

Endoscopy for Primary Treatment of Obesity

by James M Stewart, Camron Kiafar

Obesity is a major health concern in the developed world. It complicates many illnesses and its reduction offers a major opportunity for health impact. Currently, treatment for obesity relies on lifestyle modification, pharmacotherapy, endoscopic and surgical options. Endoscopic therapies offer reversibility, minimal invasion, and same day treatment options but are not commonly used in the United States. However, endoscopic therapies are used elsewhere in the world leading to some Americans to seek healthcare abroad. Some endoscopic therapies are very new and are still under active investigation. The existing endoscopic therapies are space occupying intragastric balloons, duodenal barrier sleeves, caloric removal via gastric tube, and botulinum toxin to reduce gastric motility.

BACKGROUND

Obesity has increased significantly in the United States in the last 50 years and is a major contributor to rising health care costs. The majority of this increase has occurred since 1990 and seems to be stabilizing at a prevalence of 25-35% of the US adult population, depending on the survey¹ (see Figure 1). The CDC estimates that obesity is directly responsible for \$147,000,000,000² in healthcare costs and representing anywhere between 3-8% of healthcare costs in various countries.³ The diseases directly related to obesity include diabetes type II, hyperlipidemia, cardiovascular diseases, hypertension, kidney disease, gallbladder disease, liver disease including cirrhosis, GERD, colorectal, breast and prostate cancer, polycystic

ovarian syndrome, neonatal complications, sleep apnea and depression. While research into obesity has demonstrated a complicated web of hormonal signals and neuropathways, the driving force behind the increase in obesity has been an increase in caloric intake and a decrease in physical activity leading to surplus in daily calories. Other factors such as the intrauterine environment,⁴ formula feeding,⁵ genetics,⁶ medications, and possibly viruses,⁷ are thought to also contribute to obesity. Obesity also varies by race, gender, and socioeconomic status.^{8,9}

Combating this epidemic has largely focused on methods that decrease caloric intake by either increasing satiety or blocking absorption of nutrients. Medical therapies have largely been underwhelming but there are four FDA approved medications for weight loss for the obese. Orlistat inhibits the action of pancreatic

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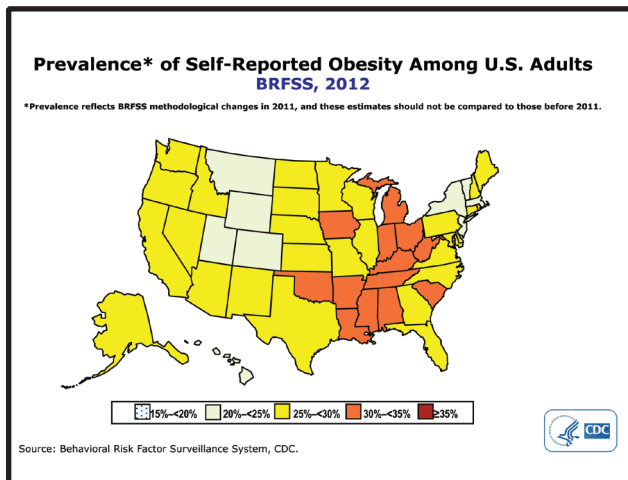


Figure 1. Prevalence of Self-Reported Obesity Among U.S. Adults BRFSS, 2012

lipases which prevents uptake of fatty acids and can lead to a 10% decrease in body weight (placebo lost 6%).¹⁰ Sibutramine, an SSRI/norepinephine inhibitor, acts to increase satiety and has been shown to cause around an 8% body weight loss but is limited by side effects on blood pressure and pulse.¹¹ In 2012 two new drugs, Qsymia (Phenteramine + topiramate) and Belviq (lorcaserin) both received FDA approval for weight loss. These medicines also act to increase satiety and offer modest weight loss over lifestyle therapy.

Surgical therapies for weight loss have been much more effective and remain the mainstay of treatment for morbid obesity at this time. Excess weight loss of ~50% can be expected after two years following bariatric surgery with proven reduction or resolution in blood pressure, diabetes, and hyperlipidemia. However, bariatric surgery carries increased cost, morbidity and mortality relative to medical therapy. Several different surgical procedures exist and most common bariatric surgery in the United States is the Roux-en-Y Gastric Bypass which combines both restrictive and malabsorptive/neurohormonal strategies. Laparoscopic Adjustable Gastric Band and Vertical Banded Gastroplasty both increase satiety by decreasing stomach volume. Biliopancreatic Diversion with Duodenal Switch decreases the effective absorptive area and alters the neurohormonal balance to increase satiety.

Curiously absent in the battle against obesity has been the gastroenterologist. This has not been for lack of trying as endoscopic treatments for obesity were

first explored in the 1980s. Some are predicting that gastroenterologists' role in obesity management will mirror that of the interventional cardiologist relative to the cardiothoracic surgeon with regards to offering a less invasive management option than surgery. However, the therapies that have been tried have largely been underwhelming and fraught with complications. As therapies improve, many have speculated that gastroenterology will play an increasing role in obesity management as therapies improve.¹²

Space Occupying Balloons

The first endoscopic therapy attempts to manage obesity were in 1982¹³ using an inflatable balloon that was placed in the stomach. The theory was that decreasing the accommodation of the stomach would cause early satiety and lead to decreased caloric intake. Early studies showed that ghrelin levels decreased in those with balloons corresponding to the increased sensation of satiety. The first balloons brought out only modest weight loss and sham studies were shown not to be superior to aggressive diet.¹⁴ Additionally, the early balloons suffered from a high degree of complications and spontaneous rupture. Further developments in intragastric balloons were made and currently the most commonly used balloon worldwide is the BioEnterics Intragastric Balloon or BIB. The deflated balloon is loaded onto a catheter and then blindly passed into the stomach. An EGD scope is then inserted alongside the balloon catheter to confirm position and placement. A needle is passed through the scope and 400–600ml of saline (often mixed with methylene blue) is injected into the filling port of the balloon. The balloon is then detached from the catheter and the EGD and catheter are removed (See Figure 2). Methylene blue, if used, is an indicator of balloon ruptures as it will dye the urine after being absorbed into the body.

While not FDA approved for US use, it is used elsewhere and has been well studied. The first large testing was done in Italy between 2000 and 2004.¹⁵ In this retrospective study, over 2500 patients had the BIB placed for 6 months with instructions on a 1000k cal diet and then the balloon was removed. The pre-placement BMI was 44.4 and the post-removal BMI was 35.4 with an extra body weight loss of 34%. Placement was successful in 99.2% of attempts. Side effects included balloon rupture (0.36%), gastric obstruction (0.76%), esophagitis (1.3%) and gastric ulcer (0.2%). There were five gastric perforations which resulted in two deaths.

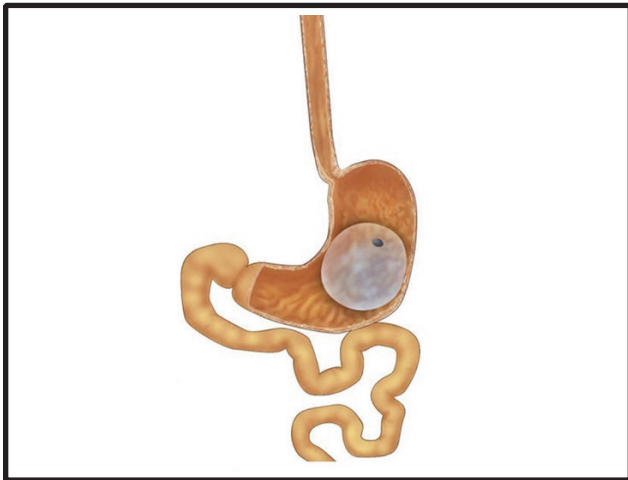


Figure 2. Intra-gastric Balloon Inflated in the Stomach

Four of the five patients with perforation had prior gastric surgery which suggested a contraindication to balloon placement.

The same authors also led a much smaller study which was a prospective double-blind, randomized, controlled with cross-over study.¹⁶ Group A had the BIB placed for three months followed by a sham procedure for three months. Group B had a sham procedure for three months followed by BIB for three months. Group A had significant weight loss within the first three months (BMI 43.5 to 38.0) and was able to maintain it following BIB extraction. Group B had no change in weight during the first three months (BMI 43.6 to 43.1) but lost weight after BIB placement (BMI 43.1 to 38.8). There was no mortality.

While the Italian studies and similar studies in Brazil¹⁷ and Spain¹⁸ demonstrated good short term data, another study by Mathus-Vliegen¹⁹ et al showed less encouraging results. Forty-three patients were enrolled with an average BMI of 43.3 and were divided into two groups. Group A would have the balloon for three months and if they lost weight were given an additional 9 months of balloon treatment. Group B was given a sham treatment for 3 months and if they lost the weight were given 9 months of BIB. Five were excluded for not meeting certain pre-trial weight loss goals and six more were excluded for either not tolerating balloon placement or for developing esophagitis and requesting the balloon be removed. In intention to treat analysis there was no difference in weight loss between group A and group B for the first three months. Once the sham group was given an additional three months of BIB

they lost more weight than the group that had the BIB from the beginning. After the balloon was removed following one year of therapy the average weight loss was 25.6kg for both groups. Follow-up another year later showed that the patients had gained half of the weight lost initially. Their conclusion was that the BIB was safe and led to weight loss although they did not see a significant benefit compared to sham in the first three months. After three months there was mild but significant weight loss.

The goal of any weight loss procedure is to achieve durable weight maintenance and a small study evaluated the long term weight trends of one hundred patients treated with six months of BIB.²⁰ The average pre-balloon BMI was 35kg/m² and after six months of therapy with the BIB, it was removed. They were not given any weight loss guidance in an attempt to measure just the balloon's effect. Average weight loss was 12.6kg and about 63% of the patients had >10% of baseline weight loss. After one year the group had gained 4.2kg back and at 2 years another 2.3kg. At 30 months after BIB placement only 24/100 patients had maintained weight loss >10%. Following intention to treat analysis, by the end of the study (4.8 years \pm 1.6 years post balloon) 28/100 patients had maintained >10% weight loss. Thirty five patient had gone on to bariatric surgery, three were lost to follow-up, and the remaining thirty four patients who had failed to maintain >10% baseline weight loss had a weight loss of 1.5kg (\pm 5.8kg). The authors' conclusion was that BIB was an effective option that provides durable weight loss in around 25% of patients.

Currently, the BIB is indicated for only six months of continuous use. The Italian group led by Genco et al designed a study that looked at the safety and efficacy of placing sequential balloons compared to a group that only had one balloon followed by diet.²¹ They took 100 patients (1:4 male:female) and randomized half of the group to receive a balloon for six months and then get seven months of diet therapy while the other group received six months of balloon therapy, one month without a balloon, and another six months of balloon therapy. Baseline BMI for both group was 42.6 and 42.9 respectively. After six months of balloon therapy both groups had achieved a BMI of 34.2 and 34.8 respectively. At the end of the study group A (one balloon followed by diet) had a mean BMI of 35.9 and the group B (two sequential balloon treatments)

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achieved a mean BMI of 30.9 ($p < 0.05$). There were no complications in either group.

Combination therapy with intragastric balloons and pharmacotherapy has been studied to boost the effect of the balloon. Farina et al.²² recently published their trial involving a small group of obese patients who were randomized to balloon therapy plus lifestyle modification with or without pharmacotherapy for one year. The group initially had the BIB for six months and then were randomized to either pharmacotherapy or lifestyle modification. A control group of patients who just received lifestyle modification with pharmacotherapy was also used. The subset that received the balloon had significantly more weight loss than the pharmacotherapy alone group (37.7% EBL vs 25.3% EBL). At one year, the group that had balloon therapy for six months followed by six months of pharmacotherapy had significantly more weight loss compared to pharmacotherapy only. The balloon+pharmacotherapy group lost 41.3% EBL, balloon+lifestyle lost 34.9% EBL, and the pharmacotherapy only group lost 22.1% EBL.

As durable weight loss remains a question with balloons, studies have assessed it as a bridge therapy to bariatric surgery in patients unsure of surgery or thought too obese for surgery. A Greek study²³ published in 2006 took 140 obese patients with a median BMI of 42 kg/m² who had previously refused bariatric surgery out of fear of complications. They were all given the BIB for 6 months and then followed for another 24 months. Seventy-one percent of the patients given the balloon had lost >25% of their calculated excess body weight. Forty percent of this group regained their weight during follow-up while 56% maintained their weight loss. Thirty-two percent of the total 140 patients eventually underwent some form of bariatric surgery. The vast majority of those that accepted surgery were from the group that failed to lose weight from the BIB or those that regained their weight after balloon extraction.

Another small study looked at super-morbid obese patients who had high risk factors to undergo weight loss surgery.²⁴ Twenty-six patients with average BMI of 65 kg/m² were given the BIB for six months in an attempt to decrease the risk factors of bariatric surgery. One patient died of cardiac arrest following an aspiration event the day after balloon placement. Twenty of the twenty-six patients lost enough weight that they were able to proceed with bariatric surgery

the day after balloon extraction.

Other studies have shown that intragastric balloons do decrease NASH scores on hepatic biopsies after six months which represents a novel treatment for NASH.²⁵ While the BIB is the most common, other balloons in development focus on delivery systems that can be deployed without endoscopy,^{26,27} or on filling the balloon with air.²⁸ Advantages of balloon therapy include quickness in placing the balloon and relative safety.

United States FDA approval is pending for intragastric balloons. It was denied in 2007 after a Cochrane review of nine randomized trials came to the conclusion that weight loss was not convincingly better than focused lifestyle modification and they could not recommend it above eating and behavioral modification.²⁹ One confounder was that the studies had difficulty separating out the balloon effect from weight loss by lifestyle modifications in motivated patients involved in the studies.

Intestinal Barrier Sleeves

Decreasing the absorptive surface of digestion decreases absorption of calories but has also been shown to alter gut hormones which helps decrease weight.³⁰ Restrictive surgeries such as the vertical banded gastroplasty and gastric bypass are proof that this method of weight loss is effective.

The first endoscopic device tried in humans was the Endobarrier made by GI Dynamics (See Figure 3). It is about 60 cm long and is endoscopically anchored in the duodenal bulb. The sleeve is passed over a guidewire so that it rests in the proximal jejunum thus inhibiting mixing of the stomach contents with pancreatic and biliary secretions. The first human study was published in 2008 and consisted of 12 patients with an average BMI of 42.³¹ Average time to implant the device was 26 minutes and average time of explantation was 43 minutes. Ten of the 12 patients were able to complete a 3-month trial of the Endobarrier sleeve and lost about 28% of their excess body weight.

One of the first randomized trials was published in 2010 from the Netherlands.³² In this study, 41 patients were recruited and randomized such that 30 patients received 12 weeks of Endobarrier sleeve and 11 patients were treated with diet counseling. The BMI in the treatment group was 48.9 and the diet group was 47.4 but this was insignificant. Twenty-six out of thirty patients had Endobarrier sleeve successfully placed

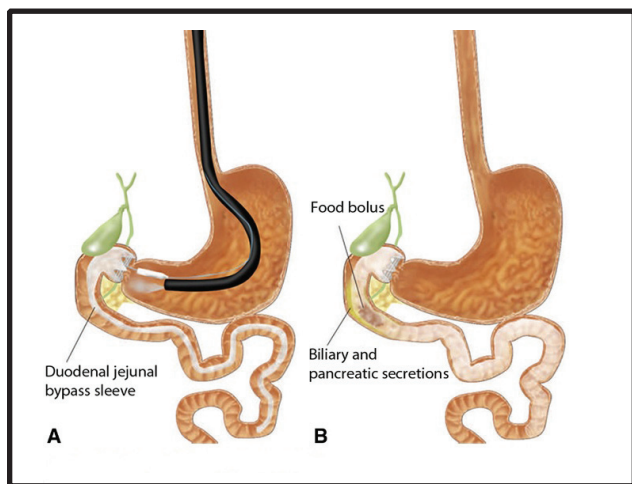


Figure 3. Placement of Intestinal Barrier Sleeve

with an average time of 35 minutes (12-102 minutes) for implantation. Four of these patients had to have the device removed prior to 12 weeks of therapy due to sleeve obstruction, sleeve migration, dislocation of the anchor, and continuous epigastric pain. All 26 patients who had the sleeve had at least one adverse event which was mainly abdominal pain or nausea. The twenty two patients that completed the 12 week trial saw an average excess body weight reduction of 19% compared to just 6.9% for the diet group. Hgb1ac was improved in diabetics that completed the trial with Endobarrier sleeve. Endoscopic time to remove the device was 17 minutes (5-99 minutes).

One of the only randomized sham controlled trial to be done on the Endobarrier was published in 2010.³³ In this study, 21 morbidly obese patients were randomized to have 12 weeks of the duodenal bypass sleeve and 26 patients were randomized to a sham procedure. Eight (41%) of the sleeve patients had to have the sleeve removed prematurely for GI bleeding, abdominal pain, nausea/vomiting, or an unrelated pre-existing illness. Comparing the remaining 13 patients who had the sleeve placed to the 26 sham control group, the excess weight loss was 11.9% to 2.7% ($p < 0.05$). Over 62% of the sleeve group achieved >10% of EWL compared to only 17% of the sham group. This study showed significance above sham trials but was still limited in its small number and the fact that the study personnel were not blinded.

A similar device studied in humans is the ValenTx barrier sleeve. This sleeve is longer (120cm) and anchors in the gastric cardia effectively bypassing the stomach as well as the duodenum. This makes it function more

like a roux-en-Y gastric bypass. The only published study looked at 24 morbidly obese patients recruited between 2008 and 2010.³⁴ The average BMI of the group was around 42 kg/m.² Twenty two of the 24 patients had the gastroduodenal bypass sleeve placed and 17/22 completed the 12 weeks of therapy. Average weight loss of the 17 patients was 39.7% of their excess body weight and there were no major complications from the procedure. Four out of four patients with elevated HgbA1c at the beginning of the trial had improved A1c scores by the end. However, this was not a randomized controlled study and further studies are needed.

Duodenal bypass sleeves offer some promise but are limited by side effects from placement of the sleeve. These side effects include failure of around 20% of patients to tolerate the sleeve due to pain or nausea as well as lesser degrees of bleeding from the anchoring site, sleeve migration, and sleeve obstruction. Additionally, no long term studies have concluded that check for durable response or the possibility of repeat sleeve placement if feasible.

Aspiration Therapy

In December 2013 a pilot study of an endoscopically placed aspiration tube was published³⁵ (See Figure 4). This study randomized 18 obese patients in a 1:2 fashion to either have lifestyle therapy (LT) training versus an endoscopically placed aspiration tube (AspireAssist (Aspire Bariatrics, King of Prussia, PA) that would assist in emptying stomach contents 20 minutes after a meal. The aspiration tube (A-tube) is placed in the usual fashion as a PEG tube but has a long fenestrated intragastric portion as well a skin port. When it is time to aspirate, a connector is attached to the skin port and water is flushed into the stomach and then aspirated into a companion reservoir that is then emptied. While the study was small there were no statistically significant differences between the LT and AT groups in age, BMI or relevant lab values. After one year 10 patients in the aspiration therapy arm and 4 patient in the lifestyle therapy arm presented for follow-up. Average % TBW [loss] was 18.6 [%] in the AT group vs 5.9% in the LT group. Adverse events in the AT group included mild/moderate abdominal pain (improved with tube redesign), mild peristomal bleeding, mild peristomal infection, mild constipation or diarrhea, and one persistent fistula after A-tube removal. All problems were treated conservatively. There were no hospitalizations required in any of the study subjects.

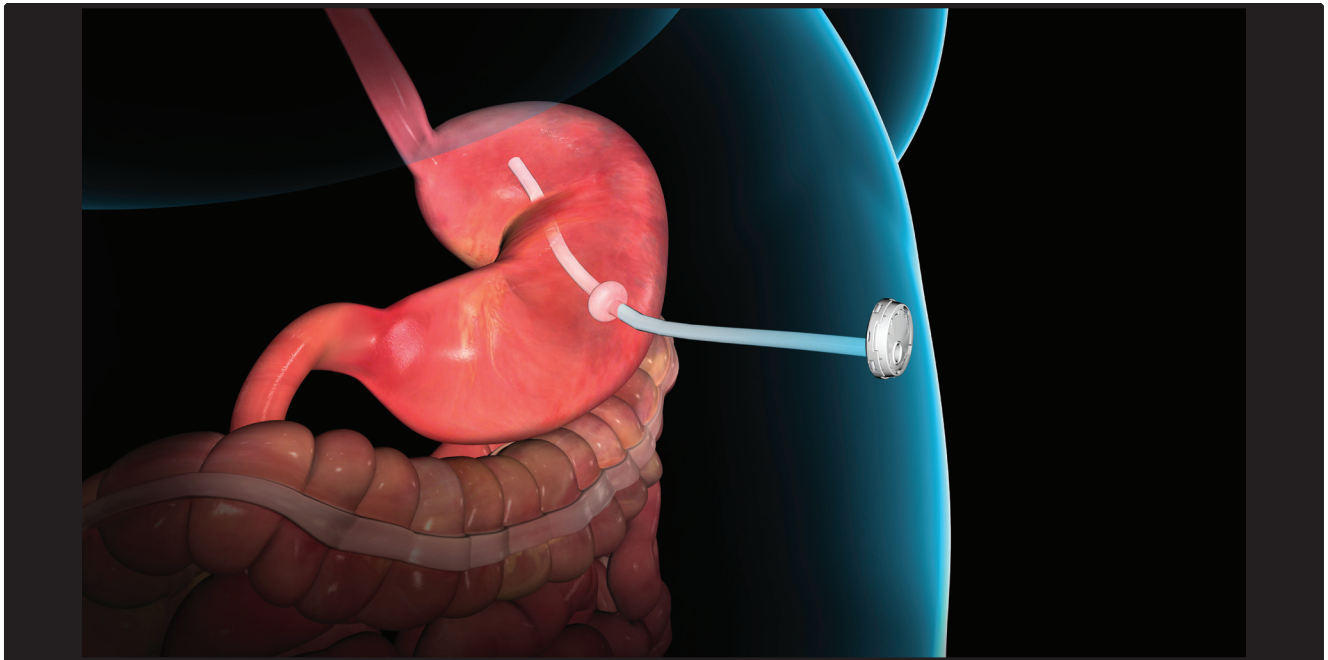


Figure 4. A representation of the AspireAssist device with gastric port flush with the abdomen allowing aspiration of gastric contents after a meal. (Photo used with permission from Aspire Bariatrics.)

Botulinum Toxin Injection

Several studies have assessed the effect of injecting botulinum toxin into the gastric muscles. The idea is that reducing the stomach's ability to empty foods will alter the gastric hormones and prolong the feeling of satiety. An initial pilot study in 2005, which injected botulinum toxin A 100u into the gastric antrum only, did not significantly decrease weight or solid gastric emptying time at 4 and 12 weeks.³⁶ However, Foschi et al found that injecting botulinum toxin 120u into the antrum AND 80u into the fundus led to small but significant decreases in weight and increases in gastric emptying time.³⁷ The group injected with botulinum lost 11.8kg after 2 months compared to 5.5kg in a control group injected with saline in both the antrum and fundus. The solid gastric emptying time increased from 83.4 minutes to 101.6 minutes with no change in the saline group. This study helped pave the way for further studies where botulinum is injected in both the antrum and the fundus. Further studies have demonstrated decreased levels of ghrelin and PYY³⁸ and no study patient has experienced any severe complications.

To date no large, randomized, prospective, sham controlled trial has been done on intragastric botulinum injections.

CONCLUSION

Primary endoscopic treatment for obesity is in its infancy but while some therapies have shown promising results, better therapies are needed to overcome the problems of lack of durability, moderate to severe side effects, time and technical skills required, and complications. For the foreseeable future, bariatric surgery will remain the most effective management of obesity. As we gain further insight in the neurohormonal gut-brain axis, medical therapies may become predominant. ■

References

1. Ogden CL, Carroll MD, Curtin LR, Lamb MM, Flegal KM. Prevalence of high body mass index in US children and adolescents, 2007–2008. *JAMA* 2010; 303(3):242–9.
2. Finkelstein EA, Trogon JG, Cohen JW, and Dietz W. Annual medical spending attributable to obesity: Payer- and service-specific estimates. *Health Affairs* 2009; 28(5): w822-w831.
3. Finkelstein EA, Fiebelkorn IC, Wang G. State-level estimates of annual medical expenditures attributable to obesity. *Obes Res* 2004; 12:18-24.
4. Toschke AM, Ehlin AG, von Kries R, et al: Maternal smoking during pregnancy and appetite control in offspring. *J Perinat Med* 2003; 31:251-256.
5. Harder T, Bergmann R, Kallischnigg G, Plagemann AL: Duration of breastfeeding and risk of overweight: A meta-analysis. *Am J Epidemiol* 2005; 162:397-403.

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6. Rankinen T, Zuberi A, Chagnon YC, et al: The human obesity gene map: The 2005 update. *Obesity* (Silver Spring) 2006; 14:529-644
7. Dhurandhar NV, Kulkarni PR, Ajinkya SM, et al: Association of adenovirus infection with human obesity. *Obes Res* 1997; 5:464-469.
8. McLaren L. Socioeconomic status and obesity. *Epidemiol Rev* 29:29-48, 2007.
9. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among United States adults, 1999-2008. *JAMA* 303:235-41, 2010.
10. Sjöström L, Rissanen A, Andersen T, et al: Randomised placebo-controlled trial of orlistat for weight loss and prevention of weight regain in obese patients. European Multicentre Orlistat Study Group. *Lancet* 1998; 352:167-172
11. Bray GA, Blackburn GL, Ferguson JM, et al: Sibutramine: A dose-ranging and long-term efficacy study in the treatment of obesity. *Obes Res* 1999; 7:189-198
12. Austin GL, Fennimore B, Ahnen DJ. Can colonoscopy remain cost-effective for colorectal cancer screening? The impact of practice patterns and the Will Rogers phenomenon on costs. *Am J Gastroenterol*. 2013 Mar;108(3):296-301
13. Nieben OG, Harboe H. Intra-gastric balloon as an artificial bezoar for treatment of obesity. *Lancet*. 1982;1:198-199
14. Hogan RB, Johnston JH, Long BW, Sones JQ, Hinton LA, Bunge J, Corrigan SA. A double-blind, randomized, sham-controlled trial of the gastric bubble for obesity. *Gastrointest Endosc*. 1989 Sep-Oct;35(5):381-5
15. Genco A, Bruni T, Doldi SB, et al. BioEnterics Intra-gastric Balloon: the Italian experience with 2515 patients. *Obes Surg*. 2005;15:1161-1164
16. Genco A, Cipriano M, Bacci V, Cuzzolaro M, Materia A, Raparelli L, Docimo C, Lorenzini M, Basso N. BioEnterics Intra-gastric Balloon (BIB): a short-term, double-blind, randomised, controlled, crossover study on weight reduction in morbidly obese patients. *Int J Obes (Lond)*. 2006 Jan;30(1):129-33
17. Sallet J, Marchesini J, Paiva D, et al. Brazilian multicenter study of the intra-gastric balloon. *Obes Surg* 2004;14:991-8.
18. Lopez-Nava G, Rubio M, Prados S, et al. BioEnterics® intra-gastric balloon (BIB®). Single ambulatory center Spanish experience with 714 consecutive patients treated with one or two consecutive balloons. *Obes Surg* 2011;21:5-9.
19. Mathus-Vliegen EM, Tytgat GN. Intra-gastric balloon for treatment-resistant obesity: safety, tolerance, and efficacy of 1-year balloon treatment followed by a 1-year balloon-free follow-up. *Gastrointest Endosc*. 2005;61:19-27
20. Dastis NS, Francois E, Deviere J, et al. Intra-gastric balloon for weight loss: results in 100 individuals followed for at least 2.5 years. *Endoscopy*. 2009;41:575-580
21. Genco A, Cipriano M, Bacci V, Maselli R, Paone E, Lorenzo M, Basso N. Intra-gastric balloon followed by diet vs intra-gastric balloon followed by another balloon: a prospective study on 100 patients. *Obes Surg*. 2010 Nov;20(11):1496-500.
22. Farina MG, Baratta R, Nigro A, Vinciguerra F, Puglisi C, Schembri R, Virgilio C, Vigneri R, Frittitta L. Intra-gastric balloon in association with lifestyle and/or pharmacotherapy in the long-term management of obesity. *Obes Surg*. 2012 Apr;22(4):565-71
23. Melissas J, Mouzas J, Filis D, Daskalakis M, Matrella E, Papadakis JA, Sevrissarianos N, Charalambides D. The intra-gastric balloon - smoothing the path to bariatric surgery. *Obes Surg*. 2006 Jul;16(7):897-902.
24. Spyropoulos C, Katsakoulis E, Mead N, Vegenas K, Kalfarentzos F. Intra-gastric balloon for high-risk super-obese patients: a prospective analysis of efficacy. *Surg Obes Relat Dis*. 2007;3:78-83
25. Lee YM, Low HC, Lim LG, Dan YY, Aung MO, Cheng CL, Wee A, Lim SG, Ho KY. Intra-gastric balloon significantly improves nonalcoholic fatty liver disease activity score in obese patients with nonalcoholic steatohepatitis: a pilot study. *Gastrointest Endosc*. 2012 Oct;76(4):756-60
26. Corby K, Martin, Drake E, Bellanger, Kristina K, Rau, Sandra Coulon, Frank L. Greenway. Safety of the Ullorex® Oral Intra-gastric Balloon for the Treatment of Obesity. *J Diabetes Sci Technol*. 2007 July; 1(4): 574-581. Published online 2007 July
27. Evzen Machytka, Pavel Klvana, et al. Adjustable Intra-gastric Balloons: A 12-Month Pilot Trial in Endoscopic Weight Loss Management. *Obes Surg*. 2011 October; 21(10): 1499-1507
28. Lecumberri E, Krekshi W, Matia P, et al. Effectiveness and safety of air-filled balloon heliosphere BAG® in 82 consecutive obese patients. *Obes Surg* 2011;21:1508-12
29. Fernandes M, Atallah AN, Soares BG, Humberto S, Guimarães S, Matos D, Monteiro L, Richter B. Intra-gastric balloon for obesity. *Cochrane Database Syst Rev*. 2007 Jan 24
30. Rubino F, Schauer PR, Kaplan LM, Cummings DE. Metabolic surgery to treat type 2 diabetes: clinical outcomes and mechanisms of action. *Annu Rev Med*. 2010;61:393-411
31. Rodriguez-Grunert L, Galvao Neto MP, Alamo M, Ramos AC, Baez PB, Tarnoff M. First human experience with endoscopically delivered and retrieved duodenal-jejunal bypass sleeve. *Surg Obes Relat Dis*. 2008 Jan-Feb;4(1):55-9
32. Schouten R, Rijs CS, Bouvy ND, Hameeteman W, Koek GH, Janssen IM, Greve JW. A multicenter, randomized efficacy study of the EndoBarrier Gastrointestinal Liner for presurgical weight loss prior to bariatric surgery. *Ann Surg*. 2010 Feb;251(2):236-43
33. Gersin KS, Rothstein RI, Rosenthal RJ, Stefanidis D, Deal SE, Kuwada TS, Laycock W, Adrales G, Vassiliou M, Szomstein S, Heller S, Joyce AM, Heiss F, Nepomnashy D. Open-label, sham-controlled trial of an endoscopic duodenal-jejunal bypass liner for preoperative weight loss in bariatric surgery candidates. *Gastrointest Endosc*. 2010 May;71(6):976-82
34. Sandler BJ, Rumbaut R, Swain CP, Torres G, Morales L, Gonzales L, Schultz S, Talamini M, Horgan S. Human experience with an endoluminal, endoscopic, gastrojejunal bypass sleeve. *Surg Endosc*. 2011 Sep;25(9):3028-33.
35. Sullivan S, Stein R, Jonnalagadda S, Mullady D, Edmundowicz S. Aspiration therapy leads to weight loss in obese subjects: a pilot study. *Gastroenterology*. 2013 Dec;145(6):1245-52.e1-5
36. Garcia-Compean D, Mendoza-Fuente E, Martinez JA, Villarreal I, Maldonado H. Endoscopic injection of botulinum toxin in the gastric antrum for the treatment of obesity. Results of a pilot study. *Gastroenterol Clin Biol*. 2005 Aug-Sep;29(8-9):789-91
37. Foschi D, Lazzaroni M, Sangaletti O, Corsi F, Trabucchi E, Bianchi Porro G. Effects of intramural administration of Botulinum Toxin A on gastric emptying and eating capacity in obese patients. *Dig Liver Dis*. 2008 Aug;40(8):667-72
38. Li L, Liu QS, Liu WH, Yang YS, Yan D, Peng LH, Li LY, Meng JY, Wang XD, Ke M. Treatment of obesity by endoscopic gastric intramural injection of botulinum toxin A: a randomized clinical trial. *Hepatogastroenterology*. 2012 Sep;59(118):2003-7

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