–78) Mean age = 33 years (range 17–51) Co-morbidities Not stated	BIB	Gastric intolerance requiring removal of balloon in 1 patient (10%)	
(Al-Momen & El-Mogy	Case series	N = 44 patients	BIB + diet	Balloon intolerance requiring removal of balloon in 6	

Study	Study design and quality appraisal	Population	Intervention	Safety outcomes	
				Primary	Secondary
2005)	pre-test/post-test Level IV intervention evidence Quality: good	Mean BMI = 45 kg/m^2 (range 27–67) Mean age = 31 years Co-morbidities Diabetes (11.4%), arterial hypertension (2.3%), myocardial valve disease (4.5%), pacemaker (2.3%), depression (27.3%), hypothyroidism (2.3%), locomotor system diseases (34.1%)		patients (13.6%) Pulmonary insufficiency in 3 patients (6.8%) Vomiting in 34 patients (77.2%) Clinical dehydration in 2 patients (4.5%) *Adverse events during the first week:* Occasional vomiting in 5 patients (11.3%) leading to asymptomatic hypokalemia in 3 patients (6.8%) and functional renal insufficiency in 2 patients (4.5%) Gastro-oesophageal reflux in 3 patients (6.8%) Abdominal pain with or without diarrhoea in 7 patients (15.9%) Gastric perforation in 1 patient (2.2%) Gastritis in 1 patient (2.2%) Abdominal pain after 2 month from mechanical ulceration of the antrum in 1 patient	
(Angrisani et al 2006)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 175 (104 females, 71 males) Mean BMI = 54.4 kg/m^2 (range 39.5–79.5) Mean age = 37.1 years (range 16–67) Co-morbidities Not stated	BIB	Psychological intolerance requiring balloon removal in 7 (4.0%) patients	Balloon rupture requiring emergency balloon removal in 2 (1.1%) patients
(Bonazzi et al 2005)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 12 (8 female, 4 male) Mean BMI = 38.5 kg/m^2 (range 32–43) Mean age = 39 years (range 26–54) Co-morbidities Not stated	BIB	Nausea in the first days following balloon placement in 12 patients (100%)	
(Busetto et al 2005)	Case series pre-test/post-test Level IV intervention	N = 18 (18 male) Mean BMI = 55.8 kg/m^2 Age range 26–62 years Co-morbidities All patients had documented	BIB	Gastric intolerance requiring removal of balloon in 1 patient (6%)	

Study	Study design and quality appraisal	Population	Intervention	Safety outcomes	
				Primary	Secondary
	evidence	obstructive sleep apnoea syndrome			
(Carbonelli et al 2003)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 20 (12 female, 8 male) BMI range 26–62 kg/m^2 Age range 17–57 years Co-morbidities Not stated	BIB	Nausea and vomiting in first week following IGB implantation (number of patients not stated)	
(de Goederen-van der Meij et al 2007)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 40 (32 female, 8 male) Mean BMI = 46.5 kg/m^2 (range 39–62) Mean age = 36.6 years (range 26–54) Co-morbidities Cardiovascular problems (3 patients), pulmonary problems (12 patients), diabetes mellitus (4 patients), hypertension (11 patients), osteoarthritis (28 patients)	BIB + later laparoscopic adjustable gastric banding		Balloon not found in stomach at the time of removal in 4 patients (10%) Suspected leakage and passage into the small intestine in 1 patient (2%)
(Doldi et al 2004)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 303 (208 female, 95 male; 349 BIB placements) Mean BMI = 42 kg/m^2 Mean age = 41.5 years Co-morbidities Hypertension (18.6%), type 2 diabetes (7.4 %), sleep apnoea (6.8%), coronary heart disease (4.8%), severe osteoarthropathy (4.2%)	BIB + 1,000 kcal diet	Balloon intolerance with removal before the due date for persistent epigastric cramp-like pain and continuing vomiting, despite appropriate treatment; the balloon was in the gastric antrum with sometimes enormous gastric stasis and dilation (7.44%) Gastric ulcers in 2 patients (0.7%) Gastric erosions in 3 patients (1.0%) 1st and 2nd degree oesophagitis (4.8%)	Deflated and passed balloons in 4 patients (1.3%) Deflated balloons in the stomach in 9 patients (3.0%)
(Evans & Scott 2001)	Case series pre-test/post-test Level IV	N = 63 (59 female, 4 male) Mean BMI = 46.3 kg/m^2 (range 36–72) Median age = 41 years (range	BIB	Nausea and/or vomiting in 31 patients (49%) Intractable vomiting requiring early balloon removal in 4 cases (6%) Abdominal pain in 10 patients (16%)	Deflation and/or displacement of balloon in 18/56 patients with follow-up data (32%), 3 requiring laparotomy (5%)

Study	Study design and quality appraisal	Population	Intervention	Safety outcomes	
				Primary	Secondary
	intervention evidence Quality: good	24–67) Co-morbidities Hypertensive (20.6%), angina (6.3%), asthma or chronic obstructive airway disease (20.6%), non-insulin dependent diabetes (6.3%), hyper-cholesterolaemia (3.2%), myocardial infection (3.2%)		Diarrhoea in 2 patients (3%) Stroke in 1 patient (1.6%)	
(Francica et al 2004)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 131 (85 females, 46 male; 151 balloon placements) Mean BMI = 43.8 kg/m^2 Mean age = 38.4 years Co-morbidities n/a	BIB	Gastric perforation in 1 patient (0.8%)	Partial or total deflation of the balloon in 18 patients (13.7%)
(Frutos et al 2007)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 31 (21 female, 10 male) Mean BMI = 55.20 kg/m^2 (range 50–78) Mean age = 40.08 years (range 18–60) Co-morbidities Hypertensive (37%), diabetic (20%), obstructive sleep apnoea syndrome (20%)	BIB	Nausea in 27 patients (87.1%) Vomiting in 25 patients (80.6%) Removal of balloon due to nausea and vomiting in 2 patients (6.5%) Epigastralgia in 3 patients (9.7%)	Bursting of the balloon in 1 patient (3.2%)
(Galloro et al 2007)	3 case series Level IV intervention evidence Quality: good [a]	N = 87 Co-morbidities n/a Group A N = 29 (19 female, 10 male) Mean BMI = 43.1 kg/m^2 (range 39.5–51.7) Mean age = 38 years	3 removal techniques BIB Group A Standard gastroscope and rat-toothed forcep		Group A 2 lost balloons during removal of the BIB

Study	Study design and quality appraisal	Population	Intervention	Safety outcomes	
				Primary	Secondary
		Group B N = 27 (19 female, 8 male) Mean BMI = 43.0 kg/m^2 (range 37.2–49.0) Mean age = 39 years Group C N = 31 (21 female, 10 male) Mean BMI = 43.6 kg/m^2 (range 39–47.3) Mean age = 39 years	Group B Standard gastroscope and retrieval snare Group C Double-channel gastroscope and rat-toothed forcep plus symmetrical 'shark model' polypectomy snare		Group B 2 lost balloons during removal of the BIB Group C No lost balloons during removal of the BIB
(Galloro et al 1999)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 10 (5 female, 5 male; 13 balloon placements) Mean BMI = 47.6 kg/m^2 (range 32.1–66.1) Mean age = 43 years	BIB	Peptic ulcer in 1 patient (10%) Foreign body sensation in 4 patients (30.8%)	
(Ganesh et al 2007)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 20 (17 female, 3 male) Mean BMI = 31.5 kg/m^2 (range 28–39) Mean age = 40 years (range 28–52) Co-morbidities Orthopaedic (65%), diabetes mellitus (5%), hypertensive (10%), hyperlipidaemia (15%), respiratory problems (20%)	BIB + 1,000 kcal diet	Nausea/vomiting in 8 patients (40%) Gastric intolerance requiring removal of the balloon in 4 patients (20%) and recurrent gastric intolerance in 12 of the 16 remaining patients (75%) Small benign gastric ulcer in 1 patient (5%)	
(Genco et al 2005)	Case series pre-test/post-test	N = 2,515 (1,793 female, 722 male) Mean BMI = 44.4 kg/m^2	BIB + 1,000 kcal diet + medical	Overall complication rate 2.8% (70 / 2,515 patients) Postoperative mortality rate 0.1% (2 / 2,515 patients) Complication during BIB positioning in 2 patients (0.1%)	Balloon rupture in 9 patients (0.4%)

Study	Study design and quality appraisal	Population	Intervention	Safety outcomes	
				Primary	**Secondary**
	Level IV intervention evidence Quality: good	(range 28–79.1) Mean age = 38.9 years Co-morbidities (n=1,394) Hypertension (509 patients, 36.5%), diabetes (488 patients, 35%), respiratory disorders (247 patients, 17.7%), osteo-arthropathy (271 patients, 19.4%), dyslipidaemia (318 patients, 22.8%), others (176 patients, 12.6%)	therapy	with acute gastric dilatation Psychological intolerance in 11 patients (0.4%) Gastric perforation in 5 patients (0.2%) Gastric obstructions during the first week after positioning in 19 patients (0.8%) Oesophagitis in 32 patients (1.3%) Gastric ulcer in 5 patients (0.2%)	
(Herve et al 2005)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 100 (77 female, 23 male) Mean BMI = 34.03 kg/m^2 (range 25.3–60.2) Mean age = 34.8 years Co-morbidities Arterial hypertension (25%), locomotion disorders (28%), lipid disorders (25%), dyspnoea (28%), sleep apnoea (10%), chronic obstructive pulmonary disease (4%), asthma (9%), gastro-oesophageal reflux (12%), oesophagitis (9%), peptic ulcer (5%), diabetes type 1 (3%), diabetes type 2 (24%), depression (14%)	BIB	*Adverse events during hospitalisation:* Nausea (78%), vomiting (66%), dehydration (5%), heartburn (27%), epigastric discomfort (46%), diarrhoea (2%), constipation (6%) Adverse events during time BIB was in place: nausea (32%), vomiting (32%), heartburn (22%), epigastric discomfort (13%), diarrhoea (13%), constipation (8%) Peptic ulcer in 2 patients (2%) Oesophagitis in 5 patients (5%) Upgrading of a pre-existing case of oesohagitis in 1 patient (1%) Psychological intolerance of the BIB in 3 patients (3%) Physical intolerance of the BIB in 12 patients (12%)	Immediate deflation of the BIB during the implantation in 1 patient (1%) Defective valve in 2 cases (2%) Spontaneous deflation and intestinal excretion in 17 patients (17%) Spontaneous deflation and vomiting in 2 patients (2%)
(Hodson et al 2001)	Case series pre-test/post-test Level IV intervention evidence	N = 10 (9 female, 1 male; 15 balloon placements) Mean BMI = 39 kg/m^2 (range 32–53) Mean age = 33 years	BIB + 800 kcal diet	Hyperemesis in 1 patient (10%) Symptoms of mild dehydration and constipation (frequently)	Balloon rupture in 1 patient (10%)
(Iordache 2005)	Case series	N = 54 (45 female, 9 male)	BIB	Vomiting in 38 patients (70.3%)	Spontaneous deinsertion of the filling tube at the

Study	Study design and quality appraisal	Population	Intervention	Safety outcomes	
				Primary	Secondary
	pre-test/post-test Level IV intervention evidence Quality: good	Mean BMI = 32 kg/m^2 (range 24–42) Mean age = 33.1 years Co-morbidities Arterial hypertension and diabetes (18.5%)		Clinical dehydration in 2 patients (3.7%) Abdominal pain in 14 patients (25.9%)	valve in 2 patients (3.7%)
(Iordache 2005)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 40 (32 females, 8 males) Mean BMI = 33 kg/m^2 (range 30–43) Mean age = 35.5 years Co-morbidities n/a	BIB	Nausea and vomiting in 24 patients (60%) Epigastric pain in 18 patients (45%)	
(Loffredo et al 2001)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 77 (54 female, 23 male; 87 balloons) Mean BMI = 46.6 kg/m^2 (range 32.1–73.8) Mean age = 38.2 years Co-morbidities n/a	BIB + diet	Gastric ulcer in 2 patients (2.6%) Transient hypokalemia due to persistent vomiting in the first days after insertion in 1 patient (1.3%) Self-induced vomiting to enable increased food intake in 1 patient (1.3%) Meteorism (ie distention of the abdomen caused by the presence of gas) in 4 patients (6.3%) Vomiting > 2 weeks and therefore BIB removal in 4 patients (6.3%)	Spontaneous balloon deflation in 15 patients (19.5%)
(Mion et al 2005)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 17 (14 female, 3 male) Mean BMI = 34.4 kg/m^2 (range 30.1–40.0) Mean age = 34.9 years Co-morbidities Gastric ulcers related to *Helicobacter pylori* gastritis in 1 patient (therefore excluded)	BIB + 1,300 kcal diet	Early removal of the balloon because of severe gastrointestinal bleeding and anaemia due to gastric ulcer in 1 patient (5.9%) Food intolerance, vomiting, dehydration in 2 patients (11.8%) Nausea and vomiting for 2 to 14 days after balloon insertion in all patients	
(Mui et al 2006)	Case series pre-test/post-test Level IV intervention	N = 15 (10 female, 5 male) Mean BMI = 40.5 kg/m^2 (range 29.6–56.9) Median age = 40 years Co-morbidities	BIB + 1,200 kcal diet +150 minutes/week moderately intense	Nausea, vomiting (60%) Biliary pancreatitis requiring early removal of the BIB in 1 patient (6.7%) Severe vomiting and dehydration in 1 patient (6.7%)	

Study	Study design and quality appraisal	Population	Intervention	Safety outcomes	
				Primary	Secondary
	evidence Quality: good	obstructive sleep apnoea syndrome (40%), diabetes mellitus (20%), hypertension (40%), degenerative joint problems with knee pain (46.7%)	exercise		
(Puglisi et al 2007)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 75 (63 female, 12 male) BMI range = 39–55 kg/m^2 Mean age = 39.5 years <u>BE group</u> N = 27 (24 female, 3 male) Mean BMI = 44.7 kg/m^2 Mean age = 38 years <u>NBE group</u> N = 48 (39 female, 9 male) Mean BMI = 47.6 kg/m^2 Mean age = 39 years <u>Co-morbidities</u> n/a	BIB + 1,000 kcal diet	<u>BE group</u> Complication rate (20.7%) BIB intolerance due to persistent vomiting and abdominal pain in 2 patients (2.7%) <u>NBE group</u> Complication rate (10.4%) BIB intolerance due to persistent vomiting and abdominal pain in 1 patient (1.3%)	
(Roman et al 2004)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 176 (161 female, 15 male) Mean BMI = 31 kg/m^2 (range 27–40) Mean age = 37.4 years <u>Co-morbidities</u> Diabetes mellitus (2.8%), arterial hypertension (6.8%), hypothyroidism (4.5%), depression (2.3%), grade I oesophagitis and/or small hiatal hernia (14.2%), gastritis or duodenitis (5.1%), mycotic oesophagitis (0.6%), oesophageal papilloma (0.6%)	BIB	Early balloon removal due to intolerance in 15 patients (8.5%) Sub-occlusion in 1 patient due to a partially deflated balloon (0.6%) Small bowel obstruction by migration of a particularly deflated balloon 14 months after BIB insertion in 1 patient (0.6%) Vomiting during the 1st week after insertion (90%) Clinical dehydration in 9 patients (5.1%) Occasional vomiting in 32 patients (18.2%) leading to asymptomatic hypokalemia in 15 patients and functional renal insufficiency in 2 patients Gastro-oesophageal reflux in 20 patients (11.8%) Abdominal pain with or without diarrhoea in 22 patients (12.5%) *Complications noted after the theoretical date of removal:*	Balloon dysfunction in 1 patient (0.6%) Partially deflated balloons in 2 patients Spontaneously deflated balloon in 49 patients (27.8%) *Complications noted after the theoretical date of removal:* Deflated BIB in 1 patient. Partially deflated BIB in 1 patient (0.6%)

Study	Study design and quality appraisal	Population	Intervention	Safety outcomes	
				Primary	**Secondary**
				Abdominal pain from mechanical ulceration of the antrum by the balloon in 2 patients (1.1%) Partial bowel obstruction secondary to deflated BIB migration in 1 patient (0.6%) Small bowel obstruction by migration of a partially deflated BIB in 1 patient (14 months after placement) (0.6%)	
(Sallet et al 2004)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 323 (196 female, 127 male) Mean BMI = 38.2 kg/m^2 Mean age = 37.5 years Co-morbidities Hypertension (31.6%), arthropathies (21.9%), hyperlipemia (13.3%), sleep apnoea (10.8%), diabetes (10.8%), cardiovascular disease (9.6%)	BIB + 1,000 kcal diet + clinical, psychiatric, physical training	Nausea, vomiting in 129 patients (39.9%) Epigastric pain in 65 patients (20.1%) Dehydration in 15 patients (4.6%) Intolerance leading to early removal of the balloon in 11 patients (3.4%) Reflux oesophagitis in 40 patients (12.4%) Symptomatic gastric stasis from transient obstruction of the pyloric antrum by the balloon in 28 patients (8.7%) Balloon impaction in the antrum with gastric hyperdistention, requiring removal of gastric content under general anaesthesia in 2 patients (0.6%) Spontaneous balloon deflation and migration into the small bowel, causing intestinal obstruction in 1 patient (0.3%)	Spontaneous balloon deflation in 1 patient (0.3%)
(Spyropoulos et al 2007)	Case series pre-test/post-test Level IV intervention evidence	N = 26 (3 female, 23 male) Mean BMI = 65.3 kg/m^2 Mean age = 40.8 years Co-morbidities Hypoventilation syndrome (50%), sleep apnoea syndrome (81%), pickwick syndrome (11.5%), insulin-dependent type 2 diabetes mellitus (69.2%), hypertension (26.9%), deep vein thrombosis / venous stasis disease (46.1%)	BIB + diet	1 patient died of complications related to the procedure (3.8%) Nausea and vomiting in 65% of the patients, treated with routine medication Continuous vomiting resulting in severe dehydration and readmission in 1 patient (3.8%) Positive CLO test in 9 patients (34.6%)	
(Totte et al 2001)	Case series pre-test/post-test Level IV intervention	N = 126 (121 female, 5 male) Mean BMI = 37.7 kg/m^2 (range 26.7–57.7) Mean age = 35.6 years	BIB + 800 kcal diet	Severe nausea and vomiting (76.8%) resulting in early removal of the balloon in 3 patients Gastric perforation presented as acute peritonitis in 2 patients (1.6%) Oesophagitis in 11 patients (22%) Diffuse gastric erosion in 1 patient (0.8%)	General anesthesia and surgical removal of the balloon by rigid oesophagoscopy, following attempted endoscopic extraction and technical failure of the balloons extraction device in 1 patient (0.8%)

Study	Study design and quality appraisal	Population	Intervention	Safety outcomes	
				Primary	Secondary
	evidence Quality: good	Co-morbidities Locomotor problems like pain in low back, ankle, feet (11.9%), arterial hypertension (3.2%), dyspnoea on effort (47.6%), depression (9.5%)			
(Vandenplas et al 1999)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 5 (3 female, 2 male) Mean age = 14.1 years Co-morbidities hypertension, genu valgum, hypercholesterolemia, orthopaedic abnormalities	BIB + hypocaloric diet + physical activity	Nausea during the first days after the balloon insertion in 3 patients (60%)	Spontaneous balloon rupture (without being noticed) in 2 patients (40%)
(Weiner et al 1999)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 15 (7 female, 8 male) Mean BMI = 60.2 kg/m^2 (range 46.6–72.0) Mean age 38.8 years Co-morbidities Pulmonary diseases (46.7%), sleep apnoea (26.7%)	BIB	Earlier balloon removal in 2 patients due to abdominal pain in 1 patient and non-compliance in 1 patient (6.7%)	Balloon dysfunction in 1 case (6.7%)

BIB = BioEnterics intragastric balloon; BMI = body mass index; BE = binge eating; NBE = non-binge eating; CLO test = rapid urease test; [a] this study was designed as a randomised controlled trial, but for the purpose of the current assessment (ie comparing balloon treatment with conventional obesity treatment), it provided only level IV intervention evidence

Table 22 Case reports reporting safety outcomes associated with the BioEnterics intragastric balloon

Study	Population	Intervention	Primary safety outcomes
(De Waele et al 2001)	*Case 1*: female Age = 48 years BMI = 28.9 kg/m^2	BIB	*Case 1:* Persistent vomiting, severe constipation
	Case 2: female Age = 48 years BMI = 34.9 kg/m^2	BIB	*Case 2:* Persistent vomiting
	Case 3: female Age = 51 years BMI = 31.6 kg/m^2 Co-morbidities: History of hyper-cholesterolemia, coronary artery disease, arthrosis and depression	BIB	*Case 3* :Persistent vomiting
	Case 4: female Age = 46 years BMI = 29.8 kg/m^2	BIB	*Case 4*: Persistent vomiting, haemoconcentration, hypokalemia, hypochloremia, alkalosis Renal insufficiency
(Giardiello et al 2003)	N = 1 female BMI = 37 kg/m^2 Age = 52 years Co-morbidities Hiatal hernia, moderate hypertension, dyspnoea	BIB + 800 kcal diet + pharmacotherapy	Gastric perforation
(Kim et al 2000)	N = 1 female BMI = 41 kg/m^2 Age = 38 years Co-morbidities n/a	BIB	Abdominal pain, nausea due to a large bowel impaction caused by migration of a BIB 9 months after BIB placement
(Nijhof et al 2006)	N = 1 female BMI = 43 kg/m^2 Age = 49 years	BIB	Oesophageal rupture
(Puglisi et al 2005)	N = 1 (male) BMI = 49 kg/m^2 Age = 39 years Co-morbidities	BIB	Atrial fibrillation 75 days after BIB placement

Study	Population	Intervention	Primary safety outcomes
	Diabetes, mild arterial hypertension, osteoarthritis		
(Roche-Nagle et al 2003)	N = 1 female	BIB	Gastric perforation
(Vanden Eynden & Urbain 2001)	N = 1 female BMI = 34.4 kg/m^2 Age = 48 years Co-morbidities Severe arthritis of both knees	BIB	Small bowel obstruction by migration of a deflated BIB

BIB = BioEnterics intragastric balloon; BMI = body mass index

Appendix F Safety outcomes of the Heliosphere intragastric balloon

Table 23 Studies reporting safety outcomes associated with the Heliosphere intragastric balloon

Study	Study design and quality appraisal	Population	Intervention	Safety outcomes	
				Primary	Secondary
(Forestieri et al 2006)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 10 (5 female, 5 male) Mean BMI = 43.40 kg/m^2 (range 35–51) Mean age = 35.20 years (range 17–49) Co-morbidities Not stated	Heliosphere + 1,000 kcal diet	Nausea and vomiting in 10 patients (100%)	Balloon failure requiring insertion of a 2nd balloon in 5 patients (50%) Balloon not found in stomach at the time of removal in 1 patient (10%)
(Mion et al 2007)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 32 (27 female, 5 male) Mean BMI = 35 kg/m^2 (range 30.1–40.0) Mean age = 35 years	Heliosphere + 1,300 kcal diet	Severe upper quadrant abdominal pain in 2 patients (6.3%) Psychological intolerance in 1 patient (3.1%) Abdominal pain (moderate to severe) in week 1 in 11 patients (34.4%) Early nausea and vomiting in 27 patients (84.4%) Mild and intermittent episodes of vomiting at week 4 in 4 patients (12.5 %) Gastric ulceration in 1 patient (3.1%)	Difficulties in opening the sheath in 2 patients (6.3%) Impression of an incomplete unfolding of the balloon in 3 patients (9.4%) Difficulty in separating the balloon from its insertion catheter in 1 patient (3.1%) Deflated balloon by > 50% in 2 patients (6.3%) Difficulty in introducing the needle of the catheter into the balloon in 1 patient (3.1%) Difficulty in grasping the balloon with the removal catheter in 6 patients (18.7%) Difficulties in removing the balloon in 11 patients (34.4%)

BMI = body mass index

Appendix G Effectiveness outcomes of the BioEnterics intragastric balloon

Table 24 Inclusion criteria for identification of studies relevant to an assessment of the effectiveness of placement of intragastric balloons for the temporary management of morbid obesity

Characteristic	Criteria
Publication type	Randomised or non-randomised controlled trials, cohort studies, case series or systematic reviews of these study designs. Non-systematic reviews, opinion letters, editorials, animal, in vitro and laboratory studies were excluded
Patient	1. Morbidly obese patients who have received previous ineffective non-surgical obesity therapy and who are at increased surgical risk (and therefore need to loose weight before surgical treatment for obesity) or have refused surgical treatment
	2. Morbidly obese patients with previous ineffective non-surgical obesity therapy who are at increased surgical risk (and therefore should lose weight before surgical treatment for obesity)
Intervention/test	1. Placement of the intragastric balloon ± continued conventional obesity treatment
	2. Placement of the intragastric balloon followed by surgical obesity treatment
Comparator	1. Continued conventional obesity treatment (diet ± physical activity ± behavioural therapy ± drug therapy)
	2. Surgical obesity treatment
Outcomes	Primary: short- and long-term weight loss, BMI, waist size, skinfold thickness, fat free mass, quality of life, mortality (all cause), obesity-related co-morbidities Secondary: technical failure
Language	Non-English language articles were excluded unless they appeared to provide a higher level of evidence than the English language articles identified

BMI = body mass index

Table 25 Comparative studies of effectiveness of the BioEnterics intragastric balloon ± continued conventional obesity treatment

Study	Study design and quality appraisal	Population	Weight loss							
(Genco et al 2006)	Randomised controlled trial (crossover) Level II intervention evidence Quality: good	N = 32 (24 female, 8 male) Mean BMI = 43.7 kg/m^2 (range 40–45) Mean age = 36.2 years (range 25–50) Co-morbidities Not stated	**Outcome**	**Group A** BIB followed by sham procedure after 3 months (+1,000 kcal diet)			**Group B** Sham procedure followed by BIB after 3 months (+1,000 kcal diet)			**Relative change**
				Before	**After 3 months**	**Change**	**Before**	**After 3 months**	**Change**	5.4 kg/m^2 (p<0.001)
			Mean BMI	43.9 ± 1.1 kg/m^2	38.0 ± 2.6 kg/m^2	5.8 ± 0.5 kg/m^2 (plus a further 1.1 ± 0.3 kg/m^2 at 3 months after crossover)	43.6 ± 1.8 kg/m^2	43.1 ± 2.8 kg/m^2	0.4 ± 0.2 kg/m^2 (plus a further 5.1 ± 0.5 kg/m^2 at 3 months after crossover)	
			Mean EW	65 ± 11 kg (43.5 ± 12.9% of weight)		34.0 ± 4.8% of initial EW (plus a further 4.6 ± 5.1% of initial EW at 3 months after crossover)	67 ± 9 kg (42.9 ± 13.2% of initial weight)		2.1 ± 1.0 % of initial EW (plus a further 31 ± 4.8 % of initial EW at 3 months after crossover)	
			Mean weight			15 ± 6 kg (plus a further 6 ± 3 kg at 3 months after crossover)			3 ± 1 kg (plus a further 13 ± 8 kg at 3 months after crossover)	12 kg (p <0.001)

Study	Study design and quality appraisal	Population	Weight loss							
(Mathus-Vliegen & Tytgat 2005)	Randomised controlled trial Level II intervention evidence Quality: good	N = 43 (36 female, 7 male) Mean BMI = 43.3 kg/m^2 (range 33.9–61.3) Mean age = 41.4 years Co-morbidities n/a	**Outcome**	**Group A** Sham balloon placement for the first 3 months, followed by a balloon every 3 months for the remainder of the first year (3 balloons) (+ 1,000–1,500 kcal diet + exercise)			**Group B** Balloon placement every 3 months for one year (4 balloons) (+ 1,000–1,500 kcal diet + exercise)			**Relative change**
				Change after 3 months	**Change after 6 months**	**Change after 12 months**	**Change after 3 months**	**Change after 6 months**	**Change after 12 months**	0 kg after 12 months (not statistically significant)
			Mean weight	11.2 kg (9.0% of initial weight)	20.0 kg (16.1% of initial weight)	21.3 kg (17.1% of initial weight)	12.9 kg (10.4% of initial weight)	16.7 kg (13.4% of initial weight)	21.3 kg (17.1% of initial weight)	
(Martinez-Brocca et al 2007)	Randomised controlled trial Level II intervention evidence Quality: fair	N = 22 (17 female, 5 male) Mean BMI = 50.4 kg/m^2 (± 7.8) Mean age = 35.9 years Co-morbidities Group A % (Group B%) Diabetes mellitus 27.3 (36.4), hyper-tension 27.3 (36.4), dyslipidaemia 54.5 (72.7),	**Outcome**	**Group A** BIB + low-fat hypocaloric diet			**Group B** Sham balloon placement + low-fat hypocaloric diet			**Relative change**
				Before	**After 4 months**	**Change**	**Before**	**After 4 months**	**Change**	1.4 kg/m^2 (not statistically significant)
			Mean BMI	50.2 ± 9.6 kg/m^2	45.7 ± 9.7 kg/m^2	4.5 kg/m^2	51.3 kg/m^2	48.2 kg/m^2	3.1 kg/m^2	
			Mean EW	72.4 ± 29.2 kg	59.7 ± 30 kg	12.7 kg	71.3 ± 19.5 kg	62.4 ± 22.8 kg	8.9 kg	3.8 kg (not statistically significant)
			Mean weight	143.8 ± 31.2 kg	131.1 ± 32.6 kg	12.7 ± 5.6 kg	138.8 ± 24.5 kg	129.9 ± 25.6 kg	8.9 ± 9.2 kg	3.8 kg (not statistically significant)
			Mean waist circumference	136.7 ± 15.7 cm	130.1 ± 20.7 cm	6.6 cm	133.1± 14.4 cm	129.8 ± 15.5 cm	3.3 cm	3.3 cm (not statistically significant)

Study	Study design and quality appraisal	Population	Weight loss							
		metabolic syndrome 36.4 (54.5), sleep disordered breathing 27.3 (0), osteo-arthropathy 27.3 (45.5), coronary heart disease 9.1 (0), thyroid dysfunction 9.1 (9.1)	**Mean fat mass**	48.3 ± 8.9%	45.6 ± 5.6%	2.7%	47.6 ± 5.2%	45.5 ± 5.2%	2.1%	0.6% (not statistically significant)
(Doldi et al 2004)	Cohort study with n=73 from a case series of 303 patients Level III-2 intervention evidence Quality: poor	Group A N = 42 (32 female, 10 male) Mean BMI = 41 kg/m^2 (range 31–58) Group B N = 31 (24 female, 7 male) Mean BMI = 43.9 kg/m^2 (range 29–66)	**Outcome**	**Group A** BIB + 1,000 kcal diet			**Group B** 18 months 1,000 kcal diet			**Relative change**
				Before	**Change after 4 months**	**Change after 12 months**	**Before**	**Change after 6 months**	**Change after 12 months**	
			Mean BMI		5.6 kg/m^2 (females) 6.8 kg/m^2 (males)	3.9 kg/m^2 (females) 8.0 kg/m^2 (males)		4.7 kg/m^2 (females) 5.6 kg/m^2 (males)	6.0 kg/m^2 (females) 6.0 kg/m^2 (males)	–3.1 kg/m^2 (females) 2.0 kg/m^2 (males)
			Mean weight		15.5 kg (females) 21.0 kg (males)	11.2 kg (females) 24.0 kg (males)		11.6 kg (females) 16.4 kg (males)	15.1 kg (females) 18.7 kg (males)	–3.9 kg (females) 5.3 kg (males)

BIB = BioEnterics intragastric balloon; EW = excess weight; EWL = excess weight loss

Table 26 Case series of effectiveness of the BioEnterics intragastric balloon ± continued conventional obesity treatment

Study	Study design and quality appraisal	Population	Length of follow-up	Intervention	Pre-intervention	Post-intervention	Difference	Statistical testing of change from baseline
(Al-Momen & El-Mogy 2005)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 44 patients Mean BMI = 45 kg/m^2 (range 27–67) Mean age = 31 years Co-morbidities Diabetes (5 patients), arterial hypertension (1 patient), myocardial valve disease (2 patients), pacemaker (1 patient), depression (12 patients), hypothyroidism (1 patient), locomotor system diseases (15 patients)	6 months	BIB + diet	Mean BMI = 45 kg/m^2	n/a	Mean weight loss = 13 kg in patients with initial BMI < 40 kg/m^2 Mean weight loss = 33 kg in patients with initial BMI > 50 kg/m^2	n/a
(Angrisani et al 2006)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 166/175 (104 females, 71 males) Mean BMI = 54.4 kg/m^2 (range 39.5–79.5) Mean age = 37.1 years (range 16–67) Co-morbidities Not stated	6 months	BIB	Mean BMI = 54.4 ± 8.1 kg/m^2 Mean %EW = 160.8 ± 32.9%	Mean BMI = 47.3 ± 8.1 kg/m^2	Mean BMI reduction = 7.1 kg/m^2 Mean %EWL= 32.1 ± 16.6%	*%EWL* p<0.0001 [95% CI 29.6, 34.6] (One sample t-test)
(Bonazzi et al 2005)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 12 (8 female, 4 male) Mean BMI = 38.5 kg/m^2 (range 32–43) Mean age = 39 years (range 26–54) Co-morbidities Not stated	6 months BIB treatment + additional 2 months follow-up	BIB	Mean BMI = 38.5 kg/m^2	n/a	*At one month:* Mean weight loss = 6.2 ± 2.3 kg *At 3 months:* Mean weight loss = 12.4 ± 5.8 kg *At 6 months:* Mean weight loss = 14.4 ± 6.6 kg *At 2 months after BIB removal:* Mean weight loss = 10.1± 4.3 kg	*At one month:* p<0.0001 [95% CI 4.7, 7.7] *At 3 months:* p<0.0001 [95% CI 8.7, 16.1] *At 6 months:* p<0.0001 [95% CI 10.2, 18.6] *At 2 months after BIB removal:* p<0.0001 [95% CI 7.4, 12.8]

Study	Study design and quality appraisal	Population	Length of follow-up	Intervention	Pre-intervention	Post-intervention	Difference	Statistical testing of change from baseline
								(One sample t-test)
(Busetto et al 2005)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 18 (18 male) Mean BMI = 55.8 kg/m^2 Age range 26–62 years Co-morbidities All patients had documented obstructive sleep apnoea syndrome	6 months	BIB + 2.5 MJ diet	Mean BW = 168.1 ± 27.9 kg Mean BMI = 55.8 ± 9.9 kg/m^2 Waist circumference = 156.4 ± 17.6 cm Sagittal abdominal diameter = 37.8 ± 3.0 cm	Mean BW = 143.9 ± 29.4 kg Mean BMI = 48.6 ± 11.2 kg/m^2 Waist circumference = 136.8 ± 18.4 cm Sagittal abdominal diameter = 32.3 ± 4 cm	Mean weight loss = 24.2 kg Mean BMI reduction = 7.2 kg/m^2 Waist circumference reduction = 19.6 cm Sagittal abdominal diameter reduction = 5.5 cm	p<0.001 (Wilcoxon rank sum test) for all four outcomes
(Doldi et al 2004)	Case series pre-test/post-test Level IV intervention evidence Quality: good	*Case series* N = 303 (208 female, 95 male; 349 BIB placements) Mean BMI = 42 kg/m^2 Mean age = 41.5 years Co-morbidities Hypertension (18.6%), type 2 diabetes (7.4 %), sleep apnoea (6.8%), coronary heart disease (4.8%), severe osteo-arthropathy (4.2%)	4-6 month	BIB + 1,000 kcal diet	Mean BMI = 42 kg/m^2 Mean weight = 118.8 kg Mean EW = 45.8 kg Mean %EW = 62.3%	*At 4 months:* Mean BMI = 37.2 kg/m^2 Mean weight = 104.9 kg *At 6 months:* Mean weight = 106.3 kg	*At 4 months:* Overall, mean weight loss = 13.9 kg Overall, mean BMI reduction = 4.8 kg/m^2 Mean weight loss = 12 kg for patients with initial BMI < 40 kg/m^2 Mean weight loss = 17 kg for patients with initial BMI > 40 kg/m^2 *At 6 months:* Overall, mean weight loss = 12.5 kg Overall, mean %EWL = 18.2% (range 0–55.8) Mean weight loss = 9 kg for patients with initial BMI < 40 kg/m^2 Mean weight loss = 13 kg for patients with initial BMI > 40 kg/m^2	n/a
(Evans & Scott 2001)	Case series pre-test/post-test	N = 63 (59 female, 4 male) Mean BMI = 46.3 kg/m^2	7 months	BIB	Median weight = 124.5 kg (range	Median weight = 109.5 kg (range 66.7–	Median %EWL = 16.4% (range –49–4.8) after first	n/a

Study	Study design and quality appraisal	Population	Length of follow-up	Intervention	Pre-intervention	Post-intervention	Difference	Statistical testing of change from baseline
	Level IV intervention evidence Quality: good	(range 36–72) Median age = 41 years (range 24–67) Co-morbidities Hypertensive (20.6%), angina (6.3%), asthma or chronic obstructive airway disease (20.6%), non-insulin dependent diabetes (6.3%), hyper-cholesterolaemia (3.2%), myocardial infection (3.2%)			89–177)	171.5)	few months Median %EWL = 18.7% (range –51.5–12.68) after 7 months	
(Frutos et al 2007)	Case series pre-test/post-test Level IV intervention Quality: good evidence	N = 31 (21 female, 10 male) Mean BMI = 55.2 kg/m^2 (range 50–78) Mean age = 40.1 years (range 18–60) Co-morbidities Hypertensive (37%), diabetic (20%), obstructive sleep apnoea syndrome (20%)	6 months	BIB	Mean weight = 149.3 ± 26.3 kg Mean BMI = 55.2 ± 6.9 kg/m^2 Mean liver volume = 2,938.53 ± 853.1 cm^3	Mean weight = 128 ± 20.1 kg Mean BMI = 47.42 ± 7.7 kg/m^2 Mean liver volume = 1,918 ± 499.8 cm^3	Mean %EWL = 22.1 ± 7.4% Mean weight loss = 21.3 kg Mean BMI reduction = 7.8 kg/m^2 Mean %WL = 12.7% Mean liver volume reduction = 31.8 ± 18.2 cm^3	*Mean %EWL* p<0.0001 [95% CI 19.4, 24.8] (One sample t-test)
(Galloro et al 1999)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 10 (5 female, 5 male; 13 balloon placements) Mean BMI = 47.6 kg/m^2 (32.1–66.1) Mean age = 43 years Co-morbidities n/a	3–5 months	BIB	Mean weight = 134.4 kg Mean BMI = 47.6 kg/m^2 (range 32.1–66.1) Mean EW = 74.7 kg	Mean weight = 124.3 kg Mean BMI = 43.5 kg/m^2	Mean %EWL = 18.3% Mean weight loss = 10.1 kg Mean BMI reduction = 4.1 kg/m^2	n/a

Study	Study design and quality appraisal	Population	Length of follow-up	Intervention	Pre-intervention	Post-intervention	Difference	Statistical testing of change from baseline
(Ganesh et al 2007)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 20 (17 female, 3 male) Mean BMI = 31.5 kg/m^2 (range 28–39) Mean age = 40 years (range 28–52) <u>Co-morbidities</u> Orthopaedic (65%), diabetes mellitus (5%), hypertensive (10%), hyperlipidaemia (15%), respiratory problems (20%)	1 year (6 months BIB treatment)	BIB + 1,000 kcal diet	Mean BMI = 31.5 kg/m^2 Mean EW = 21.2 kg	n/a	Maximum mean weight loss = 5.9 kg Mean weight loss = 4.4 kg at 6 months Mean weight loss = 1.5 kg after 1 year	p<0.0001 p<0.001 p>0.05 (Wilcoxon signed ranks test)
(Genco et al 2005)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 2,515 (1,793 female, 722 male) Mean BMI = 44.4 kg/m^2 (range 28–79.1) Mean age = 38.9 years <u>Co-morbidities</u> Hypertension (509 patients, 36.5%), diabetes (488 patients, 35%), respiratory disorders (247 patients, 17.7%), osteo-arthropathy (271 patients, 19.4%), dyslipidaemia (318 patients, 22.8%), others (176 patients, 12.6%)	6 months	BIB + 1,000 kcal diet + medical therapy	Mean BMI = 44.4 kg/m^2 (range 28–79.1) Mean EW = 59.5 ± 29.8 kg	Mean BMI = 35.4 ± 11.8 kg/m^2 (range 24–73)	Mean %EWL = 33.9 ± 18.7% (range 0–87) Mean BMI loss = 4.9 ± 12.7 kg/m^2 (range 0–25)	*Mean %EWL* p<0.0001 [95% CI 33.2, 34.6] *Mean BMI loss* p<0.0001 [95% CI 4.4, 5.4] (One sample t-test)

Study	Study design and quality appraisal	Population	Length of follow-up	Intervention	Pre-intervention	Post-intervention	Difference	Statistical testing of change from baseline
(Herve et al 2005)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 100 (77 female, 23 male) Mean BMI = 34.0 kg/m^2 (range 25.3–60.2) Mean age = 34.8 years <u>Co-morbidities</u> Arterial hypertension (25%), locomotion disorders (28%), lipid disorders (25%), dyspnoea (28%), sleep apnoea (10%), chronic obstructive pulmonary disease (4%), asthma (9%), gastro-oesophageal reflux (12%), oesophagitis (9%), peptic ulcer (5%), diabetes type 1 (3%), diabetes type 2 (24%), depression (14%)	1 year after BIB removal	BIB	Mean BMI = 34.0 kg/m^2	n/a	Overall mean weight loss = 12 kg at BIB removal Overall mean %EWL = 39.8% at BIB removal Mean weight loss = 7.1 kg at BIB removal in patients with baseline BMI 25–29.9 kg/m^2 Mean %EWL = 43.4% at BIB removal in patients with baseline BMI 25–29.9 kg/m^2 Mean weight loss = 11.7 kg at BIB removal in patients with baseline BMI 30–34.9 kg/m^2 Mean %EWL = 41.2% at BIB removal in patients with baseline BMI 30–34.9 kg/m^2 Mean weight loss = 16.6 kg at BIB removal in patients with baseline BMI 35–39 kg/m^2 Mean %EWL = 42.4% at BIB removal in patients with baseline BMI 35–39 kg/m^2 Mean weight loss = 17.2 kg at BIB removal in patients with baseline BMI > 40 kg/m^2 Mean %EWL = 25.9% at BIB removal in patients with baseline BMI > 40 kg/m^2	n/a

Study	Study design and quality appraisal	Population	Length of follow-up	Intervention	Pre-intervention	Post-intervention	Difference	Statistical testing of change from baseline
							Overall mean weight loss = 8.6 kg at 12 months after BIB removal Overall mean %EWL = 26.8% at 12 months after BIB removal Mean weight loss = 4.4 kg at 12 months after BIB removal in patients with baseline BMI 25–29.9 kg/m^2 Mean %EWL = 29.9% at 12 months after BIB removal in patients with baseline BMI 25–29.9 kg/m^2 Mean weight loss = 7.8 kg at 12 months after BIB removal in patients with baseline BMI 30–34.9 kg/m^2 Mean %EWL = 27.1% at 12 months after BIB removal in patients with baseline BMI 30–34.9 kg/m^2 Mean weight loss = 11.1 kg at 12 months after BIB removal in patients with baseline BMI 35–39 kg/m^2 Mean %EWL = 26.4% at 12 months after BIB removal in patients with baseline BMI 35–39 kg/m^2 Mean weight loss = 15.7 kg at 12 months after BIB removal in patients with baseline BMI > 40 kg/m^2	

Study	Study design and quality appraisal	Population	Length of follow-up	Intervention	Pre-intervention	Post-intervention	Difference	Statistical testing of change from baseline
							Mean %EWL = 20.4% at 12 months after BIB removal in patients with baseline BMI > 40 kg/m^2	
(Hodson et al 2001)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 10 (9 female, 1 male; 15 balloon placements) Mean BMI = 39 kg/m^2 (range 32–53) Mean age = 33 years Co-morbidities n/a	6 months	BIB + 800 kcal diet	Mean BMI = 39 kg/m^2	n/a	Mean weight loss = 18.6 kg (range 6.6–40) Mean %EWL = 40% (range 10–81) Mean weight loss = 30.3 kg (range 24–40) in 5 patients with 2 consecutive BIB placements Mean %EWL = 54% (range 29–81) in 5 patients with 2 consecutive BIB placements Mean weight loss = 10.4 kg (range 8.8–12.5) in 5 patients with a single BIB placement Mean %EWL = 19% (range 10–37) in 5 patients with a single BIB placement	n/a
(Iordache 2005)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 54 (45 female, 9 male) Mean BMI = 32 kg/m^2 (range 2–42) Mean age = 33.1 years Co-morbidities Arterial hypertension and diabetes (10 patients)	6 months	BIB	Mean BMI = 32.0 ± 4.5 kg/m^2	Mean BMI = 28.8 ± 4.7 kg/m^2	Mean BMI reduction = 3.2 kg/m^2	$p<0.05$ (unclear statistical test used)

Study	Study design and quality appraisal	Population	Length of follow-up	Intervention	Pre-intervention	Post-intervention	Difference	Statistical testing of change from baseline
(Iordache et al 2005)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 40 (32 females, 8 males) Mean BMI = 33 kg/m^2 (range 30–43) Mean age = 35.5 years Co-morbidities n/a	6 months	BIB	Mean BMI = 33 kg/m^2	Mean BMI = 27 kg/m^2	Mean BMI reduction = 6 kg/m^2 Mean weight loss = 17.5 kg (range 7–37)	p<0.01 (unclear statistical test used)
(Loffredo et al 2001)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 77 (54 female, 23 male; 87 balloons) Mean BMI = 46.6 kg/m^2 (range 32.1–73.8) Mean age = 38.2 years Co-morbidities n/a	3–6 months of BIB	BIB + diet	Mean BMI = 46.6 kg/m^2 Mean weight = 128.0 kg Mean EW = 65.0 kg	Mean BMI = 41.2 kg/m^2 Mean weight = 113.4 kg	%EWL = 22.1% Mean BMI loss = 5.4 kg/m^2 Mean weight loss = 14.3 kg	n/a
(Melissas et al 2006)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 140 (106 female, 34 male) Median BMI = 42.3 kg/m^2 (range 35–61.3) Median age = 38 years Co-morbidities n/a	6–30 months after balloon removal	BIB + 1,000 kcal diet	Median BMI = 42.3 kg/m^2 Median weight = 122 kg Median EW = 59 kg	n/a	71% of patients with %EWL ≥ 25% (range 25–88.2) at BIB removal 40% of patients with %EWL ≥ 25% after 6–30 months (mean 18.3 months)	n/a
(Mion et al 2005)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 17 (14 female, 3 male) Mean BMI = 34.4 kg/m^2 (range 30.1–40.0) Mean age = 34.9 years Co-morbidities Gastric ulcers related to *Helicobacter pylori* gastritis in 1 patient (therefore excluded)	7 months (6 months BIB)	BIB + 1,300 kcal diet	Mean BMI = 34.4 kg/m^2	n/a	Mean %WL = 9.4 ± 1.8% at BIB removal Mean weight loss = 8.7 ± 1.6 kg (range 0–21) at 1 month after BIB removal Mean BMI loss = 3.1 ± 0.7 kg/m^2 at 1 month after BIB removal	*Mean %WL* p<0.0001 [95% CI 8.5, 10.3] *Mean weight loss* p<0.0001 [95% CI 7.9, 9.5] *Mean BMI loss* p<0.0001 [95% CI 2.7, 3.5] (One sample t-test)

Study	Study design and quality appraisal	Population	Length of follow-up	Intervention	Pre-intervention	Post-intervention	Difference	Statistical testing of change from baseline
(Mui et al 2006)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 15 (10 female, 5 male) Mean BMI = 40.5 kg/m^2 (range 29.6–56.9) Median age = 40 years Co-morbidities obstructive sleep apnoea syndrome (40%), diabetes mellitus (20%), hypertension (40%), degenerative joint problems with knee pain (35%)	Median 162 days BIB	BIB + 1,200 kcal diet + 150 minutes/ week moderately intense exercise	Mean BMI = 40.5 kg/m^2 Mean weight = 109.8 kg	Mean BMI = 34.6 kg/m^2 Mean weight = 94.2 kg	Mean BMI loss = 5.9 ± 3.2 kg/m^2 (range 1.9–12.5) Mean weight loss = 15.6 ± 7.9 kg (range 5.3–30.1) Mean %WL = 14.4 ± 7.5% (range 5.9–30.7) Mean %EWL = 42.8 ± 23.0% (range 18.2–87.7)	n/a
(Puglisi et al 2007)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 75 (63 female, 12 male) BMI range = 39–55 kg/m^2 Mean age = 39.5 years BE group N = 27 (24 female, 3 male) Mean BMI = 44.7 kg/m^2 Mean age = 38 years NBE group N = 48 (39 female, 9 male) Mean BMI = 47.6 kg/m^2	9 months	BIB + 1,000 kcal diet	BE group Mean BMI = 44.7 ± 5.8 kg/m^2 Mean weight = 122.4 kg	BE group Mean BMI = 41.3 ± 4.9 kg/m^2 at BIB removal Mean weight = 106.3 kg at BIB removal Mean BMI = 41.4 ± 5.3 kg/m^2 3 months after BIB removal Mean weight = 104.2 kg 3 months after BIB removal	BE group Mean BMI loss = 3.4 kg/m^2 at BIB removal Mean weight loss = 16.1 kg at BIB removal Mean BMI loss = 3.3 kg/m^2 3 months after BIB removal Mean weight loss = 18.2 kg 3 months after BIB removal	*Mean BMI* P<0.05 from pre-implantation to removal of BIB at 3 months and 3 months after removal of BIB (Repeated measures ANOVA)

Study	Study design and quality appraisal	Population	Length of follow-up	Intervention	Pre-intervention	Post-intervention	Difference	Statistical testing of change from baseline
		Mean age = 39 years Co-morbidities n/a			NBE group Mean BMI = 47.6 ± 7.3 kg/m^2 Mean weight = 136.3 kg	NBE group Mean BMI = 42.4 ± 6.6 kg/m^2 at BIB removal Mean weight = 115.2 kg at BIB removal Mean BMI = 41.9 ± 6.8 kg/m^2 3 months after BIB removal Mean weight = 118.4 kg 3 months after BIB removal	NBE group Mean BMI loss = 5.2 kg/m^2 at BIB removal Mean weight loss = 21.1 kg at BIB removal Mean BMI loss = 5.7 kg/m^2 3 months after BIB removal Mean weight loss = 17.9 kg 3 months after BIB removal	
(Roman et al 2004)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 176 (161 female, 15 male) Mean BMI = 31 kg/m^2 (range 27–40) Mean age = 37.4 years Co-morbidities Diabetes mellitus (2.8%), arterial hypertension (6.8%), hypothyroidism (4.5%), depression (2.3%), grade I oesophagitis and/or small hiatal hernia (14.2%), gastritis or duodenitis (5.1%), mycotic	4–6 months	BIB	Mean BMI = 31 kg/m^2 Mean EW = 25.5 kg	n/a	Mean weight loss = 9.5 ± 7.1 kg Mean weight loss = 12.9 ± 7.9 kg in patients with 600 mL filled BIB Mean weight loss = 8.6 ± 6.6 kg in patients with 500 mL filled BIB Mean %EWL = 38.1 ± 28.5% Mean %EWL = 35.4 ± 27.3% in patients with 600 mL filled BIB	*Weight loss–500 mL* p<0.001 [95% CI 7.46, 9.74] *Weight loss–600 mL* p<0.001 [95% CI 10.05, 15.75] *Excess weight loss–500 mL* p<0.001 [95% CI 30.68, 40.12]

Study	Study design and quality appraisal	Population	Length of follow-up	Intervention	Pre-intervention	Post-intervention	Difference	Statistical testing of change from baseline
		oesophagitis (0.6%), oesophageal papilloma (0.6%)					Mean %EWL = 48.8 ± 31% in patients with 500 mL filled BIB	*Excess weight loss–600 mL* p<0.001 [95% CI 37.62, 59.98] (One-sample t-test)
(Sallet et al 2004)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 323 (196 female, 127 male) Mean BMI = 38.2 kg/m^2 Mean age = 37.5 years Co-morbidities Hypertension (31.6%), arthropathies (21.9%), hyperlipaemia (13.3%), sleep apnoea (10.8%), diabetes (10.8%), cardiovascular disease (9.6%)	6 months	BIB + 1,000 kcal diet + clinical, psychiatric, physical training	Mean BMI = 38.2 ± 9.4 kg/m^2 Mean weight = 110.1 kg Mean EW = 38.7 kg	Mean BMI = 32.9 ± 8.3 kg/m^2 Mean weight = 94.9 kg	Mean weight loss = 15.2 ± 10.5 kg Mean BMI loss = 5.3 ± 3.4 kg/m^2 Mean %EWL = 48.3 ± 23.3% Mean %WL = 13.6 ± 7.3 kg	*BMI reduction–6 months* p<0.001 [95% CI 5.75, 7.05] *%EWL–6 months* p<0.0001 [95% CI 51.79, 63.09] *BMI reduction–1 year* p<0.0001 [95% CI 5.10, 6.70] *%EWL–1 year* p<0.0001 [95% CI 44.69, 57.11] (One sample t-test)
(Spyropoulos et al 2007)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 26 (3 female, 23 male) Mean BMI = 65.3 kg/m^2 Mean age = 40.8 years Co-morbidities Hypoventilation syndrome (50%), sleep apnoea syndrome (81%), pickwick syndrome (11.5%), insulin-dependent type 2 diabetes mellitus (69%), hypertension (27%), deep vein thrombosis / venous stasis disease (46.1%)	6 months	BIB + diet	Mean BMI = 65.3 ± 9.8 kg/m^2 Mean weight = 193.9 ± 29.2 kg Mean EW = 124.5 ± 28.4 kg	Mean BMI = 54.3 ± 9.9 kg/m^2 Mean weight = 164.9 ± 35.7 kg Mean EW = 96.7 ± 32.9 kg	Mean %EWL = 22.4 ± 14.5% Mean BMI loss = 11 kg/m^2 Mean weight loss = 29.0 kg	Mean BMI p=0.001 Mean weight p=0.001 Mean EW p=0.001 (unclear statistical testing used)

Study	Study design and quality appraisal	Population	Length of follow-up	Intervention	Pre-intervention	Post-intervention	Difference	Statistical testing of change from baseline
(Totte et al 2001)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 126 (121 female, 5 male) Mean BMI = 37.7 kg/m^2 (26.7–57.7) Mean age = 35.6 years Co-morbidities Locomotor problems (low back pain, ankle, feet pain (11.9%), arterial hypertension (3.2%), dyspnoea on effort (47.6%), depression (9.5%)	6 months	BIB + 800 kcal diet	Mean BMI = 37.7 kg/m^2 Mean EW = 35.3 kg Mean %EW = 32.2%	Mean BMI = 32.0 kg/m^2	Mean %EWL = 50.8% Mean weight loss = 15.4 kg Mean BMI loss = 5.7 kg/m^2	n/a
(Vandenplas et al 1999)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 5 (3 female, 2 male) Mean age = 14.1 years Co-morbidities hypertension, genu valgum, hypercholesterolaechima, orthopaedic abnormalities	6 months	BIB + hypocaloric diet + physical activity	Mean BMI% = 198.6%	Mean BMI% = 187.4% at 3 months Mean BMI% = 208.8% at 6 months	Non-significant trend in BMI reduction at 3 months BMI higher than before insertion at 6 months	BMI% reduction p>0.05 (unclear statistical testing)

BIB = BioEnterics intragastric balloon; BMI = body mass index; BW = body weight; EW = excess weight; EWL = excess weight loss; LASGB = laparoscopic adjustable silicone gastric banding; n/a = not available

Table 27 Studies reporting co-morbidities related outcomes

Study	Study design and quality appraisal	Population	Length of follow-up	Intervention	Co-morbidities related outcomes	
(Genco et al 2005)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 2,515 (1,793 female, 722 male) Mean BMI = 44.4 kg/m^2 (range 28–79.1) Mean age = 38.9 years <u>Co-morbidities</u> Hypertension (509 patients, 36.5%), diabetes (488 patients, 35%), respiratory disorders (247 patients, 17.7%), osteo-arthropathy (271 patients, 19.4%), dyslipidaemia (318 patients, 22.8%), others (176 patients, 12.6%)	6 months	BIB + 1,000 kcal diet + medical therapy	Co-morbidities resolved in 44.3% of patients Co-morbidities improved in 44.8% of patients (allowing less pharmacological dosages or shift to other therapies) Co-morbidities remained unchanged in 10.9% of patients	
(Busetto et al 2005)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 18 (18 male) Mean BMI = 55.8 kg/m^2 Age range 26–62 years <u>Co-morbidities</u> All patients had documented obstructive sleep apnoea syndrome	6 months	BIB + 2.5 MJ diet	*Pre-intervention* Number obstructive apnoeas = 277 ± 105 Number central apnoeas = 7 ± 17 Number mixed apnoeas = 16 ± 17 Number hypopnea = 116 ± 83 AHI events/hour = 59.3 ± 18.1 ESS score = 11.2 ± 5.2	*Post-intervention* Number obstructive apnoeas = 90 ± 120 [a] Number central apnoeas = 1 ± 1 Number mixed apnoeas = 1 ± 1 Number hypopnea = 36 ± 55 [b] AHI events/hour =14 ± 12.4 [a] ESS score = 4.7 ± 2.3 [c]

BIB = BioEnterics intragastric balloon; BMI = body mass index; AHI = apnoea–hypopnea index; ESS = Epworth sleepiness scale; [a] p<0.01(Wilcoxon rank sum test); [b] p<0.05 (Wilcoxon rank sum test); [c] p<0.001 (Wilcoxon rank sum test)

Table 28 Studies of effectiveness of the BioEnterics intragastric balloon followed by surgical obesity treatment

Study	Study design and quality appraisal	Population	Length of follow-up	Intervention	Pre-intervention	Post-intervention	Difference
(Busetto et al 2004)	Historical control Level III-3 intervention evidence Quality: good	N = 86 Case group (BIB pre-surgical) N = 43 Mean age = 43.3 years Mean BMI = 58.4 kg/m^2 (range 47.9–74.4) Control group (only LAGB) N = 43 Mean age = 42.8 years Mean BMI = 56.9 kg/m^2 (range 46.7–70.2) Co-morbidities Type 2 diabetes 44.2 (18.6), hypertension 69.8 (53.5), dyslipidaemia 27. 16.3 (18.6)	Case group 1.1 years (0–4 years) Control group 4.4 years (range 0.5–69) (27.9), hyperuricemia and/or gout 16.3 (25.6), obstructive sleep apnoea syndrome 67.4 (62.8), osteoarthritis 69.8 (74.4), depression 14.0 (14.0), binge eating disorder years)	BIB +diet followed by surgery Vs surgery alone (Lap-Band)	Case group Mean BMI = 58.4 ± 6.6 kg/m^2	Case group Mean BMI = 49.3 ± 6.2 kg/m^2	Case group %EWL = 33.6 ± 12.5% at 6 months %EWL = 36.5 ± 12.5% at 1 year %EWL = 31.5 ± 16.0% at 2 years %EWL = 32.3 ± 20.7% at 3 years Control group %EWL = 25.3 ± 12.4% at 6 months %EWL = 32.9 ± 16.3% at 1 year %EWL = 331.5 ± 16.3% at 2 years %EWL = 34.0 ± 18.5% at 3 years
(Alfalah et al 2006)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 10 (10 female) Mean BMI = 64 kg/m^2 (range 59–78) Mean age = 33 years (range 17–51) Co-morbidities Not stated	6 months balloon treatment	BIB followed by laparoscopic surgery	Mean weight = 175 ± 25 kg BMI = 64.4 ± 7 kg/m^2	Mean weight = 165 ± 27 kg at 3 months Mean BMI = 60.8 ± 8.4 kg/m^2 at 3 months Mean weight =169 ± 26 kg at 6 months Mean BMI = 61.8 ± 8.2 kg/m^2 at 6 months	Mean weight loss = 10 kg at 3 months Mean BMI loss = 3.6 kg/m^2 at 3 months %EWL = 10 ± 7% at 3 months Mean weight loss = 6 kg at 6 months Mean BMI loss = 2.6 kg/m^2 at 6 months %EWL = 7 ± 6% at 6 months
(de Goederen-van der Meij et al 2007)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 40 (32 female, 8 male) Mean BMI = 46.5 kg/m^2 (range 39–62) Mean age = 36.6 years (range 26–54)	6 months following IGB placement + 12 months following laparoscopic adjustable gastric banding	BIB followed by laparoscopic adjustable gastric banding Group A: 10% initial weight loss after 6 months of balloon	Overall mean BMI = 46.5 kg/m^2	Overall mean BMI = 40.5 kg/m^2 after 6 months of balloon treatment Overall mean BMI = 35.2 kg/m^2 at	%EWL = 28.7% after 6 months of balloon treatment %EWL = 57.1% at 12 months after LAGB *Group A (after*

Study	Study design and quality appraisal	Population	Length of follow-up	Intervention	Pre-intervention	Post-intervention	Difference
		Co-morbidities Cardiovascular problems (7.5%), pulmonary problems (30%), diabetes mellitus (10%), hypertension (27.5%), osteoarthritis (70%)		treatment Group B: < 10% initial weight loss		12 months after LAGB	*6 months balloon and 12 months LAGB):* BMI reduction = 12.4 kg/m^2 Weight loss = 37.3 kg *Group B (after 6 months balloon and 12 months LAGB)* BMI reduction = 9.0 kg/m^2 Weight loss = 28.7 kg *Group A (after 12 months LAGB):* BMI reduction = 4.7 kg/m^2 Weight loss = 13.8 kg %EWL = 32.9% *Group* B *(after 12 months LAGB):* BMI reduction = 5.8 kg/m^2 Weight loss = 18.6 kg %EWL = 33.8%
(Weiner et al 1999)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 15 (7 female, 8 male) Mean BMI = 60.2 kg/m^2 (range 46.6–72.0) Mean age 38.8 years Co-morbidities Pulmonary diseases (46.7%), sleep apnoea (26.7%)	4–7 months	BIB followed by LAGB	Mean weight = 194 kg Mean BMI = 60.2 kg/m^2 Mean EW = 108.2 kg	Mean weight = 176 kg	Mean weight loss = 18.1 kg (range 13–30)

BIB = BioEnterics intragastric balloon; BW = body weight; EW = excess weight; EWL = excess weight loss; LAGB = laparoscopic adjustable gastric banding; LASGB = laparoscopic adjustable silicone gastric banding

Appendix H Effectiveness outcomes of the Heliosphere intragastric balloon

Table 29 Studies of effectiveness of the Heliosphere intragastric balloon ± continued conventional obesity treatment

Study	Study design and quality appraisal	Population	Length of follow-up	Intervention	Pre-intervention	Post-intervention	Difference
(Forestieri et al 2006)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 10 (5 female, 5 male) Mean BMI = 43.4 kg/m^2 (range 35–51) Mean age = 35.2 years (range 17–49) Co-morbidities Not stated	6 months	Heliosphere + 1,000 kcal diet	n/a	Mean BMI = 37.4 kg/m^2 (range 28.9–42.1)	%EWL = 29.1% (range 9–57.4) Mean BMI reduction = 5.2 kg/m^2 (range 1.9–11.2) Weight loss = 17.5 kg (range 5–33)
(Mion et al 2007)	Case series pre-test/post-test Level IV intervention evidence Quality: good	N = 32 (27 female, 5 male) Mean BMI = 35 kg/m^2 (range 30.1–40.0) Mean age = 35 years Co-morbidities n/a	1 year (4 months balloon)	Heliosphere + 1,300 kcal diet	n/a	n/a	Mean %WL = 9.3% (range 3–20) at 16 weeks Mean %WL = 8.6% (range 5–24) at 12 months after balloon removal

BMI = body mass index; EW = excess weight; EWL = excess weight loss

Appendix I Studies included in the review

Study profiles of included studies

Study and location	Level of evidence and quality assessment	Study design	Study population	Intervention	Inclusion/exclusion criteria	Outcomes assessed	Duration of follow-up
(Alfalah et al 2006) Lille, France	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 10 (10 female) Mean BMI = 64 kg/m^2 (range 59–78) Mean age = 33 years (range 17–51) Co-morbidities Not stated	BIB + surgery	Inclusion Super-obese patients scheduled for laparoscopic Roux-en-Y gastric bypass surgery Exclusion Large hiatal hernia, previous gastric surgery, pregnancy, cancer, peptic ulcer disease, bleeding disorder, oesophageal varices, Crohn's disease, psychiatric disorder, alcoholism, drugs	Safety Adverse events Effectiveness Change in BMI, weight loss, excess weight loss	6 months
(Al-Momen & El-Mogy 2005) Al-Khobar, Saudi Arabia	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 44 patients Mean BMI = 45 kg/m^2 (range 27–67) Mean age = 31 years Co-morbidities Diabetes (11.3%), arterial hypertension (2.3%), myocardial valve disease (4.5%), pacemaker (2.3%), depression (27.2%), hypothyroidism (2.3%), locomotor system diseases (34.1%)	BIB + diet	Inclusion Patients with a BMI > 30 kg/m^2 without criteria for bariatric surgery, super-obese patients to reduce the surgical risk and to select patients for gastric restrictive surgery (LAGB) if they lose weight with the balloon Patients who failed to achieve weight loss on an adequate weight control program Exclusion Neoplastic lesions, large hiatal hernia, gastric or duodenal ulcer, prior gastric or intestinal surgery, grade I or II oesophagitis	Safety Adverse events Effectiveness Excess weight loss	6 months after BIB insertion

Study and location	Level of evidence and quality assessment	Study design	Study population	Intervention	Inclusion/exclusion criteria	Outcomes assessed	Duration of follow-up
(Angrisani et al 2006)	Level IV intervention evidence Quality: good	Case series pre-test/post-test	*Case series:* N = 175 (104 females, 71 males) Mean BMI = 54.4 kg/m^2 (range 39.5–79.5) Mean age = 37.1 years (range 16–67) Co-morbidities Not stated	*Case series:* BIB	Exclusion Emergency BIB removal due to balloon rupture, early removal of BIB for psychological intolerance	Safety Adverse events Effectiveness Weight loss	6 months
(Bonazzi et al 2005)	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 12 (8 female, 4 male) Mean BMI = 38.5 kg/m^2 (range 32–43) Mean age = 39 years (range 26–54) Co-morbidities Not stated	BIB	Inclusion Not stated Exclusion Patients with endocrine or pathological causes of obesity	Safety Adverse events Effectiveness Weight loss, gastric emptying	6 months IGB treatment + additional 2 months follow-up
(Busetto et al 2004) Padova, Italy	Level III-3 intervention evidence Quality: good	Historical control	N = 86 Case group (BIB pre-surgical) N = 43 Mean age = 43.3 years Mean BMI = 58.4 kg/m^2 (range 47.9–74.4) Control group (only LAGB) N = 43 Mean age = 42.8 years Mean BMI = 56.9 kg/m^2 (range 46.7–70.2) Co-morbidities case group (control group) % Type 2 diabetes 44.2 (18.6), hypertension 69.8 (53.5), dyslipidaemia 27.9 (27.9), hyperuricaemia and/or gout	BIB before undergoing LAGB Comparator LAGB without preoperative treatment	Inclusion n/a Exclusion n/a	Safety Adverse events Effectiveness Excess weight loss, change in BMI, weight loss	Case group 1.1 years (range 0–4) Control group 4.4 years (range 0.5–6)

Study and location	Level of evidence and quality assessment	Study design	Study population	Intervention	Inclusion/exclusion criteria	Outcomes assessed	Duration of follow-up
			16.3 (25.6), obstructive sleep apnoea syndrome 67.4 (62.8), Osteoarthritis 69.8 (74.4), depression 14.0 (14.0), binge eating disorder 16.3 (18.6)				
(Busetto et al 2005) Padova, Italy	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 18 (18 male) Mean BMI = 55.8 kg/m^2 Age range 26–62 years Co-morbidities All patients had documented obstructive sleep apnoea syndrome	BIB + 2.5 MJ diet	Inclusion Morbidly obese men with obstructive sleep apnoea syndrome Exclusion Smoking	Safety Adverse events Effectiveness Change in BMI, weight loss, change in waist circumference, change in sagittal abdominal diameter, change in neck circumference, change in measures of pulmonary function, change in measures of sleep apnoea	6 months
(de Goederen-van der Meij et al 2007) Amsterdam, The Netherlands	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 40 (32 female, 8 male) Mean BMI = 46.5 kg/m^2 (range 39–62) Mean age = 36.6 years (range 26–54) Co-morbidities Cardiovascular problems (7.5%), pulmonary problems (30%), diabetes mellitus (10%), hypertension (27.5%), osteoarthritis (70%).)	BIB + laparoscopic adjustable gastric banding	Inclusion Low probability of success with non-surgical measures, BMI > 40 kg/m^2 or BMI > 35 kg/m^2 with significant co-morbidities, age between 18 and 55 years, not pregnant, no prior bariatric surgery, suitable candidate for IGB according to psychologist, no large hiatal hernia, no severe gastro-oesophageal reflux, no use of anticoagulants, aspirin and NSAIDs Exclusion Balloon-related problems and subsequent refusal of gastric banding	Safety Adverse events Effectiveness Change in BMI, weight loss, excess weight loss	6 months following IGB placement + 12 months following laparoscopic adjustable gastric banding
(De Waele et al 2001) Brussels, Belgium	n/a	Case reports	*Case 1*: female, Age = 48 years	BIB	Inclusion n/a	Safety Adverse events	Up to 7 months

Study and location	Level of evidence and quality assessment	Study design	Study population	Intervention	Inclusion/exclusion criteria	Outcomes assessed	Duration of follow-up
			BMI = 28.9 kg/m^2 *Case 2*: female Age = 48 years BMI = 34.9 kg/m^2 *Case 3*: female Age = 51 years BMI = 31.6 kg/m^2 Co-morbidities: History of hyper-cholesterolemia, coronary artery disease, arthrosis and depression *Case 4:* female Age = 46 years BMI = 29.8 kg/m^2		Exclusion n/a		
(Doldi et al 2004) Milan, Italy	Level IV intervention evidence Quality: good	Case series pre-test/post-test	*Case series* N = 303 (208 female, 95 male; 349 BIB placements) Mean BMI = 42 kg/m^2 Mean age = 41.5 years Co-morbidities Hypertension (18.6%), type 2 diabetes (7.4 %), sleep apnoea (6.8%), coronary heart disease (4.8%), severe osteoarthropathy (4.2%)	*Case series* BIB + 1,000 kcal diet	Inclusion Morbid obese (BMI > 40 kg/m^2) and super-obese patients (BMI > 50 kg/m^2) in preparation for bariatric surgery, to reduce surgical risk; BMI 35-40 kg/m^2 with the presence of some obesity-related diseases; BMI < 35 kg/m^2 in patients who failed many attempts at weight loss; overweight patients (BMI < 30 kg/m^2) with a psychological indication in a multidisciplinary treatment program Exclusion Presence of an organic disease of the upper digestive tract, Crohn's disease on anti-inflammatory agents, anticoagulants or steroids, alcoholism or drug addiction, a hiatus hernia of diameter > 5 cm	Safety Adverse events Effectiveness Weight loss, change in BMI, change in co-morbidities	*Case series* 6 months
	Level III-2 intervention evidence Quality: poor	Cohort study with n=31 of the above patients and 42 controls	*Cohort study* Group A (diet) N = 42 (32 female, 10 male) Mean BMI = 41 kg/m^2 (range 31–58) Group B (BIB + diet) N = 31 (24 female, 7 male) Mean BMI = 43.9 kg/m^2 (range 29–66)	*Cohort study* BIB + 1,000 kcal diet vs 18 month 1,000 kcal diet			*Cohort study* 18 months

Study and location	Level of evidence and quality assessment	Study design	Study population	Intervention	Inclusion/exclusion criteria	Outcomes assessed	Duration of follow-up
(Evans & Scott 2001) Merseyside, UK	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 63 (59 female, 4 male) Mean BMI = 46.3 kg/m^2 (range 36–72) Median age = 41 years (range 24–67) Co-morbidities Hypertensive (20.6%), angina (6.3%), asthma or chronic obstructive airway disease (20.6%), non-insulin dependent diabetes (6.3%), hyper-cholesterolaemia (3.2%), myocardial infection (3.2%)	BIB	Inclusion Patients obese for a minimum of 5 years and had failed conservative therapy Exclusion No major psychiatric disorder, alcoholism	Safety Adverse events Effectiveness Weight loss, excess weight loss	7 months
(Forestieri et al 2006) Naples, Italy	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 10 (5 female, 5 male) Mean BMI = 43.4 kg/m^2 (range 35–51) Mean age = 35.2 years (range 17–49) Co-morbidities Not stated	Heliosphere + 1,000 kcal diet	Inclusion Low probability of success with non-surgical measures, BMI > 40 kg/m^2 or BMI > 35 kg/m^2 with significant co-morbidities, age between 18 and 55 years, suitable candidate for IGB according to psychologist Exclusion Previous bariatric surgery, pregnancy, large hiatal hernia, severe gastroesophageal reflux, use of anticoagulants, aspirin or NSAIDs	Safety Adverse events Effectiveness Change in BMI, weight loss, excess weight loss	6 months
(Francica et al 2004) Napoli, Italy	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 131 (85 females, 46 male; 151 balloon placements) Mean BMI = 43.8 kg/m^2 Mean age = 38.4 years Co-morbidities n/a	BIB	Inclusion n/a Exclusion n/a	Safety Adverse events, technical failure	Not stated
(Frutos et al 2007) Murcia, Spain	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 31 (21 female, 10 male) Mean BMI = 55.2 kg/m^2 (range 50–78)	BIB	Inclusion Not stated Exclusion	Safety Adverse events Effectiveness	6 months

Study and location	Level of evidence and quality assessment	Study design	Study population	Intervention	Inclusion/exclusion criteria	Outcomes assessed	Duration of follow-up
			Mean age = 40.1 years (range 18–60) Co-morbidities Hypertensive (37%), diabetic (20%), obstructive sleep apnoea syndrome (20%)		Previous gastric surgery, hiatus hernia, pregnancy, cancer, ulcer disease, haematological diseases, oesophageal varices, Crohn's disease, psychiatric disease, alcoholism, drugs	Change in BMI, weight loss, excess weight loss	
(Galloro et al 1999) Naples, Italy	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 10 (5 female/ 5 male; 13 balloon placements) Mean BMI = 47.6 kg/m^2 (range 32.1–66.1) Mean age = 43 years Co-morbidities n/a	BIB	Inclusion n/a Exclusion Structural abnormalities in the oesophagus or pharynx, such as strictures or diverticula, large hiatal hernia, potential upper gastrointestinal bleeding conditions such as oesophageal or gastric varices or congenital or acquired gastrointestinal telangiectasis, congenital anomalies of the gastrointestinal tract such as atresia or stenosis, prior gastric or intestinal surgery, aspirin, anti-inflammatory agents or other gastric irritants taken by patients, alcoholism or drug addiction, psychiatric disorders, unwillingness of patients to participate in an established medically supervised diet and behaviour modification program, pregnancy or breastfeeding, peptic diseases (oesophagitis, gastric or duodenal erosions, gastric or duodenal ulcer) and *Helicobacter pylori* contamination allow BIB placement only after treatment	Safety Adverse events Effectiveness Weight loss, change in BMI, excess weight loss	5 months
(Galloro et al 2007) Naples, Italy	Level IV intervention evidence	3 case series	N = 87 Co-morbidities	3 removal techniques for BIB	Inclusion n/a	Safety Adverse events during	n/a

Study and location	Level of evidence and quality assessment	Study design	Study population	Intervention	Inclusion/exclusion criteria	Outcomes assessed	Duration of follow-up
	Quality: fair		n/a Group A N = 29 (19 female, 10 male) Mean BMI = 43.1 kg/m^2 (range 39.5–51.7) Mean age = 38 years Group B N = 27 (19 female, 8 male) Mean BMI = 43.0 kg/m^2 (range 37.2–49) Mean age = 39 years Group C N = 31 (21 female, 10 male) Mean BMI = 43.6 kg/m^2 (range 39–47.3) Mean age = 39 years	Group A Standard gastroscope and rat-toothed forcep Group B Standard gastroscope and retrieval snare Group C Double-channel gastroscope and rat-toothed forcep plus symmetrical 'shark model' polypectomy snare	Exclusion n/a	the removal of the balloon	
(Ganesh et al 2007) Singapore	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 20 (17 female, 3 male) Mean BMI = 31.5 kg/m^2 (range 28–39) Mean age = 40 years (range 28–52) Co-morbidities Orthopaedic (65%), diabetes mellitus (5%), hypertensive (10%), hyperlipidaemia (15%), respiratory problems (20%)	BIB + 1,000 kcal diet	Inclusion BMI > 32.5 kg/m^2 or BMI > 27.5 kg/m^2 with significant co-morbidities Exclusion Peptic ulcer disease, large hiatus hernia	Safety Adverse events Effectiveness Weight loss, excess weight loss	1 year (6 months BIB)
(Genco et al 2005) Naples, Italy	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 2,515 (1,793 female, 722 male) Mean BMI = 44.4 kg/m^2 (range 28–79.1) Mean age = 38.9 years Co-morbidities Hypertension (509 patients, 36.5%), diabetes (488 patients,	BIB + 1,000 kcal diet + medical therapy	Inclusion Patients who meet the NIH criteria and guidelines for bariatric surgery Exclusion Physical inability to maintain regular follow-up, problems precluding safe endoscopy,	Safety Adverse events Effectiveness Mortality, change in BMI, excess weight loss	6 months

Study and location	Level of evidence and quality assessment	Study design	Study population	Intervention	Inclusion/exclusion criteria	Outcomes assessed	Duration of follow-up
			35%), respiratory disorders (247 patients, 17.7%), osteo-arthropathy (271 patients, 19.4%), dyslipidaemia (318 patients, 22.8%), others (176 patients, 12.6%)		oesophagitis (grade 1), hiatal hernia (> 5 cm), chronic therapy with steroids, non-steroidal anti-inflammatory drugs, or anticoagulants, active peptic ulcer or its previous complications, previous GI resections, structural abnormalities of the GI tract, lesions considered at risk for bleeding, pregnancy, disorders of eating pattern		
(Genco et al 2006) Naples, Italy	Level II intervention evidence Quality: good	Randomised controlled trial (crossover)	N = 32 (24 female, 8 male) Mean BMI = 43.7 kg/m^2 (range 40–45) Mean age = 36.2 years (range 25–50) Co-morbidities Not stated	Group A (N=16) BIB followed by sham procedure after 3 months (+ 1,000 kcal diet) Group B (N=16) Sham procedure followed by BIB after 3 months (+ 1,000 kcal diet)	Inclusion Low probability of success with non-surgical measures, BMI > 40 kg/m^2 or BMI > 35 kg/m^2 with significant co-morbidities, age between 18 and 55 years, suitable candidate for IGB according to psychologist Exclusion Severe oesophagitis, hiatal hernia > 5 cm, peptic ulcer, Crohn's disease, major psychiatric disease, disorders of alimentary pattern, pregnancy, previous gastric surgery, use of anticoagulants, steroids or NSAIDs, alcoholism, drugs, structural abnormalities of gastrointestinal tract, lesions with increased risk of bleeding, severe liver disease, any contraindication to endoscopy, sibutramine treatment, orlistat treatment	Safety Adverse events Effectiveness Change in BMI, excess weight loss	6 months
(Giardiello et al 2003) Naples, Italy	n/a	Case report	N = 1 female BMI = 37 kg/m^2 Age = 52 years Co-morbidities	BIB + 800 kcal diet + pharmacologic therapy	Inclusion n/a Exclusion n/a	Safety Adverse events	6 months

Study and location	Level of evidence and quality assessment	Study design	Study population	Intervention	Inclusion/exclusion criteria	Outcomes assessed	Duration of follow-up
			Hiatal hernia, moderate hypertension, dyspnoea				
(Herve et al 2005) Liège, Belgium	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 100 (77 female, 23 male) Mean BMI = 34.03 kg/m^2 (range 25.3–60.2) Mean age = 34.8 years Co-morbidities Arterial hypertension (25%), locomotion disorders (28%), lipid disorders (25%), dyspnoea (28%), sleep apnoea (10%), chronic obstructive pulmonary disease (4%), asthma (9%), gastro-oesophageal reflux (12%), oesophagitis (9%), peptic ulcer (5%), diabetes type 1 (3%), diabetes type 2 (24%), depression (14%)	BIB	Inclusion Patients who refuse surgery or who do not meet the IFSO standards for bariatric surgery; super-obese patients who have to reduce the operative risk before surgery (bariatric surgery or other) Exclusion Large hiatal hernia or a large peptic ulcer	Safety Adverse events, technical failure Effectiveness Weight loss, excess weight loss, change in BMI	1 year after BIB removal
(Hodson et al 2001) East Yorkshire, UK	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 10 (9 female, 1 male; 15 balloon placements) Mean BMI = 39 kg/m^2 (range 32–53) Mean age = 33 years Co-morbidities n/a	BIB + 800 kcal diet	Inclusion n/a Exclusion Previous gastric surgery, large hiatal hernia, gastro-oesophageal varices, congenital or acquired telangiectasis, use of aspirin or other gastric irritants, psychiatric disorders, pregnancy	Safety Adverse events, technical failure Effectiveness Weight loss, excess weight loss	6 months
(Iordache 2005)	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 54 (45 female, 9 male) Mean BMI = 32 kg/m^2 (range 24–42) Mean age = 33.1 years Co-morbidities Arterial hypertension and diabetes (18.5%)	BIB	Inclusion BMI 30–35 kg/m^2, BMI 35–40-kg/m^2 for patients that do not accept bariatric surgery, super-obese patients for preoperative weight loss, screening for evaluating the indication for gastric bending, failure of diet and medication for the patients with at	Safety Adverse events, technical failure Effectiveness Change in BMI, change in co-morbidities	6 months

Study and location	Level of evidence and quality assessment	Study design	Study population	Intervention	Inclusion/exclusion criteria	Outcomes assessed	Duration of follow-up
					least 10 kg above the ideal weight Exclusion n/a		
(Iordache et al 2005)	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 40 (32 females, 8 males) Mean BMI = 33 kg/m^2 (range 30–43) Mean age = 35.5 years Co-morbidities n/a	BIB	Inclusion n/a Exclusion n/a	Safety Adverse events Effectiveness Weight loss, change in BMI	6 months
(Kim et al 2000) Warrington, UK	n/a	Case report	N = 1 female BMI = 41 kg/m^2 Age = 38 years Co-morbidities n/a	BIB (placement 9 months ago)	Inclusion n/a Exclusion n/a	Safety Adverse event	n/a
(Loffredo et al 2001) Naples, Italy	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 77 (54 female, 23 male; 87 balloons) Mean BMI = 46.6 kg/m^2 (range 32.1–73.8) Mean age = 38.2 years Co-morbidities n/a	BIB + diet	Inclusion BMI > 35 kg/m^2, BMI > 30 kg/m^2 with correlated pathologies, reduction of anaesthesia risk (bariatric or other surgery), reduction of disabling disease, BIB-test in sweets-eaters or snackers and binge- or compulsive-eaters Exclusion Active oesophagitis, active gastric or duodenal ulcer, Crohn's disease, cancer, potential or active GI bleeding, alcoholism or drug addiction, large hiatal hernia (> 5 cm), prior gastric or intestinal resection, patients on anticoagulants or gastric irritants, psychiatric disorders Relative exclusion included oesophagitis, gastric or duodenal peptic disease and helicobacter	Safety Adverse events Effectiveness Weight loss, change in BMI, excess weight loss	Until removal of the BIB (3–6 months)

Study and location	Level of evidence and quality assessment	Study design	Study population	Intervention	Inclusion/exclusion criteria	Outcomes assessed	Duration of follow-up
					pylori infection		
(Martinez-Brocca et al 2007) Seville, Spain	Level II intervention evidence Quality: fair	Randomised controlled trial	N = 22 (17 female, 5 male) Mean BMI = 50.4 kg/m^2 (± 7.8) Mean age = 35.9 years Co-morbidities group BIB (group sham) % Diabetes mellitus 27.3 (36.4), hypertension 27.3 (36.4), dyslipidaemia 54.5 (72.7), metabolic syndrome 36.4 (54.5), sleep disordered breathing 27.3 (0), osteoarthropathy 27.3 (45.5), coronary heart disease 9.1 (0), thyroid dysfunction 9.1 (9.1)	BIB + low-fat hypocaloric diet Comparator Sham balloon placement	Inclusion Candidates for bariatric surgery, failure to sustain weight loss within a supervised weight-control program, agreement with the follow-up controls Exclusion Severe GI or hepatic disease, previous gastrointestinal surgery, structural abnormalities of gastrointestinal tract (hiatal hernial > 5 cm) and/or lesions with increased risk of bleeding (varices, peptic ulcer or > 3 gastric erosions assessed by endoscopic evaluation), persistent *Helicobacter pylori* infection defined as positive urea breath test in spite of proton-pump-inhibitor-based triple therapy, chronic therapy with steroids, NSAIDs or anticoagulants, therapy with sibutramine, orlistat, selective serotonin reuptake inhibitors, antidepressants, neuroleptics and/or antihistaminic drugs	Effectiveness Weight loss, excess weight loss, change in BMI, change in waist circumference, change in fat mass	4 months
(Mathus-Vliegen & Tytgat 2005) Amsterdam, The Netherlands	Level II intervention evidence Quality: good	Randomised controlled trial	N = 43 (36 female, 7 male) Mean BMI = 43.3 kg/m^2 (range 33.9–61.3) Mean age = 41.4 years Co-morbidities n/a	BIB + 1,000–1,500 kcal diet + exercise Group 1 (N=23) sham balloon placement for the first 3 months; followed by a balloon every 3 months for the remainder of the first	Inclusion Age 18 years or older, failure to achieve weight loss within a supervised weight-control program, BMI of at least 32 kg/m^2 (fluctuation of no more than one BMI unit over the previous 4 months) Exclusion A hormonal or genetic cause for	Safety Adverse events, technical failure Effectiveness Weight loss, change in co-morbidities	2 years

Study and location	Level of evidence and quality assessment	Study design	Study population	Intervention	Inclusion/exclusion criteria	Outcomes assessed	Duration of follow-up
				year (3 balloons) Group 2 (N=20) Balloon placement every 3 months for one year (4 balloons)	the obese state, malignancy within the previous 5 years, pregnancy or a desire to become pregnant, alcoholism, drug abuse, GI lesions (eg a large (> 3 cm), hiatal hernia, grade C–D oesophagitis, peptic ulceration, varices or angiectasias), abdominal surgery, patients unable to cooperate at endoscopy, patients whose general health would preclude surgery, use of antiobesity drugs, anticoagulants and NSAIDs		
Melissas et al, 2006 Paphos, Cyprus	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 140 (106 female/ 34 male) Mean BMI = 42.3 kg/m^2 (range 35–61.3) Mean age = 38 years Co-morbidities n/a	BIB + 1,000 kcal diet	Inclusion Preoperative preparation of super-obese patients in an attempt to minimise weight and reduce operative risk, contraindications to bariatric surgery, ie aged > 70 years, BMI 30–35 kg/m^2 with severe obesity co-morbidities, morbidly obese patients with BMI ≥ 35 kg/m^2 refusing conventional surgical treatment because of fear of complications and/or mortality Exclusion n/a	Safety n/a Effectiveness Excess weight loss, weight loss, change in BMI	6–30 months after balloon removal
(Mion et al 2005) Lyon France	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 17 (14 female, 3 male) Mean BMI = 34.4 kg/m^2 (range 30.1–40.0) Mean age = 34.9 years Co-morbidities Gastric ulcers related to *Helicobacter pylori* gastritis in one patient (therefore excluded)	BIB + 1,300 kcal diet	Inclusion BMI > 30 kg/m^2 and ≤ 40 kg/m^2, age > 18 years and < 60 years Exclusion n/a	Safety Adverse events Effectiveness Weight loss, change in BMI	1 month after balloon removal

Study and location	Level of evidence and quality assessment	Study design	Study population	Intervention	Inclusion/exclusion criteria	Outcomes assessed	Duration of follow-up
(Mion et al 2007) Lyon, France	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 32 (27 female, 5 male) Mean BMI = 35 kg/m^2 (range 30.1–40.0) Mean age = 35 years Co-morbidities n/a	Heliosphere + 1,300 kcal diet	Inclusion Failed previous attempts to lose weight by dietary restrictions Exclusion Previous digestive surgery (except for gallbladder removal and appendectomy), past history of gastric ulcer, or presence of a large hiatal hernia, severe oesophagitis (≥ class B of Los Angeles classification) or severe gastritis at the time endoscopy	Safety Adverse events, technical failure, endoscopic difficulties Effectiveness Weight loss, change in BMI, change in co-morbidities	1 year
(Mui et al 2006) Hong Kong SAR, China	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 15 (10 female, 5 male) Mean BMI = 40.5 kg/m^2 (range 29.6–56.9) Median age = 40 years Co-morbidities obstructive sleep apnoea syndrome (40%), diabetes mellitus (20%), hypertension (40%), degenerative joint problems with knee pain (46.7%)	BIB + 1,200 kcal diet +150 minutes/week moderately intense exercise	Inclusion Age 18–65 years, long history of obesity (> 5 years), failed previous conservative weight reduction therapy (lifestyle and pharmacotherapy), BMI > 50 kg/m^2 as a pre-surgical treatment to minimise surgical risk OR BMI > 37 kg/m^2 who are not suitable candidates or reluctant for obesity surgery OR BMI > 30 kg/m^2 with repetitive failure of previous weight reduction therapy and are not recommended for obesity surgery OR BMI < 30 kg/m^2 with obesity-related diseases with repetitive failure of previous weight reduction therapy Exclusion Secondary cause of obesity, not compliant to clinician or dietician advice for follow-up, presence of contraindications like active peptic ulcer disease, previous upper gastrointestinal surgery, large hiatus hernia, active psychiatric	Safety Adverse events Effectiveness Weight loss, excess weight loss, change in BMI, waist circumference loss	n/a

Study and location	Level of evidence and quality assessment	Study design	Study population	Intervention	Inclusion/exclusion criteria	Outcomes assessed	Duration of follow-up
					illness or drug addiction, alcoholism, pregnancy or breastfeeding		
(Nijhof et al 2006) Leiden, The Netherlands		Case report	N = 1 female BMI = 43 kg/m^2 Age = 49 years Co-morbidities n/a	BIB	Inclusion n/a Exclusion n/a	Safety Adverse events	n/a
(Puglisi et al 2005) Bari, Italy		Case report	N = 1 (male) BMI = 49 kg/m^2 Age = 39 years Co-morbidities Diabetes, mild arterial hypertension, osteoarthritis	BIB	Inclusion Not stated Exclusion Not stated	Safety Adverse events	6 months
(Puglisi et al 2007) Bari, Italy	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 75 (63 female, 12 male) BMI range = 39–55 kg/m^2 Mean age = 39.5 years BE group N = 27 (24 female, 3 male) Mean BMI = 44.7 kg/m^2 Mean age = 38 years NBE group N = 48 (39 female, 9 male) Mean BMI = 47.6 kg/m^2 Mean age = 39 years Co-morbidities n/a	BIB + 1,000 kcal diet	Inclusion n/a Exclusion n/a	Safety Adverse events Effectiveness Change in BMI, change in weight	9 months
(Roche-Nagle et al 2003) Dublin, Ireland		Case report	N = 1 female Age = 46 years Co-morbidities n/a	BIB	Inclusion n/a Exclusion n/a	Safety Adverse events	n/a
(Roman et al 2004) Lyon, France	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 176 (161 female, 15 male) Mean BMI = 31 kg/m^2 (range 27–40)	BIB	Inclusion Failed to achieve weight loss on an adequate weight control	Safety Adverse events, technical failure	4 and 6 months

Study and location	Level of evidence and quality assessment	Study design	Study population	Intervention	Inclusion/exclusion criteria	Outcomes assessed	Duration of follow-up
			Mean age = 37.4 years Co-morbidities Diabetes mellitus (2.8%), arterial hypertension (6.8%), hypothyroidism (4.5%), depression (2.3%), grade I oesophagitis and/or small hiatal hernia (14.2%), gastritis or duodenitis (5.1%), mycotic oesophagitis (0.6%), oesophageal papilloma (0.6%)		program Exclusion Large hiatal hernia, gastric or duodenal ulcer, prior gastric or intestinal surgery	Effectiveness Weight loss, excess weight loss	
(Sallet et al 2004) São Paulo, Brazil	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 323 (196 female, 127 male) Mean BMI = 38.2 kg/m^2 Mean age = 37.5 years Co-morbidities Hypertension (31.6%), arthropathies (22%), hyperlipemia (13.3%), sleep apnoea (10.8%), diabetes (10.8%), cardiovascular disease (9.6%)	BIB + 1,000 kcal diet + clinical, psychiatric, physical training	Inclusion n/a Exclusion n/a	Safety Adverse events Effectiveness Weight loss, excess weight loss, change in BMI	6 months after BIB placement
(Spyropoulos et al 2007) Rion, Greece	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 26 (3 female, 23 male) Mean BMI = 65.3 kg/m^2 Mean age = 40.8 years Co-morbidities Hypoventilation syndrome (50%), sleep apnoea syndrome (81%), pickwick syndrome (11.5%), insulin-dependent type 2 diabetes mellitus (69%), hypertension (27%), deep vein thrombosis/ venous stasis disease (46.1%),	BIB + diet	Inclusion A BMI of ≥ 50 kg/m^2 and the presence of ≥ 3 risk factors Exclusion n/a	Safety Adverse events Effectiveness Weight loss, change in BMI, change in excess weight loss, change in co-morbidities	6 months after BIB placement
(Totte et al 2001) Antwerp, Belgium	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 126 (121 female, 5 male) Mean BMI = 37.7 kg/m^2 (range 26.7–57.7)	BIB + 800 kcal diet	Inclusion Patients refusing surgery or not meeting the IFSO standards for	Safety Adverse events,	6 months after BIB placement

Study and location	Level of evidence and quality assessment	Study design	Study population	Intervention	Inclusion/exclusion criteria	Outcomes assessed	Duration of follow-up
			Mean age = 35.6 years Co-morbidities Locomotor problems like pain in low back, ankle, feet (11.9%), arterial hypertension (3.2%), dyspnoea on effort (47.6%), depression (9.5%)		operation Exclusion Structural abnormalities in the oesophagus, such as strictures or diverticula; large hiatal hernia; potential upper gastrointestinal bleeding such as oesophageal or gastric varices, or congenital or acquired telangiectasis; congenital abnormalities of the gastrointestinal tract, such as atresia or stenosis; prior gastric or intestinal surgery; aspirin, anti-inflammatory agents, or other gastric irritants; alcoholism or drug addiction; psychiatric disorders; unwillingness to participate in a medically supervised diet and behaviour modification program; pregnancy or breastfeeding Peptic disease (oesophagitis, gastric or duodenal erosions, gastric or duodenal ulcer) and Helicobacter pylori infection requires specific pharmacologic therapy before undergoing BIB placement	technical failure Effectiveness Weight loss, excess weight loss, change in BMI	
(Vanden Eynden & Urbain 2001) Baudour, Belgium		Case report	N = 1 female BMI = 34.4 kg/m^2 Age = 48 years Co-morbidities Severe arthritis of both knees	BIB	Inclusion n/a Exclusion n/a	Safety Adverse events	n/a
(Vandenplas et al 1999) Brussels, Belgium	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 5 (3 female, 2 male) Mean age = 14.1 years Co-morbidities Hypertension, genu valgum,	BIB + hypocaloric diet + physical activity	Inclusion Failed previous attempts to loose weight with hypocaloric diet, physical activity, group programmes etc	Safety Adverse events Effectiveness Change in BMI	6 months after BIB placement

Study and location	Level of evidence and quality assessment	Study design	Study population	Intervention	Inclusion/exclusion criteria	Outcomes assessed	Duration of follow-up
			hypercholesterolaechima, orthopaedic abnormalities		Exclusion Pathology of the mucosa of the oesophagus, stomach and duodenum		
(Weiner et al 1999) Frankfurt, Germany	Level IV intervention evidence Quality: good	Case series pre-test/post-test	N = 15 (7 female, 8 male) Mean BMI = 60.2 kg/m^2 (range 46.6–72.0) Mean age 38.8 years Co-morbidities Pulmonary diseases (46.7%), sleep apnoea (26.7%)	BIB + LAGB	Inclusion Patients with a BMI > 60 kg/m^2 and an extreme abdominal fat deposition Exclusion Not reported	Safety Adverse events Effectiveness Weight loss	4–7 months

BMI = body mass index; BIB = BioEnterics intragastric balloon; LAGB = laparoscopic adjustable gastric banding; BE = binge eating; NBE = not binge eating; LSG = laparoscopic sleeve gastrectomy; GI = gastrointestinal; NSAIDs = non-steroidal anti-inflammatory drugs

Appendix J Excluded studies

Irrelevant population

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Abbreviations

ARTG	Australian Register of Therapeutic Goods
BIB	BioEnterics intragastric balloon
BE	binge eating
BMI	body mass index
EWL	excess weight loss
GI	gastrointestinal
IGB	intragastric balloon
LAGB	laparoscopic adjustable gastric banding
LSG	laparoscopic sleeve gastrectomy
MSAC	Medical Services Advisory Committee
MBS	Medicare Benefits Schedule
NBG	non-binge eating
NHMRC	National Health and Medical Research Council
NSAIDs	non-steroidal anti-inflammatory drugs
PBS	Pharmaceutical Benefits Scheme

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