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Obesity Surgery

Clinical Policy Bulletins | Medical Clinical Policy Bulletins

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Table Of Contents

Policy History

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06/21/2022

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Review History

Definitions

Additional Information

Clinical Policy Bulletin Notes

State Information

Maryland

Policy

Scope of Policy

This Clinical Policy Bulletin addresses obesity surgery.

Note: Most Aetna HMO and QPOS plans exclude coverage of surgical operations, procedures, or treatment of obesity unless approved by Aetna. Some Aetna plans entirely exclude coverage of surgical treatment of obesity. Please check benefit plan descriptions for details.

I. Medical Necessity

A. *Roux-en-Y Gastric Bypass (RYGB), Laparoscopic Adjustable Silicone Gastric Banding (LASGB), Sleeve Gastrectomy, Biliopancreatic Diversion (BPD) and Duodenal Switch (DS) Procedures*

Open or laparoscopic short or long-limb Roux-en-Y gastric bypass (RYGB), open or laparoscopic sleeve gastrectomy, open or laparoscopic biliopancreatic diversion (BPD) with or without duodenal switch (DS), or laparoscopic adjustable silicone gastric banding (LASGB) is considered medically necessary when the selection criteria listed below are met:

1. Must meet *either* a (adults) or b (adolescents):

    a. For adults aged 18 years or older, presence of persistent severe obesity, documented in contemporaneous clinical records, defined as *any* of the following:

        i. Body mass index (BMI) (see Appendix) exceeding 40 measured prior to preoperative preparatory program; *or*
        ii. BMI greater than 35 measured prior to preoperative preparatory program in conjunction with *any* of the following severe co-morbidities:

            a. Clinically significant obstructive sleep apnea (i.e., person meets the criteria for treatment of obstructive sleep apnea set forth in CPB 0004 - Obstructive Sleep Apnea in Adults (../1_99/0004.html)); *or*
            b. Coronary heart disease, with objective documentation (by exercise stress test, radionuclide stress test, pharmacologic stress test, stress echocardiography, CT angiography, coronary angiography, heart failure or prior myocardial infarction); *or*
            c. Medically refractory hypertension (blood pressure greater than 140 mmHg systolic and/or 90 mmHg

diastolic despite concurrent use of 3 anti-hypertensive agents of different classes); *or*

d. Type 2 diabetes mellitus; *or*
e. Nonalcoholic steatohepatitis (NASH)*; *or*

b. For adolescents who have completed bone growth (generally age of 13 in girls and age of 15 in boys), presence of obesity with severe co-morbidities:

i. BMI exceeding 40 with one or more of the following serious co-morbidities:

a. Clinically significant obstructive sleep apnea; *or*
b. Type 2 diabetes mellitus; *or*
c. Nonalcoholic steatohepatitis (NASH)*; *or*
d. Pseudotumor comorbidities;

* Note: NASH determination may include either a liver biopsy or the presence of advanced hepatic fibrosis identified by FibroScan, FibroTest-ActiTest, magnetic resonance elastography, or Enhanced Liver Fibrosis (ELF) test (see also CPB 0690 - Noninvasive Tests for Hepatic Fibrosis (../600_699/0690.html)).

ii. BMI exceeding 50 with one or more of the following less serious co-morbidities:

a. Medically refractory hypertension; *or*
b. Dyslipidemias; *or*
c. Nonalcoholic steatohepatitis; *or*
d. Venous stasis disease; *or*
e. Significant impairment in activities of daily living; *or*
f. Intertriginous soft-tissue infections; *or*
g. Stress urinary incontinence; *or*
h. Gastroesophageal reflux disease; *or*
i. Weight-related arthropathies that impair physical activity; *or*

j. Obesity-related psychosocial distress;

2. Member has attempted weight loss in the past without successful long-term weight reduction; *and*

   Member has participated in an intensive multicomponent behavioral intervention designed to help participants achieve or maintain weight loss through a combination of dietary changes and increased physical activity. This intensive multicomponent behavioral intervention must meet *all* of the following criteria:

   a. Member's participation in an intensive multicomponent behavioral intervention must be documented in the medical record. Records must document compliance with the program. Note: A summary letter, without evidence of contemporaneous oversight, is not sufficient documentation. Documentation should include medical records of contemporaneous assessment of member's progress throughout the course of the nutrition and exercise program. For members who participate in an intensive multicomponent behavioral intervention (e.g., Weight Watchers, Jenny Craig, MediFast, OptiFast), program records documenting the member's participation and progress may substitute for medical records; *and*
   b. Intensive multicomponent behavioral intervention may be in-person or remote, and may be group or individual-based; *and*
   c. Program must be intensive (12 or more sessions on separate dates over any duration of time) and occur within 2 years prior to surgery. Note: Programs may extend beyond two years if the final session occurred within two years prior to surgery; *and*
   d. The intensive multicomponent behavioral intervention program must have components focusing on nutrition, physical activity, and behavioral modification (e.g., self-monitoring, identifying barriers, and problem solving). The multicomponent behavioral intervention

program may be supervised by behavioral therapists, psychologists, registered dietitians, exercise physiologists, lifestyle coaches or other staff; *and*

3. Screening for diabetes, with initiation of appropriate treatment for persons diagnosed with diabetes based on a HgbA1c of 6.5% or above, a fasting blood glucose (FBG) of 126 mg/dL or above, or an oral glucose tolerance test (OGTT) of 200 mg/dL or above at 2 hours. Note: Screening is not required for persons already diagnosed with diabetes; *and*
4. Screening for obstructive sleep apnea (OSA), using a validated screening questionnaire (including the ESS, STOP Questionnaire (Snoring, Tiredness, Observed Apnea, High Blood Pressure), STOP-Bang Questionnaire (STOP Questionnaire plus BMI, Age, Neck Circumference, and Gender), Berlin Questionnaire, Wisconsin Sleep Questionnaire, or the Multivariable Apnea Prediction (MVAP) tool). The medical records should document that OSA screening has been performed, although the results of such screening do not need to be forwarded to Aetna for review. Note: Screening is not required for persons already diagnosed with OSA; *and*
5. Cardiac clearance by a cardiologist for persons with a history of cardiac disease; *and*
6. Optimized glycemic control, as evidenced by any of the following: fasting blood glucose less than 110 mg/dL, two hour postprandial blood glucose level less than 140 mg/dL, or hemoglobin A1C (HbA1c) less than 7 percent (less than 8 percent in persons with a history of poorly controlled type 2 diabetes) within 6 months prior to surgery (within 3 months prior to surgery for persons with diabetes); for persons with diabetes who are unable to achieve glycemic control (i.e., persons with a HbA1c greater than 8 percent), there should be documentation of consultation with an endocrinologist or diabetologist prior to surgery to ensure that all appropriate actions have been taken to improve glycemic control; *and*

7. For members who have a history of severe psychiatric disturbance (schizophrenia, borderline personality disorder, suicidal ideation, severe depression) or who are currently under the care of a psychologist/psychiatrist or who are on psychotropic medications, pre-operative psychological clearance is necessary in order to exclude members who are unable to provide informed consent or who are unable to comply with the pre- and post-operative regimen. Note: The presence of depression due to obesity is not normally considered a contraindication to obesity surgery.

B. *Vertical Banded Gastroplasty (VBG)*

Open or laparoscopic vertical banded gastroplasty (VBG) is considered medically necessary for members who meet the selection criteria for obesity surgery and who are at increased risk of adverse consequences of a RYGB due to the presence of *any* of the following co-morbid medical conditions:

1. Demonstrated complications from extensive adhesions involving the intestines from prior major abdominal surgery, multiple minor surgeries, or major trauma; *or*
2. Hepatic cirrhosis with elevated liver function tests; *or*
3. Inflammatory bowel disease (Crohn's disease or ulcerative colitis); *or*
4. Poorly controlled systemic disease (American Society of Anesthesiology (ASA) Class IV) (see Appendix); *or*
5. Radiation enteritis.

Aetna considers VBG experimental and investigational when medical necessity criteria are not met.

C. *Bariatric Surgery Complications*

The following are considered medically necessary:

1. Removal of a gastric band when recommended by the member's physician;

2. Surgery to correct complications from bariatric surgery, such as obstruction, stricture, erosion, or band slippage;
3. Surgery for Candy cane syndrome (Roux syndrome) when member is symptomatic (abdominal pain, nausea, and emesis) and diagnosis is confirmed by endoscopy or upper gastrointestinal contrast studies;
4. Replacement of an adjustable band is considered medically necessary if there are complications (e.g., port leakage, slippage) that cannot be corrected with band manipulation or adjustments;
5. Conversion of sleeve gastrectomy to Roux-en-Y gastric bypass is considered medically necessary for the treatment of symptomatic gastroesophageal reflux disease (GERD) meeting the following criteria:

    a. Reflux is documented by abnormal 24-hour pH monitoring or endoscopically proven esophagitis performed after the sleeve gastrectomy; and
    b. Symptoms persist despite optimal medical therapy, including behavioral modification and at least one month of maximum proton pump inhibitor (PPI) therapy. Note: When performed primarily for the purpose of treating reflux meeting these criteria, conversion of sleeve gastrectomy to Roux-en-Y gastric bypass is not considered repeat bariatric surgery;

6. Repeat bariatric surgery for members whose initial bariatric surgery was medically necessary (i.e., who met medical necessity criteria for their initial bariatric surgery), and who meet *any* of the following medical necessity criteria:

    a. Conversion to a sleeve gastrectomy, RYGB or BPD/DS is considered medically necessary for members who have not had adequate success (defined as loss of more than 50 % of excess body weight) 2 years following the primary bariatric surgery procedure and the member has been compliant with a prescribed nutrition and exercise program following the procedure; *or*

b. Revision of a primary bariatric surgery procedure that has failed due to dilation of the gastric pouch, dilated gastrojejunal stoma, or dilation of the gastrojejunostomy anastomosis is considered medically necessary if the primary procedure was successful in inducing weight loss prior to the dilation of the pouch or GJ anastomosis, and the member has been compliant with a prescribed nutrition and exercise program following the procedure; *or*

c. Conversion from an adjustable band to a sleeve gastrectomy, RYGB or BPD/DS is considered medically necessary for members who have been compliant with a prescribed nutrition and exercise program following the band procedure, and there are complications that cannot be corrected with band manipulation, adjustments or replacement.

D. *Cholecystectomy*

As a high incidence of gallbladder disease (28%) has been documented after surgery for morbid obesity, Aetna considers routine cholecystectomy medically necessary when performed in concert with elective bariatric procedures.

E. *Liver Biopsy*

Aetna considers routine liver biopsy during bariatric surgery to be not medically necessary in the absence of signs or symptoms of liver disease (e.g., elevated liver enzymes, enlarged liver).

II. **Experimental and Investigational**

A. The following procedures are considered experimental and investigational because the peer-reviewed medical literature shows them to be either unsafe or inadequately studied:

1. Adjunctive omentectomy to bariatric surgery
2. AspireAssist aspiration therapy

3. "Band over bypass" or LASGB revision of prior Roux-en-Y gastric bypass
4. "Band over sleeve" or LASGB revision of prior sleeve gastrectomy
5. Bariatric surgery as a treatment for idiopathic intracranial hypertension in persons not meeting medical necessity criteria for obesity surgery above
6. Bariatric surgery as a treatment for infertility in persons not meeting medical necessity criteria for obesity surgery above
7. Bariatric surgery as a treatment for type-2 diabetes in persons with a BMI less than 35
8. Conversion of a sleeve gastrectomy to a Roux-en-Y gastric bypass for the treatment of bile reflux
9. Conversion to sleeve gastrectomy for hypoglycemia post-RYGB
10. Gastric bypass as a treatment for gastroparesis in persons not meeting medical necessity criteria for obesity surgery above
11. Gastroplasty, more commonly known as "stomach stapling" (see below for clarification from vertical band gastroplasty)
12. Laparoscopic gastric diversion with gastro-jejunal reconstruction for the treatment of GERD with esophagitis
13. Laparoscopic gastric plication (also known as laparoscopic greater curvature plication [LGCP]), with or without gastric banding
14. Laparoscopic single-anastomosis duodeno-ileal bypass with gastric plication
15. LASGB, RYGB, and BPD/DS procedures not meeting the medical necessity criteria above
16. Liposuction (suction-assisted lipectomy; ultrasonic assisted liposuction)
17. Loop gastric bypass
18. Mini gastric bypass
19. Natural orifice transoral endoscopic surgery (NOTES) techniques for bariatric surgery including, but may not be limited to, the following:

    a. Gastrointestinal liners (endoscopic duodenal-jejunal bypass, endoscopic gastrointestinal bypass devices; e.g.,

EndoBarrier and the ValenTx Endo Bypass System); *or*

b. Intragastric balloon (e.g., the Obalon Balloon System, and the ReShape Integrated Dual Balloon System); *or*

c. Mini sleeve gastrectomy; *or*

d. Restorative obesity surgery, endoluminal (ROSE) procedure for the treatment of weight regain after gastric bypass surgery; *or*

e. Transoral gastroplasty (TG) (vertical sutured gastroplasty; endoluminal vertical gastroplasty; endoscopic sleeve gastroplasty); *or*

f. Use of any endoscopic closure device (Over the Scope clip [OTSC] system set, Apollo OverStitch endoscopic suturing system, StomaphyX endoluminal fastener and delivery system) in conjunction with NOTES;

20. Open adjustable gastric banding
21. Prophylactic mesh placement for prevention of incisional hernia after open bariatric surgery
22. Prophylactic pyloroplasty via botulinum toxin injection following laparoscopic sleeve gastrectomy
23. Roux-en-Y gastric bypass as a treatment for gastroesophageal reflux in persons not meeting medical necessity criteria for obesity surgery
24. Roux-en-Y gastrojejunostomy for the treatment of persistent gastro-esophageal reflux disease following antireflux surgery in persons not meeting medical necessity criteria for obesity surgery above
25. Sclerotherapy for the treatment of dilated gastrojejunostomy following bariatric surgery
26. Silastic ring vertical gastric bypass (Fobi pouch)
27. Sleeve gastrectomy with single anastomosis duodeno-ileal bypass (SIPS)
28. Vagus nerve blocking (e.g., the VBLOC device, also known as the Maestro Implant or the Maestro Rechargeable System)
29. VBG, except in limited circumstances noted above.

B. Measurement of serum C-reactive protein as a predictor for complications following bariatric surgery because the effectiveness of this approach has not been established.

III. Related Policies

- CPB 0004 - Obstructive Sleep Apnea in Adults (../1_99/0004.html)
- CPB 0039 - Weight Reduction Medications and Programs (../1_99/0039.html)
- CPB 0690 - Noninvasive Tests for Hepatic Fibrosis (../600_699/0690.html)

Applicable CPT / HCPCS / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

Code	Code Description
CPT codes covered if selection criteria are met:	
43644	Laparoscopy, surgical, gastric restrictive procedure; with gastric bypass and Roux-en-Y gastroenterostomy (Roux Limb 150 cm or less)
43645	with gastric bypass and small intestine reconstruction to limit absorption [laparoscopic gastric diversion with gastro-jejunal reconstruction]
43770	Laparoscopy, surgical, gastric restrictive procedure; placement of adjustable gastric restrictive device (eg, gastric band and subcutaneous port components) [not covered if history of prior Roux-en-Y gastric bypass or sleeve gastrectomy] [not covered with gastric plication]
43771	revision of adjustable gastric restrictive device component only
43772	removal of adjustable gastric restrictive device component only
43773	removal and replacement of adjustable gastric restrictive device component only

Code	Code Description
43774	removal of adjustable gastric restrictive device and subcutaneous port components
43775	longitudinal gastrectomy (ie, sleeve gastrectomy)
43842	Gastric restrictive procedure, without gastric bypass, for morbid obesity; vertical-banded gastroplasty
43843	other than vertical-banded gastroplasty [not covered for transoral gastroplasty (TG), vertical sutured gastroplasty, endoluminal vertical gastroplasty, endoscopic sleeve gastroplasty] [not covered for open gastric banding]
43845	Gastric restrictive procedure with partial gastrectomy, pylorus-preserving duodenoileostomy and ileoileostomy (50 to 100 cm common channel) to limit absorption (biliopancreatic diversion with duodenal switch)
43846	Gastric restrictive procedure, with gastric bypass for morbid obesity; with short limb (150 cm or less) Roux-en-Y gastroenterostomy
43847	with small intestine reconstruction to limit absorption
43848	Revision, open, of gastric restrictive procedure for morbid obesity, other than adjustable gastric restrictive device (separate procedure)
43886	Gastric restrictive procedure, open; revision of subcutaneous port component only
43887	removal of subcutaneous port component only
43888	removal and replacement of subcutaneous port component only
CPT codes not covered for indications listed in the CPB (not all-inclusive) [incorrect for reporting bariatric surgery]:	
Sleeve gastrectomy with SIPS, Laparoscopic single-anastomosis duodeno-ileal bypass with gastric plication - no specific code:	
0312T	Vagus nerve blocking therapy (morbid obesity); laparoscopic implantation of neurostimulator electrode array, anterior and posterior vagal trunks adjacent to esophagogastric junction (EGJ), with implantation of pulse generator, includes programming

Code	Code Description
0313T	Vagus nerve blocking therapy (morbid obesity); laparoscopic revision or replacement of vagal trunk neurostimulator electrode array, including connection to existing pulse generator
0317T	Vagus nerve blocking therapy (morbid obesity); neurostimulator pulse generator electronic analysis, includes reprogramming when performed
15876 - 15879	Suction assisted lipectomy; head and neck, trunk, upper/lower extremities
43620	Gastrectomy, total; with esophagoenterostomy
43621	with Roux-en-Y reconstruction
43622	with formation of intestinal pouch, any type
43631	Gastrectomy, partial, distal; with gastroduodenostomy
43632	with gastrojejunostomy
43633	with Roux-en-Y reconstruction
43634	with formation of intestinal pouch
+ 43635	Vagotomy when performed with partial distal gastrectomy (List separately in addition to code(s) for primary procedure)
47000	Biopsy of liver, needle; percutaneous [in the absence of signs or symptoms of liver disease (e.g., elevated liver enzymes, enlarged liver)]
47001	Biopsy of liver, needle; when done for indicated purpose at tine of other major procedure (list separately in addition to code for primary procedure) [in the absence of signs or symptoms of liver disease (e.g., elevated liver disease, enlarged liver)]
47100	Biopsy of liver, wedge [in the absence of signs or symptoms of liver disease (e.g., elevated liver disease, enlarged liver)]
49255	Omentectomy, epiploectomy, resection of omentum (separate procedure)
86140	C-reactive protein
86141	C-reactive protein; high sensitivity (hsCRP)
Other CPT codes related to the CPB:	
43659	Unlisted laparoscopy procedure, stomach

Code	Code Description
43800	Pyloroplasty [prophylactic]
43999	Unlisted procedure, stomach
47562 - 47620	Cholecystectomy
74240	Radiologic examination, upper gastrointestinal tract, including scout abdominal radiograph(s) and delayed image(s), when performed; single-contrast (eg, barium) study
74246	Radiologic examination, upper gastrointestinal tract, including scout abdominal radiograph(s) and delayed image(s), when performed; double-contrast (eg, high-density barium and effervescent agent) study, including glucagon, when administered
HCPCS codes not covered for indications listed in the CPB:	
J0585	Injection, onabotulinumtoxina, 1 unit
Other HCPCS codes related to the CPB:	
S2083	Adjustment of gastric band diameter via subcutaneous port by injection or aspiration of saline
S9449	Weight management classes, non-physician provider, per session
S9451	Exercise classes, non-physician provider, per session
S9452	Nutrition classes, non-physician provider, per session
ICD-10 codes covered if selection criteria are met:	
E66.01	Morbid (severe) obesity due to excess calories
E66.09	Obesity, unspecified
E66.3	Overweight
E67.8	Other specified hyperalimentation
K75.81	Nonalcoholic steatohepatitis (NASH)
K91.1	Postgastric surgery syndromes [Roux syndrome]
K95.09	Other complications of gastric band procedure [dilated gastrojejunal stoma]
K95.89	Other complications of other bariatric procedure [dilated gastrojejunal stoma]
R63.2	Polyphagia

Code	Code Description
R63.5	Abnormal weight gain
Z46.51	Encounter for fitting and adjustment of gastric lap band
Z68.35 - Z68.39	Body mass index [BMI] 35.0 - 39.9 or greater, adult [see criteria]
Z68.41 - Z68.45	Body mass index [BMI] 40 or greater, adult
Z68.54	Body mass index [BMI] pediatric, greater than or equal to 95th percentile for age [BMI of 40 or greater for adolescents who have completed bone growth]
Z98.84	Bariatric surgery status
ICD-10 codes not covered for indications listed in the CPB:	
E11.00 - E11.9	Type II diabetes [not covered for persons with BMI less than 35]
E16.1	Other hypoglycemia [hypoglycemia]
G93.2	Benign intracranial hypertension [Idiopathic] [for persons not meeting medical necessity criteria for obesity surgery]
K21.00 - K21.01	Gastro-esophageal reflux disease with esophagitis [for persons not meeting medical necessity criteria for obesity surgery]
K31.84	Gastroparesis [for persons not meeting medical necessity criteria for obesity surgery]
N46.01 - N46.9	Male infertility [for persons not meeting medical necessity criteria for obesity surgery]
N97.0 - N97.9	Female infertility [for persons not meeting medical necessity criteria for obesity surgery]
Z68.1 - Z68.34	Body Mass Index 0 - 34.9
Z98.84	Bariatric surgery status
Z98.890	Other specified postprocedural states [post anti-reflux surgery] [for persons not meeting medical necessity criteria for obesity surgery]
Sclerotherapy for Dilated Gastrojejunostomy:	
CPT codes covered if selection criteria are met:	
43236	Esophagogastroduodenoscopy, flexible, transoral; with directed submucosal injection(s), any substance

Code	Code Description
43253	Esophagogastroduodenoscopy, flexible, transoral; with transendoscopic ultrasound-guided transmural injection of diagnostic or therapeutic substance(s) (eg, anesthetic, neurolytic agent) or fiducial marker(s) (includes endoscopic ultrasound examination of the esophagus, stomach, and either the duodenum or a surgically altered stomach where the jejunum is examined distal to the anastomosis)
ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):	
K30	Functional dyspepsia [dilated gastrojejunostomy]
K59.8	Other specified functional intestinal disorders [dilated gastrojejunostomy]
K95.09	Other complications of gastric band procedure [dilated gastrojejunostomy]
K95.89	Other complications of other bariatric procedure [dilated gastrojejunostomy]
Conversion of sleeve gastrectomy to Roux-en-Y gastric bypass:	
CPT codes covered if selection criteria are met:	
43644	Laparoscopy, surgical, gastric restrictive procedure; with gastric bypass and Roux-en-Y gastroenterostomy (Roux Limb 150 cm or less)
43848	Revision, open, of gastric restrictive procedure for morbid obesity, other than adjustable gastric restrictive device (separate procedure)
43886	Gastric restrictive procedure, open; revision of subcutaneous port component only
ICD-10 codes covered if selection criteria are met:	
K21.0 - K21.9	Gastro-esophageal reflux disease
ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):	
K83.8	Other specified diseases of biliary tract [Bile reflux]

Background

These criteria were adapted from the NIH Consensus Conference on Surgical Treatment of Morbid Obesity (1998) which state that obesity surgery should be reserved only for patients who have first attempted medical therapy: "Weight loss surgery should be reserved for patients in whom efforts at medical therapy have failed and who are suffering from the complications of extreme obesity."

Rationale for Intensive Multicomponent Behavioral Intervention

The U.S. Preventive Services Task Force (USPSTF, 2019) recommends that clinicians offer or refer obese adults to intensive, multicomponent behavioral interventions (ie, behavior-based weight loss and weight loss maintenance interventions). The USPSTF found adequate evidence that behavior-based weight loss interventions in adults with obesity can lead to clinically significant improvements in weight status and reduced incidence of type 2 diabetes among adults with obesity and elevated plasma glucose levels. The USPSTF found adequate evidence to bound the harms of intensive, multicomponent behavioral interventions in adults with obesity as small to none, based on the absence of reported harms in the evidence and the noninvasive nature of the interventions.

Most of the intensive behavioral weight loss interventions considered by the USPSTF lasted for 1 to 2 years, and the majority had 12 or more sessions in the first year (USPSTF, 2019; LeBlanc, et al., 2018). Most behavioral interventions encouraged self-monitoring of weight and provided tools to support weight loss or weight loss maintenance (eg, pedometers, food scales, or exercise videos).

Interventionists varied across the trials, and interventions included varied interactions with a primary care clinician (USPSTF, 2019; LeBlanc, et al., 2018). Primary care clinician involvement ranged from limited interactions with participants in interventions conducted by other practitioners or individuals (ie, group-based interventions conducted by lifestyle coaches or registered dietitians) to reinforcing intervention messages through brief counseling sessions. Few interventions included a primary care clinician as the primary interventionist over 3 to 12 months of individual counseling. In the trials not involving a primary care clinician, the

interventionists were highly diverse and included behavioral therapists, psychologists, registered dietitians, exercise physiologists, lifestyle coaches, and other staff.

Trials used various delivery methods (group, individual, mixed, and technology- or print-based). Group-based interventions ranged from 8 group sessions over 2.5 months to weekly group sessions over 1 year (median, 23 total sessions in the first year (USPSTF, 2019; LeBlanc, et al., 2018). These interventions consisted of classroom-style sessions lasting 1 to 2 hours. Most of the individual-based interventions provided individual counseling sessions, with or without ongoing telephone support. The remaining interventions were provided remotely through telephone counseling calls (average time, 15-30 minutes) and web-based self-monitoring and support. The median number of sessions in the first year for individual-based interventions was 12. Mixed interventions included comparatively equal numbers of group- and individual-based counseling sessions, with or without other forms of support (eg, telephone-, print-, or web-based). Most of these interventions took place for more than 1 year and involved more than 12 sessions (median, 23 total sessions in the first year).

Among technology-based interventions, intervention components included computer- or web-based intervention modules, web-based self-monitoring, mobile phone–based text messages, smartphone applications, social networking platforms, or DVD learning (USPSTF, 2019; LeBlanc, et al., 2018). Only 1 trial delivered its intervention through print-based tailored materials.

The NIH Consensus Conference on Surgical Treatment of Morbid Obesity states that the initial goal of medical therapy is a 10% reduction in weight, and that a reasonable duration for medical therapy is 6 months. The Consensus Conference stated: "The initial goal of weight loss therapy is to reduce body weight by approximately 10% from baseline. If this goal is achieved, further weight loss can be attempted, if indicated through further evaluation. A reasonable time line for a 10% reduction in body weight is 6 months of therapy."

The NIH Consensus Conference Statement (1998) explained "The rationale for this initial goal is that even moderate weight loss, i.e., 10% of initial body weight, can significantly decrease the severity of obesity-associated risk factors." The NIH Consensus Conference (1998) states that the combination of a reduced calorie diet and increased physical activity can result in substantial improvements in blood pressure, glucose tolerance, lipid profile, and cardiorespiratory fitness.

The NIH Consensus Conference (1998) has stated that the patient should begin a nutrition and exercise program prior to surgery: "An integrated program must be in place to provide guidance on diet, physical activity, and behavioral and social support both prior to and after the surgery."

The American Dietetic Association (1997), in their position statement obesity surgery, recommends dietetic counseling and behavioral modification commencing prior to, not after, surgery: "Careful dietetics evaluation is needed to determine if the patient will be able to comply with the postoperative diet. A preoperative behavior change program with psychological evaluation should be required."

More recently, evidence-based guidelines from the Scottish Intercollegiate Guidelines Network (2010) have stated that bariatric surgery should be considered on an individual case basis following assessment of risk/benefit in obese patients with "evidence of completion of a structured weight management programme involving diet, physical activity, psychological and drug interventions, not resulting in significant and sustained improvement in the comorbidities."

Candidates for obesity surgery should begin a weight reduction diet prior to surgery. The purpose of a pre-operative nutrition program prior to obesity surgery are to test patient motivation, to reduce perioperative morbidity, to accustom patients to the restriction of food intake after surgery, and to increase total weight loss (van de Weijgert et al,1999; Jung and Cusciheri, 2000; Pekkarinen et al, 1997; Martin et al, 1995). Even super obese patients (BMI greater than 50) may benefit from initiating a nutrition and exercise program prior to surgery. Obesity itself increases the likelihood of pulmonary complications and wound infections (Choban et al, 1995; Abdel-Moneim, 1985; Holley et al, 1990; Myles et al, 2002; Nair et al, 2002; Bumgardner et al, 1995; Perez et al, 2001; Chang

et al, 2000; Printken et al, 1975). The higher the patient's BMI, the higher the surgical risk, and the highest risks occur among patients with a BMI over 50 (Gonzalez et al, 2003; Oelschlager and Pellegrini, 2003). Even relatively modest weight loss prior to surgery can result in substantial improvements in pulmonary function, blood glucose control, blood pressure, and other physiological parameters (Anderson et al, 2000; Hakala et al, 1995; Kansanen et al, 1998; Pekkarinen et al, 1998). Factors such as blood glucose control, hypertension, etc., affect surgical risk. Garza (2003) explained that the patient should lose weight prior to surgery to reduce surgical risks. "The overall health of patients should be optimized prior to surgery to reduce the potential for complications. Patients ought to be encouraged to lose as much weight as possible before surgery" (Garza, 2003). Although the long-term effectiveness of weight reduction programs has been questioned, the Institute of Medicine (1995) has reported the substantial short-term effectiveness of certain organized physician-supervised weight reduction programs.

For maximal benefit, dieting should occur proximal to the time of surgery, and not in the remote past to reduce surgical risks and improve outcomes. Even if the patient has not been able to keep weight off long-term with prior dieting, the patient may be able to lose significant weight short term prior to surgery in order to improve the outcome of surgery.

Given the importance of patient compliance in diet and self-care in improving patient outcomes after surgery, the appropriateness of obesity surgery in noncompliant patients should be questioned. The American College of Surgeons has stated: "Not all persons who are obese or who consider themselves overweight are candidates for bariatric surgery. These procedures are not for cosmesis but for prevention of the pathologic consequences of morbid obesity. The patient must be committed to the appropriate work-up for the procedure and for continuing long-term postoperative medical management, and understand and be adequately prepared for the potential complications of the procedure. Screening of the patients to ensure appropriate selection is a critical responsibility of the surgeon and the supporting health care team."

A Multidisciplinary Care Task Group (Saltzman et al, 2005) conducted a systematic review of the literature and recommended an attempt at modest weight loss before obesity surgery, citing evidence that modest

reductions in weight (5 to 10% of initial weight) reduce factors known to increase surgical risk (e.g., sleep disordered breathing, hypertension, hyperglycemia), and that with weight loss, obese patients had significantly shorter operating room times and length of stay. The Task Group stated that registered dietitians are best qualified to provide nutritional care, including pre-operative assessment and nutritional education and counseling.

Rationale for Completing Program Prior to Surgery

The patient's ability to lose weight prior to surgery makes surgical intervention easier and also provides an indication of the likelihood of compliance with the severe dietary restriction imposed on patients following surgery.

Given the importance of patient compliance on diet and self-care in improving patient outcomes after surgery, the patient's refusal to even attempt to comply with a nutrition and exercise regimen prior to surgery portends poor compliance with nutritional and self-care requirements after surgery. Therefore, the appropriateness of obesity surgery in non-compliant patients should be questioned.

The patient must be committed to the appropriate work-up for the procedure and for continuing long-term post-operative medical management, and must understand and be adequately prepared for the potential complications of the procedure.

There is rarely a good reason why obese patients (even super obese patients) can not delay surgery in order to undergo behavioral modification to improve their dietary and exercise habits in order to reduce surgical risks and improve surgical outcomes. The patient may be able to lose significant weight prior to surgery in order to improve the outcome of surgery.

An individual's understanding of the procedure and ability to comply with life-long follow-up and life-style changes (e.g., as exemplified by compliance with previous medical care) are necessary for the success of the procedure.

Obesity makes many types of surgery more technically difficult to perform and hazardous. Weight loss prior to surgery makes the procedure easier to perform. Weight reduction reduces the size of the liver, making surgical access to the stomach easier. By contrast, the liver enlarges and becomes increasingly infiltrated with fat when weight is gained prior to surgery. A fatty liver is heavy, brittle, and more likely to suffer injury during surgery. Moreover, following surgery, patients have to follow a careful diet of nutritious, high-fiber foods in order to avoid nutritional deficiencies, dumping syndrome, and other complications. The total weight loss from surgery can be enhanced if it is combined with a low-calorie diet. For these reasons, it is therefore best for patients to develop good eating and exercise habits before they undergo surgery.

The pre-operative surgical preparatory regimen should include cessation counseling for smokers. The National Institutes of Health Consensus Statement (1998) states that all smokers should be encouraged to quit, regardless of weight. Smoking cessation is especially important in obese persons, as obesity places them at increased risk for cardiovascular disease. Severely obese persons are at increased risk of surgical complications. Smoking cessation reduces the risk of pulmonary complications from surgery.

Ideally, the surgical center where surgery is to be performed should be accomplished in bariatric surgery with a demonstrated commitment to provide adequate facilities and equipment, as well as a properly trained and funded appropriate bariatric surgery support staff. Minimal standards in these areas are set by the institution and maintained under the direction of a qualified surgeon who is in charge of an experienced and comprehensive bariatric surgery team. This team should include experienced surgeons and physicians, skilled nurses, specialty-educated nutritionists, experienced anesthesiologists, and, as needed, cardiologists, pulmonologists, rehabilitation therapists, and psychiatric staff. The American College of Surgeons (ACS) has stated that the surgeon performing the bariatric surgery be committed to the multidisciplinary management of the patient, both before and after surgery. The ACS recommended: "They develop skills in patient education and selection and are committed to long-term patient management and follow-up. There is active collaboration with multiple patient care disciplines including nutrition, anesthesiology, cardiology,

pulmonary medicine, orthopedic surgery, diabetology, psychiatry, and rehabilitation medicine. Appropriate technical skills in the performance of bariatric surgical procedures are acquired."

Although not a requirement for coverage, ideally, the bariatric surgeon should be board certified by the American Board of Surgery or in the process of certification within 5 years after completion of an accredited residency program in general or gastrointestinal surgery, and recertification has been obtained by the American Board of Surgery on an every 10-year basis, if applicable. Appropriate qualifications for a bariatric surgeon include either fellowship training or extended mentoring by an experienced surgeon, preferably by members of international/national bariatric societies, in all aspects of bariatric surgery, advanced laparoscopic techniques, and additional training in re-operative techniques.

A number of studies have demonstrated a relationship between surgical volumes and outcomes of obesity surgery. Most recently, an assessment by the Canadian Agency for Drugs and Technologies in Health (CADTH) (Klarenbach et al, 2010) stated that their volume-outcome review found that higher surgical volumes were associated with better clinical outcomes. CADTH was not, however, able to identify specific thresholds for surgical volume that were associated with better clinical outcomes.

A Multidisciplinary Care Task Group (Saltzman et al, 2005) conducted a systematic review of the literature to to provide evidence-based guidelines for patient selection and to recommend the medical and nutritional aspects of multi-disciplinary care required to minimize peri-operative and post-operative risks in patients with severe obesity who undergo weight loss surgery. The Task Group recommended multi-disciplinary screening of weight loss surgery patients to ensure appropriate selection; pre-operative assessment for cardiovascular, pulmonary, gastrointestinal, endocrine, and other obesity-related diseases associated with increased risk for complications or mortality; pre-operative weight loss and cessation of smoking; peri-operative prophylaxis for deep vein thrombosis and pulmonary embolism (PE); pre-operative and post-operative education and counseling by a registered dietitian; and a well-defined post-surgical diet progression. The authors explained that obesity-related diseases are often undiagnosed before

weight loss surgery, putting patients at increased risk for complications and/or early mortality. Multi-disciplinary assessment and care to minimize short- and long-term risks include: comprehensive medical screening; appropriate pre-, peri-, and post-operative preparation; collaboration with multiple patient care disciplines (e.g., anesthesiology, pulmonary medicine, cardiology, and psychology); and long-term nutrition education/counseling.

A Multidisciplinary Care Task Group (Saltzman et al, 2005) recommended that operative candidates must be committed to the appropriate work-up for the procedure and to continued long-term post-operative medical management. They must also be able to understand, and be adequately prepared for, potential complications. The Multidisciplinary Care Task Group recommended the use of patient selection criteria from the NIH Consensus Development Conference on Gastrointestinal Surgery for Severe Obesity, which are consistent with those of other organizations. These include: BMI greater than or equal to 40 kg/m2 or BMI greater than or equal to 35 kg/m2 in the presence of significant co-morbidities, a well-informed and motivated patient with a strong desire for substantial weight loss, failure of non-surgical approaches to long-term weight loss, and acceptable operative risks.

The Task Group recommended that all weight loss surgery patients be encouraged to lose weight before surgery, and to promote 5 to 10% pre-operative weight loss in patients with a BMI greater than 50 kg/m2 or obesity-related comorbidities (Saltzman et al, 2005). The Task Group recommended to decide on a case-by-case basis whether to proceed with surgery in patients who are unable to lose weight. The Task Group stated that registered dietitians are best qualified to provide nutritional care, including pre-operative assessment and post-operative education, counseling, and follow-up. Weight loss surgery patients need to learn important new skills, including self-monitoring and meal planning. Many forms of weight loss surgery require patients to take lifelong nutritional supplements and to have lifelong medical monitoring. Dedicated dietitians can help patients during their pre-operative education on new dietary requirements and stipulations and their post-surgical adjustment to those requirements. The Task Group also recommended a pre-operative assessment for micronutrient deficiencies.

The Task Group recommended that smokers should be encouraged to stop, preferably at least 6 to 8 weeks before surgery (Saltzman et al, 2005). Bupropion and/or nicotine replacements are recommended to help minimize weight gain associated with smoking cessation. Patients should be encouraged to remain non-smokers after weight loss surgery to reduce the negative long-term health effects of smoking.

Anderin et al (2015) found that weight loss before bariatric surgery is associated with marked reduction of risk of postoperative complications. The investigators reported that the degree of risk reduction seems to be related to amount of weight lost and patients in the higher range of BMI are likely to benefit most from pre-operative weight reduction. The investigators noted that a pre-operative weight-reducing regimen is usually adhered to in most centers performing bariatric surgery for obesity, and that the potential to reduce post-operative complications by such a routine is yet to be defined. The investigators analyzed data from the Scandanavian Obesity Registry on 22,327 patients undergoing primary gastric bypass from January 1, 2008, to June 30, 2012. In all patients, median pre-operative total weight change was −4.8%. Corresponding values in the 25th, 50th, and 75th percentile were 0.5, −4.7, and −9.5%, respectively. Complications were noted in 9.1% of the patients. When comparing patients in the 75th with those in the 25th percentile of pre-operative weight loss, the risk of complications was reduced by 13%. For specific complications, the corresponding risks were reduced for anastomotic leakage by 24%, for deep infection/abscess by 37%, and for minor wound complications by 54%. Similarly, however, less pronounced risk reductions were found when comparing patients in the 50th with those in the 25th percentile of pre-operative weight loss. For patients in the highest range of body mass index (BMI), the risk reduction associated with pre-operative weight loss was statistically significant for all analyzed complications, whereas corresponding risk reductions were only occasionally encountered and less pronounced in patients with lower BMI.

Body Mass Index as a Criterion for Candidacy for Obesity Surgery

Surgery for severe obesity is usually considered an intervention of last resort with patients having attempted other forms of medical management (such as behavior change, increased physical activity and drug therapy)

but without achieving permanent weight loss (Colquitt et al, 2002; NIH, 1995). Surgery is indicated for persons with severe obesity (BMI of 40 kg/m2 or more) or for persons with a BMI of 35 kg/m2 or more and serious co-morbidities such as diabetes, coronary heart disease, or obstructive sleep apnea. Ideally patients selected for surgery should have no major perioperative risk factors, a stable personality, no eating disorders, and have lost some weight prior to surgery. The patient's ability to lose weight prior to surgery makes surgical intervention easier and also provides an indication of the likelihood of compliance with the severe dietary restriction imposed on patients following surgery.

Contraindications to Obesity Surgery

Surgery for severe obesity is a major surgical intervention with a risk of significant early and late morbidity and of perioperative mortality (Colquitt, 2002; Oelschlager and Pellegrini, 2003). Contraindications for these surgical procedures include peri-operative risk of cardiac complications, poor myocardial reserve, significant chronic obstructive airways disease or respiratory dysfunction, non-compliance of medical treatment, psychological disorders of a significant degree that a psychologist/psychiatrist would have thought would be exacerbated or interfere with the long-term management of the patient after the operation, significant eating disorders, or severe hiatal hernia/gastroesophageal reflux.

A Multidisciplinary Care Task Group (Saltzman et al, 2005) identified contraindications to weight loss surgery, including unstable or severe coronary artery disease, severe pulmonary disease, portal hypertension with gastric or intestinal varices, and/or other conditions thought to seriously compromise anesthesia or wound healing. The Task Group also noted that weight loss surgery is contraindicated in those who are unable to comprehend basic principles of weight loss surgery or follow operative instructions. The Task Group stated that any combination of the following factors – revisional surgery, male, greater than 50 years of age, BMI greater than 50 kg/m2, and obstructive sleep apnea, hypertension, and type 2 diabetes – indicates high risk.

Requirement that Obesity be Persistent

Obesity surgery is not indicated for persons with transient increases in weight (Collazo-Clavell, 1999). Guidelines of the American Association of Clinical Endocrinologists and the American College of Endocrinology (1998) and guidelines on obesity surgery from the Massachusetts Department of Health and Human Services (2006) state that surgery candidates should be severely obese for a period of time.

Obesity Surgery in Children and Adolescents

According to available guidelines, obesity surgery is generally indicated for persons age 18 and older (AACE, 1998). Children and adolescents are rapidly growing, and are therefore especially susceptible to adverse long-term consequences of nutritional deficiencies from the reduced nutrient intake and malabsorption that is induced by obesity surgery. It is not known whether the benefits of obesity surgery in children and adolescents outweigh the increased risks.

According to a panel of experts (Inge et al, 2004; Lawson et al, 2006), bariatric surgery may be an appropriate treatment for severe obesity in adolescents who have completed bone growth. According to the recommendations by the expert panel, potential candidates for bariatric surgery should be referred to centers with multi-disciplinary weight management teams that have expertise in meeting the unique needs of overweight adolescents. Consideration for bariatric surgery is generally warranted only when adolescents have experienced failure of 6 months of organized weight loss attempts and have met certain criteria: severe obesity (a BMI of 40) and severe co-morbidities, or super obesity (BMI of 50) and less severe co-morbidities that may be remedied with weight loss; and have attained a majority of skeletal maturity (generally 13 years of age for girls and 15 years of age for boys). Surgery should only be performed at facilities that are equipped to collect long-term data on clinical outcomes. The panel recommended the Roux-en-Y gastric bypass method of surgery over the simpler, newer technique of implanting an adjustable gastric band since gastric bands are less effective and younger patients would probably need replacement as they age.

Requirement for Program Documentation

Aetna’s policy states that the member should participate in an intensive multicomponent behavioral intervention, and that this participation be documented in the medical record. Program records documenting participation in an intensive multicomponent behavioral intervention such as Weight Watchers or Jenny Craig may substitute for medical record documentation. As is true generally, physicians should document their assessment of the patient, what health interventions are prescribed, and their assessment of the patient’s progress. There is established evidence that medical supervision of a nutrition and exercise program increases the likelihood of success (Blackburn, 1993). The American Medical Association Council on Scientific Affairs recommends that "any person considering a weight loss program first consult a physician for a physical examination and an objective evaluation of the proposed weight loss program as it relates to the individual’s physical condition … Various health organizations recommend that physicians assess their patients for overweight and that patients receive appropriate counseling about safe weight management and the benefits of physical activity and a healthy diet [citing guidelines from the National Heart, Lung and Blood Institute, the AACE/ACE, the Institute of Medicine of the National Academy of Sciences, the U.S. Preventive Services Task Force, the American Obesity Association, the American Medical Association, and an expert committee of pediatric experts convened by the Health Resources and Services Administration]" (Lyznicki et al, 2001). "If treatment is indicated, physicians can help patients develop weight loss or management plans tailored to individual needs; this includes setting reasonable weight loss goals; selecting appropriate weight loss programs; referring patients to ancillary personnel when appropriate; and providing monitoring, support and encouragement" (Lyznicki et al, 2001).

Requirement for Psychological Evaluation

Candidates for obesity surgery who have a history of severe psychiatric disturbance (schizophrenia, borderline personality disorder, suicidal ideation, severe depression) or who are currently under the care of a psychologist/psychiatrist or who are on psychotropic medications should undergo a comprehensive evaluation by a licensed psychologist or psychiatrist to assess the patient’s suitability for surgery, the absence of significant psychopathology that can limit an individual’s understanding of

the procedure or ability to comply with life-long follow-up (e.g., defined noncompliance with previous medical care, active substance abuse, schizophrenia, borderline personality disorder, uncontrolled depression).

Routine Liver Biopsy for Bariatric Surgery

Society of American Gastrointestinal and Endoscopic Surgeons (SAGES), with input from the Clinical Issues Committee of the American Society for Metabolic and Bariatric Surgery (ASMBS), have issued the following guideline for liver biopsy as a part of preoperative medical evaluation bariatric surgery: "The liver may be assessed by hepatic profile and ultrasound. In cases of suspected cirrhosis, biopsy may be indicated."

The American Association of Clinical Endocrinologists, Obesity Society, American Society for Metabolic & Bariatric Surgery's clinical practice guidelines on "The perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient" (Mechanick et al, 2013) stated that "Consideration can be made for liver biopsy at the time of surgery to document steatohepatitis and/or cirrhosis that may otherwise be unknown due to normal appearance and/or liver function tests (Grade D)" (Grade D recommendation is based on expert opinion because of a lack of conclusive clinical evidence; if a 2/3 consensus cannot be reached, then the recommendation grade is D).

An UpToDate review on "Bariatric operations for management of obesity: Indications and preoperative preparation" (Lim, 2015) states that "For patients suspected to have nonalcoholic fatty liver disease (NAFLD) on the basis of hepatomegaly on the physical examination, liver function tests are obtained. In addition, radiographic imaging is obtained, such as an ultrasound or a computed tomography scan, or a biopsy may be required to evaluate for cirrhosis".

Cazzo et al (2014) stated that non-alcoholic fatty liver disease (NAFLD) is common among subjects who undergo bariatric surgery and its post-surgical improvement has been reported. This study aimed to determine the evolution of liver disease evaluated through NAFLD fibrosis score 12 months after surgery. It is a prospective cohort study which evaluated patients immediately before and 12 months following Roux-en-Y gastric

bypass (RYGB). Mean score decreased from 1.142 to 0.066; surgery led to a resolution rate of advanced fibrosis of 55%. Resolution was statistically associated with female gender, percentage of excess weight loss, post-surgical BMI, post-surgical platelet count, and diabetes resolution. The authors concluded that as previously reported by studies in which post-surgical biopsies were performed, RYGB leads to a great resolution rate of liver fibrosis. Since post-surgical biopsy is not widely available and has a significant risk, calculation of NAFLD fibrosis score is a simple tool to evaluate this evolution through a non-invasive approach.

Shalhub et al (2004) noted that non-alcoholic steatohepatitis (NASH) commonly occurs in obese patients and predisposes to cirrhosis. Prevalence of NASH in bariatric patients is unknown. The aim of this study was to determine the role of routine liver biopsy in managing bariatric patients. Prospective data on patients undergoing Roux-en-Y gastric bypass (RYGBP) was analyzed. One pathologist graded all liver biopsies as mild, moderate or severe steatohepatitis. NASH was defined as steatohepatitis without alcoholic or viral hepatitis. Consecutive liver biopsies were compared to those liver biopsies selected because of grossly fatty livers. A total of 242 patients underwent open and laparoscopic RYGBP from 1998 to 2001. Routine liver biopsies (68 consecutive patients) and selective liver biopsies (additional 86/174, 49%) were obtained. Findings of cirrhosis on frozen section changed the operation from a distal to a proximal RYGBP. The two groups were similar in age, gender, and BMI. The group with the routine liver biopsies showed a statistically significant larger preponderance of NASH (37% versus 32%). Both groups had a similar prevalence of cirrhosis. Neither BMI nor liver enzymes predicted the presence or severity of NASH. The authors concluded that routine liver biopsy documented significant liver abnormalities in a larger group of patients compared with selective liver biopsies, thereby suggesting that liver appearance is not predictive of NASH. Liver biopsy remains the gold-standard for diagnosing NASH. The authors recommended routine liver biopsy during bariatric operations to determine the prevalence and natural history of NASH, which will have important implications in directing future therapeutics for obese patients with NASH and for patients undergoing bariatric procedures.

Oliveira et al (2005) stated that pathogenesis of non-alcoholic fatty liver disease (NAFLD) remains incompletely known, and oxidative stress is

one of the mechanisms incriminated. The aim of this study was to evaluate the role of liver oxidative stress in NAFLD affecting morbidly obese patients. A total of 39 consecutive patients with BMI > 40 kg/m2 submitted to Roux-en-Y gastric bypass were enrolled, and wedge liver biopsy was obtained during operation. Oxidative stress was measured by concentration of hydroperoxides (CEOOH) in liver tissue. Female gender was dominant (89.7%) and median age was 43.6 +/- 11.1 years. Histology showed fatty liver in 92.3%, including 43.6% with NASH, 48.7% with isolated steatosis and just 7.7% with normal liver. Liver cirrhosis was present in 11.7% of those with NASH. Concentration of CEOOH was increased in the liver of patients with NASH when compared to isolated steatosis and normal liver (0.26 +/- 0.17, 0.20 +/- 0.01 and 0.14 +/- 0.00 nmol/mg protein, respectively) ($p < 0.01$). Liver biochemical variables were normal in 92.3% of all cases, and no difference between NASH and isolated steatosis could be demonstrated. The authors concluded that (i) non-alcoholic steatosis, steatohepatitis and cirrhosis were identified in substantial numbers of morbidly obese patients; and (ii) concentration of hydroperoxides was increased in steatohepatitis, consistent with a pathogenetic role for oxidative stress in this condition.

Arun et al (2007) stated that NAFLD is a chronic condition that can progress to cirrhosis and hepatocellular cancer. The most progressive form of NAFLD is NASH. Currently, the only method to diagnose NASH is with a liver biopsy; however, sampling error may limit diagnostic accuracy. These researchers investigated the discordance of paired liver biopsies in individuals undergoing gastric bypass. Two liver biopsies, composite size of > or = 25 mm and > or = 8 portal tracts (PTs), were obtained from the left lobe in 31 subjects. Group 1 included specimens at least 15 mm in length with > or = 4 PTs compared to a second biopsy of at least 10 mm and > or = 4 PTs (Group 2). The mean specimen size (number of PTs) for group 1 was 20.4 +/- 4.2 mm (11.7 +/- 5.5 PTs) and group 2 was 16.1 +/- 5.3 mm (8.2 +/- 4.1 PTs). Prevalence of NASH was 26% in Group 1 and 32% in Group 2. Sampling discordance was greatest for portal fibrosis (26%), followed by zone 3 fibrosis (13%) and ballooning degeneration (3%). The negative predictive values from Group 1 liver biopsies for NASH and portal fibrosis were only 83% and 67%, respectively. The authors concluded that the results demonstrate that significant sampling

variability exists in class 2 and 3 obese individuals undergoing screening liver biopsies for NAFLD. The degree and histopathological discordance is dependent upon zonal location and types of injury. Nevertheless, a 25-mm biopsy specimen without zone 3 cellular ballooning or fibrosis appears adequate to exclude the diagnosis of NASH.

Roux-en-Y Gastric Bypass (RYGB) and Vertical Banded Gastroplasty (VBG)

Surgery for obesity, termed bariatric surgery, includes gastric restrictive procedures and gastric bypass. The gastric restrictive procedures include vertical banded gastroplasty accompanied by gastric banding which attempt to induce weight loss by creating an intake-limiting gastric pouch by segmenting the stomach along its vertical axis. The process of digestion is more or less normal. In the United States, the primary operative choice for severely obese patients has recently shifted from vertical banded gastroplasty (VBG) to the Roux-en-Y gastric bypass (RYGB) (Fisher and Schauer, 2002; Mason et al, 1997). Vertical banded gastroplasty (VBG), a purely restrictive procedure, has fallen into disfavor because of inadequate long-term weight loss.

Roux-en-Y gastric bypass (RYGB) combines restriction and malabsorption principles, and combines gastric segmentation along its vertical axis with a Roux-en-Y procedure, such that the food bypasses the duodenum and proximal small bowel. Long-limb RYGB is similar to standard RYGB, except that the limb through which food passes is longer and is often used to treat super obese individuals. Because the normal flow of food is disrupted, available literature indicates that there is a greater potential for metabolic complications compared to gastric restrictive surgeries, including iron deficiency anemia, vitamin B-12 deficiency and hypocalcemia, all of which can be corrected by oral supplementation. Several studies have suggested that RYGB is a more effective weight loss procedure than VBG, offering the best combination of maximum weight control and minimum nutritional risk (Sugerman et al, 1989; Howard et al, 1995). Pories et al (1995) reported 57.7%, 54.7%, and 49.2% excess weight loss with RYGB at 5, 10, and 14 years, respectively, in a large series with 95% follow-up. Thus, the RYGB is "the current procedure of choice for patients requiring surgery for morbid obesity" (Barrow; 2002). An assessment conducted by the French

National Technology Assessment Agency (ANAES, 2001; Msika, 2003) found that surgical mortality for RYGB and VBG is about the same. However, RYGB is associated with significantly more weight loss, and has become the procedure of choice for obesity surgery.

Gentileschi et al (2002) systematically reviewed the published literature on open and bariatric laparoscopic obesity surgery and concluded that the available evidence indicates that laparoscopic VBG and laparoscopic RYGB are as effective as their open counterparts.

An assessment of laparoscopic RYGB by the BlueCross BlueShield Association Technology Evaluation Center (BCBSA, 2005) stated that among available bariatric surgical procedures, RYGB appears to have the most favorable risk-to-benefit ratio, and that the overall risk-to-benefit ratio of laparoscopic RGBY is similar to that of open RGBY. The assessment found that open and laparoscopic RYGB induces similar amounts of weight loss. However, the assessment found that the profile of adverse events differs between the two approaches. Laparoscopic RYGB is a less invasive approach that results in a shorter hospital stay and earlier return to usual activities. The assessment found that the estimated mortality rate was low for both procedures, but somewhat lower for laparoscopic surgery than open surgery (0.3% versus 1.1%). Laparoscopic RGBY had a higher rate of postoperative anastomotic leaks than open RGBY (3.7% versus 1.9%), and a somewhat higher rate of bleeding (4.1% versus 2.4%). The report found, on the other hand, that open surgery had higher rates of cardiopulmonary complications (2.6% versus 1.0%) and wound infections (11.0% versus 4.7%). Regarding long-term adverse events, the rates of reoperation (9.9%) and anastomotic problems (8.0%) may be higher for laparoscopic RGBY than for open RGBY (6.0% and 2.0%, respectively), while the rate of incisional hernia is higher for open RGBY than laparoscopic RGBY (9.0% versus 0%).

An assessment by the Institute for Clinical Systems Improvement (ICSI, 2005) found that large studies have shown that RYGB may result in weight loss of 60% to 70% of excess weight. It also found that VBG shows substantial weight loss efficacy but less than that for RYGB. In addition, VBG has a high rate of serious morbidity, including a re-

operation rate of up to 30% from stoma obstruction and staple-line disruption. Therefore, the evidence supports the overall superiority of RYGB over VBG in safety and efficacy for bariatric surgery.

A decision memorandum from the Centers for Medicare and Medicaid Services (CMS, 2006) concluded that the evidence is sufficient that open and laparoscopic RYGB is reasonable and necessary for Medicare beneficiaries who have a BMI greater than 35 and have at least one co-morbidity related to obesity, and have been previously unsuccessful with medical treatment for obesity. The assessment concluded that the evidence is not adequate to conclude that open or laparoscopic vertical banded gastroplasty is reasonable and necessary and they are therefore non-covered for all Medicare beneficiaries.

A systematic evidence review by the Canadian Agency for Drugs and Technologies in Health (CADTH) (Klarenbach et al, 2010) found that, although data from large, adequately powered, long-term randomized controlled trials are lacking, bariatric surgery seems to be more effective than standard care for the treatment of severe obesity in adults. Procedures that are mainly diversionary (e.g., biliopancreatic diversion (BPD)) result in the greatest amounts of weight loss, hybrid procedures are of intermediate effectiveness (e.g., RYGB), and restrictive procedures (e.g., adjustable gastric banding) result in the least amounts of weight loss. RYGB and adjustable gastric banding tended to lead to trade-offs between the risk of adverse events and the need for procedure conversion or reversals.

Biliopancreatic Diversion (BPD) (Jejunoilieal Bypass, Scorpinaro Procedure) and Duodenal Switch (DS) Procedures

While appropriate surgical procedures for severe obesity primarily produce weight loss by restricting intake, intestinal bypass procedures produce weight loss by inducing a malabsorptive effect. Biliopancreatic bypass or diversion (BPD) (also called jejunoileal bypass or the Scopinaro procedure) consists of a subtotal gastrectomy and diversion of the biliopancreatic juices into the distal ileum by a long Roux-en-Y procedure; the result is a 200-cm long alimentary tract, a 300- to 400-cm biliary tract, and after these 2 tracts are joined at the distal anastomosis, there is a 50-cm common absorptive alimentary tract. The BPD was

designed to address some of the drawbacks of the original intestinal bypass procedures, which resulted in unacceptable metabolic complications of diarrhea, hyperoxaluria, nephrolithiasis, cholelithiasis and liver failure.

The duodenal switch (DS) is a variant of the BPD procedure with a vertical subtotal gastrectomy and pylorus preservation, which eliminates the "dumping syndrome". The duodenum is divided just beyond the pylorus. The small bowel is then divided, and the end going to the cecum of the colon is connected to the short stump of the duodenum. This becomes the "enteral limb". The other end, leading from the gallbladder and pancreatic ducts, is connected onto the enteral limb at about 75 to 100 cm from the iliocecal valve. This limb is the "biliopancreatic limb". The last 75-100 cm then becomes the "common channel", measuring about 10% of the total small bowel length and is the only portion that can absorb fat. Some have advocated use of the DS procedure in the super-obese (i.e., persons with BMI greater than 50) because of the substantial weight loss induced by this procedure. Patients who have this operation must have lifelong medical follow-up, since the side effects can be subtle, and can appear months to years after the surgery.

A decision memorandum from the Centers for Medicare and Medicaid Services (CMS, 2006) concluded that open or laparoscopic BPD with or without DS are reasonable and necessary for Medicare beneficiaries.

Gastroplasty ("Stomach Stapling")

Gastroplasty, more commonly known as "stomach stapling" and not to be confused with vertical banded gastroplasty (VBG), is a technically simple operation, accomplished by stapling the upper stomach to create a small pouch into which food flows after it is swallowed. The outlet of this pouch is restricted by a band of synthetic mesh, which slows its emptying, so that the person having it feels full after only a few bites of food. According to the available literature, patients who have this procedure seldom experience any satisfaction from eating, and tend to seek ways to get around the operation by eating more. This causes vomiting, which can tear out the staple line and destroy the operation. Overall, clinical studies have shown that about 40% of persons who have this operation do not achieve loss of more than half of their excess body weight. In the long-

term, 5 or more years after surgery, only about 30% of patients have maintained a successful weight loss. Studies have reported that many patients must undergo another revisional operation to obtain the results they seek.

Sleeve Gastrectomy

Sleeve gastrectomy is a 70 to 80% greater curvature gastrectomy (sleeve resection of the stomach) with continuity of the gastric lesser curve being maintained while simultaneously reducing stomach volume (CMS, 2005). It is often the first step in a 2-stage procedure when performing RYGB or duodenal switch.

A decision memorandum from the Centers for Medicare and Medicaid Services (CMS, 2012) found that open or laparoscopic sleeve gastrectomy may be reasonable and necessary for beneficiaries with a BMI greater than or equal to 35 with comorbidities.

A systematic evidence review prepared for *Clinical Evidence* concluded that the effectiveness of sleeve gastrectomy for morbid obesity is unknown (DeLaet and Schauer, 2009). The evidence review found no clinically important results from randomized controlled clinical trials about sleeve gastrectomy compared with non-surgical treatment, or compared with vertical banded gastroplasty or biliopancreatic diversion. They found low quality evidence that sleeve gastrectomy may be more effective than gastric banding at increasing weight loss at 1 and 3 years, and moderate quality evidence that sleeve gastrectomy seems more effective than gastric bypass at increasing mean excess-weight loss at 1 to 2 years.

A systematic evidence review of sleeve gastrectomy by the Australia and New Zealand Horizon Scanning Network (ANZHSN) (Lee, 2007) found that the evidence showed that laparoscopic sleeve gastrectomy can induce substantial excess weight loss at least as effectively as LASGB (in one study up to 3-years post surgery) but less effectively than gastric bypass and duodenal switch in the short-term. The report noted, however, that these results should be viewed in light of the ease and simplicity of laparoscopic sleeve gastrectomy relative to the other more invasive procedures. The report found a comparable reduction in co-morbidities in patients who underwent laparoscopic sleeve gastrectomy or RYGB, most

notably in resolution rates of diabetes within 4 months after surgery despite laparoscopic gastric banding patients being significantly more obese than the RYGB patients in the study. Evidence suggested that, compared to LASGB, laparoscopic sleeve gastrectomy had lower complication rates but more severe complications. The report found laparoscopic sleeve gastrectomy safer than laparoscopic RYGB or intragastric balloon implantation. The report stated that evidence of the safety of laparoscopic sleeve gastrectomy compared with duodenal switch is conflicting possibly because of differences in baseline patient characteristics. The report stated that the incidence of gastric sleeve dilatation appears to be an uncommon event, but the evidence is far from conclusive at this point. The report noted that one study found that laparoscopic sleeve gastrectomy and LASGB had significantly shorter operative times compared to RYGB and duodenal switch. Laparoscopic sleeve gastrectomy had a significantly longer length of stay compared to LASGB, but a significantly shorter length of stay compared to RYGB and duodenal switch. The report found that knowledge gaps include: comparing the effectiveness of laparoscopic sleeve gastrectomy to established bariatric procedures in super-obese (BMI greater than or equal to 50) as a stand alone procedure; long-term (greater than 5 years) safety, durability of weight loss and comorbidity data for laparoscopic sleeve gastrectomy relative to existing bariatric procedures; and effects of laparoscopic sleeve gastrectomy on plasma ghrelin levels and subsequent effect on appetite. More recently, a review of the literature by the Veterans Health Administration Technology Assessment Program (Adams, 2008) found no new literature that would not alter the conclusions of the ANZHSN review.

A randomized controlled clinical trial comparing short-term (1-year) outcomes of laparoscopic sleeve gastrectomy to laparoscopic RYGB found comparable reductions in body weight and BMI (Karamanakos et al, 2008). However, power calculations were not reported, and the study (n = 32) was likely under-powered to detect clinically signficant differences in effectiveness between the 2 procedures. This study was poorly reported, failing to discuss inclusion criteria for the trial and adverse events associated with the procedures.

An earlier retrospective study by Lee et al (2007) (n = 846) found similar rates of short-term weight loss in persons who elected sleeve gastrectomy and persons who elected RYGB or duodenal switch procedures. However, the lack of randomization and retrospective nature of the study results in a substantial risk of bias in the results.

The strongest arguments for sleeve gastrectomy relate to the comparatively poor outcomes of LASGB, which is the competing option for persons wishing to undergo a restrictive (non-malabsorptive) procedure. A randomized clinical study by Himpens et al (2006) compared laparoscopic sleeve gastrectomy to LASGB (n = 80). Although median weight loss was significantly greater after 1 and 3 years with sleeve gastrectomy (65 lbs) than with LASGB (37.5 lbs), the total weight loss with either procedure was insufficient for most potential candidates. The study also found that sleeve gastrectomy was associated with more severe complications than LASGB. The study was also poorly reported, including failure to discuss randomization and blinding procedures, and whether any subjects did not comply with randomization or were lost to follow-up. Clinical studies have reported long-term reoperation rates with LASGB of up to 60% (see, e.g., Scozzari et al, 2009; Camerini et al, 2004; Tweddle et al, 2004; Morino et al, 2002). Australia has reported that the costs of band adjustments with LASGB has exceeded the costs of the primary LASGB procedure.

A Cochrane review of the evidence for bariatric surgical procedures (Colquitt et al, 2009) found that, although the effects of the available bariatric procedures compared with medical management and with each other are uncertain, "limited" evidence suggests that sleeve gastrectomy results in weight loss similar to RYGB and greater than with LASGB. The assessment stated that information from the included trials did not allow the authors to reach any conclusions about the safety of these procedures compared with each other. The assessment noted that, due to limited evidence and poor quality of the trials comparing each pair of procedures, these conclusions should be viewed with caution.

In a position statement, the American Society for Metabolic and Bariatric Surgery (2009) determined that sleeve gastrectomy is an "approved bariatric surgical procedure" despite finding only "limited" intermediate term data and a lack of long-term data on the effectiveness of the

procedure. The ASMBS position statement explained that the Society has accepted sleeve gastrectomy as an approved bariatric surgical procedure primarily because of its potential value as a first-stage operation for high-risk patients, primarily super-obese patients with an average BMI of 60 kg/m2. The ASMBS reached this conclusion despite not knowing what proportion of super-obese patients will achieve satisfactory outcomes with sleeve gastrectomy alone without conversion to RYGB or duodenal switch, and despite a lack of evidence that accomplishing RYGB or duodenal switch as a staged procedure results in better outcomes (fewer risks) than accomplishing these procedures as a single surgery.

An assessment by the California Technology Assessment Forum (CTAF) (Walsh, 2010) concluded that sleeve gastrectomy does not meet CTAF technology assessment criteria for improvement in health outcomes for the treatment of obesity. The CTAF assessment reported that the results of multiple case series and retrospective studies have suggested that sleeve gastrectomy as a primary procedure is associated with a significant reduction in excess weight loss. The CTAF assessment reported that the complication rate from sleeve gastrectomy ranged from 0% to 4.1% and complications included leaks, bleeding, strictures and mortality. The CTAF assessment found few comparative studies of sleeve gastrectomy. CTAF identified only 2 randomized controlled trials that have compared sleeve gastrectomy to another surgical procedure (citing Himpens et al, 2006; Karamanakos et al, 2008). These trials included a total of 112 participants who were followed from 1 to 3 years. Among the 80 subjects followed for 3 years, there were a similar number of complications in the sleeve gastrectomy and the RYGB groups, although the complications in the sleeve gastrectomy group were more severe. The CTAF assessment stated that, "[t]o date, long term outcomes from registry studies are relatively limited, but longer term follow-up will provide additional important information."

An assessment of surgical treatment for obesity from the Canadian Agency for Drugs and Technologies in Health (CADTH) (Klarenbach et al, 2010) also concluded that the evidence base for sleeve gastrectomy is limited.

Loop Gastric Bypass

Although the basic concept of gastric bypass remains intact, numerous variations are being performed at this time. Recent data demonstrate that surgeons are moving from simple gastroplasty procedures, favoring the more complex gastric bypass procedures as the surgical treatment of choice for the severely obese patient. The gastric bypass operation can be modified, to alter absorption of food, by moving the Roux-en-Y-connection distally down the jejunum, effectively shortening the bowel available for absorption of food. The weight loss effect is then a combination of the very small stomach, which limits intake of food, with malabsorption of the nutrients, which are eaten, reducing caloric intake even further. In a sense, this procedure combines the least desirable features of the gastric bypass with the most troublesome aspects of the biliopancreatic diversion. Although patients can have increased frequency of bowel movements, increased fat in their stools, and impaired absorption of vitamins, recent studies have reported good results. The loop gastric bypass developed years ago has generally been abandoned by most bariatric surgeons as unsafe. Although easier to perform than the RYGB, it has been shown to create a severe hazard in the event of any leakage after surgery, and seriously increases the risk of ulcer forrmation, and irritation of the stomach pouch by bile.

Laparoscopic Adjustable Silicone Gastric Banding (LASGB)

Recent advances in laparoscopy have renewed the interest in gastric banding techniques for the control of severe obesity. Laparoscopic adjustable silicone gastric banding (LASGB) has become an attractive method because it is minimally invasive and allows modulation of weight loss. Available brands of LASGB include the Lap-Band System (Allergan, Inc., Irvine, CA) and the Realize Adjustable Gastric Band (Ethicon Endo-Surgery, Cincinnati, OH). The claimed advantage of LASGB is the adjustability of the band, which can be inflated or deflated percutaneously according to weight loss without altering the anatomy of the stomach. This method entails encircling the upper part of the stomach using bands made of synthetic materials, creating a small upper pouch that empties into the lower stomach through a narrow, non-stretchable stoma. The reduced capacity of the pouch and the restriction caused by the band diminish caloric intake, depending on important technical details, thus producing weight loss comparable to vertical gastroplasties, without the possibility of staple-line disruption and lesser incidence of infectious

complications. However, distension of the pouch, slippage of the band and entrapment of the foreign material by the stomach have been described and are worrisome.

A decision memorandum from the CMS (2006) found that there was sufficient evidence to support LASGB as reasonable and necessary for Medicare beneficiaries with a BMI greater than 35 and co-morbid medical conditions. Sustained weight loss was well documented, ranging from an approximate mean of 30 to 50% excess weight loss in LASGB, compared to an approximate mean of 50% excess weight loss in RYGB. The CMS decision memorandum found that short-and-long-term mortality associated with both LASGB and RYGB were low (less than 2%) in this younger age group.

Regarding performing adjustable gastric banding as an open procedure, the CMS decision memorandum (2006) concluded that the evidence is not adequate to conclude that open adjustable gastric banding is reasonable and necessary and therefore this procedure remains noncovered for Medicare beneficiaries.

Mini Gastric Bypass

The "mini gastric bypass" has been promoted as a new surgical treatment for severe obesity. It involves laparoscopic construction of a large and elongated gastric pouch and a loop gastric bypass with distal diversion (200 cm or up to 50% of the small bowel) to reduce food absorption. While the name mini gastric bypass implies "small" and "simple", this is a major surgical procedure. The mini-gastric bypass uses a jejunal loop directly connected to a small gastric pouch, instead of a Roux-en-Y anastomosis. In this way, the mini-gastric bypass is similar to the loop gastric bypass; the latter procedure that has been abandoned by bariatric surgeons because of its inherent risks. Specifically, performing a loop, rather than a Roux-en-Y, anastomosis to a small gastric pouch in the stomach may permit reflux of bile and digestive juice into the esophagus where it can cause esophagitis and ulceration, and may thus increase the risk of esophageal cancer. The Roux-en-Y modification of the loop bypass was designed to divert bile downstream, several feet below the gastric pouch and esophagus to minimize the risk of reflux. The trend towards use of Roux-en-Y and away from loop gastric bypass was based on

sound surgical experience of multiple surgeons with large series of patients. The published evidence supporting the mini-gastric bypass comes from descriptive reports and case series; the potential biases inherent in reports of case series are well known in clinical epidemiology. The evidence for the mini gastric bypass has come from a single investigator, thus raising questions about the generalization and validity of the reported findings. The mini-gastric bypass has not been subjected to a prospective clinical outcome study in peer-reviewed publication.

Silastic Ring Vertical Gastric Bypass (Fobi Pouch)

The Fobi pouch, developed by California surgeon Mathias A.L. Fobi, is a modification of gastric bypass surgery. The modifications to gastric bypass surgery are designed to prevent post-surgical enlargement of the gastric pouch and stoma.

In a traditional gastric bypass procedure, surgeons create a smaller stomach by stapling off a large section. A problem with the traditional procedure is that the staples can break down, causing the stomach to regain its original shape – and patients to start gaining weight again. Also, the stomach opening that leads into the intestines, which in surgery is made smaller to allow less food to pass through, often stretches as the years go by. With the Fobi pouch, there is no use of staples; rather, the stomach is bisected and hand-sewn them to maintain the separation. A synthetic band is placed around the stomach opening to keep it from stretching.

However, there is a paucity of direct comparative studies of the Fobi pouch to traditional gastric bypass surgery, causing colleagues to "question whether his technique is really an improvement on the traditional procedure" (Davis, 2000). All of the published literature has been limited to descriptive articles, case series, and a prospective non-randomized controlled study. These studies were from a single group of investigators, raising questions about the generalization of the findings.

Intragastric Balloon

The intragastric balloon (also known as the silicone intragastric balloon or SIB) has been developed as a temporary aid for obese patients who have had unsatisfactory results in their clinical treatment for obesity and super obese patients with higher surgical (Fernandes et al, 2004). Intragastric balloon is intended to reduce gastric capacity, causing satiety, making it easier for patients to take smaller amounts of food. Randomized, controlled clinical studies, however, have found no increase in weight loss with the intragastric balloon plus dieting versus dieting alone (Rigaud et al, 1995; Geliebter et al, 1991; Mathus-Vliegen et al, 1990; Lindor et al, 1987). One non-randomized controlled clinical study that reported positive results reported that results were not maintained after gastric balloon removal (Ramhamadany et al, 1989). In addition, the intragastric balloon has been associated with potentially severe adverse effects, including gastric erosion, reflux, and obstruction. An assessment of the intragastric balloon from the Canadian Coordinating Office for Health Technology Assessment (2006) concluded that "[m]ore data on the benefits, harms, and cost-effectiveness are required before the intragastric balloon can be compared with other short-term weight loss interventions, including low-calorie diets."

On July 28, 2015, the Food and Drug administration (FDA) approved the ReShape Integrated Dual Balloon System (ReShape Medical Inc., San Clemente, CA) to treat obesity without the need for invasive surgery (FDA, 2015). This new device is intended to facilitate weight loss in obese adult patients by occupying space in the stomach, which may trigger feelings of fullness, or by other mechanisms that are not yet understood. The ReShape Dual Balloon device is delivered into the stomach via the mouth through a minimally invasive endoscopic procedure. The outpatient procedure usually takes less than 30 minutes while a patient is under mild sedation. Once in place, the balloon device is inflated with a sterile solution, which takes up room in the stomach. The device does not change or alter the stomach’s natural anatomy. Patients are advised to follow a medically supervised diet and exercise plan to augment their weight loss efforts while using the ReShape Dual Balloon and to maintain their weight loss following its removal. It is meant to be temporary and should be removed 6 months after it is inserted.

The ReShape Dual Balloon was studied in a clinical trial with 326 obese participants aged 22 to 60 (with a BMI of 30 kg/m2 to 40 kg/m2) who had at least 1 obesity-related health condition (FDA, 2015). In the study (Ponce et al, 2015), 187 individuals randomly selected to receive the ReShape Dual Balloon lost 14.3 pounds on average (6.8% of their total body weight) when the device was removed at 6 months, while the control group (who underwent an endoscopic procedure but were not given the device) lost an average of 7.2 pounds (3.3% of their total body weight). Six months following the device removal, patients treated with the ReShape Dual Balloon device kept off an average of 9.9 pounds of the 14.3 pounds they lost. Potential side effects for the procedure include headache, muscle pain, and nausea from the sedation and procedure; in rare cases, severe allergic reaction, heart attack, esophageal tear, infection, and breathing difficulties can occur. Once the device is placed in the stomach, patients may experience vomiting, nausea, abdominal pain, gastric ulcers, and feelings of indigestion. This device should not be used in patients who have had previous gastro-intestinal or bariatric surgery or who have been diagnosed with inflammatory intestinal or bowel disease, large hiatal hernia, symptoms of delayed gastric emptying or active H. Pylori infection; those who are pregnant or use aspirin daily should also avoid the device (FDA, 2015).

There is a lack of data on the durability of the results with the ReShape Integrated Dual Balloon System. It is unclear what benefit there is from a temporary reduction in weight. An UpToDate review on "Obesity in adults: Overview of management" (Bray, 2015) does not mention intragastric balloon as a therapeutic option. Furthermore, an UpToDate review on " Bariatric surgical operations for the management of severe obesity: Descriptions " (Lim, 2015) lists intragastric balloon as an investigational procedure. It states that "As much as 33% excess weight loss has been reported in trials conducted outside of the United States with devices not approved by the FDA. After 5 years of surveillance, however, only 23% of patients maintained more than 20% of their excess weight loss".

Popov and colleagues (2017) examined the effect of intra-gastric balloons (IGBs) on metabolic outcomes associated with obesity. Medline, Embase, and Cochrane Database were searched through July 2016. Dual extraction and quality assessment of studies using Cochrane risk of bias tool were performed independently by 2 authors. Primary outcomes

included the change from baseline in metabolic parameters. Secondary outcomes included resolution and/or improvement in metabolic co-morbidities and association with baseline parameters. A total of 10 randomized controlled trial (RCTs) and 30 observational studies including 5,668 subjects were analyzed. There was moderate-quality evidence for improvement in most metabolic parameters in subjects assigned to IGB therapy as compared to conventional non-surgical therapy in RCTs: mean difference (MD) in fasting glucose change: -12.7 mg/dL (95% confidence interval [CI]: -21.5 to -4); MD in triglycerides: -19 mg/dL (95% CI: -42 to 3.5); MD in waist circumference: -4.1 cm (95% CI: -6.9 to -1.4); MD in diastolic blood pressure: -2.9 mm Hg (95% CI: -4.1 to -1.8). The OR for diabetes resolution after IGB therapy was 1.4 (95% CI: 1.3 to 1.6). The rate of serious AES was 1.3%. The authors concluded that IGBs were more effective than diet in improving obesity-related metabolic risk factors with a low rate of AEs, however the strength of the evidence was limited given the small number of participants and lack of long-term follow-up.

On August 10, 2017, the FDA announced that it has received 5 reports of unanticipated deaths that occurred from 2016 to the present in patients who received a liquid-filled intra-gastric balloon system to treat obesity; 4 reports involve the Orbera Intragastric Balloon System (Apollo Endosurgery) and 1 report involves the ReShape Integrated Dual Balloon System (ReShape Medical). All 5 patients died within 1 month or less of balloon placement; 3 patients died 1 to 3 days after the balloon was placed. The FDA stated that "At this time, we do not know the root cause or incidence rate of patient death, nor have we been able to definitively attribute the deaths to the devices or the insertion procedures for these devices (e.g., gastric and esophageal perforation, or intestinal obstruction)". The FDA has also received 2 additional reports of deaths from 2016 to the present related to potential complications associated with balloon treatment: 1 gastric perforation with the Orbera Intragastric Balloon System and 1 esophageal perforation with the ReShape Integrated Dual Balloon System. As part of the ongoing, FDA-mandated post-approval studies for these devices, the FDA will obtain more information to help evaluate the continued safety and effectiveness of these approved medical devices (Brooks, 2017).

StomaphyX

In March 2007, the FDA granted 510(k) pre-marketing clearance to the StomaphyX (EndoGastric Solutions, Inc.), an endoluminal fastener and delivery system used to tighten esophageal tissue. There is only limited evidence on the effectiveness of the StomaphyX in bariatric surgery repair/revision.

Overcash (2008) reported 2 cases of the safe and successful use of the StomaphyX device to alter the flow of gastric contents and repair gastric leaks resulting from bariatric revision surgery. Both patients were at a high risk and could not undergo another open or laparoscopic surgery to correct the leaks that were not healing. The author reported that the StomaphyX procedures lasted approximately 30 mins, were performed without any complications, and resulted in the resolution of the gastric leaks in both patients. The findings of these cases needs to be validated by well-designed clinical studies.

In a prospective, single-center, randomized, single-blinded study, Eid et al (2014) examined the safety and effectiveness of endoscopic gastric plication with the StomaphyX device versus a sham procedure for revisional surgery in RYGB (performed at least 2 years earlier) patients to reduce regained weight. These researchers planned for 120 patients to be randomized 2:1 to multiple full-thickness plications within the gastric pouch and stoma using the StomaphyX device with SerosFuse fasteners or a sham endoscopic procedure and followed up for 1 year. The primary efficacy end-point was reduction in pre-RYGB excess weight by 15% or more excess BMI (calculated as weight in kilograms divided by height in meters squared) loss and BMI less than 35 at 12 months after the procedure. Adverse events were recorded. Enrollment was closed prematurely because preliminary results indicated failure to achieve the primary efficacy end-point in at least 50% of StomaphyX-treated patients. One-year follow-up was completed by 45 patients treated with StomaphyX and 29 patients in the sham treatment group. Primary efficacy outcome was achieved by 22.2% (10) with StomaphyX versus 3.4% (1) with the sham procedure ($p < 0.01$). Patients undergoing StomaphyX treatment experienced significantly greater reduction in weight and BMI at 3, 6, and 12 months ($p \leq 0.05$). There was one causally related adverse event with StomaphyX, that required laparoscopic

exploration and repair. The authors concluded that StomaphyX treatment failed to achieve the primary efficacy target and resulted in early termination of the study.

Bariatric Surgery and Pregnancy

The American College of Obstetricians and Gynecologists' practice bulletin on bariatric surgery and pregnancy (ACOG, 2009) stated that bariatric surgery should not be considered a treatment for infertility.

Bariatric Surgery for the Treatment of Idiopathic Intracranial Hypertension

Fridley et al (2011) reviewed the literature on the effectiveness of bariatric surgery for obese patients with idiopathic intracranial hypertension (IIH) with regard to both symptom resolution and resolution of visual deficits. The published literature was reviewed using manual and electronic search techniques. Data from each relevant manuscript were gathered, analyzed, and compared. These included demographic data, pre- and post-operative symptoms, pre- and post-operative visual field deficits, bariatric procedure type, absolute weight loss, changes in BMI, and changes in cerebrospinal fluid (CSF) opening pressure. A total of 11 relevant publications (including 6 individual case reports) were found, reporting on a total of 62 patients. The Roux-en-Y gastric bypass was the most common bariatric procedure performed. Fifty-six (92%) of 61 patients with recorded post-operative clinical history had resolution of their presenting IIH symptoms following bariatric surgery. Thirty-four (97%) of 35 patients who had undergone pre- and post-operative funduscopy were found to have resolution of papilledema post-operatively. Eleven (92%) of 12 patients who had undergone pre- and post-operative formal visual field testing had complete or nearly complete resolution of visual field deficits, and the remaining patient had stabilization of previously progressive vision loss. In 13 patients both pre- and post-operative CSF pressures were recorded, with an average post-operative pressure decrease of 254 mm H(2)O. Changes in weight loss and BMI varied depending on the reported post-operative follow-up interval. The authors concluded that the published Class IV evidence suggested that bariatric surgery may be an effective treatment for IIH in

obese patients, both in terms of symptom resolution and visual outcome. They stated that prospective, controlled studies are needed for better elucidation of its role.

Levin and colleagues (2015) stated that IIH occurs most frequently in young, obese women. Gastric bypass surgery has been used to treat morbid obesity and its co-morbidities, and IIH has recently been considered among these indications. These investigators presented a case report of a 29-year old female with a maximum BMI of 50.3 and a 5-year history of severe headaches and moderate papilledema due to IIH. She also developed migraine headaches. After a waxing and waning course and various medical treatments, the patient underwent laparoscopic Roux-en-Y gastric bypass surgery with anterior repair of hiatal hernia. Dramatic improvement in IIH headaches occurred by 4 months post-procedure and was maintained at 1 year, when she reached her weight plateau with a BMI of 35. Pre-surgery migraines persisted. This added to the small number of case reports and retrospective analyses of the successful treatment of IIH with gastric bypass surgery, and brought this data from the surgical literature into the neurological domain. It offered insight into an early time course for symptom resolution, and explored the impact of weight-loss surgery on migraine headaches. The authors concluded that this treatment modality should be further investigated prospectively to analyze the rate of headache improvement with weight loss, the amount of weight loss needed for clinical improvement, and the possible correlation with improvement in papilledema.

Handley et al (2015) systematically reviewed the effect of bariatric weight reduction surgery as a treatment for IIH. These investigators performed a comprehensive literature search using the following databases: MEDLINE, EMBASE, PubMed, Scopus, Web of Sciences, and the Cochrane Library. No restrictions were placed on these searches, including the date of publication. A total of 85 publications were identified, and after initial appraisal, 17 were included in the final review. Overall improvement in symptoms of IIH after bariatric surgery was observed in 60 of the 65 patients observed (92%). Post-operative lumbar puncture opening pressure was shown to decrease by an average of 18.9 cmH2 O in the 12 patients who had this recorded. The authors concluded that bariatric surgery for weight loss is associated with alleviation of IIH

symptoms and a reduction in intracranial pressure. Furthermore, an improvement was observed in patients where conventional treatments, including neurosurgery, were ineffective. They stated that further prospective randomized studies with control groups and a larger number of participants are lacking within the published studies to date.

Laparoscopic Gastric Plication

Pujol Gebelli et al (20110 stated that laparoscopic gastric plication is a new technique derived from sleeve gastrectomy. Plication of the greater curvature produces a restrictive mechanism that causes weight loss. The results of the first cases where this technique has been applied in this hospital were presented. A review was made of patients operated on in the authors' hospital between November 2009 and December 2010. Plication of the gastric greater curvature was performed under general anesthetic and by laparoscopy using 3 lines of sutures and with an orogastric probe as a guide. Results of the morbidity, mortality and weight loss were presented. A total of 13 patients were operated on (7 women). The maximum BMI varied between 37.11 kg/m² and 51.22 kg/m² at the time of the operation. The most frequently found morbidity was nausea and vomiting. Two patients required further surgery due intractable vomiting and total dysphagia; in 1 the plication unfolded, and in the 2nd it was converted into vertical gastrectomy. The authors concluded that laparoscopic gastric plication is a new surgical technique which gives equivalent short-term results as vertical gastrectomy. It is a reproducible and reversible technique with results and indications still to be validated.

Brethauer et al (2011) presented the results of a feasibility study using laparoscopic gastric plication for weight loss achieved without stapling or banding. After institutional review board approval, 2 methods were used to achieve laparoscopic gastric volume reduction. In the 1st group (anterior plication [AP]), the anterior gastric wall was folded inward from the fundus to the antrum using 2 rows of running sutures. The greater and lesser curvatures were approximated to create an intraluminal fold of the stomach. In the 2nd group (greater curvature plication [GCP]), the short gastric vessels were divided, and the greater curvature was folded inward, with 2 suture lines to reduce the gastric capacity by a large intraluminal gastric fold. The average pre-operative body mass index was 43.3 kg/m(2) (range of 36.9 to 49.0), and 3 patients were men. Of the 15

patients, 9 underwent AP. For the 9 patients who underwent AP, the 6- and 12-month endoscopic evaluations demonstrated comparable-size plications over time, except for in 1 patient, who had a partially disrupted fold. Of the 6 patients who underwent GCP, the 6- and 12-month follow-up endoscopic examinations demonstrated a durable intraluminal fold, except for in 1 patient, with a partial disruption at the distal fold owing to a broken suture. For patients completing 1 year of follow-up, the percentage of excess weight loss was 23.3% +/- 24.8% in the AP group (n = 5) and 53.4% +/- 22.7% in the GCP group (n = 6). No bleeding or infectious complications developed. The 1st patient in the GCP group required re-operation and plication reduction owing to gastric obstruction. The authors concluded that their initial experience has suggested that a reduction in gastric capacity can be achieved by way of plication of the anterior stomach and greater curvature. The early weight loss results have been encouraging, with better weight loss in patients who underwent GCP. They stated that the use of laparoscopic GCP warrants additional investigation as a primary bariatric procedure.

Huang et al (2012) noted that the laparoscopic adjustable gastric band has been widely accepted as 1 of the safest bariatric procedures to treat morbid obesity. However, because of variations in the results and the complications that tend to arise from port adjustment, alternative procedures are needed. These researchers have demonstrated, in a university hospital setting, the safety and feasibility of a novel technique, laparoscopic adjustable gastric banded plication, designed to improve the weight loss effect and decrease gastric band adjustment frequency. These investigators enrolled 26 patients from May 2009 to August 2010. Laparoscopic adjustable gastric banded plication was performed using 5-port surgery. They placed Swedish bands using the pars flaccida method, divided the greater omentum, and performed gastric plication below the band to 3 cm from the pylorus using a single-row continuous suture. The data were collected and analyzed pre- and post-operatively. The mean operative time was 87.3 mins without any intra-operative complications. The average post-operative hospitalization was 1.33 days. The mean excess weight loss at 1, 3, 6, 9, and 12 months after surgery was 21.9%, 31.9%, 41.3%, 55.2%, and 59.5%, respectively. The mean follow-up time was 8.1 months (range of 2 to 15), and the gastric band adjustment rate was 1.1 times per patient during this period. Two complications

developed: (i) gastrogastric intussusception and (ii) tube kinking at the subcutaneous layer. Both cases were corrected by reoperation. No mortality was observed. The authors concluded that laparoscopic adjustable gastric banded plication provides both restrictive and reductive effects and is reversible. The technique is safe, feasible, and reproducible and can be used as an alternative bariatric procedure. Moreover, the authors stated that comparative studies and long-term follow-up are needed to confirm their findings.

Ji et al (2014) conducted a systematic review of the currently available literature regarding the outcomes of laparoscopic gastric plication (LGP) for the treatment of obesity. The authors' systematic review yielded 14 studies encompassing 1,450 LGP patients. Peri-operative data were collected from each study and recorded. Mean pre-operative BMI ranged from 31.2 to 44.5 kg/m2, and 80.8% of the patients were female. Operative time ranged from 50 to 117.9 mins (average of 79.2 mins). Hospital stay varied from 0.75 to 5 days (average of 2.4 days). The percentage of excess weight loss (% EWL) for LGP varied from 31.8% to 74.4% with follow-up from 6 months to 24 months. No mortality was reported in these studies and the rate of major complications requiring re-operation ranged from 0% to 15.4% (average of 3.7%). The authors concluded that early reports with LGP were promising with a favorable short-term safety profile. However, it remains unclear if weight loss following LGP is durable in the long-term. They stated that additional prospective comparative trials and long-term follow-up are needed to further define the role of LGP in the surgical management of obesity.

In a prospective study, Zeinoddini (2014) evaluated safety and effectiveness of LGP on adolescents. Measured parameters included%EWL, percentage of BMI loss (%BMIL), obesity related co-morbidities, operative time, and length of hospitalization and complications. Laparoscopic gastric plication was performed in 12 adolescents (9 females and 3 males). Mean (SD) age of the patients was 13.8 ± 1 year. Mean pre-operative weight and BMI were 112.4 ± 19.7 kg and 46.0 ± 4 kg/m2, respectively. Mean (SD)%EWL and%EBMIL were 68.2 ± 9.9% and 79.0 ± 9.0%, respectively after 2 years. All medical co-morbidities were improved after LGP. There were no deaths. One patient required replication 4 days post-operatively due to obstruction at the site

of the last knot. No other major complications were observed. No patient required re-hospitalization. The authors concluded that LGP has the potential of being an ideal weight loss surgery for adolescents, resulting in excellent weight loss and minimal psychological disruption. It is associated with a minimal risk of leakage, bleeding, and nutritional deficiency. However, they stated that large well-designed studies with long-term follow-up are needed.

Sclerotherapy for Dilated Gastrojejunostomy

The textbook Townsend: Sabiston Textbook of Surgery (2012) states that, in regard to investigational bariatric procedures, "endoscopic incisionless surgery has focused on patients after Roux-en-Y gastric bypass (RYGB) who have inadequate weight loss or significant weight regain and who have a dilated gastrojejunostomy. It is thought that these patients lose restriction because of the dilated gastrojejunostomy and thus overeat. Surgeons have tried endoscopic injection of sclerosing agents to create scar and a smaller anastomosis, with variable effects."

In 2008, Loewen and Barba evaluated the injection of morrhuate sodium as sclerotherapy to decrease the diameter of the gastrojejunostomy anastomosis following gastric bypass. A total of 71 patients underwent sclerotherapy at their gastrojejunostomy from July 2004 to August 2006. A retrospective review was performed of this group, including chart review, follow-up data with weight checks, and telephone interview findings. The average age of the patients was 45 years and all but 4 patients were women. Sclerotherapy was done an average of 2.9 years after gastric bypass. The starting weight at endoscopy was an average of 218 lb-18 lb heavier than the average nadir weight. The average diameter of the gastrojejunostomy was 2.3 cm. An average of 13 mL morrhuate sodium was injected circumferentially. Repeat therapy was performed in 35 patients (49%). No hospital admissions or complications occurred in relation to the procedure. During the 12-month follow-up period, 72% of patients maintained or lost weight. The analysis showed a high body mass index (at endoscopy) to be the only predictive factor for successful weight maintenance or loss. The authors reported, "a randomized controlled study is necessary to validate these findings."

In a 2007 article, Spaulding, Osler and Patlak studied endoscopic sclerotherapy with sodium morrhuate of a dilated gastrojejunostomy in 147 gastric bypass patients. In a retrospective review, 32 patients were identified for whom > or =12 months of postprocedure data were available. Their weight trends before and after treatment were assessed by paired t test. A total of 32 patients who were gaining weight after gastric bypass underwent sclerotherapy of their dilated gastrojejunostomy. The timing of treatment ranged from 10 to 140 months (average 56) after Roux-en-Y gastric bypass. Before sclerotherapy, patients were gaining weight at a rate of .36 kg/mo. After treatment, they were losing weight at a rate of .39 kg/mo. After treatment, 56.3% of patients began to lose weight, 34.4% had their weight stabilize, and 9.4% continued to gain weight.

Gastrointestinal Liners (EndoBarrier) for the Treatment of Obesity

Endoscopic duodenal-jejunal bypass is the endoscopic placement of a duodenal-jejunal bypass sleeve (eg, EndoBarrier) which lines the first section of the small intestine causing food to be absorbed further along the intestine. Once implanted, the device is purported to influence gastrointestinal hormones and satiety. It is suggested to promote weight loss in individuals who are potential candidates for bariatric surgery, but are too heavy to safely undergo the procedure.

An UpToDate review on "Bariatric surgical operations for the management of severe obesity: Descriptions" (Lim, 2015) lists "Endoscopic gastrointestinal bypass devices" as investigational. It states that "Endoscopic gastrointestinal bypass devices (EGIBD) – A barrier device is deployed to prevent luminal contents from being absorbed in the proximal small intestine. The EndoBarrier is 60-cm long and it extends from the proximal duodenum to the mid-jejunum and thus mimics a duodenojejunal bypass. It is a safe procedure but is hallmarked by an up to 20% rate of early removal due to patient intolerance. The ValenTx is a 120-cm barrier device that extends from the gastroesophageal junction to the jejunum. This too has a high rate of early removal, but excess weight loss at 3 months was reported to be 40%, and significant improvement was seen in 7 out of 7 diabetic patients within those 3 months. Data are still lacking about the longevity of these endobarriers and their outcomes once the barrier is removed".

The EndoBarrier, an endoscopically delivered duodeno-jejunal bypass liner (DJBL), is a plastic flexible tube that is placed in the duodenal bulb, directly behind the pylorus. It extends from the duodenum to the proximal jejunum. Recent studies have suggested that the use of EndoBarrier has resulted in significant weight reduction in comparison to control-diet patients.

Schouten et al (2010) noted that the endoscopically placed duodenal-jejunal bypass sleeve or EndoBarrier Gastrointestinal Liner has been designed to achieve weight loss in morbidly obese patients. These researchers reported on the first European experience with this device. A multi-center, randomized clinical trial was performed. A total of 41 patients were included and 30 underwent sleeve implantation; 11 patients served as a diet control group. All patients followed the same low-calorie diet during the study period. The purpose of the study was to determine the safety and effectiveness of the device. A total of 26 devices were successfully implanted. In 4 patients, implantation could not be achieved. Four devices were explanted prior to the initial protocol end point because of migration (n = 1), dislocation of the anchor (n = 1), sleeve obstruction (n = 1), and continuous epigastric pain (n = 1). The remaining patients all completed the study. Mean procedure time was 35 mins (range of 12 to 102) for a successful implantation and 17 mins (range of 5 to 99) for explantation. There were no procedure related adverse events. During the study period the 26 duodenal-jejunal bypass sleeve patients (100%) had at least 1 adverse event, mainly abdominal pain and nausea during the first week after implantation. Initial mean BMI was 48.9 and 47.4 kg/m2 for the device and control patients, respectively. Mean excess weight loss after 3 months was 19.0% for device patients versus 6.9% for control patients ($p < 0.002$). Absolute change in BMI at 3 months was 5.5 and 1.9 kg/m2, respectively. Type 2 diabetes mellitus was present at baseline in 8 patients of the device group and improved in 7 patients during the study period (lower glucose levels, glycated hemoglobin [HbA1c], and medication requirements). The authors concluded that the EndoBarrier Gastrointestinal Liner is a feasible and safe non-invasive device with excellent short-term weight loss results. The device also has a significant positive effect on type 2 diabetes mellitus. Moreover, they stated that long-term randomized and sham studies for weight loss and treatment of diabetes are necessary to determine the role of the device in the treatment of morbid obesity.

Gersin et al (2010) examined the effects of an endoscopic DJBL for pre-operative weight loss in bariatric surgery candidates. A total of 21 obese subjects in the DJBL arm and 26 obese subjects in the sham arm composed the intent-to-treat population. The subjects in the sham arm underwent an esophagogastroduodenoscopy and mock implantation. Both groups received identical nutritional counseling. The primary endpoint was the difference in the percentage of EWL at week 12 between the 2 groups. Secondary endpoints were the percentage of subjects achieving 10% EWL, total weight change, and device safety. A total of 13 DJBL arm subjects and 24 sham arm subjects completed the 12-week study. EWL was 11.9% +/- 1.4% and 2.7% +/- 2.0% for the DJBL and sham arms, respectively ($p < 0.05$). In the DJBL arm, 62% achieved 10% or more EWL compared with 17% of the subjects in the sham arm ($p < 0.05$). Total weight change in the DJBL arm was -8.2 +/- 1.3 kg compared with -2.1 +/- 1.1 kg in the sham arm ($p < 0.05$). Eight DJBL subjects terminated early because of gastrointestinal bleeding (n = 3), abdominal pain (n = 2), nausea and vomiting (n = 2), and an unrelated preexisting illness (n = 1). None had further clinical symptoms after DJBL explantation. The authors concluded that the DJBL achieved endoscopic duodenal exclusion and promoted significant weight loss beyond a minimal sham effect in candidates for bariatric surgery. The main drawbacks of this study were: (i) study personnel were not blinded, and (ii) there was a lack of data on caloric intake.

Escalona et al (2012) evaluated safety, weight loss, and cardio-metabolic changes in obese subjects implanted with the DJBL for 1 year. Morbidly obese subjects were enrolled in a single-arm, open-label, prospective trial and implanted with the DJBL. Primary endpoints included safety and weight change from baseline to week 52. Secondary endpoints included changes in waist circumference, blood pressure, lipids, glycemic control, and metabolic syndrome. The DJBL was implanted endoscopically in 39 of 42 subjects (mean age of 36 +/- 10 years; 80% female; mean weight of 109 +/- 18 kg; mean BMI of 43.7 +/- 5.9 kg/m); 24 completed 52 weeks of follow-up. Three subjects could not be implanted due to short duodenal bulb. Implantation time was 24 +/- 2 mins. There were no procedure-related complications and there were 15 early endoscopic removals. In the 52-week completer population, total body weight change from baseline was -22.1 +/- 2.1 kg ($p < 0.0001$) corresponding to 19.9 +/- 1.8%

of total body weight and 47.0 +/- 4.4% excess of weight loss. There were also significant improvements in waist circumference, blood pressure, total and low-density lipoprotein cholesterol, triglycerides, and fasting glucose. The authors concluded that the DJBL is safe when implanted for 1 year, and results in significant weight loss and improvements in cardio-metabolic risk factors. They stated that these results suggested that this device may be suitable for the treatment of morbid obesity and its related comorbidities. Main drawbacks of this study were its small sample size and only 24 of 39 subjects (62%) completed the 52-week followed-up.

Verdam et al (2012) stated that the prevalence of obesity is increasing worldwide. Its primary treatment consists of lifestyle changes. In severely obese (BMI greater than 40 kg/m2 or greater than or equal to 35 kg/m2 with co-morbidity) patients though, bariatric surgery has been found to be the only way to achieve permanent weight loss. Operations such as the placement of a gastric band or a gastric bypass can, however, lead to complications and necessitate secondary interventions. In search of less invasive treatments, placement of the EndoBarrier duodenal jejunal bypass liner appears to be a promising, safe and effective method for facilitating weight loss. Concomitant positive effects on cardiovascular risk factors including diabetes type 2 were observed. The authors noted that a multi-center trial is currently underway to examine the mechanism behind these effects.

Mathus-Vliegen (2012) stated that the EndoBarrier is a unique concept that starts to ameliorate the symptoms of diabetes mellitus type 2, soon after positioning. Weight-loss results are moderate, with 85% of patients showing a more than 10% excess weight loss in the 12 weeks pre-operatively. Sufficient implant training is required, but problems can still occur (e.g., due to a short duodenal bulb length). The stability of the anchors and the tolerability of the device still leave much to be desired. In 25% of patients the EndoBarrier is explanted early, because of migration, physical symptoms, gastrointestinal hemorrhage, rotation and obstruction. Only 7 studies on the EndoBarrier are available and these are mostly small in size, short-term and with limited follow-up, and many questions regarding the safety and long-term effects of the device remain. The author concluded that this calls for a large, long-term, randomized,

placebo-controlled, double-blind trial. Lessons should have been learned from the disastrous results with intra-gastric balloon implantation before commercializing another such product.

The OverStitch Suturing Device

Bolton et al (2013) stated that weight regain secondary to VBG pouch dilation is a typical referral for bariatric surgeons. In this study these investigators compared an endoluminal pouch reduction (StomaphyX) to RYGB for revision. A retrospective review was completed for patients with a previous VBG presenting with weight regain between 2003 to 2010. A total of 30 patients were identified (StomaphyX; n = 14). Significant post procedure BMI loss was seen in each cohort (RYGB, 47.7 ± 7 kg/m(2) to 35 ± 7 kg/m(2); StomaphyX 43 ± 10 kg/m(2) to 40 ± 9 kg/m(2), p = 0.0007). Whereas nausea and headache were the only complications observed in StomaphyX patients, the RYGB group had a 43.5% complication rate and 1 mortality. Complications following RYGB include: incisional hernia (13%), anastomotic leak (8.7%), respiratory failure (8.7%), fistula (8.7%), and perforation (4.35%). The median length of stay following RYGB was 6 days compared to 1.5 ± 0.5 days following StomaphyX. The authors concluded that the findings of this study suggested that while RYGB revision may achieve greater weight loss, the complication rates and severity is discouraging. StomaphyX may be a safe alternative. Moreover, they stated that further technical modifications of the device and longer follow-up may clarify the role of this approach.

Goyal et al (2013) examined if endoluminal reduction of gastric pouch and stoma using StomaphyX results in sustained weight loss in patients who regain weight after gastric bypass. Retrospective chart review was performed on 59 post-gastric bypass patients who underwent revision of gastric pouch using StomaphyX from 2007 to 2008. Post-procedure weight at 1 week, 1 month, and 6 months follow-up as well as weight at the time of the review was recorded for each patient. Average weight loss and excess body weight loss (EBWL) were 2.6 ± 2.3 kg and 7.3 ± 7.1% (n = 42) at 1 week, 3.7 ± 2.9 kg and 11.6 ± 12.1% (n = 31) at 1 month, and 3.8 ± 4.5 kg and 11.5 ± 17.9% (n = 10) at 6 months, respectively. At the time of review, the average follow-up was 41 months, average weight loss was 1.7 ± 9.7 kg, and EBWL was 4.3 ± 29.8% (n = 53). Endoscopy in 12 patients at average 18 months follow-up showed no sustained reduction

in pouch and stoma size. The authors concluded that StomaphyX resulted in weight loss that is not sustained on long-term follow-up. Pouch and stoma tend to regain their pre-procedure size on follow-up. They stated that StomaphyX cannot be recommended as a weight loss strategy in post-gastric bypass patients who regain weight.

Campos et al (2012) stated that RYGB may result in stenosis of the gastro-jejunal anastomosis (GJA). There is currently no well-defined management protocol for this complication. Through systematic review, these investigators analyzed the results of endoscopic dilation in patients with stenosis, including complication and success rates. The PubMed database was searched for relevant studies published each year from 1988 to 2010, and 23 studies were identified for analysis. Only papers describing the treatment of anastomotic stricture after RYGB were included, and case-reports featuring less than 3 patients were excluded. The mean age of the trial populations was 42.3 years and mean pre-operative BMI was 48.8 kg/m². A total of 1,298 procedures were undertaken in 760 patients (81% female), performing 1.7 dilations per patient. Through-the-scope balloons were used in 16 studies (69.5%) and Savary-Gilliard bougies in 4 studies. Only 2% of patients needed surgical revision after dilation; the reported complication rate was 2.5% (n = 19). Annual success rate was greater than 98% each year from 1992 to 2010, except for a 73% success rate in 2004; 7 studies reported complications, perforation being the most common, reported in 14 patients (1.82%) and requiring immediate operation in 2 patients. Other complications were also reported: 1 esophageal hematoma, 1 Mallory-Weiss tear, 1 case of severe nausea and vomiting, and 2 cases of severe abdominal pain. The authors concluded that endoscopic treatment of stenosis is safe and effective; however, further high-quality randomized controlled trials are needed to confirm these findings.

Thompson et al (2013) stated that weight regain or insufficient loss after RYGB is common. This is partially attributable to dilatation of the gastro-jejunostomy, which diminishes the restrictive capacity of RYGB. Endoluminal interventions for GJ reduction are being explored as alternatives to revision surgery. These researchers performed a randomized, blinded, sham-controlled trial to evaluate weight loss after sutured transoral outlet reduction (TORe). Patients with weight regain or inadequate loss after RYGB and GJ diameter greater than 2 cm were

assigned randomly to groups that underwent TORe (n = 50) or a sham procedure (controls, n = 27). Intra-operative performance, safety, weight loss, and clinical outcomes were assessed. Subjects who received TORe had a significantly greater mean percentage weight loss from baseline (3.5%; 95% CI: 1.8% to 5.3%) than controls (0.4%; 95% CI: 2.3% weight gain to 3.0% weight loss) (p = 0.021), using a last observation carried forward intent-to-treat analysis. As-treated analysis also showed greater mean percentage weight loss in the TORe group than controls (3.9% and 0.2%, respectively; p = 0.014). Weight loss or stabilization was achieved in 96% subjects receiving TORe and 78% of controls (p = 0.019). The TORe group had reduced systolic and diastolic blood pressure (p < 0.001) and a trend toward improved metabolic indices. In addition, 85% of the TORe group reported compliance with the healthy lifestyle eating program, compared with 53.8% of controls; 83% of TORe subjects said they would undergo the procedure again, and 78% said they would recommend the procedure to a friend. The groups had similar frequencies of adverse events. The authors concluded that a multi-center randomized trial provided Level I evidence that TORe reduces weight regain after RYGB. These results were achieved using a superficial suction-based device; greater levels of weight loss could be achieved with newer, full-thickness suturing devices. These researchers stated that TORe is one approach to avoid weight regain; moreover, they noted that a longitudinal multi-disciplinary approach with dietary counseling and behavioral changes are needed for long-term results.

Jirapinyo et al (2013) evaluated the technical feasibility, safety, and early outcomes of a procedure using a commercially available endoscopic suturing device to reduce the diameter of the GJA. This was a retrospective analysis of 25 consecutive patients who underwent TORe for dilated GJA and weight regain. An endoscopic suturing device was used to place sutures at the margin of the GJA in order to reduce its aperture. On chart review, clinical data were available at 3, 6, and 12 months. Patients had regained a mean of 24 kg from their weight loss nadir and had a mean BMI of 43 kg/m2 at the time of endoscopic revision. Average anastomosis diameter was 26.4 mm. Technical success was achieved in all patients (100%) with a mean reduction in anastomosis diameter to 6 mm (range of 3 to 10), representing a 77.3% reduction. The mean weight loss in successful cases was 11.5 kg, 11.7 kg, and 10.8 kg at 3, 6, and 12 months, respectively. There were no major complications.

The authors concluded that this case series demonstrated the technical feasibility, safety, and effectiveness of performing GJ reduction using a commercially available endoscopic suturing device. They stated that this technique may represent an effective and minimally invasive option for the management of weight regain in patients with RYGB.

Dakin and colleagues (2013) noted that weight recidivism after RYGB is a challenging problem for patients and bariatric surgeons alike. Traditional operative strategies to combat weight regain are technically challenging and associated with a high morbidity rate. Endoluminal interventions are thus an attractive alternative that may offer a good combination of results coupled with lower peri-procedure risk that might one day provide a solution to this increasingly prevalent problem. These investigators systematically reviewed the available literature on endoluminal procedures used to address weight regain after RYGB, with specific attention to the safety profile, effectiveness, cost, and current availability. This retrospective review focused only on endoluminal procedures that were performed for weight regain after RYGB, as opposed to primary endoluminal obesity procedures. Several methods of endoluminal intervention for weight regain were reviewed, ranging from injection of inert substances to suturing and clipping devices. The literature review showed the procedures on the whole to be well-tolerated with limited effectiveness. The majority of the literature was limited to small case-series. Most of the reviewed devices were no longer commercially available. The authors concluded that endoluminal therapy represents an intriguing strategy for weight regain after RYGB. However, the current and future technologies must be rigorously studied and improved such that they offer durable, repeatable, cost-effective solutions.

Pauli et al (2013) stated that despite advances in many areas of therapeutic endoscopy, the development of an effective endoscopic suturing device has been elusive. These researchers evaluated the safety and effectiveness of a suturing device to place and secure sutures within normal, in-vivo human colonic tissue prior to surgical resection. Patients undergoing elective colectomy were enrolled in this treat-and-resect model. The OverStitch endoscopic suturing device (Apollo Endosurgery, Austin, TX) was used to place sutures in healthy colonic tissue during a 15-min, time-limited period. Following colectomy, the explanted tissue was evaluated to determine the depth of suture penetration and the

effectiveness of the suture/cinch element. Clinical and operative data were recorded. A total of 4 patients (50% female) were enrolled. Seven sutures were successfully placed, incorporating a total of 10 tissue bites in a mean of 13.5 mins. On inspection of the explanted tissue, all sutures were found to be located sub-serosal (no full thickness bites were taken). The suture and cinch elements were judged to be effective in the majority of cases. One device-related issue did not inhibit the ability to oppose tissue or place the cinch. There were no intra-operative or post-operative complications. The authors concluded that the OverStitch permitted safe and effective suturing in an in-vivo human colon model. The sutures were placed at a consistent sub-serosal depth and at no point risked iatrogenic injury to adjacent structures. Technical issues with the device were infrequent and did not inhibit the ability to place sutures effectively.

A clinical trial entitled "Endoscopic Surgery for Bariatric Revision after Weight Loss Failure" is not yet open for participant recruitment (NIH, 2014). This clinical trial is designed to study the Apollo OverStitch endoscopic suturing device that has already been approved by the FDA as an option for bariatric surgery revision without having to re-operate on the patient. The investigators believe that the endoscopic technique may be able to provide weight loss without having to re-operate on the patient.

Laparoscopic Greater Curvature Plication

Shen described the surgical technique of laparoscopic greater curvature plication (LGCP) and validated the safety and effectiveness of LGCP for the treatment of obesity in Chinese patients with a relatively low BMI. A total of 22 obese patients (mean age of 33.8 ± 6.0 years; mean BMI of 37.0 ± 7.0 kg/m(2)) underwent LGCP between September 2011 and September 2012. After dissecting the greater omentum and short gastric vessels, the gastric greater curvature plication with 2 rows of non-absorbable suture was performed under the guidance of a 32-F bougie. The data were collected during follow-up examinations performed at 1, 3, 6, and 12 months post-operatively. All procedures were performed laparoscopically. The mean operative time was 84.1 mins (50 to 120 mins), and the mean length of hospital stay was 3.8 days (2 to 10 days). There were no deaths or post-operative major complications that needed re-operation. The mean%EWL was 22.9% ± 6.9%, 38.6% ± 9.8%, 51.5% ± 13.5%, and 61.1% ± 15.9% at 1, 3, 6, and 12 months post-operatively.

At 6 months, type 2 diabetes was in remission in 2 (50%) patients, hypertension in 1 (33.3%) patient, and dyslipidemia in 11 (78.6%) patients. Decreases in the index for homeostasis model assessment of insulin resistance (HOMA-IR) and in insulin and glucose concentrations were observed. The authors concluded that the early outcomes of LGCP as a novel treatment for obese Chinese with a relatively low BMI were satisfactory with respect to the effectiveness and low incidence of major complications. They stated that additional long-term follow-up and prospective, comparative trials are still needed.

Transoral Mucosal Excision Sutured Gastroplasty

In a pilot study, Legner et al (2014) examined the effectiveness of transoral mucosal excision sutured gastroplasty for the treatment of gastro-esophageal reflux disease (GERD) and obesity. A total of 8 patients (GERD, n =3 and obesity = 5) were selected according to a pre-approved study protocol. All GERD patients had pre-procedure manometry and pH monitoring to document GERD as well as quality of life and symptom questionnaires. Obese patients (BMI greater than 35) underwent a psychological evaluation and tests for co-morbidities. Under general anesthesia, a procedure was performed at the gastro-esophageal junction including mucosal excision, suturing of the excision beds for apposition, and suture knotting. One patient with micrognathia could not undergo the required pre-procedural passage of a 60 F dilator and was excluded. The first 2 GERD patients had incomplete procedures due to instrument malfunction. The subsequent 5 subjects had a successfully completed procedure. Four patients were treated for obesity and had an average excess weight loss of 30.3% at 2-year follow-up. Of these patients, 1 had an 8-mm outlet at the end of the procedure recognized on video review – a correctable error – and another vomited multiple times post-operatively and loosened the gastroplasty sutures. The treated GERD patient had resolution of reflux-related symptoms and is off all anti-secretory medications at 2-year follow-up. Her DeMeester score was 8.9 at 24 months. The authors concluded that the initial human clinical experience showed promising results for effective and safe GERD and obesity therapy.

Laparoscopic Mini-Gastric Bypass

Georgiadou et al (2014) summarized the available evidence about the efficacy and safety of laparoscopic mini-gastric bypass (LMGB). These investigators performed a systematic search in the literature, and PubMed and reference lists were scrutinized (end-of-search date: July 15, 2013). For the assessment of the eligible articles, the Newcastle-Ottawa quality assessment scale was used. A total of 10 eligible studies were included in this study, reporting data on 4,899 patients. According to all included studies, LMGB induced substantial weight and BMI reduction, as well as substantial excess weight loss. Moreover, resolution or improvement in all major associated medical illnesses and improvement in overall Gastrointestinal Quality of Life Index score were recorded. Major bleeding and anastomotic ulcer were the most commonly reported complications. Re-admission rate ranged from 0% to 11%, whereas the rate of revision operations ranged from 0.3% to 6%. The latter were conducted due to a variety of medical reasons such as inadequate or excessive weight loss, malnutrition, and upper gastro-intestinal bleeding. Finally, the mortality rate ranged between 0% and 0.5% among primary LMGB procedures. The authors concluded that LMGB represents an effective bariatric procedure; its safety and minimal post-operative morbidity seem remarkable. They stated that randomized comparative studies seem mandatory for the further evaluation of LMGB.

Bariatric Surgery for Type-2 Diabetes

Zechmeister-Koss et al (2014) applied the GRADE approach to evaluate the safety and effectiveness of the duodenal-jejunal bypass liner (DJBL) for the treatment of; (i) patients with obesity greater than or equal to grade II (with co-morbidities) and (ii) patients with type 2 diabetes mellitus + obesity greater than or equal to grade I. These researchers included 10 studies with a total of 342 patients that primarily investigated a prototype of the DJBL. In high-grade obese patients, short-term excess weight loss was observed. For the remaining patient-relevant endpoints and patient populations, evidence was either not available or ambiguous. Complications (mostly minor) occurred in 64 to 100% of DJBL patients compared to 0 to 27% in the control groups. Gastro-intestinal bleeding was observed in 4% of patients. The authors do not yet recommend the device for routine use.

Parikh et al (2014) compared bariatric surgery versus intensive medical weight management (MWM) in patients with type 2 diabetes mellitus (T2DM) who do not meet current National Institutes of Health criteria for bariatric surgery and examined if the soluble form of receptor for advanced glycation end products (sRAGE) is a biomarker to identify patients most likely to benefit from surgery. A total of 57 patients with T2DM and BMI 30 to 35, who otherwise met the criteria for bariatric surgery were randomized to MWM versus surgery (bypass, sleeve or band, based on patient preference). The primary outcomes assessed at 6 months were change in homeostatic model of insulin resistance (HOMA-IR) and diabetes remission. Secondary outcomes included changes in HbA1c, weight, and sRAGE. The surgery group had improved HOMA-IR (-4.6 versus +1.6; p = 0.0004) and higher diabetes remission (65% versus 0%, p < 0.0001) than the MWM group at 6 months. Compared to MWM, the surgery group had lower HbA1c (6.2 versus 7.8, p = 0.002), lower fasting glucose (99.5 vs 157; P = 0.0068), and fewer T2DM medication requirements (20% vs 88%; P < 0.0001) at 6 months. The surgery group lost more weight (7. vs 1.0 BMI decrease, P < 0.0001). Higher baseline sRAGE was associated with better weight loss outcomes (r = -0.641; p = 0.046). There were no mortalities. The authors concluded that surgery was very effective short-term in patients with T2DM and BMI 30 to 35. Baseline sRAGE may predict patients most likely to benefit from surgery. However, they stated that these findings need to be confirmed with larger studies.

Sjostrom et al (2014) noted that short-term studies showed that bariatric surgery causes remission of diabetes. The long-term outcomes for remission and diabetes-related complications are not known. These researchers determined the long-term diabetes remission rates and the cumulative incidence of microvascular and macrovascular diabetes complications after bariatric surgery. The Swedish Obese Subjects (SOS) is a prospective matched cohort study conducted at 25 surgical departments and 480 primary health care centers in Sweden. Of patients recruited between September 1, 1987, and January 31, 2001, 260 of 2,037 control patients and 343 of 2,010 surgery patients had type-2 diabetes at baseline. For the current analysis, diabetes status was determined at SOS health examinations until May 22, 2013. Information on diabetes complications was obtained from national health registers until December 31, 2012. Participation rates at the 2-, 10-, and 15-year

examinations were 81%, 58%, and 41% in the control group and 90%, 76%, and 47% in the surgery group. For diabetes assessment, the median follow-up time was 10 years (interquartile range [IQR], 2 to 15) and 10 years (IQR, 10 to 15) in the control and surgery groups, respectively. For diabetes complications, the median follow-up time was 17.6 years (IQR, 14.2 to 19.8) and 18.1 years (IQR, 15.2 to 21.1) in the control and surgery groups, respectively. Adjustable or non-adjustable banding (n = 61), vertical banded gastroplasty (n = 227), or gastric bypass (n = 55) procedures were performed in the surgery group, and usual obesity and diabetes care was provided to the control group. Main outcome measures were diabetes remission, relapse, and diabetes complications. Remission was defined as blood glucose less than 110 mg/dL and no diabetes medication. The diabetes remission rate 2 years after surgery was 16.4% (95% CI: 11.7% to 22.2%; 34/207) for control patients and 72.3% (95% CI: 66.9% to 77.2%; 219/303) for bariatric surgery patients (odds ratio [OR], 13.3; 95% CI: 8.5 to 20.7; $p < 0.001$). At 15 years, the diabetes remission rates decreased to 6.5% (4/62) for control patients and to 30.4% (35/115) for bariatric surgery patients (OR, 6.3; 95% CI: 2.1 to 18.9; $p < 0.001$). With long-term follow-up, the cumulative incidence of microvascular complications was 41.8 per 1,000 person-years (95% CI: 35.3 to 49.5) for control patients and 20.6 per 1,000 person-years (95% CI: 17.0 to 24.9) in the surgery group (hazard ratio [HR], 0.44; 95% CI: 0.34 to 0.56; $p < 0.001$). Macrovascular complications were observed in 44.2 per 1,000 person-years (95% CI: 37.5-52.1) in control patients and 31.7 per 1,000 person-years (95% CI: 27.0 to 37.2) for the surgical group (HR, 0.68; 95% CI: 0.54 to 0.85; $p = 0.001$). The authors concluded that in this very long-term follow-up observational study of obese patients with type 2 diabetes, bariatric surgery was associated with more frequent diabetes remission and fewer complications than usual care. Moreover, they stated that these findings require confirmation in randomized trials.

Yu et al (2015) evaluated the long-term effects of bariatric surgery on type 2 diabetic patients. These investigators searched Cochrane Library, PubMed, and EMbase up to Dec 2013; RCTs and cohort studies of bariatric surgery for diabetes patients that reported data with more than 2 years of follow-up were included. They used rigorous methods to screen studies for eligibility and collected data using standardized forms. Where applicable, these investigators pooled data by meta-analyses. A total of

26 studies, including 2 RCTs and 24 cohort studies that enrolled 7,883 patients, proved eligible. Despite the differences in the design, those studies consistently showed that bariatric surgery offered better treatment outcomes than non-surgical options. Pooling of cohort studies showed that BMI decreased by 13.4 kg/m(2) (95% confidence interval (CI): -17.7 to -9.1), fasting blood glucose by 59.7 mg/dl (95% CI: -74.6 to -44.9), and glycated hemoglobin by 1.8% (95% CI: -2.4 to -1.3). Diabetes was improved or in remission in 89.2% of patients, and 64.7% of patients was in remission. Weight loss and diabetes remission were greatest in patients undergoing bilio-pancreatic diversion/duodenal switch, followed by gastric bypass, sleeve gastrectomy, and adjustable gastric banding. The authors noted that bariatric surgery may achieve sustained weight loss, glucose control, and diabetes remission. Moreover, they stated that large randomized trials with long-term follow-up are warranted to demonstrate the effect on outcomes important to patients (e.g., cardiovascular events).

Furthermore, an UpToDate review on "Management of persistent hyperglycemia in type 2 diabetes mellitus" (McCullock, 2014) states that "Surgical treatment of obese patients with diabetes results in the largest degree of sustained weight loss (20 to 30 percent after one to two years) and, in parallel, the largest improvements in blood glucose control. There are a growing number of unblinded trials comparing bariatric surgery with medical therapy for the treatment of type 2 diabetes …. Despite these impressive metabolic results, concerns remain about acute post-operative complications including need for re-operations and re-hospitalizations and rare, but potentially severe, adverse events; the long-term success rates in maintaining weight loss; and the reproducibility of the results in patients with an extensive history of diabetes or with a different surgical team. Some weight regain is typical within two to three years of bariatric procedures, and different bariatric procedures result in different levels of weight loss and corresponding reductions in glycemia. Longer-term follow-up of clinically important endpoints, such as effects on microvascular and macrovascular complications and mortality, are required before laparoscopic banding or other bariatric surgery procedures can be routinely recommended for the treatment of persistent hyperglycemia, resistant to multiple medications, in obesity-related type 2 diabetes".

Cummings and Cohen (2016) stated that global usage of bariatric surgery has been dictated for the past quarter century by National Institutes of Health (NIH) recommendations restricting these operations to individuals with a BMI ≥ 35 kg/m(2). Strong evidence now demonstrates that bariatric procedures markedly improve or cause remission of type 2 diabetes mellitus (T2DM), in part through weight-independent mechanisms, and that baseline BMI does not predict surgical benefits on glycemic or cardiovascular outcomes. This impels consideration of such operations as "metabolic surgery", which is used expressly to treat T2DM, including among patients with a BMI < 35 kg/m(2) who constitute the majority of people with diabetes worldwide. These investigators reviewed available evidence to inform that consideration. A meta-analysis of the 11 published randomized clinical trials (RCTs) directly comparing bariatric/metabolic surgery versus a variety of medical/lifestyle interventions for T2DM provided level 1A evidence that surgery is superior for T2DM remission, glycemic control, and HbA1c lowering. Importantly, this is equally true for patients whose baseline BMI is below or above 35 kg/m(2). Similar conclusions were derived from meta-analyses of high-quality non-randomized prospective comparisons. Meta-analysis of all pertinent published studies indicated that T2DM remission rates following bariatric/metabolic surgery are comparable above and below the 35 kg/m(2) BMI threshold. The safety, anti-diabetes durability, and benefits on other cardiovascular risk factors from bariatric/metabolic surgery appeared roughly comparable among patients with a BMI below or above 35 kg/m(2). They stated that further studies are needed to extend long-term findings and measure "hard" macrovascular/microvascular outcomes and mortality in RCTs. The authors concluded that available data, including level 1A evidence from numerous RCTs, support new guidelines from the 2nd Diabetes Surgery Summit that advocate for the consideration of bariatric/metabolic surgery as one option, along with lifestyle and medical therapy, to treat T2DM among patients with a BMI < 35 kg/m(2).

The authors also noted that "long-term data regarding bariatric surgery in lower-BMI patients is relatively limited … long-term results from RCTs of lower-BMI patients are still pending. Another understudied area is the relative cost-effectiveness of bariatric/metabolic surgery compared with

conventional care among less obese patients with T2DM, and RCTs powered to observe "hard" outcomes such as cardiovascular events, cancer, and death are needed among patients of any BMI level".

Rubino et al (2016) stated that despite growing evidence that bariatric/metabolic surgery powerfully improves T2DM, existing diabetes treatment algorithms do not include surgical options. The 2nd Diabetes Surgery Summit (DSS-II), an international consensus conference, was convened in collaboration with leading diabetes organizations to develop global guidelines to inform clinicians and policymakers about benefits and limitations of metabolic surgery for T2DM. A multi-disciplinary group of 48 international clinicians/scholars (75% non-surgeons), including representatives of leading diabetes organizations, participated in DSS-II. After evidence appraisal (Medline (January 1, 2005 to September 30, 2015]), 3 rounds of Delphi-like questionnaires were used to measure consensus for 32 data-based conclusions. These drafts were presented at the combined DSS-II and 3rd World Congress on Interventional Therapies for Type 2 Diabetes (London, U.K., September 28 to 30, 2015), where they were open to public comment by other professionals and amended face-to-face by the Expert Committee. Given its role in metabolic regulation, the gastro-intestinal tract constitutes a meaningful target to manage T2DM. Numerous randomized clinical trials, albeit mostly short/mid-term, demonstrated that metabolic surgery achieves excellent glycemic control and reduces cardiovascular risk factors. On the basis of such evidence, metabolic surgery should be recommended to treat T2DM in patients with class III obesity (BMI ≥ 40 kg/m(2)) and in those with class II obesity (BMI 35.0 to 39.9 kg/m(2)) when hyperglycemia is inadequately controlled by lifestyle and optimal medical therapy. Surgery should also be considered for patients with T2DM and BMI 30.0 to 34.9 kg/m(2) if hyperglycemia is inadequately controlled despite optimal treatment with either oral or injectable medications. These BMI thresholds should be reduced by 2.5 kg/m(2) for Asian patients. The authors concluded that although additional studies are needed to further demonstrate long-term benefits, there is sufficient clinical and mechanistic evidence to support inclusion of metabolic surgery among anti-diabetes interventions for people with T2DM and obesity. To date, the DSS-II guidelines have been formally endorsed by 45 worldwide medical and scientific societies. Health care regulators should introduce appropriate reimbursement policies.

Yan et al (2016) compared Roux-en-Y gastric bypass (RYGB) surgery versus medical treatment for T2DM in obese patients. Bariatric surgery can achieve remission of T2DM in obese patients. RYGB surgery has been performed as one of the most common surgical treatment options for obese patients with T2DM, but the efficacy of RYGB surgery comparing with medical treatment alone has not been conclusively determined. These investigators performed a systematic literature search and identified RCTs evaluating RYGB surgery versus medical treatment for T2DM in obese patients in PubMed, Embase, Cochrane Database, and Cochrane Clinical Trials Registry. This systematic review and meta-analysis were performed according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. The primary outcome was T2DM remission. Additional analyses comprised hemoglobin A1c (HbA1c), fasting plasma glucose (FPG), BMI, waist circumference, serum lipid level, blood pressure, medication use, and adverse events. Random-effects meta-analyses were calculated and presented as weighted odds ratio (OR) or mean difference (MD) with 95% confidence intervals (CI). A total of 6 RCTs concerning 410 total obese T2DM patients were included. Follow-up ranged from 12 to 60 months. RYGB surgery was associated with a higher T2DM remission rate (OR: 76.37, 95% CI: 20.70 to 281.73, $p<0.001$) and serum level of high-density lipoprotein cholesterol (MD: 0.24 mmol/L, 95% CI: 0.18 to 0.30 mmol/L, $p<0.001$) than medical treatment alone. HbA1c (MD: -1.25%, 95% CI: -1.88% to -0.63%, $p<0.001$), BMI (MD: -6.54 kg/m, 95% CI: -9.28 to -3.80 kg/m, $p<0.001$), waist circumference (MD: -15.60 cm, 95% CI: -18.21 to -13.00 cm, $p<0.001$), triglyceride (MD: -0.87 mmol/L, 95% CI: -1.17 to -0.57 mmol/L, $p<0.001$), low-density lipoprotein cholesterol (MD: -0.32 mmol/L, 95% CI: -0.62 to -0.02 mmol/L, $p=0.04$), systolic blood pressure (MD: -2.83 mm Hg, 95% CI: -4.88 to -0.78 mm Hg, $p<0.01$) were lower after RYGB surgery. However, FPG (MD: -1.58 mmol/L, 95% CI: -3.58 to 0.41 mmol/L, $p=0.12$), total cholesterol (MD: -0.40 mmol/L, 95% CI: -0.92 to 0.12 mmol/L, $p=0.13$), and diastolic blood pressure (MD: 0.28 mm Hg, 95% CI: -1.89 to 2.45 mm Hg, $p=0.80$) were not significantly different between the 2 treatment groups. The medicine use and quality of life were solely improved in the surgical group. Nutritional deficiencies and anemia were noted more frequently in the RYGB group. The authors concluded that RYGB surgery was superior to medical treatment for short- to medium-term remission of T2DM, improvement of metabolic

condition, and cardiovascular risk factors. Moreover, they stated that further RCTs should address the safety and long-term benefits of RYGB surgery on obese patients with T2DM.

Friedman and Wolfe (2016) stated that a number of important questions need to be addressed before recommending bariatric surgery as a treatment for type II diabetic kidney disease (DKD). First, does bariatric surgery actually slow progression of DKD? If so, which patients with DKD should be targeted for such an approach? Which bariatric procedure offers the best reno-protective effects? Are kidney-related benefits proportional to the weight lost? What effect does weight re-accumulation have on remission of DKD? Is actual remission required to treat DKD, or can more modest improvements suffice? What are the rates of complications and mortality after bariatric surgery in patients with DKD, and are these risks out-weighed by the kidney-related and other benefits? What additional benefits, such as improvements in dialysis access placement or transplantation wait-listing rates, can bariatric surgery offer?

These researchers noted that answering these questions will be challenging. A recent NIH symposium on long-term outcomes in bariatric surgery reviewed, in detail, the major hurdles in conducting well-powered, randomized, controlled bariatric surgery trials, specifically with regard to recruitment, sample size, and length of follow-up. Given the current funding environment, it was felt that alternative research strategies, including large observational studies using existing or prospective databases, should be considered. This may be especially relevant when considering the extended length of time that it could take to reverse DKD. These investigators and associated collaborators are currently working on just such a strategy.

The authors concluded that DKD is devastating to individuals and society. By inducing regression or remission of T2DM, bariatric surgery may also have the capability to effectively treat DKD. Small, short-term studies of bariatric surgery in patients with T2DM and DKD suggest a reno-protective effect primarily as reflected by a reduction in albuminuria, but effects on harder, more clinically relevant outcomes are lacking. The field is, therefore, ripe for clinical studies designed to elucidate the kidney-related benefits of bariatric surgery.

Panosian et al (2017) compared effects of Roux-en-Y gastric bypass versus a multi-disciplinary, group-based medical diabetes and weight management program on physical fitness and behaviors. Physical behavior and fitness were assessed in participants of the study Surgery or Lifestyle With Intensive Medical Management in the Treatment of Type 2 Diabetes (SLIMM-T2D) (NCT01073020), a randomized, parallel-group trial conducted at a US academic hospital and diabetes clinic with 18- to 24-month follow-up. A total of 38 T2DM patients with hemoglobin A1c ≥ 6.5% and BMI of 30 to 42 kg/m2 were randomized to Roux-en-Y gastric bypass or the medical program. A 6-minute walk test to evaluate fitness, self-reported physical activity, standardized physical surveys, and cardio-metabolic risk assessment were performed at baseline and after intervention. Both groups similarly improved 6-minute walk test distance, with greater improvements in oxygen saturation and reduced heart rate after surgery. Self-reported physical activity improved similarly at 18 to 24 months after interventions, although exercise increased gradually after surgery, whereas early substantial increases in the medical group were not fully sustained. Self-reported total and physical health were similar by Short Form-36 but improved more in the Impact of Weight on Quality of Life survey after surgery. Improvement in cardiovascular risk scores, HbA1c, and BMI were greater after surgery. The authors concluded that in this small, randomized study, both interventions led to therapeutic lifestyle changes and improved objective and self-reported physical fitness. Greater improvements in heart rate, oxygen saturation, and perceived impact of weight on health were seen after surgery, which could be attributable to greater weight loss. They stated that the clinical importance of these improvements with greater weight loss warrants further investigation.

Ikramuddin and associates (2018) compared durability of RNYGB added to intensive lifestyle and medical management in achieving diabetes control targets. Observational follow-up of a randomized clinical trial at 4 sites in the United States and Taiwan, involving 120 participants who had a hemoglobin A1c (HbA1c) level of 8.0% or higher and a BMI between 30.0 and 39.9 (enrolled between April 2008 and December 2011) were followed-up for 5 years, ending in November 2016. Lifestyle-intensive medical management intervention based on the Diabetes Prevention Program and LookAHEAD trials for 2 years, with and without (60 participants each) RNYBP followed by observation to year 5. Main

outcome measures were the American Diabetes Association composite triple end-point of hemoglobin A1c less than 7.0%, low-density lipoprotein cholesterol (LDL-C) less than 100 mg/dL, and systolic blood pressure less than 130 mm Hg at 5 years. Of 120 participants who were initially randomized (mean age, 49 years [SD, 8 years], 72 women [60%]), 98 (82%) completed 5 years of follow-up. Baseline characteristics were similar between groups: mean (SD) BMI 34.4 (3.2) for the lifestyle-medical management group and 34.9 (3.0) for the gastric bypass group and had hemoglobin A1c levels of 9.6% (1.2) and 9.6% (1.0), respectively. At 5 years, 13 participants (23%) in the gastric bypass group and 2 (4%) in the lifestyle-intensive medical management group had achieved the composite triple end-point (difference, 19%; 95% CI: 4% to 34%; p = 0.01). In the 5th year, 31 patients (55%) in the gastric bypass group versus 8 (14%) in the lifestyle-medical management group achieved an HbA1c level of less than 7.0% (difference, 41%; 95% CI: 19% to 63%; p = 0.002). Gastric bypass had more serious AEs than did the lifestyle-medical management intervention, 66 events versus 38 events, most frequently GII events and surgical complications such as strictures, small bowel obstructions, and leaks. Gastric bypass had more parathyroid hormone elevation but no difference in B12 deficiency. The authors concluded that in extended follow-up of obese adults with T2DM randomized to adding gastric bypass compared with lifestyle-medical management and intensive medical management alone, there remained a significantly better composite triple end-point in the surgical group at 5 years. However, because the effect size diminished over 5 years, further follow-up is needed to understand the durability of the improvement.

The authors stated that this study had several drawbacks. The mean baseline HbA1c concentration of 9.6% indicated that this was a group of participants with relatively poorly controlled glycemia, so whether the results would be different with better controlled glycemia at baseline could not be determined. Similarly, the participants had diabetes for a mean of 9 years at study entry, so treatment effect on diabetes of lesser duration could be different. Conversely, blood pressure and LDL-C levels were relatively well-controlled among the study participants, so it was possible that individuals with less control might receive greater treatment benefit. Follow-up was incomplete (82% at 5 years), creating an opportunity for bias. Statistical analyses assumed missing data were missing at random, which may not have been true. Cross-overs, which were analyzed on an

intention-to-treat basis, may have reduced observed treatment differences. The study tested a single type of bariatric surgery, the gastric bypass procedure which was most common at study initiation, so whether these conclusions apply to other surgical approaches will have to be assessed.

In a retrospective, matched cohort study, Fisher and colleagues (2018) examined the relationship between bariatric surgery and incident macrovascular (coronary artery disease and cerebrovascular diseases) events in patients with severe obesity and T2DM. Patients with severe obesity (BMI greater than or equal to 35) aged 19 to 79 years with diabetes who underwent bariatric surgery from 2005 to 2011 in 4 integrated health systems in the United States (n = 5,301) were matched to 14,934 control patients on site, age, sex, BMI, hemoglobin A1c, insulin use, observed diabetes duration, and prior health care utilization, with follow-up through September 2015. Bariatric procedures (76% RYGB, 17% sleeve gastrectomy, and 7% adjustable gastric banding) were compared with usual care for diabetes. Multivariable-adjusted Cox regression analysis investigated time to incident macrovascular disease (defined as first occurrence of coronary artery disease [acute myocardial infarction, unstable angina, percutaneous coronary intervention, or coronary artery bypass grafting] or cerebrovascular events [ischemic stroke, hemorrhagic stroke, carotid stenting, or carotid endarterectomy]). Secondary outcomes included coronary artery disease and cerebrovascular outcomes separately. Among a combined 20,235 surgical and non-surgical patients, the mean (SD) age was 50 (10) years; 76% of the surgical and 75% of the non-surgical patients were women; and the baseline mean (SD) BMI was 44.7 (6.9) and 43.8 (6.7) in the surgical and non-surgical groups, respectively. At the end of the study period, there were 106 macrovascular events in surgical patients (including 37 cerebrovascular and 78 coronary artery events over a median of 4.7 years; IQR, 3.2 to 6.2 years) and 596 events in the matched control patients (including 227 cerebrovascular and 398 coronary artery events over a median of 4.6 years; IQR, 3.1 to 6.1 years). Bariatric surgery was associated with a lower composite incidence of macrovascular events at 5 years (2.1% in the surgical group versus 4.3% in the non-surgical group; HR, 0.60 [95% CI: 0.42 to 0.86]), as well as a lower incidence of coronary artery disease (1.6% in the surgical group versus 2.8% in the non-surgical group; HR, 0.64 [95% CI: 0.42 to 0.99]).

The incidence of cerebrovascular disease was not significantly different between groups at 5 years (0.7% in the surgical group versus 1.7% in the non-surgical group; HR, 0.69 [95% CI: 0.38 to 1.25]). The authors concluded that in this observational study of patients with T2DM and severe obesity who underwent surgery, compared with those who did not undergo surgery, bariatric surgery was associated with a lower risk of macrovascular outcomes. Moreover, they stated that these findings need confirmation in randomized clinical trials. Health care professionals should engage patients with severe obesity and T2DM in a shared decision-making conversation regarding the potential role of bariatric surgery in the prevention of macrovascular events.

The authors stated that this study had several drawbacks. First, the observational design precluded causal inference, and unmeasured confounding may have persisted despite model adjustment for all major cardiovascular risk factors. However, the sensitivity analysis using E-value methodology (relative risk) indicated that the observed 5-year HR of 0.60 for incident macrovascular disease could only be explained by an unmeasured confounder that was associated with both receipt of bariatric surgery and risk of macrovascular disease by a risk ratio of more than 2.72 above and beyond that of the confounders that were measured in this study (upper confidence bound, 1.60). Given that this risk ratio was much greater than any observed for known macrovascular disease risk factors examined in the current study, such as hypertension, diabetes, or hyperlipidemia, it was implausible that an unmeasured confounder existed that could overcome the effect of bariatric surgery observed in the current analysis study. Second, baseline health characteristics and outcomes were established using data collected during routine medical care and billing, which meant that some information was missing and some co-morbid conditions could be misclassified (e.g., ICD-9 diagnosis codes could be misapplied); however, major cardiac and cerebrovascular outcomes were more likely to be accurately captured claims for all diagnoses and procedures associated with emergency department and hospital admissions. Third, cause-specific mortality was not examined because cause of death data were not extracted a priori. Fourth, loss to follow-up could bias the result if patients who underwent bariatric surgery and left the integrated health care systems in this study had very different macrovascular outcomes than the non-surgical patients who left these systems. Fifth, the sample size was insufficient to compare the

effectiveness of alternative bariatric procedures for these outcomes. There has been a shift toward increased use of the sleeve gastrectomy (SG) procedure in recent years in the United States, and although this study included 17% SG, it was unclear whether the benefits observed in a primarily RYGB population would be seen with SG. Sixth, given sample size and statistical constraints related to the number of variables that could be accommodated in the matching process, the authors could not match on every available characteristic. This left some imbalances in other variables that were not part of the matching algorithm. To further address confounding, all variables were adjusted for in their multi-variable Cox models.

Vagus Nerve Blocking (VBLOC Therapy)

Vagus/vagal nerve block, vagal blocking for obesity control (VBLOC [eg, Maestro]) involves laparoscopic placement of two leads (electrodes) in contact with vagal nerve trunks and a subcutaneously implanted neuromodulation device which is externally programmed to intermittently send electrical impulses via the implanted electrodes. The electrical impulses are purported to block vagus nerve signals in the abdominal region, inhibiting gastric motility and increasing satiety.

On January 15, 2015, the FDA approved VBLOC vagal blocking therapy, delivered via the Maestro System, for the treatment of adult patients with obesity who have a BMI of at least 40 to 45 kg/m2, or a BMI of at least 35 to 39.9 kg/m2 with a related health condition (e.g., high blood pressure or high cholesterol levels, and who have tried to lose weight in a supervised weight management program within the past 5years).

However, there is currently insufficient evidence to support the VBLOC vagal nerve blocking therapy for the treatment of obesity.

In an open-label, 3-center study, Camilleri et al (2008) evaluated the effects of vagal blocking (VBLOC therapy) on excess weight loss (EWL), safety, dietary intake, and vagal function. This clinical trial was conducted in obese subjects (BMI of 35 to 50 kg/m(2)). Electrodes were implanted laparoscopically on both vagi near the esophago-gastric junction to provide electrical block. Patients were followed for 6 months for body weight, safety, electrocardiogram, dietary intake, satiation, satiety, and

plasma pancreatic polypeptide (PP) response to sham feeding. To specifically assess device effects alone, no diet or exercise programs were instituted. A total of 31 patients (mean BMI of 41.2 +/- 1.4 kg/m(2)) received the device. Mean EWL at 4 and 12 weeks and 6 months after implant was 7.5%, 11.6%, and 14.2%, respectively (all $p < 0.001$); 25% of patients lost greater than 25% EWL at 6 months (maximum of 36.8%). There were no deaths or device-related serious adverse events (AEs). Calorie intake decreased by greater than 30% at 4 and 12 weeks and 6 months (all $p <$ or $= 0.01$), with earlier satiation ($p < 0.001$) and reduced hunger ($p = 0.005$). After 12 weeks, plasma PP responses were suppressed (20 +/- 7 versus 42 +/- 19 pg/ml). Average percent EWL in patients with PP response less than 25 pg/ml was double that with PP response greater than 25 pg/ml ($p = 0.02$). Three patients had serious AEs that required brief hospitalization, 1 each for lower respiratory tract, subcutaneous implant site seroma, and Clostridium difficile diarrhea. The authors concluded that intermittent, intra-abdominal vagal blocking is associated with significant EWL and a desirable safety profile. This was a small study (n = 31) with shorter-term follow-up (6 months); its findings need to be validated by well-designed studies with larger sample size and longer follow-up.

In a prospective, double-blind, RCT, Sarr et al (2012) examined the feasibility of vagal blockade (VBLOC therapy) to induce weight loss in patients with morbid obesity. A total of 503 subjects were enrolled at 15 centers. After informed consent, 294 subjects were implanted with the vagal blocking system and randomized to the treated (n = 192) or control (n = 102) group. Main outcome measures were percentage EWL (% EWL) at 12 months and serious AEs. Subjects controlled duration of therapy using an external power source; therapy involved a programmed algorithm of electrical energy delivered to the sub-diaphragmatic vagal nerves to inhibit afferent/efferent vagal transmission. Devices in both groups performed regular, low-energy safety checks. Data were mean ± SEM. Study subjects consisted of 90% females, BMI of 41 ± 1 kg/m(2), and age of 46 ± 1 years. Device-related complications occurred in 3% of subjects. There was no mortality; 12-month% EWL was 17 ± 2% for the treated and 16 ± 2% for the control group. Weight loss was related linearly to hours of device use; treated and controls with greater than or equal to 12 hours/day use achieved 30 ± 4 and 22 ± 8% EWL, respectively. The authors concluded that VBLOC therapy to treat morbid

obesity was safe, but weight loss was not greater in treated compared to controls; clinically important weight loss, however, was related to hours of device use. Post-study analysis suggested that the system electrical safety checks (low charge delivered via the system for electrical impedance, safety, and diagnostic checks) may have contributed to weight loss in the control group.

In an open-label study, Shikora et al (2013) evaluated the effect of intermittent vagal blocking (VBLOC) on weight loss, glycemic control, and blood pressure (BP) in obese subjects with diabetes mellitus type-2 (DM2). A total of 28 subjects were implanted with a VBLOC device (Maestro Rechargeable System) at 5 centers. Effects on weight loss, HbA1c, fasting blood glucose, and BP were evaluated at 1 week to 12 months; 26 subjects (17 females/9 males, 51 ± 2 years, BMI of 37 ± 1 kg/m(2), mean ± SEM) completed 12 months follow-up. One serious AE (pain at implant site) was easily resolved. At 1 week and 12 months, mean% EWL were 9 ± 1% and 25 ± 4% ($p < 0.0001$), and HbA1c declined by 0.3 ± 0.1% and 1.0 ± 0.2% ($p = 0.02$, baseline 7.8 ± 0.2%). In DM2 subjects with elevated BP (n = 15), mean arterial pressure reduced by 7 ± 3 mmHg and 8 ± 3 mmHg ($p = 0.04$, baseline 100 ± 2 mmHg) at 1 week and 12 months. All subjects MAP decreased by 3 ± 2 mmHg (baseline 95 ± 2 mmHg) at 12 months. The authors concluded that VBLOC was safe in obese DM2 subjects and associated with meaningful weight loss, early and sustained improvements in HbA1c, and reductions in BP in hypertensive DM2 subjects. This was a small study (n = 28) with shorter-term follow-up (12 months); its findings need to be validated by well-designed studies with larger sample size and longer follow-up.

Shikora et al (2015) noted that the ReCharge trial is a double-blind, RCT of 239 participants with BMI of 40 to 45 kg/m or 35 to 40 kg/m with one or more obesity-related conditions. Interventions were implantation of either vBloc or sham devices and weight management counseling. Mixed models assessed percent excess weight loss (%EWL) and total weight loss (%TWL) in intent-to-treat analyses. At 18 months, 142 (88%) vBloc and 64 (83%) sham patients remained enrolled in the study. 18-month weight loss was 23% EWL (8.8% TWL) for vBloc and 10% EWL (3.8% TWL) for sham ($p < 0.0001$). vBloc patients largely maintained 12-month weight loss of 26% EWL (9.7% TWL). Sham regained over 40% of the 17% EWL (6.4% TWL) by 18 months. Most weight regain preceded

unblinding. Common adverse events of vBloc through 18 months were heartburn/dyspepsia and abdominal pain; 98% of events were reported as mild or moderate and 79% had resolved. The authors concluded that weight loss with vBloc was sustained through 18 months, while sham regained weight between 12 and 18 months. They stated that vBloc is effective with a low rate of serious complications. This study had several drawbacks: (i) frequency of missing data was appreciable at 18 months, (ii) statistical analysis of the ReCharge study was not pre-specified after 12 months, and (iii) all participants were not blinded through 18 months and were unblinded on a rolling basis, making interpretation more difficult. The authors stated that additional long-term data and continued follow-up of the ReCharge study are needed to further characterize the safety and effectiveness profile of vBloc therapy.

Natural Orifice Transluminal Endoscopic Surgery (NOTES)

Natural orifice transluminal endoscopic surgery (NOTES) is being explored for a variety of surgeries, including bariatric procedures. NOTES procedures are incisionless surgeries performed with an endoscope passed through the mouth. Tissue approximation and closure devices are being developed for use in conjunction with various endoscopic procedures, including NOTES. Examples of NOTES techniques for bariatric surgery include, but may not be limited to, endoscopic duodenal-jejunal bypass, intragastric balloon (also called gastric balloon), restorative obesity surgery, endoluminal (ROSE) procedure, and transoral gastroplasty (TG) (also referred to as vertical sutured gastroplasty or endoluminal vertical gastroplasty). Endoscopic closure devices proposed for use in conjunction with NOTES include: Over the Scope Clip (OTSC) System Set, OverStitch Endoscopic Suturing System, and StomaphyX Endoluminal Fastener and Delivery System.

Restorative obesity surgery, endoluminal (ROSE) procedure is suggested for the treatment of weight regain following gastric bypass surgery due to a gradual expansion of the gastric pouch. The stomach is accessed orally via an endoscope and reduced in size using an endoscopic closure device.

Endoscopic Sleeve Gastroplasty

Transoral gastroplasty (TG), also referred to as vertical sutured gastroplasty or endoluminal vertical gastroplasty, is an incisionless procedure in which the stomach is purportedly restricted with staples or sutures by using endoscopic surgical tools guided through the mouth and esophagus.

In a single-center, pilot feasibility study (n = 4), Abu Dayyeh et al (2013) demonstrated the technical feasibility of transoral endoscopic gastric volume reduction with an endoscopic suturing device in a fashion similar to sleeve gastrectomy for the treatment of obesity. Main outcome measure was technical feasibility. These researchers successfully used an endoscopic free-hand suturing system in 4 subjects, thus demonstrating the technical feasibility of a novel technique to mimic the anatomic manipulations created by surgical sleeve gastrectomy endoscopically. The authors concluded that endoscopic sleeve gastroplasty (ESG) for treatment of obesity is feasible. The main drawback of this study was that it was a pilot feasibility study with small number of subjects.

Sharaiha et al (2015) stated that novel endoscopic techniques have been developed as effective treatments for obesity. Recently, reduction of gastric volume via endoscopic placement of full-thickness sutures, termed ESG, has been described. These investigators evaluated the safety, technical feasibility, and clinical outcomes for ESG. Between August 2013 and May 2014, ESG was performed on 10 patients using an endoscopic suturing device. Their weight loss, waist circumference, and clinical outcomes were assessed. Mean patient age was 43.7 years and mean BMI was 45.2kg/m(2). There were no significant adverse events noted. After 1 month, 3 months, and 6 months, excess weight loss of 18%, 26%, and 30%, and mean weight loss of 11.5kg, 19.4kg, and 33.0kg, respectively, were observed. The differences observed in mean BMI and waist circumference were 4.9kg/m(2) (p=0.0004) and 21.7cm (p =0.003), respectively. The authors concluded that ESG is effective in achieving weight loss with minimal adverse events. They stated that this approach may provide a cost-effective out-patient procedure to add to the steadily growing armamentarium available for treatment of this significant epidemic. These findings from a small (n = 10) study need to be validated by well-designed studies.

Lopez-Nava et al (2015) described the ESG used in 50 patients. The goal of this procedure is to reduce the gastric lumen into a tubular configuration, with the greater curvature modified by a line of sutured plications. General anesthesia with endotracheal intubation is needed. An endoscopic suturing system requiring a specific double-channel endoscope delivers full-thickness sets of running sutures from the antrum to the fundus. Patients were admitted and observed, with discharge planned within 24 hours. Post-procedure out-patient care included diet instruction with intensive follow-up by a multi-disciplinary team. Voluntary oral contrast and endoscopy studies were scheduled to evaluate the gastroplasty at 3, 6, and 12 months. The technique was applied in 50 patients (13 men) with an average BMI of 37.7 kg/m(2) (range of 30 to 47) with 13 having reached 1 year. Procedure duration averaged 66 mins during which 6 to 8 sutures on average were placed. All patients were discharged in less than 24 hours. There were no major intra-procedural, early, or delayed adverse events. Weight loss parameters were satisfactory, mean BMI changes from 37.7 ± 4.6 to 30.9 ± 5.1 kg/m(2) at 1 year, and mean%TBWL was 19.0 ± 10.8. Oral contrast studies and endoscopy revealed sleeve gastroplasty configuration at least until 1 year of follow-up. The authors concluded that ESG is a safe, effective, and reproducible primary weight loss technique. The main drawbacks of this study were its small sample size (n = 50) and short-term follow-up (1 year and only 13 subjects reached 1-year follow-up).

Furthermore, a Cochrane review on "Surgery for weight loss in adults" (Colquitt et al, 2014) as well as an UpToDate review on "Bariatric surgical operations for the management of severe obesity: Descriptions" (Lim, 2015) do not mention endoscopic sleeve gastroplasty as a therapeutic option.

AspireAssist Aspiration Therapy

In a pilot study, Sullivan and colleagues (2013) evaluated the use of endoscopic aspiration therapy for the treatment of obesity. This method entails endoscopic placement of a gastrostomy tube (A-Tube) and the AspireAssist siphon assembly (Aspire Bariatrics, King of Prussia, PA) to aspirate gastric contents 20 minutes after meal consumption. These researchers performed a study of 18 obese subjects who were randomly assigned (2:1) to groups that underwent aspiration therapy for 1 year plus

lifestyle therapy (n = 11; mean BMI, 42.6 ± 1.4 kg/m(2)) or lifestyle therapy only (n = 7; mean BMI, 43.4 ± 2.0 kg/m(2)). Lifestyle intervention comprised a 15-session diet and behavioral education program; 10 of the 11 subjects who underwent aspiration therapy and 4 of the 7 subjects who underwent lifestyle therapy completed the 1st year of the study. After 1 year, subjects in the aspiration therapy group lost 18.6% ± 2.3% of their body weight (49.0% ± 7.7% of EWL) and those in the lifestyle therapy group lost 5.9% ± 5.0% (14.9% ± 12.2% of EWL) ($p < 0.04$); 7 of the 10 subjects in the aspiration therapy group completed an additional year of therapy and maintained a 20.1% ± 3.5% body weight loss (54.6% ± 12.0% of EWL). There were no AEs of aspiration therapy on eating behavior and no evidence of compensation for aspirated calories with increased food intake. No episodes of binge eating in the aspiration therapy group or serious AEs were reported. The authors concluded that aspiration therapy appeared to be a safe and effective long-term weight loss therapy for obesity. These preliminary findings from a pilot study need to be validated by well-designed studies.

Forssell and Noren (2015) evaluated the effectiveness of a novel device, the AspireAssist aspiration therapy system, for the treatment of obesity. After 4 weeks taking a very-low-calorie diet, 25 obese men and women (BMI 39.8 ±0.9kg/m(2)) had the AspireAssist gastrostomy tube placed during a gastroscopy. A low-profile valve was installed 14 days later and aspiration of gastric contents was performed approximately 20 minutes after meals 3 times per day. Cognitive behavioral therapy was also started. At month 6, mean weight lost was 16.5 ± 7.8kg in the 22 subjects who completed 26 weeks of therapy ($p=0.001$). The mean percentage EWL was 40.8 ± 19.8% ($p=0.001$); 2 subjects were hospitalized for complications: 1 subject for pain after gastrostomy tube placement, which was treated with analgesics, and another because of an aseptic intra-abdominal fluid collection 1 day after gastrostomy tube placement. No clinically significant changes in serum potassium or other electrolytes occurred. The authors concluded that in this study, substantial weight loss was achieved with few complications using the AspireAssist system, suggesting its potential as an attractive therapeutic device for obese patients.

In a prospective observational study, Noren and Forssell (2016) evaluated the safety and effectiveness of the novel AspireAssist Aspiration Therapy System for treatment of obesity, and its effect on patient's quality of life. A total of 25 obese subjects, mean age of 48 years (range of 33 to 65) were included in this study. A custom gastrostomy tube (A-tube) was percutaneously inserted during a gastroscopy performed under conscious sedation. Drainage and irrigation of the stomach were performed 3 times daily, 20 mins after each meal, for 1 to 2 years. Efficient aspiration required thorough chewing of ingested food. Treatment included a cognitive behavioral weight loss program. Mean BMI at inclusion was 39.8 kg/m2 (range of 35 to 49). After 1 year mean (SD) BMI was 32.1 kg/m2 (5.4), $p < 0.01$, and EWL was 54.4% (28.8), $p < 0.01$. Quality of life, as measured with EQ-5D, improved from 0.73 (0.27) to 0.88 (0.13), $p < 0.01$. After 2 years BMI was 31.0 kg/m2 (5.1), $p < 0.01$, and EWL was 61.5% (28.5), $p < 0.01$. There were no serious AEs or electrolyte disorders. Compliance was 80% after 1 year and 60% after 2 years. The authors concluded that aspiration therapy is a safe and efficient treatment for obesity, and weight reduction improves quality of life. Excess weight was approximately halved in a year, with weight stability if treatment was continued; and long-term results remain to be investigated.

This study by Noren and Forssell (2016; n = 25; 2-year follow-up) appeared to be an extension of their 2015 study (n = 25; 6-month follow-up). It is unclear whether firm conclusions can be drawn from a 25-person observational study. Furthermore, the authors noted that "Limitation of this study is the combination of aspiration therapy and CBT without any control group. This study only encompasses treatment during 1 to 2 years. Long-term patency is still unknown. It is our belief that once the desired weight goal is achieved many, if not most, patients will need to continue aspiration therapy, albeit possibly at a reduced frequency, to maintain weight stability. In order to determine this, we have started a prospective study in which we will follow 50 patients with AspireAssist and 50 patients with laparoscopic gastric bypass procedure for 5 years".

Thompson and colleagues (2017) stated that the AspireAssist System (AspireAssist) is an endoscopic weight loss device that is comprised of an endoscopically placed percutaneous gastrostomy tube and an external device to facilitate drainage of about 30% of the calories consumed in a meal, in conjunction with lifestyle (diet and exercise) counseling. In this

52-week clinical trial, a total of 207 subjects with a BMI of 35.0 to 55.0 kg/m2 were randomly assigned in a 2:1 ratio to treatment with AspireAssist plus Lifestyle Counseling (n = 137; mean BMI was 42.2 ± 5.1 kg/m2) or Lifestyle Counseling alone (n = 70; mean BMI was 40.9 ± 3.9 kg/m2). The co-primary end-points were mean percent excess weight loss and the proportion of participants who achieved at least a 25% excess weight loss. At 52 weeks, participants in the AspireAssist group, on a modified intent-to-treat basis, had lost a mean (± S.D.) of 31.5 ± 26.7% of their excess body weight (12.1 ± 9.6% total body weight), whereas those in the Lifestyle Counseling group had lost a mean of 9.8 ± 15.5% of their excess body weight (3.5 ± 6.0% total body weight) ($p < 0.001$). A total of 58.6% of participants in the AspireAssist group and 15.3% of participants in the Lifestyle Counseling group lost at least 25% of their excess body weight ($p < 0.001$). The most frequently reported AEs were abdominal pain and discomfort in the peri-operative period and peristomal granulation tissue and peristomal irritation in the post-operative period. Serious AEs were reported in 3.6% of participants in the AspireAssist group. The authors concluded that the weight loss efficacy and safety profile of the AspireAssist System suggested that this treatment approach may bridge the therapeutic gap between more conservative lifestyle modification and the established bariatric surgical procedures for people with class II and III obesity.

The authors noted that this study has several drawbacks: (i) although this was a RCT, subjects could not be blinded as to treatment group because of the nature of the therapy. However, all other aspects of the study protocol, such as weight management counseling and study visits, were the same in the AspireAssist and Lifestyle Counseling groups to minimize any additional potential influences on the outcome measures, (ii) it was possible that bias was introduced into the study by the high number of pre-enrollment withdrawals (approximately 14% in each treatment group) and post-enrollment withdrawals (26% in the AspireAssist group and 48% in the Lifestyle Counseling group), which is a common problem in weight loss intervention studies. However, the baseline and demographic characteristics of the randomized, enrolled, and completer populations were analyzed for homogeneity and were not different in the AspireAssist and Lifestyle Counseling groups. The consistency of

study results by using different statistical analyses further indicated that withdrawals did not bias the results, (iii) this report included only 1-year results, and hence did not provide longer term safety and effectiveness of the AspireAssist therapy. However, approximately 90% of the AEs associated with AspireAssist are related to the A-tube, with about 50% occurring within the first week of implantation. The placement and management of the A-tube was similar to percutaneous endoscopic gastrostomy tubes, which have been used in clinical practice for more than 35 years, so the short-term and long-term complications of this device are already well known, and (iv) the study population contained a high percentage of female participants, which is a common problem of weight loss studies. Thus, these findings might not necessarily apply to men with obesity.

On June 14, 2016, the FDA approved the AspireAssist device to assist in weight loss in patients aged 22 and older who are obese, with a BMI of 35 to 55, and who have failed to achieve and maintain weight loss through non-surgical weight-loss therapy. Side effects related to use of the AspireAssist include occasional indigestion, nausea, vomiting, constipation and diarrhea. The AspireAssist is contraindicated in those with certain conditions, including uncontrolled hypertension, diagnosed bulimia, diagnosed binge eating disorder, night eating syndrome, certain types of previous abdominal surgery, pregnancy or lactation, inflammatory bowel disease or stomach ulcers. The AspireAssist is also contraindicated in patients with a history of serious pulmonary or cardiovascular disease, coagulation disorders, chronic abdominal pain or those at a high-risk of medical complications from an endoscopic procedure. Furthermore, the AspireAssist device it is not indicated for use in short durations in those who are moderately overweight.

In a post-market study, Nystrom and colleagues (2018) evaluated long-term safety and efficacy of aspiration therapy (AT) in a clinical setting in 5 European clinics. A total of 201 participants, with BMI of 35.0 to 70.0 kg/m2, were enrolled in this study from June 2012 to December 2016. Mean baseline BMI was 43.6 ± 7.2 kg/m2. Mean percent total weight loss at 1, 2, 3, and 4 years, respectively, was 18.2% ± 9.4% (n/N = 155/173), 19.8% ± 11.3% (n/N = 82/114), 21.3% ± 9.6% (n/N = 24/43), and 19.2% ± 13.1% (n/N = 12/30), where n is the number of measured participants and

N is the number of participants in the absence of withdrawals or lost to follow-up. Clinically significant reductions in HbA1C, triglycerides, and blood pressure were observed. For participants with diabetes, HbA1C decreased by 1% ($p < 0.0001$) from 7.8% at baseline to 6.8% at 1 year. The only serious complications were buried bumpers, experienced by 7 participants and resolved by removal/replacement of the A-Tube, and a single case of peritonitis, resolved with a 2-day course of intravenous antibiotics. The authors concluded that the findings of this study established that AT is a safe, effective, and durable weight loss therapy in people with classes II and III obesity in a clinical setting. The high withdrawals/lost to follow-up rates were of concerns – 10%, 18%, 44% and 60% for years 1 to 4.

Kumar and associates (2017) noted that weight management is increasingly incorporating endoscopic bariatric therapy (EBT). As the global burden of obesity and its co-morbidities has increased, it is evident that novel therapeutic approaches will be necessary to address the obesity epidemic. EBTs offer greater efficacy than diet and lifestyle modification and lower invasiveness than bariatric surgery. The FDA has approved 2 intra-gastric balloons and aspiration therapy (AT) for the treatment of obesity: Apollo Orbera is indicated for the treatment of Class I and Class II obesity, Re Shape Integrated Dual Balloon system is indicated for the same range with a co-morbidity, and Aspire Bariatrics AspireAssist is approved for patients with a BMI of 35 to 55 kg/m2. These devices have proven safe and effective in clinical trials and are gaining commercial acceptance in the USA; the Orbera has been used extensively outside the USA for over 20 years. These devices will need to be delivered in the context of a multi-disciplinary weight loss program, integrating comprehensive care of obesity. Patient selection is important, and ensuring appropriate patient expectations and understanding of alternatives such as pharmacologic therapy and surgery is essential. With several EBTs on the horizon, patients with obesity will have an even broader array of safe and effective options for weight management in the future. The authors stated that AT addresses a broader BMI range and offers the potential for a significant and durable weight loss.

Pajot and co-workers (2017) stated that EBT is a rapidly developing area that has now seen FDA approval of 6 endoscopic bariatric devices and procedures and there are a number of other novel EBTs progressing

through various stages of development with newly published findings. This paper aimed to assist readers in either selecting an appropriate therapy for their patient or deciding to incorporate these therapies into their practice. This paper provided an updated review of the available data on EBTs, both FDA approved and not, with a particular focus on safety and effectiveness, as well as guidance for discussing with patients the decision to use endoscopic therapies. The authors of a large meta-analysis of Orbera concluded its ideal balloon volume to be 600 to 650 ml. AspireAssist has had favorable effectiveness and safety data published in a large RCT. A large study of endoscopic sleeve gastroplasty has published findings at up to 24 months showing promising durability. Elipse, a swallowed intra-gastric balloon not requiring endoscopy for either insertion or removal, has had early favorable results published. A magnet-based system for creation of a gastrojejunostomy has published favorable findings from its pilot study. The authors concluded that EBTs are safe and effective therapies for weight loss when used in conjunction with lifestyle changes and fill an important gap in the management of obesity. There are now 6 FDA-approved EBTs available and several more in ongoing trials with favorable early findings. These researchers stated that more study is needed to understand the role of EBTs used in combination or in sequence with medications and bariatric surgery.

Christensen and colleagues (2017) noted that AT with AspireAssist is a novel endoscopic obesity treatment. Patients aspirate approximately 30% of an ingested meal through a draining system connected to a percutaneous endoscopic gastrostomy tube. AspireAssist was recently approved by the FDA, and it induced weight loss comparable to the weight loss observed after bariatric surgery, but with a lower risk of complications. The authors stated that few clinical studies about the safety and efficacy of AspireAssist have been carried out and published. Thus, further intervention studies evaluating acute as well as long-term effects are needed.

Moreover, an UpToDate review on "Bariatric procedures for the management of severe obesity: Descriptions" (Lim, 2018) lists aspiration therapy as an investigational procedure.

In a post-market European registry study, Nystrom and colleagues (2018) evaluated the long-term safety and efficacy of the AspireAssist System in a clinical setting in 5 clinics. A total of 201 subjects, with BMI of 35.0 to 70.0 kg/m2, were enrolled in this study from June 2012 to December 2016. Mean baseline BMI was 43.6 ± 7.2 kg/m2. Mean percent total weight loss at 1, 2, 3, and 4 years, respectively, was 18.2% ± 9.4% (n/N = 155/173), 19.8% ± 11.3% (n/N = 82/114), 21.3% ± 9.6% (n/N = 24/43), and 19.2% ± 13.1% (n/N = 12/30), where n is the number of measured participants and N is the number of participants in the absence of withdrawals or lost to follow-up. Clinically significant reductions in HbA1C, triglycerides, and blood pressure were observed. For participants with diabetes, HbA1C decreased by 1% ($p < 0.0001$) from 7.8% at baseline to 6.8% at 1 year. The only serious complications were buried bumpers, experienced by 7 participants and resolved by removal/replacement of the A-Tube, and a single case of peritonitis, resolved with a 2-day course of intravenous antibiotics. The authors concluded that the findings of this study established that aspiration therapy is a safe, effective, and durable weight loss therapy in people with classes II and III obesity in a clinical setting. Moreover, they noted that although the therapy required a substantial commitment on the part of the patient, the data suggested that a very large percentage of patients were willing and able to make the commitment to succeed with this therapy. Furthermore, the ability to perform the gastrostomy on an out-patient basis and the very low incidence of costly, serious complications suggested that aspiration therapy may be a lower cost alternative to bariatric surgery.

The authors stated that this study had several drawbacks. First, this report lacked a control group to provide a comparative base. Second, only 2 sites reported cardio-metabolic data; however, the weight loss from these 2 sites was no greater than that of the sites not reporting cardio-metabolic data, suggesting that it was unlikely that the results would differ substantially had there been data from all 5 clinics. Third, this report only provided results through 4 years of therapy and the number of participants in years 2 to 4 was less than in year 1; however, the durability of weight loss and relatively narrow band of 95% confidence intervals suggested robustness of the data. With regard to safety, the excellent and consistent safety data between this report and the PATHWAY trial, coupled with the 30 years of widespread usage of the AspireAssist's

nearest analog, the PEG tube, suggested that longer-term safety results are not apt to substantially differ from the post-procedural results reported here.

Bariatric Surgery Prior to Total Hip or Knee Arthroplasty to Reduce Post-Operative Complications and Improve Clinical Outcomes for Obese Individuals

Smith et al (2016) examined if bariatric surgery prior to total hip arthroplasty (THA) or total knee arthroplasty (TKA) reduces the complication rates and improves the outcome following arthroplasty in obese patients. These researchers performed a systematic literature search of published and unpublished databases on the November 5, 2015. All papers reporting studies comparing obese patients who had undergone bariatric surgery prior to arthroplasty, or not, were included. E ach study was assessed using the Downs and Black appraisal tool. A meta-analysis of RR and 95% CI was performed to determine the incidence of complications including wound infection, deep vein thrombosis (DVT), pulmonary embolism (PE), revision surgery and mortality. From 156 potential studies, 5 were considered to be eligible for inclusion in the study. A total of 23,348 patients (657 who had undergone bariatric surgery, 22,691 who had not) were analyzed. The evidence-base was moderate in quality. There was no statistically significant difference in outcomes such as superficial wound infection (RR 1.88; 95% CI: 0.95 to 0.37), deep wound infection (RR 1.04; 95% CI: 0.65 to 1.66), DVT (RR 0.57; 95% CI: 0.13 to 2.44), PE (RR 0.51; 95% CI: 0.03 to 8.26), revision surgery (RR 1.24; 95% CI: 0.75 to 2.05) or mortality (RR 1.25; 95% CI: 0.16 to 9.89) between the 2 groups. The authors concluded that for most peri-operative outcomes, bariatric surgery prior to THA or TKA did not significantly reduce the complication rates or improve the clinical outcome. They stated that the findings of this study questions the previous belief that bariatric surgery prior to arthroplasty may improve the clinical outcomes for patients who are obese or morbidly obese. This finding is based on moderate quality evidence.

Conversion of Sleeve Gastrectomy to Roux-En-Y Gastric Bypass as a Treatment of Gastro-Esophageal Reflux Disease

Abdemur et al (2016) stated that laparoscopic sleeve gastrectomy (LSG) as a primary bariatric procedure has gained significant popularity. Conversion to RYGBP or Roux-en-Y esophagojejunostomy (LRYEJ) has been described as a therapeutic option for inadequate weight loss after LSG and unresolved co-morbidities or complications such as leak, stricture, and severe GERD. These researchers determine reasons and outcomes of conversions of LSG to RYGBP. Between January 2004 and August 2014, a total of 1,118 patients underwent primary LSG for morbid obesity. A retrospective review of a prospectively collected database was conducted for laparoscopic conversions of LSG to RYGBP or LRYEJ, describing reasons and outcomes. Conversion to RYGBP was identified in 30 (2.7%) patients, of whom only 9 (0.8%) were originally from the authors' institution. Of the entire cohort of revisions, 9 (0.8%) had intractable GERD; only 4 (0.4% of total LSGs reviewed) were originally from the authors' institution; 7 (0.6%) patients were revised for inadequate weight loss: 5 (0.4%) originally from the authors' institution, 2 (0.2%) for stricture, and 12 (1.1%) for leak. Both the stricture and the leak patients were referred from outside institutions. All procedures were performed laparoscopically. The additional mean excess weight loss after conversion to RYGBP was 30.9% with no mortalities. The authors concluded that the most common reason for conversion was chronic leak. The conversion rate of LSG to RYGBP due to inadequate weight loss, GERD, and stricture was 1.6% for the entire group, with 0.8% from the authors' institution. They stated that additional follow-up and studies are needed to define real incidence of GERD after LSG.

El Chaar et al (2017) noted that bariatric surgery is the only proven and effective long-term treatment for morbid obesity, with LSG being the most commonly performed weight loss procedure in the United States. Despite its safety and effectiveness, LSG's association with both de-novo and pre-existing GERD remains controversial. Therefore, this retrospective study determined the incidence, indications, and outcomes of revisional surgery following LSG in adult patients at the authors’ institution from 2010 to 2014. Descriptive outcomes were reported due to the small sample size. Of the 630 LSGs performed, 481 patients were included in the analysis (mean age and BMI = 46.2 and 44.3, respectively; 79.5% female; 82.3% white). A total of 12/481 patients underwent conversion to a different bariatric procedure due to inadequate weight loss, GERD, or both. The 6/12 patients with GERD-related symptoms and failed medical

management underwent conversion to RYGBP following pre-operative wireless Bravo pH monitoring (Given Imaging) to confirm the diagnosis objectively. The other 6/12 patients with inadequate weight loss received either RYGBP or bilio-pancreatic diversion with duodenal switch (BPD/DS) based on personal choice. Overall, 9/12 patients underwent conversion to RYGBP, and 3/12 underwent conversion to BPD/DS. Median time from the initial surgery to conversion was 27 months (range of 17 to 41). Median operating room time was 168 minutes (range of 130 to 268). Median length of stay was 48 hours (range of 24 to 72). The follow-up rate at 3 months was 100% (12/12 patients). The authors concluded that the findings of this study showed that some patients may present following LSG with refractory GERD or inadequate weight loss, but that conversion to RYGBP or BPD/DS may be done safely and effectively.

Langer and colleagues (2010) noted that due to excellent weight loss (WL) success in the short-time follow-up, sleeve gastrectomy (SG) has gained popularity as the sole and definitive bariatric procedure. In the long-term follow-up, WL failure and intractable severe reflux can necessitate further surgical intervention. These investigators carried out a retrospective analysis of laparoscopic conversions from SG to Roux-en-Y gastric bypass (RYGB) to assess the efficacy for reflux relief and WL success; 8 out of 73 patients (11%) underwent conversion to RYGB for severe reflux (n = 3) or weight regain (WR; n = 5) after a median interval of 33 months following laparoscopic SG (LSG). In 1 of the patients, a banded gastric bypass was performed. In both groups, conversion to RYGB was successful, as proton pump inhibitor (PPI) medication could be discontinued in all patients presenting with severe reflux, and a significant WL could be achieved in the patients with WR within a median follow-up of 33 months. Post-operative complications were observed in only 1 patient as leakage at the gastrojejunostomy was successfully treated by temporary stent placement. The authors concluded that conversion to RYGB was an effective treatment for WR or intractable reflux symptoms following SG. Therefore, SG could be performed, intended as the sole and definitive bariatric intervention, with conversion from SG to RYGB as an exit strategy for these complications.

Iannelli and co-workers (2016) reported their preliminary results within the 2 main indications for laparoscopic conversion of SG to RYGB. Data from all patients who underwent laparoscopic conversion from SG to RYGB were retrospectively analyzed as to indications for revisional surgery, WL, and complications. A total of 40 patients underwent conversion, 29 cases (72.5%) for WL failure and 11 cases for refractory gastro-esophageal reflux disease (GERD; 27.5%). The mean interval from SG to RYGB was 32.6 months (range of 8 to 113). Revisional surgery was attempted by laparoscopy in all cases, and conversion to laparotomy was necessary in 3 patients (7.5%). Mean length of follow-up was 18.6 months (range of 9 to 60) after conversion. Follow-up rate was 100%. Mean percent total WL (TWL) and percent excess WL (EWL) were 34.7% and 64%, respectively, when calculated from weight before SG. Remission rate for GERD was 100%; improvement was observed for all co-morbidities after conversion. There was no immediate post-operative mortality. The post-operative complication rate was 16.7%. According to the Clavien-Dindo classification, there were 5 grade-II and 2 grade-IIIa complications. The authors concluded that laparoscopic conversion of SG to RYGB was safe and feasible. In the short-term, it appeared to be effective in treating GERD and inducing significant additional WL and improvement of co-morbidities.

Casillas and associates (2016) evaluated the indications and outcomes of revision of SG to laparoscopic RYGB (LRYGB) at a single community hospital. These researchers carried out a retrospective review of a prospectively collected database identifying SG operations done from February 2009 to June 2014. All patients who underwent revision from SG to RYGB were studied. A total of 48 patients underwent revision of SG to RYGB. Mean time to revision was 26 months (range of 2 to 60 months) and mean follow-up after RYGB was 20 months (range of 4 to 48 months). Indications for revision were reflux (n = 14), inadequate WL (IWL; n = 11), reflux and IWL (n = 16), stricture (n = 4), chronic leak (n = 1), and recurrent diabetes and reflux (n = 2). Reflux symptoms resolved in 96% of patients after revision, and hiatal hernias were repaired in 50% of patients. Percentage TWL at 3, 6, 12, 24, and 36 months was 9.0%, 12.9%, 15.7%, 13.3%, and 6.5%, respectively . The overall rate of complication was 31%; there were no mortalities. The authors concluded that revision of SG to RYGB was a potentially effective means of treating SG complications, particularly reflux. Reflux was the most common

indication for revision and was often associated with a hiatal hernia. These researchers stated that further studies are needed to evaluate the long-term maintenance of additional WL after revision of SG to RYGB.

Quezada and co-workers (2016) reported their results in converting SG to revisional LRYGB (R-LRYGB). Patients who underwent R-LRYGB after SG between June 2005 and April 2015 were identified. Demographic characteristics, anthropometrics, pre-operative work-up, and peri-operative data were retrieved; TWL, EWL, and clinical progression over 3 years were registered. A total of 50 patients were identified, mean age of 39 ± 8.4 years, 42 (84%) women; median body mass index (BMI) prior to R-LRYGB was 33.8 (31 to 36) kg/m2. Indications for revision were weight regain (n = 28, 56%), GERD (n = 16, 32%), and gastric stenosis (n = 6, 12%). In WR patients, mean follow-up at 3 years was 72.2% and median percentage of TWL at 12 and 36 months was 18.5 (12 to 24) and 19.3 (8 to 23), respectively; percentage of EWL at 12 and 36 months was 60.7 (37 to 82) and 66.9 (26 to 90), respectively. Over 90% of GERD patients resolved or improved symptoms. All patients with gastric stenosis resolved symptoms after conversion; there were no major complications. The authors concluded that R-LRYGB was a feasible, effective, and well-tolerated alternative in selected patients with failed SG in which other therapies have been insufficient to either maintain WL or resolve complications. However, long-term follow-up is still needed.

Parmar and colleagues (2017) noted that IWL / WR and GERD unresponsive to medical management are 2 most common indications for conversion of SG to RYGB. These investigators reported detailed outcomes of conversion of SG to RYGB for these 2 indications separately. They examined prospectively maintained database to identify patients who underwent a conversion of their SG to RYGB in their unit. Outcomes in patients converted for IWL / WR and those converted for GERD were evaluated separately. These researchers performed 22 SG to RYGB in their unit between August 2012 and April 2015 with a mean follow-up of 16 months. Indication for conversion was GERD in 10/22 (45.5%) patients and IWL / WR in 11/22 (50.0%) patients. Patients undergoing conversion for GERD were significantly lighter (BMI 30.5) than those converted for IWL / WR (BMI 43.3) at the time of conversion. The conversion was very effective for GERD with 100% patients reporting improvement in symptoms, and 80% patients were able to stop their

antacid medications; IWL / WR group achieved a further BMI drop of 2.5 points 2 years after surgery (final BMI 40.8) in comparison with 2.0 points BMI drop achieved by the GERD group (final BMI 28.5). The authors concluded that this study demonstrated that conversion of SG to RYGB was effective for GERD symptoms; but not for further WL, which was modest in both groups. These researchers stated that future studies are needed to examine the best revisional procedure for IWL / WR after SG.

Chang and co-workers (2018) stated that LSG has been validated as a safe and effective treatment for morbid obesity. However, data of the long-term outcome remains lacking. A total of 1,759 LSG was performed as primary bariatric procedure from 2005 to 2017 with mean age of 35.2 ± 10.3 years (14 to 71), female 69.7%, mean BMI 37.9 ± 7.7 kg/m2, and mean waist width 113.7 ± 17.9 cm. All patients were evaluated and managed under a strict multi-disciplinary team approach. These researchers carried out a retrospective analysis of a prospective bariatric database and telephone interview of patients who defaulted clinic follow-up at 10 years. The mean operating time, intra-operative blood, and hospital LOS of LSG were 121.5 ± 36.5 mins, 40.8 ± 69.7 ml, and 2.8 ± 2.7 days, respectively. The 30-day post-operative major complication occurred in 25 (1.4%) patients. The major complication rate was 15% at 1st year and 0% at the last year. The follow-up rate at 1, 5 and 10 years were 89.3%, 52.1% and 64.4%, respectively. At post-operative 1, 5, and 10 years, the mean percentage of TWL (%TWL) and EWL (EWL%) of LSG patients were 33.4, 28.3, and 26.6% and 92.2, 80.1, and 70.5%, respectively. The mean BMI became 27, 26.2, and 27.1 kg/m2 at post-operative 1, 5, and 10 years. At follow-up, a total of 69 patients needed surgical revision due to reflux disease (n = 45), WR (n = 19), persistent diabetes (n = 2), and chronic fistula (n = 3). The type of revision procedures were hiatal repair and gastropexy (n = 29), RYGB (n = 23), and single anastomosis bypass (n = 17) with median time to revision of 33 months (range of 3 to 62). At 10 years, the overall revision rate was 21.5% (14/65) and 11 (16.9%) of 65 patients were converted to RYGB. The other 54 patients remained at LSG anatomy, but 45% of them required PPI for reflux symptoms. The authors concluded that these findings showed that primary LSG was a durable primary bariatric procedure with sustained WL and a high resolution of co-morbidities at 10 years, but about 50% the patients had de-novo GERD; and the need for conversion to RYGB was 16.9% at 10 years.

Boru and associates (2018) evaluated incidence, indications, and short-term outcomes of laparoscopic SG (LSG) conversion to LRYGB in 3 bariatric centers. Patients operated between January 2012 and December 2016 by primary LSG, with mean follow-up of 24 months and converted to LRYGB for IWL, WR, and/or GERD, were retrospectively analyzed for demographics, operative details, peri-operative complications, co-morbidities evolution, and further WL. A total of 30 patients (2.76%, 7 males / 23 females, mean age of 41 ± 10.1 years, initial mean BMI of 46.9 ± 6.3 kg/m2) were successfully converted after a mean period of 33 ± 27.8 months for severe GERD (15 patients, 50%), GERD and IWL / WR (3 patients, 10%), and IWL / WR (12 patients, 40%). Surgical complications occurred in 3 patients (10%). Mean BMI at revision time was 36 ± 9 kg/m2, and 30.8 ± 5.2 kg/m2, 28 ± 4.9 kg/m2, and 28 ± 4.3 kg/m2 after 6, 12, and 24 months, respectively. Resolution of GERD was achieved in 83% of cases. Overall, post-operative satisfaction was reported by 96% of the cases, after mean follow-up of 24 ± 8.9 months. The authors concluded that in high-volume centers, where strict criteria for patients' selection for LSG were applied, the expected incidence of re-operations for "non-responder" (IWL / WR) or de-novo or persistent severe GERD non-responder to medical treatment was low (less than 3%). These researchers stated that conversion of "non-responder" LSG to LRYGB was effective for further WL and GERD remission at short-term (2 years follow-up); however, a high post-operative complication rate was observed; long-term multi-disciplinary follow-up is mandatory to confirm data on WL durability and co-morbidity control.

Raj and co-workers (2019) stated that the development of GERD following LSG is a major concern as it affects the quality of life (QOL) of the patients and potentially exposes them to the complications of GERD. The reported incidence of GERD after LSG was up to 35%; and LRYGB is considered the procedure of choice for patients with morbid obesity with GERD but objective evidence based on physiologic studies for the same are limited. These researchers determined the physiologic changes related to GER based on symptoms index, 24-hour pH study, impedance, and manometry following LSG and LRYGB. This registered study is a prospective, non-randomized, open-label clinical trial comparing the incidence of GERD after LSG and LRYGB. In this study, non-GERD patients were evaluated for GERD based on clinical questionnaires, 24-hour pH study, and impedance manometry pre-operatively and 6 months

post-operatively. A total of 30 patients underwent LSG, and 16 patients underwent LRYGB. The mean DeMeester score increased from 10.9 ± 11.8 to 40.2 ± 38.6 (p = 0.006) after LSG. The incidence of GERD after LSG was 66.6%. The increase in DeMeester score from 9.5 ± 4.6 to 12.2 ± 17.2 after LRYGB was not significant (p = 0.7). There was a significant increase in the non-acid reflux both following LSG and LRYGB. The authors concluded that the incidence of GERD following LSG was high, making it a contraindication for LSG. These researchers stated that LRYGB remains the preferred procedure for patients with GERD; however, more studies are needed to understand the physiologic changes in patients with pre-existing GERD.

An UpToDate review on "Late complications of bariatric surgical operations" (Ellsmere, 2019) states that "Gastroesophageal reflux after SG presents with classic symptoms such as burning pain, heartburn, and regurgitation. It can occur as an early and late complication. The first-line treatment is anti-reflux medical therapy. GERD unresponsive to anti-reflux medical therapy with no clear anatomic abnormalities, such as stoma stenosis or a hiatal hernia, can be effectively treated by conversion to RYGB".

Prophylactic Mesh Placement for Prevention of Incisional Hernia after Open Bariatric Surgery

In a systematic review and meta-analysis, Dasari and colleagues (2016) examined if mesh prevents post-operative incisional hernia (IH) in open and laparoscopic bariatric surgery patients. A total of 7 studies met inclusion criteria. These investigators abstracted data regarding post-operative IH development, surgical site infection, and seroma or wound leakage and performed a meta-analysis. The prophylactic mesh group had significantly decreased odds of developing IH than the standard closure group (odds ratio, 0.30, 95% CI: 0.13 to .68, p = 0.004). No included studies evaluated outcomes after prophylactic mesh during laparoscopic bariatric surgery. The authors concluded that prophylactic mesh during open bariatric surgery appeared to be beneficial in reducing post-operative IH without significant increasing the odds of surgical site infection or seroma or wound leakage. Moreover, they stated that higher quality studies, including those in laparoscopic patients, and cost-utility analysis, are needed to support routine use of this intervention.

Single-Incision Laparoscopic Sleeve Gastrectomy

Dimitrokallis and colleagues (2017) noted that single-incision laparoscopic surgery has attracted a great deal of interest in the surgical community in recent years, including bariatric surgery. Single-incision laparoscopic sleeve gastrectomy (SILSG) has been proposed as an alternative to the multi-port laparoscopic procedure; however, it has yet to meet wide acceptance and application. These researchers summarized existing data on SILSG and checked the procedure's feasibility, technical details, safety, and, if possible, outcomes. They checked the most important databases for studies concerning SILSG and included all these that summarized the criteria placed and contained the data needed for this review. They excluded case reports. A total of 19 studies (1,679 patients) met the selection criteria of this review. Their mean age was 38.91 years and the mean pre-operative BMI was 41.8 kg/m2. In the majority of cases (60.5%), a left upper quadrant incision was carried out; and in 97.6%, a commercially available multi-port system was employed. A wide variety of instruments had been used and mean operating time was 94.6 minutes. One conversion to open surgery was reported and 7.4% required the placement of additional ports. There was a complication rate of 7.38% (most common being bleeding with a rate of 2.5%) and a re-operation rate of 2.8%. Mean EWL for a follow-up of 1 year was achieved in 53.7% of patients and was 70.06%. A tendency for less analgesia and better wound satisfaction was reported. The authors concluded that SILSG was safe and feasible. However, there is insufficient evidence to recommend it as the new gold standard for sleeve gastrectomy in the place of conventional laparoscopic sleeve gastrectomy. These investigators stated that RCTs are needed to analyze the results and the possible benefits of this technique.

Sleeve Gastrectomy with Single Anastomosis Duodeno-Ileal Bypass (SIPS) for the Treatment of Morbid Obesity

Zaveri et al (2015) noted that the increase in the prevalence of obesity and gastro-esophageal reflux disease (GERD) has paralleled one another. Laparoscopic fundoplication (LF) (Nissen or Toupet) is a minimally invasive form of anti-reflux surgery. The duodenal switch (DS) is a highly effective weight loss surgery with a proven record of long-term weight loss success. However, fundoplication alone does not give

satisfactory results when used for GERD in morbidly obese patients. These researchers presented a novel approach combining stomach intestinal pylorus sparing surgery (SIPS) with LF for morbidly obese patients with GERD. The data from patients who underwent the SIPS procedure along with LF in past year was retrospectively analyzed. The variables collected were age, sex, height, weight, intra-operative and post-operative complications, length of stay, operative time, and estimated blood loss. All revisions were excluded. Descriptive statistics such as mean and standard deviation were used to analyze the data. The total sample size of the study was 5 patients, with a mean age of 59.6 ± 16.4 years, a mean weight of 292.1 ± 73.6 lbs., and a mean body mass index (BMI) of 43.4 ± 6.3. Weight loss patterns were the same as those without LF. All 5 patients had resolution or improvement in their GERD symptoms within 6 months. The authors concluded that SIPS with LF provided substantial and sustained weight loss and GERD resolution.; however, long-term follow-ups and further study on this novel surgical technique is recommended.

This study had 2 main drawbacks: (i) this was a small (n = 5) study. This study was not meant to provide definitive superiority to LF or LRYGBP alone in the setting of obesity but as a possibility in patients who both LF and LRYGBP are not options for various reasons. Consequently predicting its widespread applicability to all bariatric patients with reflux is premature and awaits larger trials, (ii) these researchers could not evaluate endoscopy or pH testing post-operatively in their patients, which is fundamental to evaluate the effect of anti-reflux surgery. Although they could get GERD-HRQL questionnaires for all their patients, these investigators could not compare the data pre- and post-surgery.

Mitzman et al (2016) stated that although the DS has been the most effective weight loss surgical procedure, it is a small minority of the total bariatric surgical cases performed. Modifications that can make the operation technically simpler and reduce a long-term risk of short bowel syndrome would be of benefit. These investigators detailed their initial experience with a modified DS called SIPS procedure. Data from patients who underwent a primary SIPS procedure performed by 2 surgeons at 2 centers from January 2013 to August 2014 were retrospectively analyzed.

All revisions of prior bariatric procedures were excluded. Regression analyses were performed for all follow-up weight loss data. A total of 123 patients were available; 102 patients were beyond 1 year post-operative, with data available for 64 (62% followed-up). The mean BMI was 49.4 kg/m(2); 2 patients had diarrhea (1.6%), 4 had abdominal hematoma (3.2%), and 1 had a stricture (0.8%) in the gastric sleeve; 2 patients (1.6%) were re-admitted within 30 days; 1 patient (0.8%) was re-operated due to an early post-operative ulcer. At 1 year, patients had an average change in BMI of 19 units (kg/m(2)), which was compared to an average of 38% of TWL or 72% of EWL. The authors concluded that modification of the classic DS to one with a single anastomosis and a longer common channel had effective weight loss results. Morbidity appeared comparable to other stapling reconstructive procedures. Moreover, they stated that future analyses are needed to determine whether a SIPS procedure reduces the risk of future small bowel obstructions and micronutrient deficiencies.

Cottam and colleagues (2017) stated that in bariatric surgery, the procedure with the highest average weight loss is the bilio-pancreatic diversion with duodenal switch (BPDDS). A new simplified duodenal switch called the SIPS surgery with less malabsorption and 1 fewer anastomosis claims to have similar outcomes when compared to the BPDDS. These researchers performed a retrospective matched cohort analysis of SIPS versus BPDDS patients in a single private practice by matching every BPDDS to a SIPS patient of the same gender and BMI. Excess weight loss (EWL) percentage, BMI, and percentage total weight loss (% TWL) were compared. Additionally, co-morbidity resolution, nutritional data, and complications were also compared. Data were analyzed using both descriptive and comparative statistics. Over 2 years, there was no statistical difference in weight loss between BPDDS and SIPS. There also was no difference in nutritional data between the 2 procedures pre- and post-op. Complication rates were lower in SIPS however, due to the small sample sizes this is not statistically significant. The authors concluded that weight loss and nutritional results between SIPS and BPDDS were similar at 2 years. However, there are fewer complications with SIPS. The main drawbacks of this study were its retrospective design and small sample size.

Shoar et al (2018) noted that owing to the possibility of weight regain after the long-term follow-up of gastric bypass patients and because of the high morbidity of bilio-pancreatic diversion with duodenal switch (BPD-DS), single-anastomosis duodeno-ileal switch (SADIS) has emerged as a rescue procedure in bariatric surgery. These researchers summarized the literature data on SADIS. They carried out a comprehensive literature review through October 2016 to identify English studies on SADIS performed in human subjects. Outcomes of interest were technical considerations, post-operative complications, weight loss outcome, co-morbidity resolution rate, and nutritional deficiency after SADIS. A total of 12 studies including 581 SADIS patients (217 males and 364 females) were included. SADIS was a primary procedure in 508 patients (87.4%) and a conversion procedure in 73 patients (12.6%). The length of common limb was 300 cm in 54.2%, 250 cm in 23%, and 200 cm in 13.4% of patients. Anastomosis technique was a linear stapler in 26.7% and a hand-sewn suture technique in 73.3% of patients. Diarrhea was the most common complication (1.2%). The average%EWL was 30% at 3 months, 55% at 6 months, 70% at 1 year, and 85% at 2 years. Co-morbidity resolution rate was 74.1% for T2DM, 96.3% for hypertension, 68.3% for dyslipidemia, 63.3% for OSA, and 87.5% for GERD. Overall, vitamin A, selenium, and iron deficiency were the most common nutritional deficiencies with the possibility of the protein malnutrition in up to 34% of the patients when measured. The authors concluded that as a modified bariatric procedure, SADIS has promising outcomes for weight loss and co-morbidity resolution in morbidly obese patients. When measured, there was a high prevalence of macro-nutrient deficiencies following SADIS. There is a high technical variability, and long-term data are needed before any meaningful conclusion can be made.

In a systematic review and meta-analysis Lee et al (2019) compared the safety and efficacy between single-anastomosis duodeno-ileal bypass (SADI) or BPD-DS versus RYGB as a revisional procedure for sleeve gastrectomy (SG). Medline, Embase, Cochrane Central Register of Controlled Trials, and PubMed were searched up to August 2018. Studies were eligible for inclusion if they compared SADI or BPD-DS with RYGB as a revisional bariatric procedure for SG. Primary outcome was absolute% TWL. Secondary outcomes were LOS, AEs, and improvement or resolution of co-morbidities (diabetes, hypertension, or hypercholesterolemia). Pooled MDs were calculated using random effects

meta-analysis. A total of 6 retrospective cohort studies involving 377 patients met the inclusion criteria. The SADI/BPD-DS group achieved a significantly higher% TWL compared with RYGB by 10.22% (95% CI: -17.46 to -2.97; p = 0.006). However, there was significant baseline equivalence bias with 4 studies reporting higher initial BMI in the SADI/BPD-DS group. There were no significant differences in LOS, AEs, or improvement of co-morbidities between the 2 groups. The authors concluded that SADI, BPD-DS, and RYGB were safe and effective revisional surgeries for SG. Both SADI and RYGB were effective in lowering initial BMI but there is more evidence for excellent WL outcomes with the conversion to BPD-DS when the starting BMI was high. Moreover, these researchers stated that further RCTs are needed for definitive conclusions.

In a retrospective, 3-year trial, Ozmen et al (2020) examined the early effects of "Single Anastomosis Duodenal Switch-proximal approach" (SADS-p) and "One Anastomosis Gastric Bypass-Mini Gastric Bypass (OAGB-MGB) on the "homeostasis model assessment of insulin resistance" (HOMA-IR) index levels in morbidly obese patients with T2DM. Outcomes of SADS-p and OAGB-MGB patients were compared considering the changes in HOMA-IR index levels. All bariatric procedures were performed by a single primary surgeon recognized as a surgeon of excellence by IFSO-EC with the assistance of 1 or 2 additional attending surgeons. SADS-p was performed on 60 (10 males) patients, and 200 (27 males) patients underwent OAGB-MGB; 46 patients (78%) in the SADS-p group and 125 (63%) in the OAGB-MGB group had T2DM. Patients were evaluated before surgery and 1, 3, 9, and 12 months after surgery. In both groups, the HOMA-IR index levels decreased significantly after surgery ($p < 0.05$), and both procedures markedly improved glycemic control. In the SADS-p group the HOMA-IR index levels significantly decreased from 6.2 to 1.4 after the 12th month of surgery ($p < 0.05$); in OAGB-MGB group HOMA-IR index levels significantly decreased from 5.9 to 1.7 after the 12th month of surgery ($p < 0.05$). The authors concluded that both procedures are promising operations that offer excellent control on weight, HOMA-IR index and diabetes.

In a retrospective study, Finno et al (2020) examined WL, co-morbidity remission, complications, and nutritional deficits after duodenal switch (DS) and single-anastomosis DS with sleeve gastrectomy (SADI-S). A

total of 440 patients underwent DS (n = 259) or SADI-S (n = 181). Mean pre-operative BMI was 50.8 ± 6.4 kg/m2. Mean follow-up was 56.1 ± 37.2 months for DS and 27.2 ± 18.9 months for SADI-S. Global mean EWL was 77.4% at 2 years similar for SADI-S and DS, and 72.1% at 10 years after DS. Although early complications were similar in SADI-S and DS (13.3% versus 18.9%, p = n.s.), long-term complications and vitamin and micro-nutrient deficiencies were superior after DS. Rate of co-morbidities remission was 85.2% for diabetes, 63.9% for hypertension, 77.6% for dyslipidemia, and 82.1% for sleep apnea, with no differences between both techniques. In patients with initial BMI of greater than 55 kg/m2 (n = 91), DS achieved higher percentage of BMI of less than 35 kg/m2 (80% versus 50%, p = 0.025) and higher rate of diabetes remission (100% versus 75%, p = 0050). The authors concluded that DS and SADI-S showed similar WL and co-morbidity remission rates at 2 years. In patients with initial BMI of greater than 55 kg/m2, DS obtained better BMI control at 2 years and better diabetes remission, but more long-term complications and supplementation needs.

Cottam et al (2020) noted that the SADS procedure has been suggested to be an effective bariatric procedure that offers excellent WL and by lengthening the common channel the potential to reduce micro-nutrient deficiencies. These researchers examined the WL, co-morbidity resolution and the 1-year nutritional outcomes of the SADS procedure. From October 2014 to January 2017, a total of 120 patients were enrolled at 6 sites across the U.S. and underwent the SADS procedure; WL, co-morbidities, QOL, and AEs were followed post-procedure for 12 months. At 1, 6, and 12 months, 98.3%, 85.5%, and 77.1% of the patients were available for assessment, respectively. At 12 months, patients showed significantly reduced BMI when compared to baseline (46.8 ± 5.8 versus 29.8 ± 4.4, p < 0.001 respectively); 65 patients had T2DM at baseline; however, 11 patients were lost to follow-up. Of the available data (54 patients), 96.3% of the patients had a resolution of T2DM by 12 months with a mean A1C reduction from 7.8 ± 1.6 to 5.3 ± 0.7. Furthermore, there were reductions in hyperlipidemia, sleep apnea, and hypertension at 12 months. Patient GERD satisfaction and QOL (SF-36) scores were significantly higher at 12 months post-procedure (p < 0.001 in all cases) while 12-month protein levels remained at normal values. There were abnormalities of parathyroid hormone (PTH) and vitamin D at 1 year with all other nutritional markers being not significantly different at 1 year from

baseline. There were 10, III-b or greater complications according to the Clavien-Dindo scoring system during the study period, not all of which were related to the surgery. The authors concluded that SADS was a highly effective WL procedure with significant co-morbidity reduction at 1 year. At 1 year, complications and vitamin and mineral deficits appeared to be consistent with other mal-absorption operations. The authors concluded that long-term follow-up is needed, especially around complications and vitamin deficiencies.

Surve et al (2020a) noted that the long-term outcomes of primary single-anastomosis duodeno-ileal bypass with sleeve gastrectomy (SADI-S) have never been reported in the literature. In a retrospective study, these researchers examined the long-term outcomes after primary laparoscopic SADI-S (LSADI-S). Data from 750 patients who underwent a primary LSADI-S from June 2013 through November 2019 by 3 surgeons were analyzed. The mean age and pre-operative body mass index (BMI) were 49.3 ± 13.1 years and 50 ± 12.6 kg/m2, respectively. Follow-up was available on 109 patients (61%) at 5 years and on 87 patients (53%) at 6 years; 6 patients did not have any follow-up. The average operative time and length of stay (LOS) were 67.6 ± 27.4 mins and 1.5 ± .8 days, respectively. The intra-operative, short-term, and long-term complication rates were 0%, 7.8%, 11.7%, respectively . The 30-day emergency room (ER) visit, re-admission, and re-operation rates were 0.4%, 1.1%, and 1.1%, respectively. In total, there were 15 (2%) grade IIIb long-term complications unique to LSADI-S. Complete remission of type 2 diabetes mellitus (T2DM) was observed in 77% of the diabetic population. At 5 and 6 years, the mean change in BMI was 17.5 ± 6.9 and 17.6 ± 6.4 kg/m2, respectively. The mortality rate was 0.5%. The authors concluded that LSADI-S was effective in this retrospective review in achieving good initial weight loss and weight maintenance. Moreover, these researchers stated that although these findings showed acceptable nutritional complications, questions still remain because of the retrospective nature of the study. They stated that further long-term outcome studies with better follow-up rates are needed to confirm the long-term nutritional results of LSADI-S.

The authors stated that this study’s main drawback was the follow-up percentage. The long-term follow-up rate was 61% at 5 years, and 53% at 6 years. Because there are no long-term outcomes article in the literature, and the mid-term data were limited, these researchers believed it is

important to report the long-term outcomes even with what they would consider a limited patient follow-up. However, there were enough patients past 5 years, so that the probability of the weight loss data changing would be minimal with the acquisition of more patients. There also were enough patient years that any common long-term complication should have been seen. In addition, as this was the authors' total experience with this procedure, it included their learning curve. The complication rate has fallen as these investigators have become more skilled at performing this procedure. This article was not and should not be the final word on SADI-S. There are many issues unresolved. For example, what is the optimal SG size and what is the optimal CCL for BMI or co-existing conditions. The question has not been answered by this article, and they deserve to be. Furthermore, what is the optimal length of the common channel to avoid diarrhea post-operatively, and what level of post-operative revisions for diarrhea is acceptable; these researchers simply do not know. For this reason, further long-term studies are needed to confirm the safety and efficacy of this procedure.

Surve et al (2020b) stated that the long-term effectiveness of RYGB and SADI-S is unknown. These investigators compared the long-term outcomes. Data from 1,254 patients who underwent primary RYGB or SADI-S were used for a retrospective matched cohort. Data were obtained by matching every RYGB patient to a SADI-S patient of the same sex, BMI, and weight. Only patients out 5 years and had at least 1 greater than 5-year follow-up visit were included. The matched cohort included 61 RYGB and 61 SADI-S patients. There was no statistical, demographic difference between the 2 groups. At 5 years, a 100% follow-up was available in each group. The intra-operative outcomes were significantly better with SADI-S. The 30-day re-admission, re-operation, emergency department (ED) visits, and complication rates were statistically similar between the 2 groups. The long-term complication rates, Clavien-Dindo grade IIIb complications, and number of patients with more than 1 complication were significantly lower with SADI-S. Weight loss was significantly greater in the SADI-S group at 5 years. The long-term weight-loss failure rate was significantly higher in the RYGB group. The SADI-S procedure was associated with fewer re-intervention through 6 years (14.7% patients versus 39.3% patients, $p = 0.001$). Conversion or reversal of the procedure was required only in the RYGB group. There also was no significant difference in nutritional outcomes

between the 2 procedures. The authors concluded that in this matched cohort comparison of long-term outcomes, the SADI-S procedure was superior to the RYGB procedure with regard to operative outcomes, lethal long-term complications, number of patients with more than 1 complication, re-intervention rates, weight loss, weight-loss failure rates, and conversion rates. Moreover, these researchers stated that more such studies with a larger sample size are needed. They stated that the SADI-S may be considered one of the viable alternatives to RYGB.

The authors stated that this study had several drawbacks. First, the small sample size of the cohort. The study had 61 patients in each group, with a 100% follow-up at 5 years. In the majority of bariatric practices, only 20% to 25% of the patient population followed-up after 5 years. Moreover, getting labs after 5 years is even more difficult. These researchers were still able to compare their findings with other long-term outcome studies in the literature because most studies on the long-term outcome of RYGB had less than 200 patients, specifically at 5 years. Second was the lack of long-term co-morbidity outcomes. These investigators had sufficient long-term co-morbidity data for 1 of the 2 procedures; however, since this was a comparative study, they decided not to present them. Third, the number of available labs was insufficient to make any definite conclusion on the nutritional outcomes. Surgeons will rightly be skeptical of this paper showing SADI-S with fewer nutritional complications than RYGB (especially calcium). Fourth was the retrospective nature of the study. Fifth was the learning curve of the SADI-S procedures. These investigators' practice began to perform the SADI-S procedure in 2013. Around 55% of the SADI-S patients that have been included in the study had been operated in the first 2 years.

Enochs et al (2020) noted that the sleeve gastrectomy (SG), Roux-en-Y gastric bypass (RYGB), and SADI-S are recognized bariatric procedures. A comparison has never been made between these 3 procedures and especially in different BMI categories. These researchers analyzed a large cohort of patients undergoing either laparoscopic (L) SG, LRYGB, or LSADI-S to examine and compare weight loss and glycosylated hemoglobin level. The secondary objective was to compare the nutritional outcomes between LRYGB and LSADI-S. This was a retrospective review of 878 patients who underwent LSG, LRYGB, or LSADI-S from April 2014 through October 2015 by 5 surgeons in a single institution. For weight

loss analysis, the patients were categorized into 4 different categories as follows: patients regardless of their pre-operative BMI, patients with pre-operative BMI of less than 45 kg/m2, patients with pre-operative BMI 45 to 55 kg/m2, and patients with pre-operative BMI of greater than 55 kg/m2. A total of 878 patients were identified for analysis. Of 878 patients, 448 patients, 270 patients, and 160 patients underwent LSG, LRYGB, and LSADI-S, respectively. Overall, at 12 and 24 months, the weight loss was highest with LSADI-S, followed by LRYGB and LSG in all 4 categories. At 2 years, the patients lost 19.5, 16.1, and 11.3 BMI points after LSADI-S, LRYGB, and LSG, respectively. Furthermore, the weight loss was highest in patients with pre-operative BMI of less than 45 kg/m2 and lowest in patients with pre-operative BMI of greater than 55 kg/m2 at 12 and 24 months. In addition, there were no statistically significant differences between the nutritional outcomes between LRYGB and LSADI-S. The LSADI-S had significantly lower rates of abnormal glycosylated hemoglobin than LRYGB and LSG at 12 months ($p < 0.001$). The authors concluded that the weight loss outcomes and glycosylated hemoglobin rates were better with LSADI-S than LRYGB or LSG. The nutritional outcomes between LRYGB and LSADI-S were similar.

The authors stated that this study had several drawbacks. The first was the fact that it was retrospective rather than prospective. At 2 years, these researchers had a follow-up of 50% for the LSG group. The study did not include complication data and analysis of other obesity-related co-existing condition data in any of the groups. Moreover, they were unable to make a definite conclusion for patients with BMI 0.55 kg/m2, as the group had a small number of patients. Another drawback was the lack of similarity between the 3 groups. In all 4 BMI categories, the patients that underwent LSADI-S had highest pre-operative weight and BMI. Despite these differences, LSADI-S had better weight loss than LSG and LRYGB. Moreover, the T2D resolution rate was highest with LSADI-S. Also, the study did not include some of the nutritional data points like prealbumin, parathyroid hormone, and vitamins B1 and B9.

Kallies and Rogers (2020) provided an updated statement on single-anastomosis duodenal switch by the American Society for Metabolic and Bariatric Surgery (ASMBS) in response to numerous inquiries made to the Society by patients, physicians, society members, hospitals, and others regarding single-anastomosis duodenal switch as a treatment for

obesity and metabolic disease. This recommendation is based on current clinical knowledge, expert opinion, and published peer-reviewed scientific evidence available at this time. With additional publications reporting outcomes of many more patients who have undergone SADI-S since the previous ASMBS statement (amounting to a total of approximately 1,500 currently reported patients), the ASMBS has reached the conclusion that SADI-S provides for similar outcomes to those reported after classic DS and should therefore be endorsed, similar to the ASMBS' endorsement of the predicate procedure of BPD-DS. The conclusion from the current review is that the currently available peer-reviewed literature does not suggest outcomes will differ substantially from those seen with classic DS. The ASMBS will continue to monitor and evaluate emerging data on this procedure and, when appropriate, will issue an updated evidence-based position statement at a future time. The following recommendations are currently endorsed by the ASMBS regarding SADI-S for the primary treatment of obesity or metabolic disease:

- SADI-S, a modification of classic Roux-en-Y DS, is therefore endorsed by ASMBS as an appropriate metabolic bariatric surgical procedure.
- Publication of long-term safety and efficacy outcomes is still needed and is strongly encouraged, particularly with published details on SG size and common channel length.
- Data for these procedures from accredited centers should be reported to the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program database and separately recorded as single-anastomosis DS procedures to allow for accurate data collection.
- There remain concerns about intestinal adaptation, nutritional issues, optimal limb lengths, and long-term weight loss/regain after this procedure. As such, ASMBS recommends a cautious approach to the adoption of this procedure, with attention to ASMBS-published guidelines on nutritional and metabolic support of bariatric patients, in particular for DS patient.

While the updated ASMBS statement (Kallies and Rogers, 2020) endorses SADI-S as an appropriate metabolic bariatric surgical procedure, it also points out that studies of long-term safety and efficacy

are still needed – a view that is supported by the studies described above.

Furthermore, an UpToDate review on "Bariatric procedures for the management of severe obesity: Descriptions" (Lim, 2020) states that "Several other procedures, including one-anastomosis gastric bypass (OAGB) and single anastomosis duodeno-ileal bypass (SADI), are still considered investigational in terms of being a standard bariatric procedure".

Yashkov et al (2021) stated that there are only a small number of studies providing a comparison between SADI-S and Hess-Marceau's BPD/Duodenal Switch (RY-DS) operations. These researchers compared 5-year results of SADI-S 250 (common limb 250 cm) with RY-DS. Data of patients who underwent open SADI-S (n 226) and RY-DS (n 528) were retrospectively studied. EWL(%), EBMIL(%), TWL(%), anti-diabetic effect, complications, and revision rate were compared between the 2 groups. After the first 12 months, EWL% (77.0% versus 73.3%) and TWL% (39.4% versus 38.9%) were statistically significantly better after SADI-S ($p < 0.01$, and $p < 0.05$, respectively), but not EBMIL% ($p > 0.05$). At nadir to 24-36 months, EWL, TBWL, and EBMIL after SADI-S was comparable to the RY-DS group. Up to the 4th and 5th year, better weight loss (TBWL, EBMIL, EWL) was observed after RY-DS than after SADI-S. Early complication rate was less (2.65%) in the SADI-S group versus 5.1% in the RY-DS. Protein deficiency and small bowel obstruction rates were also lower after SADI-S; 93.4% of patients achieved total remission of their diabetes; 7.5% of patients in the SADI-S group had symptoms of bile reflux, which was a main indication for revisions. The authors concluded that SADI-S has many advantages over RY-DS; however, weight loss and anti-diabetic effects after the 3rd year were marginally lower after SADI-S compared to RY-DS. SADI-S was less dangerous in terms of malabsorption and appeared to be a reasonable alternative to RY-DS as a metabolic operation. RY-DS could be implemented for weight regain and/or bile reflux after SADI-S.

This study had several drawbacks. This was a retrospective analysis of 2 modifications of BPD/DS, one of which (RY-DS) had been performed between 2003 and 2015 and another one (SADI-S), since 2014. For this reason, these investigators compared more recent information regarding

5-year anti-diabetic effects of SADI-S with their preliminary published data regarding 5-year results of RY-DS. There was no learning curve period in the SADI-S group, but there was in RY-DS group. Although the initial weight of the patients in the SADI-S group was higher ($p < 0.01$), they were also taller, so there was no statistically significant difference in the initial BMI between the 2 groups. More patients from the SADI-S group suffered from diabetes mellitus type 2 (DM2). In the period when thee investigators used SADI-S, a significant number of "easier" patients were suggested as candidates for a sleeve gastrectomy. In cases of DM2, SADI-S was preferable over a sleeve gastrectomy alone. Furthermore, the percentage of patients with DM2 has increased over the last 5 to 10 years because more patients considered their diabetes to be a more significant health problem than obesity itself. Another limitation was that both RY-DSs and SADI-Ss were performed by the authors using an open technique. Although laparotomies are infrequently used in metabolic surgery, in their experience both open RY-DSs and SADI-Ss could be performed safely by laparotomy with a minimal 30-day morbidity (0.38% for RY-DS and 0.44% for SADI-S) with low early morbidity (5.1% and 2.65% accordingly). In the recently published study from Brazil [Kim, 2016] using a laparoscopic technique, the authors demonstrated 18.9% early complications after RY-DS and 13.3% after SADI-S.

Spinos et al (2021) noted that single-anastomosis duodenoileal bypass with sleeve gastrectomy/one anastomosis duodenal switch (SADI-S/OADS) was developed as a bariatric operation with reduced overall morbidity and lasting weight loss results. These investigators carried out a systematic review of the literature, including 14 studies reporting on weight loss, co-morbidity resolution, post-operative complications, and nutritional deficiencies following SADI-S. Twelve months after SADI-S, the mean total body weight lost ranged from 21.5% to 41.2%, with no weight regain being observed after 24 months. The co-morbidity resolution rate was 72.6% for diabetes, 77.2% for dyslipidemia, and 59.0% for hypertension cases. The need for re-operation was the most common post-operative complication. While several patients developed nutrient deficiencies, SADI-S appeared to be an overall safe and effective bariatric operation. The authors concluded that since the initial conception, the popularity of SADI-S has increased. SADI-S offers the benefits of a combined malabsorptive and restrictive bariatric operation, with fewer post-operative complications than the traditional DS and has drawn the

interest of several different authors to study it further. The next step for the scientific community now will be to organize randomized controlled trials (RCTs) with long-term follow-ups to ensure the consistency of high-quality outcomes reported so far.

The authors stated that the findings of this systematic review warrant careful interpretation, due to its inherent limitations. Due to the heterogeneity in the technical aspects of these operations, as well as the reported outcomes, these researchers were unable to perform a comparative study or meta-analysis on the outcomes of SADI-S. All studies included in this systematic review were either cohort studies or case series, and retrospective in nature; therefore, the overall level of evidence presented was low. There was significant heterogeneity in the reported outcomes, their definitions, and their categorization. Finally, the follow-up of most studies was rather short, which could be explained by the novelty of the technique as most studies were published in or after 2018.

Adjunctive Omentectomy to Bariatric Surgery

Fabbrini and associates (2010) noted that visceral adipose tissue (VAT) is an important risk factor for the metabolic complications associated with obesity. Thus, a reduction in VAT is considered an important target of obesity therapy. These investigators examined if reducing VAT mass by surgical removal of the omentum would improve insulin sensitivity and metabolic function in obese patients. They conducted a 12-month RCT to determine whether reducing VAT by omentectomy in 22 obese subjects increased their improvement following RYGB surgery in hepatic and skeletal muscle sensitivity to insulin (study 1). Improvement was assessed by using the hyperinsulinemic-euglycemic clamp technique. These researchers also performed a 3-month, longitudinal, single-arm study to determine whether laparoscopic omentectomy alone, in 7 obese subjects with T2DM, improved insulin sensitivity (study 2). Improvement was assessed by using the Frequently Sampled Intravenous Glucose Tolerance Test. The greater omentum, which weighed 0.82 kg (95% CI: 0.67 to 0.97), was removed from subjects who had omentectomy in both studies. In study 1, there was an approximate 2-fold increase in muscle insulin sensitivity (relative increase in glucose disposal during insulin infusion) and a 4-fold increase in hepatic insulin sensitivity 12 months

after RYGB alone and RYGB plus omentectomy, compared with baseline values ($p < 0.001$). There were no significant differences between groups ($p > 0.87$) or group x time interactions ($p > 0.36$). In study 2, surgery had no effect on insulin sensitivity ($p = 0.844$) or use of diabetes medications. The authors concluded that these findings demonstrated that decreasing VAT through omentectomy, alone or in combination with RYGB surgery, did not improve metabolic function in obese patients.

In a double-blind RCT, Andersson and colleagues (2014) examined if removal of a large amount of visceral fat by omentectomy in conjunction with RYGB would result in enhanced improvement of insulin sensitivity compared to gastric bypass surgery alone. A total of 81 obese women scheduled for RYGB were included in the study. They were randomized to RYGB or RYGB in conjunction with omentectomy. Insulin sensitivity was measured by hyperinsulinemic euglycemic clamp before operation and 62 women were also re-examined 2 years post-operatively. The primary outcome measure was insulin sensitivity and secondary outcome measures included cardio-metabolic risk factors. Two-year weight loss was profound but unaffected by omentectomy. Before intervention, there were no clinical or metabolic differences between the 2 groups. The difference in primary outcome measure, insulin sensitivity, was not significant between the non-omentectomy (6.7 ± 1.6 mg/kg body weight/min) and omentectomy groups (6.6 ± 1.5 mg/kg body weight/min) after 2 years. Nor did any of the cardio-metabolic risk factors that were secondary outcome measures differed significantly. The authors concluded that addition of omentectomy to gastric bypass operation did not result in an incremental effect on long-term insulin sensitivity or cardio-metabolic risk factors. They stated that the clinical value of adjunctive omentectomy to gastric bypass operation is highly questionable.

Lee and co-workers (2018) stated that excess visceral adipose tissue has been identified as an important risk factor for obesity-related co-morbidities. Conflicting information exists on whether omentectomy added to bariatric surgery is beneficial to metabolic variables. These researchers evaluated the impact of omentectomy added to bariatric surgery on metabolic outcomes. Medline, Embase, and PubMed were searched up to May 2018. Studies were eligible for inclusion if they were RCTs comparing omentectomy added to bariatric surgery with bariatric surgery

alone. Primary outcome measures were absolute change in metabolic variables (BMI, insulin, glucose, cholesterol, lipoproteins, and triglycerides); secondary outcomes were changes in adipocytokines. Pooled mean differences (mean deviation; MD) were calculated using random effects meta-analyses, and heterogeneity was quantified using the I2 statistic. A total of 10 trials involving 366 patients met the inclusion criteria with a median follow-up time of 1 year after surgery. Adding omentectomy to bariatric surgery demonstrated a minimal but statistically significant decrease in BMI compared with bariatric surgery alone (MD 1.29, 95% CI: 0.35 to 2.23, p = 0.007, I2 = 0%, 10 trials). Conversely, patients who underwent bariatric surgery alone had significant increases in high-density lipoprotein (MD -2.12, 95% CI: -4.13 to -0.11, p = 0.04, I2 = 0%, 6 trials). Other metabolic outcomes and adipocytokines showed no significant difference between procedures. The authors concluded that the addition of omentectomy to bariatric surgery resulted in minimal reduction of BMI. They stated that considering no overall improvement in metabolic outcomes and the time and effort required, the therapeutic use of omentectomy added to bariatric surgery is not warranted.

Gastric Bypass for Craniopharyngioma-Related Hypothalamic Obesity

Ni and Shi (2018) stated that craniopharyngiomas (CPs) and their treatment are associated with hypothalamic damage that causes hypothalamic obesity (HO) in 30% to 70% of cases. Therefore, there is ongoing investigation regarding solutions for HO because these patients have unrelenting resistance to basic weight-loss interventions. These investigators summarized the interventions that are used to treat CP-related HO (CP-HO), including pharmacotherapy and bariatric surgery. The Cochrane Library, Embase, and PubMed databases were searched up to June 2017 for relevant reports; 2 reviewers conducted independent evaluations of the studies identified. A total of 18 articles were included in the systematic review, with 3 reports describing pharmacotherapy in RCTs and 15 reports describing bariatric surgery. Although several studies described effective interventions for treating CP-HO, the evidence base was limited by its low quality and the inability to perform a meta-analysis, which was related to a lack of adequate or integrated data. The authors concluded that octreotide appeared to be a preferred treatment for patients with CP-HO, based on limited data. Gastric bypass surgery

may also be suitable for select patients with CP-HO, based on a review of various procedures in this setting. Microsurgical preservation of the hypothalamic structures is mandatory to decrease CP-HO-related morbidity and mortality. Moreover, they stated that further studies with adequate analytical power and sufficient follow-up are needed to identify effective strategies for CP-HO treatment.

Conversion to Sleeve Gastrectomy for Hypoglycemia Post-RYGB

Carter and colleagues (2016) stated complications after RYGB are well-documented. Reversal of RYGB is indicated in select cases but can lead to weight gain. Conversion from RYGB to sleeve gastrectomy (SG) has been proposed for correction of complications of RYGB without associated weight gain. However, little is known about outcomes after this procedure. These researchers carried out a retrospective study of patients who underwent RYGB to SG conversion. A total of 12 patients underwent RYGB to SG conversion for refractory marginal ulceration, stricture, dumping, gastro-gastric fistula, hypoglycemia, and failed weight loss. No deaths occurred; 4 patients experienced 7 major complications, including portal vein thrombosis, bleeding, pancreatic leak, pulmonary embolus, seroma, anastomotic leak, and stricture; 2 required re-operation, and 6 were re-admitted within 30 days; 4 required naso-enteric feeding post-operatively because of prolonged nausea. The complication of RYGB resolved in 11 of 12 patients. At 14.7 months, change in BMI for all patients was a decrease of 2.2 kg/m(2). In 5 patients with morbid obesity at conversion, the change in BMI was a decrease of 6.4 kg/m(2) at 19 months. The authors concluded that laparoscopic conversion from RYGB to SG was successful in resolving certain complications of RYGB and did not result in short-term weight gain. However, conversion had a high rate of major complications as well as a high rate of re-admission and need for supplemental nutrition. They stated that although conversion to SG may be appropriate in carefully-selected patients, other options for patients with severe chronic complications after RYGB should be considered.

The 2017 American Society of Metabolic and Bariatric Surgery (ASMBS) position statement on "Postprandial hyperinsulinemic hypoglycemia after bariatric surgery" (Eisenberg et al, 2017) stated that "Conversion of RYGB to SG (primary or staged) has also been described in a few small

series/case reports for complications related to RYGB. Reversal of RYGB with the addition of primary or staged SG specifically for treatment of refractory hyperinsulinemic hypoglycemia has been described in less than 10 patients with resolution of hypoglycemia symptoms in the majority without findings of short-term weight gain. As with RYGB reversal, these are technically challenging procedures with increased risk of complications, including a greater incidence of gastroesophageal reflux related to the addition of the SG. Currently, there is insufficient evidence to recommend this as treatment for hyperinsulinemic hypoglycemia".

An UpToDate review on "Late complications of bariatric surgical operations" (Ellsmere, 2018) states that "Based on the theory that severe, disabling hypoglycemia after gastric bypass surgery occurs in a subset of patients with loss of gastric restriction, with resultant rapid food passage and absorption, restoration of gastric restriction can result in symptom resolution. Gastric restriction can be restored by surgical placement of a silastic ring or an adjustable gastric band around the pouch. In one series, symptoms resolved in 11 of 12 patients with this approach".

Gastrojejunostomy for the Treatment of Gastro-Esophageal Reflux Disease following Anti-Reflux Surgery

Grover and Kothari (2015) stated that patient satisfaction with primary anti-reflux surgery is high, but a small percentage of patients experience recurrent reflux and dysphagia, requiring re-operation. The major anatomic causes of failed fundoplication are slipped fundoplication, failure to identify a short esophagus, and problems with the wrap. Minimally invasive surgery has become more common for these procedures. Options for surgery include redo fundoplication with hiatal hernia repair if needed, conversion to RNY anatomy, or, as a last resort, esophagectomy. The authors asserted that conversion to RNY anatomy had a high rate of success, making this approach an important option in the properly selected patient. This review did not provide any clinical data; however, it did cite the studies by Awais et al (2008) and Makris et al (2012).

Awais and co-workers (2008) stated that intractable GERD after prior anti-reflux operation presents a difficult challenge. These investigators examined the role of Roux-en-Y near esophago-jejunostomy (RNYNEJ) in the management of intractable reflux symptoms after prior anti-reflux

surgery. Between June 2000 and October 2005, a total of 25 patients with GERD after anti-reflux surgery underwent RNYNEJ. The end-points evaluated were improvement in GERD symptoms using the GERD-Health Related Quality of Life (HRQL) scale, overall patient satisfaction, overall patient weight loss, and improvement of co-morbid conditions. There were 4 men and 21 women (mean age of 51 years; range of 35 to 74); 72% had a BMI of greater than 30; 44% had more than 1 anti-reflux surgery and 40% had a previous Collis gastroplasty. The peri-operative mortality was 0%; 6 patients (24%) developed major post-operative complications, including anastomotic leak (n = 2) and Roux-limb obstruction (n = 1). The median length of stay (LOS) was 6 days; 80% of the patients reported satisfaction at mean follow-up time of 16.5 months. Their BMI reduced from 35.8 to 27.7 ($p < 0.001$); 73% of co-morbid conditions were improved and the GERD HRQL score improved from 29.9 to 7.3 ($p < 0.001$). The authors concluded that the RNYNEJ for persistent GERD after prior anti-reflux surgery was technically challenging with significant morbidity. However, the majority of the patients reported satisfaction with significant improvement in symptoms. Many patients had associated benefits of weight loss and improvement in co-morbid conditions. They stated that RNYNEJ should be considered as an important option for the treatment of intractable GERD after prior anti-reflux surgery, particularly in the obese. Moreover, they stated that there is a need to further investigate and analyze patient variables that influence outcomes because this may help physicians/surgeons to better select patients for a particular type of operation. They noted that these variables need to be prospectively studied to define optimal candidates, and further work is needed for optimizing patient selection. This was a small study (n = 25) with short-term follow-up (mean of 16.5 months).

Makris and colleagues (2012) stated that revisionary fundoplication is the mainstay of treatment for failed previous fundoplication, but is not always feasible. These investigators reported their experience with use of short-limb RNY reconstruction for failed anti-reflux procedures. Prospectively collected data were retrospectively analyzed for morbidity, mortality, pre- and post-procedure symptom scores (scale 0 to 3), BMI, and patient satisfaction (scale 1 to 10). A total of 72 patients with 1 to 4 (median 1) previous anti-reflux procedures underwent RNY reconstruction, either to gastric pouch (n = 64) or to the esophagus (n = 8). There were 37 laparoscopic, 24 open abdominal, and 2 combined thoracic-abdominal

procedures; 9 additional patients underwent conversion from laparoscopy to open surgery. Mean follow-up of 20.7 months (± 12.9 months) was available in 63 (88%) patients. The overall median scores for heart-burn, regurgitation, dysphagia, chest pain, and nausea were 0 or 1. There were 72 major and minor complications noted that affected 33 (46%) patients, with no in-hospital or 30-day mortality observed. The most common complications were anastomotic strictures, bowel obstructions, respiratory complications, and dumping. Mean post-operative BMI was 24.6 (± 4.4) kg/m(2) compared with pre-operative BMI of 31.4 (± 6.1) kg/m(2). Mean reported satisfaction score was 8.2 (± 2.1), and 89% of the patients would recommend the procedure to a friend. Pre- and post-operative symptoms could be compared in 57 patients, and significant decrease in median symptom scores for heart-burn (2-0, $p < 0.05$), regurgitation (1-0, $p < 0.05$), and dysphagia (2-0, $p < 0.05$) was confirmed. There was an increase in reported nausea (0-1, $p < 0.05$). The authors concluded that short-limb RNY reconstruction was an effective remedial procedure for a subset of patients with failed anti-reflux surgery, but morbidity was significant. Moreover, they stated that the main drawback of this study was retrospective studies performed on prospective databases. Furthermore, they stated that studies with longer follow-up are needed to validate these findings.

Mini Sleeve Gastrectomy by Natural Orifice Trans-endoluminal Endoscopic Surgery (NOTES)

Erridge and colleagues (2016) summarized the clinical applications of natural orifice transluminal endoscopic surgery (NOTES) in bariatric surgery. These investigators carried out a review of data, until December 2014 regarding techniques and outcomes of bariatric NOTES procedures. A total of 9 publications were included in the final analysis, with another 6 papers describing endolumenal procedures included for comparison. All NOTES studies adopted a hybrid procedure. Hybrid NOTES sleeve gastrectomy (hNSG) was described in 4 humans and 2 porcine studies. In humans, 6 subjects (23.1%) were converted to conventional laparoscopic methods, and 1 post-operative complication (3.8%) was reported. Mean excess weight loss was 46.6% (range of 35.2 to 58.9). The authors concluded that transvaginal-assisted sleeve gastrectomy appeared

feasible and safe when performed by appropriately trained professionals. However, they stated that improvements must be made to overcome current technical limitations.

An UpToDate review on "Natural orifice transluminal endoscopic surgery (NOTES)" (Pasricha and Rivas, 2018) states that "Natural orifice transluminal endoscopic surgery (NOTES) is an emerging field within gastrointestinal surgery and interventional gastroenterology in which the surgeon accesses the peritoneal cavity via a hollow viscus and performs diagnostic and therapeutic procedures … There is much more that needs to be learned about this procedure, including the risk of peritoneal contamination. So far, the available body of clinical experience does not demonstrate deleterious effects related to contamination and subsequent infection. At present, NOTES still should be considered primarily experimental and should be performed only in a research setting".

Brunaldi et al (2018) stated that RYGB is the most commonly performed bariatric procedure. Despite its high efficacy, some patients regain part of their lost weight. Several endoscopic therapies have been introduced as alternatives to treat weight regain; however, most of the articles were relatively small with unclear long-term data. In a systematic review and meta-analysis, these researchers examined the efficacy of endoscopic therapies for weight regain after RYGB. They searched Medline, Embase, Scopus, Web of Science, Cochrane, Ovid, CINAHL/EBSCo, LILACS/Bireme, and gray literature. Primary outcomes were absolute weight loss (AWL), EWL, and TWL. A total of 32 studies were included in qualitative analysis; 26 described full-thickness (FT) endoscopic suturing and pooled AWL, EWL, and TWL at 3 months were 8.5 ± 2.9 kg, 21.6 ± 9.3 %, and 7.3 ± 2.6 %, respectively. At 6 months, they were 8.6 ± 3.5 kg, 23.7 ± 12.3 %, and 8.0 ± 3.9 %, respectively. At 12 months, they were 7.63 ± 4.3 kg, 16.9 ± 11.1 %, and 6.6 ± 5.0 %, respectively. Subgroup analysis showed that all outcomes were significantly higher in the group with FT suturing combined with argon plasma coagulation (APC) ($p < 0.0001$). Meta-analysis included 15 FT studies and showed greater results; 3 studies described superficial-thickness suturing with pooled AWL of 3.0 ± 3.8, 4.4 ± 0.07, and 3.7 ± 7.4 kg at 3, 6, and 12 months, respectively; 2 articles described APC alone with mean AWL of 15.4 ± 2.0 and 15.4 ± 9.1 kg at 3 and 6 months, respectively. The authors concluded that full-thickness suturing was effective at treating weight

regain after RYGB; and performing APC before suturing appeared to result in greater weight loss. Moreover, these researchers stated that head-to-head studies are needed to confirm these findings; and few studies adequately examined the effectiveness of other endoscopic techniques.

Fayad et al (2019) stated that TORe by devitalization and/or endoscopic suturing (ES) has been implemented in the management of weight regain post-RYGB. These investigators examined the safety and efficacy of TORe following an insurance-based algorithm. They reviewed the prospectively maintained database of patients who underwent TORe between September 2015 and January 2018 at a single academic center. An algorithm was followed whereby management was based on insurance coverage. As part of the algorithm, all patients presented for a repeat endoscopy at 8 weeks. Patients did not receive any diet, lifestyle intervention, or pharmacotherapy. A total of 55 patients were included (median age of 48 years), out of which 50 were women (90.9 %). Patients presented for evaluation at a mean of 8.7 years post-RYGB. The main presenting symptom was combined dumping syndrome (DS) and weight regain (49.1 %), followed by weight regain alone (45.5 %); 29 patients required treatment at their 2nd procedure, and 11 required treatment at their 3rd procedure. Average percent TWL (%TWL) after TORe observed at 3-, 6-, 9-, and 12-month follow-up was 8.2, 9.3, 8.4, and 5.5 %, respectively. The mean DS Severity Score was significantly reduced from 23.3 ± 12.4 before TORe to 16.3 ± 6.51 after TORe ($p < 0.01$). The AE rate from TORe was 14.5 %. The authors concluded that TORe was effective in halting ongoing weight regain and achieving moderate short-term weight loss as well as improving DS in post-RYGB patients. Moreover, durability at 1 year remains questionable due to weight recidivism.

Jirapinyo et al (2020) noted that TORe is an endoscopic approach for patients with weight regain after RYGB with a dilated GJA. In a retrospective review of prospectively collected data, these researchers examined the long-term efficacy of TORe. This trial included RYGB patients who underwent TORe for weight regain or inadequate weight loss after RYGB. The primary outcome was efficacy of TORe at 1, 3, and 5 years; and secondary outcomes were procedure details, safety profile, and predictors of long-term weight loss after TORe. A total of 331 RYGB

patients underwent 342 TORe procedures and met inclusion criteria. Of these, 331, 258, and 123 patients were eligible for 1-, 3- and 5-year follow-ups, respectively. Mean BMI was 40 ± 9 kg/m2. Pre-TORe GJA size was 23.4 ± 6.0 mm, which decreased to 8.4 ± 1.6 mm after TORe. Patients experienced 8.5 % ± 8.5 %, 6.9 % ± 10.1 %, and 8.8 % ± 12.5 % TWL at 1, 3, and 5 years with follow-up rates of 83.3 %, 81.8 %, and 82.9 %, respectively. Of 342 TORe procedures, 76 %, 17.5 %, 4.4 %, and 2.1 % were performed using single purse-string, interrupted, double purse-string, and running suture patterns, respectively, with an average of 9 ± 4 stitches per GJA. Pouch reinforcement suturing was carried out in 57.3 %, with an average of 3 ± 2 stitches per pouch. There were no severe AEs. Some patients (39.3 %) had additional weight loss therapy (pharmacotherapy or procedure), with 3.6 % getting repeat TORe. Amount of weight loss at 1 year ($\beta = 0.43$, $p = 0.01$) and an additional endoscopic weight loss procedure ($\beta = 8.52$, $P = 0.01$) were predictors of percentage of TWL at 5 years. The authors concluded that TORe appeared to be safe, effective, and durable at treating weight regain after RYGB.

The authors stated that this study had several drawbacks. First, the study was conducted at a single bariatric center of excellence. Although this may affect the generalizability of the findings, most cases were carried out with the participation of trainees under the supervision of an expert bariatric endoscopist. Furthermore, all consecutive TORe cases that met the inclusion and exclusion criteria from 2010 to 2018 were included in the analysis. Throughout this period, techniques at the authors' institution continued to evolve, such as APC settings, suture pattern, and final GJA size. Thus, these investigators suspected that the heterogeneity of experience levels and techniques would reflect real life experience of TORe. Another drawback was a retrospective design without a control group, which may have introduced bias. In addition, it was possible that patients who were willing to undergo TORe were more ready to adhere to lifestyle modification compared to the general weight regain population, leading to selection bias. Also, in this study, about 1/3 of the patients received adjunctive therapy after the initial TORe. Nevertheless, the majority were APC alone, which was performed as a reinforcing procedure, with a small number of patients undergoing repeat TORe. This report likely reflected the real-life experience where an adjunctive weight loss procedure may be added to enhance and maintain the long-

term outcome. In the regression analysis, any patient who received at least 1 prescription for any of the FDA-approved medications for obesity between TORe and 5-year follow-up were included regardless of the duration of medication usage and/or early discontinuation due to intolerance and/or AEs. As most patients were prescribed medications when they experienced early weight plateau or inadequate weight loss after initial TORe and duration of usage was unclear, the negative correlation between adjunctive medication usage and amount of weight loss at 5 years must be interpreted with caution.

Dhindsa et al (2020) stated that TORe is an endoscopic procedure used in patients with weight gain after RYGB. In a systematic review and meta-analysis, these researchers examined the safety and efficacy of TORe with a FT suturing device for treating patients with weight regain after RYGB. They carried out a comprehensive search of several databases and conference proceedings including PubMed, Embase, Google-Scholar, Medline, Scopus, and Web of Science databases (earliest inception to March 2020). The primary outcomes evaluated were technical success, AWL and % TWL at 3, 6, and 12 months after the procedure. The secondary outcomes evaluated were pooled rate of AEs, AE subtypes and association of size of GJA and %TWL. A total of 13 studies on 850 patients were included. The pooled rate of technical success was 99.89 %. The absolute weight loss (kg) at 3, 6, and 12 months was 6.14, 10.15, and 7.14, respectively. The %TWL at 3, 6, and 12 months was 6.69, 11.34, and 8.55, respectively. The pooled rate of AE was 11.4 % with abdominal pain being the most common AE. The correlation coefficient (r) was -0.11 between post-TORe GJA size and weight loss at 12 months. The authors concluded that TORe is an endoscopic procedure that is safe and technically feasible for post-RYGB with weight gain. These researchers stated that TORe showed promising results in the short-term; however, more studies are needed to evaluation long-term success of this procedure.

The authors stated that the drawbacks of this review/meta-analysis included some of the studies being retrospective in nature, most of the studies had short-term follow-up, and there was loss of follow-up. Moreover, their pooled rates were limited by heterogeneity and there was increased risk of confounding bias due to the majority of the studies being retrospective. For unexperienced endoscopists, this procedure may be

technically challenging; thus, affecting the generalizability. These investigators stated that more long-term studies should be carried out to determine the durability; future studies should include follow-up endoscopy post-TORe to examine the GJA to evaluate its durability and to see if this correlates with weight recidivism after TORe is done.

Dolan et al (2021) noted that an enlarged GJA is associated with weight regain after RYGB and can be corrected with endoscopic (ENDO) or surgical (SURG) revision; however, there has been no direct comparison between techniques. In a retrospective study, these researchers compared serious AE (SAE) rates and weight loss profiles between ENDO and SURG revisional techniques over a 5-year period. This trial included RYGB patients who underwent ENDO or SURG revision for weight regain with an enlarged GJA (greater than 12 mm). ENDO patients were matched 1:1 to SURG patients based on completion of 5-year follow-up, age, sex, BMI, initial weight loss, and weight regain. Demographics, GJA size, SAEs, and weight profiles were collected. The primary outcome was comparison of SAE rates between groups; and secondary outcomes included weight loss comparisons. A Fisher exact test was used to compare the SAE rate, and a Student t-test was used for weight comparisons. A total of 62 RYGB patients with weight regain and an enlarged GJA (31 ENDO, 31 matched SURG) were included. Baseline characteristics were similar between the 2 groups. The AE rate in the ENDO group (6.5 %) was lower than the SURG group (29.0 %); p = 0.043. There was a total of 0 (0 %) and 6 (19.4 %) SAEs in the ENDO and SURG groups, respectively (p = 0.02). There was no significant difference in weight loss at 1, 3, and 5 years. The authors concluded that endoscopic revision of the GJA was associated with significantly fewer total and severe AEs and similar long-term weight loss when compared with surgical revision. The main drawbacks of this study were its retrospective design and relatively small sample size (n = 31 for the ENDO group). These findings need to be validated by well-designed studies.

Furthermore, an UpToDate review on “Endoscopy in patients who have undergone bariatric surgery” (Huang, 2021) states that “A multicenter randomized, sham-controlled trial evaluated the effectiveness of transoral outlet reduction (TORe) via endoscopic suturing in 77 patients who had undergone RYGB with inadequate weight loss or weight regain. Subjects

who underwent TORe had a greater mean weight loss from baseline than those who underwent a sham procedure (3.5 versus 0.4 %). Weight loss or stabilization was achieved in 96 % of TORe subjects, compared with 78 % of controls. Full-thickness suturing has also been combined with APC therapy to promote greater weight loss than suturing alone". TORe is not mentioned in the "Summary and Recommendations" section of this UTD review.

Candy Cane Syndrome (Roux Syndrome)

Candy cane syndrome (CCS), which is also known as Roux syndrome or Candy cane Roux syndrome, is a rare complication in patients after Roux-en-Y gastric bypass surgery. It occurs when there is an excessive length of roux limb proximal to gastrojejunostomy, creating the possibility for food particles to lodge and remain in the blind redundant limb.

Aryaie and colleagues (2017) noted that CCS has been implicated as a cause of abdominal pain, nausea, and emesis after RYGB; however, it remains poorly described. These investigators reported that CCS is real and can be treated effectively with revisional bariatric surgery. All patients who underwent resection of the "Candy cane" between January 2011 and July 2015 were included in this study. All had pre-operative work-up to identify CCS. Demographic data; pre-, peri-, and post-operative symptoms; data regarding hospitalization; and post-operative weight loss were examined via retrospective chart review. Data were analyzed using Student's t test and $\chi 2$ analysis where appropriate. A total of 19 patients had resection of the "Candy cane" (94% women, mean age of 50 ± 11 years), within 3 to 11 years after initial RYGB. Primary presenting symptoms were epigastric abdominal pain (68%) and nausea/vomiting (32%), especially with fibrous foods and meats. On upper gastro-intestinal (GI) study and endoscopy, the afferent blind limb was the most direct outlet from the gastrojejunostomy. Only patients with these pre-operative findings were deemed to have CCS; 18 (94%) cases were completed laparoscopically. Length of the "Candy cane" ranged from 3 to 22 cm; median length of stay was 1 day. After resection, 18 (94%) patients had complete resolution of their symptoms ($p < 0.001$). Mean BMI decreased from 33.9 ± 6.1 kg/m2 pre-operatively to 31.7 ± 5.6 kg/m2 at 6 months (17.4% EWL) and 30.5 ± 6.9 kg/m2 at 1 year (25.7% EWL). The average length of latest follow-up was 20.7 months. The authors concluded that

CCS is a real phenomenon that could be managed safely with excellent outcomes with resection of the blind afferent limb. A thorough diagnostic work-up is critical for proper identification of CCS; and surgeons should minimize the size of the blind afferent loop left at the time of initial RYGB.

Stier and associates (2020) CCS is a rarely reported and neglected complication of proximal RYGB surgery. In a retrospective study, a total of 47 cases of CCS that underwent Candy cane (CC) resection were analyzed for pain remission to examine if intussusception is a possible underlying mechanism. A total of 43 patients (89.6%) benefited from laparoscopic CC resection ($p < 0.001$). The highly sensitive diagnostic tests were upper GI series (91%) and gastroscopy (96%). Intussusception of the CC into the gastric pouch was demonstrated in most cases and was postulated as the trigger for CCS. In some cases, retro-peristaltic intussusception led to non-specific upper GI bleeding. The authors concluded that a vast majority of CCS cases benefited significantly from CC resection. The long-described retro-peristaltic intussusception of the CC was suggested as an important underlying mechanism of the symptoms. These researchers stated that although CC resection remains a stop-gap, evidence on its clinical significance has been shown for a century. Building on this wealth of experience and the already vast storage of practical knowledge, awareness of this under-estimated complication after RYGB should be raised.

In an observational study, Kamocka and co-workers (2020) examined the sensitivity of pre-operative diagnostic tools for CC, as well as peri-operative outcomes and symptom resolution following CC revision surgery. A total of 28 CC revision cases were identified (mean age of 45 ± 9 years, women/men – 9:1). Presenting symptoms were abdominal pain (86%), regurgitation/vomiting (43%), suboptimal weight loss (36%) and acid reflux (21%). Pre-operative tests provided correct diagnosis in 63% of barium contrast swallows, 50% of upper GI endoscopies and 29% computed tomographies. Patients presenting with pain had significantly higher CC size as compared with pain-free group (4.2 versus 2 cm, $p = 0.001$). Peri-operative complications occurred in 25% of cases. Complete or partial symptom resolution was documented in 73% of patients undergoing CC revision. Highest success rates were recorded in the regurgitation/vomiting group (67%). The authors concluded that surgical revision of CC was associated with good symptom resolution in the

majority of patients, especially those presenting with regurgitation/vomiting. However, it carried certain risk of complications. These investigators stated that CC diagnosis may frequently be missed; hence more than 1 diagnostic tool should be considered when examining symptomatic patients after RYGB.

Furthermore, an UpToDate review on "Late complications of bariatric surgical operations" (Ellsmere, 2020) states that "Candy cane Roux syndrome in patients who have undergone RYGB refers to an excessively long blind afferent Roux limb at the gastrojejunostomy causing postprandial pain often relieved by vomiting. It is believed that the blind afferent limb ("candy cane") acts as an obstructed loop when filled with food (often preferentially), and the distention of the loop causes pain until the food either spills into the Roux limb or is vomited back out. Patients have been reported presenting as early as 3 months and as late as 11 years after their initial RYGB, typically with symptoms of postprandial epigastric pain, nausea, vomiting, and reflux or food regurgitation. The diagnosis is confirmed by upper gastrointestinal contrast studies or endoscopy. On upper gastrointestinal series, the afferent limb fills before contrast spills into the Roux limb. On upper endoscopy, the afferent limb is usually the most direct outlet of the gastrojejunostomy. The treatment is revision bariatric surgery, most commonly laparoscopic resection of the afferent limb, which ranged in length from 3 to 22 cm in one study (mean of 7.6 cm). Symptoms resolve after revision surgery in most patients. Surgeons should minimize the length of the blind afferent loop left at the time of initial RYGB to prevent candy cane Roux syndrome".

Measurement of Serum C-Reactive Protein as a Predictor for Complications Following Bariatric Surgery

Kroll and colleagues (2018) stated that early intra-abdominal infections (IAI) compromise short-term outcomes in bariatric surgery. The timely detection of IAI is challenging but essential to prevent major sequelae of such complications. C-reactive protein (CRP) is a reliable marker for detecting IAI after colorectal surgery. In bariatric surgery, data on CRP as a marker for IAI are limited, especially for post-operative day-1 (POD1). These researchers evaluated CRP on POD1 as a predictor for early IAI (within 7 days following surgery) in patients after LSG and LRYGB. Patients with bariatric surgery between August 2010 and June 2017 were

included. The predictive capacity of CRP for early IAI was determined using a receiver operating characteristics (ROC) analysis. In 523 patients (68.5% female, LSG = 358, LRYGB = 165), 16 (3%) early IAI were observed. ROC analysis revealed a significant predictive capacity of POD1 CRP for early IAI, with a sensitivity and a specificity of 81.2% and 94.3%, respectively, at a CRP cut-off value of 70 mg/L. In patients with confirmed early IAI, 81.3% had a CRP level of greater than or equal to 70 mg/L (LSG 85.7%, LRYGB 77.8%). The negative predictive value (NPV) for a CRP level of less than 70 mg/L was 99.4% overall and was 100% and 98% for LSG and LRYGB, respectively. The authors concluded that in patients with a CRP level of less than 70 mg/L on POD1, early IAI could be excluded with high accuracy in bariatric patients; thus, these researchers stated that early post-operative CRP may be used to examine the risk of early IAI in enhanced recovery programs.

Bona and associates (2019) noted that post-operative leak and IAI are common following bariatric surgery with a significant impact on peri-operative outcomes, hospital LOS, and re-admission rates. In the era of enhanced recovery programs, with patients being discharged from the hospital 24 to 36 hours following surgery and potentially before developing any complications, an early indicator of post-operative complications may be decisive. These researchers examined the predictive role of the CRP in the early diagnosis of complications in patients undergoing LSG and LRYGB. PubMed, Embase, and Web of Science databases were consulted. A systematic review and a fully Bayesian meta-analysis were conducted. A total of 7 studies (1,401 patients) met the inclusion criteria. Overall, 57.7% underwent LSG while 42.3% underwent LRYGB. The pooled prevalence of post-operative complications was 9.8% (95% CI: 5% to 16%). The estimated pooled CRP cut-off value on POD1 was 6.1 mg/dL with a significant diagnostic accuracy and a pooled area under the curve of 0.92 (95% CI: 0.73 to 0.98). The positive and negative likelihood ratios (PLR and NLR) were 13.6 (95% CI: 8.40 to 15.9) and 0.16 (95% CI: 0.04 to 0.31), respectively. The authors concluded that a CRP value lower than the derived cut-off of 6.1 mg/dL on POD1, combined with reassuring clinical signs, could be useful to rule out early post-operative leak and complications following LSG and LRYGB. In the context of enhanced recovery after surgery

protocols, the integration of a CRP-based diagnostic algorithm as an additional complementary instrument may be valuable to reduce cost and improve outcomes and patient care.

In a retrospective chart review, Villard and co-workers (2019) examined the use of CRP in early identification of post-operative complications following bariatric surgery. The ability of this marker to acutely predict post-operative complications in bariatric surgery patients has not been determined. This trial was carried out in adult patients who underwent a primary and revisional LRYGB or LSG between 2013 and 2017 at a single institution. Patients were identified using the prospective Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program data-base; CRP levels were drawn on POD1 per standard protocol. Univariate analyses were carried out to determine the predictive impact of CRP levels on post-operative complications, re-admissions, and re-operations. There were 275 patients who underwent bariatric surgery, 222 primary and 53 revisional. Of the 275 patients, 36 (13.1%) had a complication. Bariatric surgery patients with a post-operative complication had higher CRP levels compared to those who did not (4.8 ± 4.6 versus 2.9 ± 2.0; p = 0.02). A CRP of greater than or equal to 5 mg/dL had a sensitivity for a complication of 27% and a specificity of 88%. There was no difference in CRP levels for patients with a 30-day re-operation or re-admission; and there were no mortalities. The authors concluded that bariatric surgery patients with elevated post-operative CRP levels were at increased risk for 30-day complications. The low sensitivity of a CRP of greater than or equal to 5 mg/dL suggested that a normal CRP level alone did not rule out the possibility of a post-operative complication; however, with its high specificity, there should be an elevated clinical suspicion of a post-operative complication in patients with a CRP of greater than or equal to 5 mg/dL.

Laparoscopic Single-Anastomosis Duodeno-Ileal Bypass with Gastric Plication

Balint and colleagues (2021) noted that bariatric surgery is more effective in the management of morbid obesity and related co-morbidities than is conservative therapy. Pylorus-preserving single-anastomosis duodeno-ileal bypass with sleeve gastrectomy (SADI-SG) is a modified duodenal switch technique; gastric plication (GP) is an alternate to SG. In a cohort

study, morbidly obese (BMI of greater than 40, or greater than 35 in the presence of diabetes or pre-diabetes) patients were recruited and operated on to perform SADI with GP. Complications related to surgery were recorded to assess the feasibility of the procedure. Weight-loss outcomes were analyzed to determine effectiveness. Minnesota Multiphasic Personality Inventory 2 (MMPI-2) was recorded after 1 year of follow-up, and test scales were used to describe physiological phenomena. A total of 17 middle-aged (mean of 40 years) patients were involved in this trial; 15 of them were women. The mean duration of surgery was 205 mins. There were no complications of conversion, death, bleeding, venous thrombo-embolism (VTE) or 30-day re-admission to hospital. These researchers did experience CD4a (pulmonary insufficiency due to chronic lung disease) and a CD3b (anastomosis leakage treated laparoscopically) complications. Vomiting occurred in 3 cases (CD1). Obesity-related co-morbidities showed favorable resolution rates (77.8 % for hypertension, 81.2 % for dyslipidemia, 100 % for diabetes at the 1-year follow-up). Weight-loss outcomes were favorable (53.20 EWL%, and 35.58 TWL% at 1-year follow-up). Greater weight loss caused significantly higher levels of Depression ($t(13.958) = -2.373$; $p = 0.00$; $p < 0.05$) and Low Positive Emotions ($t(13.301) = -2.954$; $p = 0.00$; $p < 0.05$) and Introversion/Low Positive Emotionality ($t(13.408) = -1.914$; $p = 0.02$; $p < 0.05$) in MMPI-2 data. The authors concluded that according to this safety study, SADI-GP is a promising malabsorptive procedure, but a long-term, high-volume case series or a RCT is needed to examine complication rates and weight-loss outcomes.

The authors stated that this study had limitations due to the small sample size (n = 17) and study design. These researchers did not reach the projected number of included cases because they experienced a higher-than-expected drop-out rate, and the number of patients with obesity applied for screening was too low considering the strict selection criteria. There was a huge selection bias in this cohort because 88 % of the study population were women. It could skew these findings that there was no control endoscopic or radiologic examination scheduled for gastric plicated patients. Routine cholecystectomy was carried out in 15 cases that could bias operating time and occurrence of some complications. These investigators noted that this study presented only short-term results; thus, the effectiveness of the procedure could not be determined this time.

Osorio et al (2021) stated that SADI-S is being proposed for obese patients with insufficient weight loss or weight regain after SG; however, limited information is available. These researchers examined the safety and effectiveness of SADI-S as a revisional surgery after SG, compared with standard DS. This as a cohort, single-center study that entailed all patients submitted to SADI-S and DS after failed SG in a high-volume institution, between 2008 and 2020. A total of 46 patients submitted to SADI-S and 55 to DS were included, 37.2 and 41.5 months after SG ($p = 0.447$), with initial BMI of 56.2 versus 56.6 ($p = 0.777$) and 39.2 versus 39.7 before revisional surgery ($p = 0.675$). All surgeries were laparoscopic. Clavien-Dindo > II complication rate was 6.5 % for SADI-S and 10.9 % for DS ($p = 0.095$), with no 90-day mortality. Follow-up at 2 years was available for 38 SADI-S' and 38 DS' patients, with TWL of 35.3 % versus 41.7 % ($p = 0.009$), and EWL of 64.1 % versus 75.3 % ($p = 0.014$). Co-morbidities resolution for SADI-S and DS was: 44.4 % versus 76.9 % for diabetes ($p = 0.029$) and 36.4 % versus 87.5 % for hypertension ($p = 0.006$); with no differences for resolution of dyslipidemia (72.7 % versus 88.9 %, $p = 0.369$) and obstructive sleep apnea (93.3 % versus 91.7 %, $p = 0.869$). DS' patients required more extra nutritional supplementation; 3 SADI-S patients needed conversion to DS -- 2 for biliary reflux and 1 for weight regain. The authors concluded that after a failed SG, revisional DS permitted better weight control and diabetes and hypertension resolution than SADI-S, at the expense of higher supplementation needs.

Admella et al (2021) stated that SADI-S is a bariatric surgery conceived to simplify the DS in order to reduce its post-operative complications. These researchers examined the safety and effectiveness of SADI-S, comparing its results in both direct and 2-step procedure. A total of 232 patients were included, 192 were submitted to direct SADI-S and 40 had previously undergone a SG. The severe complications rate (Clavien-Dindo greater than or equal to IIIA) was 7.8 %, being hemo-peritoneum and duodenal stump leak the most frequent ones. One patient was exitus between the first 90 days after surgery (0.4 %). Patients submitted to direct SADI-S had an initial BMI of 49.6 kg/m2 in comparison of 56.2 kg/m2 in the 2-step SADI-S ($p < 0.001$). The mean EWL at 2 years was higher in direct SADI-S (77.3 % versus 59.3 %, $p < 0.05$). Rate of co-morbidities resolution was 88.5 % for diabetes, 73.0 % for hypertension, 77.0 % for dyslipidemia and 85.7 % for sleep apnea, with no differences

between both techniques. The authors concluded that in medium-term, SADI-S was a safe and effective technique that offered a satisfactory weight loss and remission of comorbidities. Patients submitted to 2-step SADI-S had a higher initial BMI and presented a lower EWL than direct SADI-S.

Prophylactic Pyloroplasty via Botulinum Toxin Injection Following Laparoscopic Sleeve Gastrectomy

Yang et al (2019) stated that gastric leakage is a common complication after LSG and causes severe morbidity and mortality. Recent reports suggested that non-operative management is favored for the leaks following LSG whenever possible. Endoscopic treatments, including self-expanding stent, clips, and glue, have been used to treat the leaks; however, the outcome varied in different situations. Recently, several improvements have been made in the designs and sizes of through the scope (TTS) clips, which induced the precise location of placement and extend the limitation in the management of perforations. Over-the-scope clip (OTSC) is a novel clipping system of endo-therapy. The edges of the lesion are grasped by the jaw of the grasper; thus, the OTSC system could accomplish a full thickness or near fullness closure. Furthermore, given that high intra-gastric pressure after LSG5 is one of the risk factors that delays the healing of perforation, these investigators added botulinum toxin (BTX) injection to keep the pylorus open to release the intra-gastric pressure to enhance recovery. These researchers reported on the case of a 30-year-old diabetic woman with severe obesity who received LSG for her weight regain 4 years after primary bariatric surgery. However, an oral contrast-enhanced computed tomography (CT) scan 12 days after LSG showed gastric leak. Esophagogastroduodenoscopy confirmed 3 perforators over the gastro-esophageal junction and upper body of stomach; multiple Sureclips were applied to the leaks. Furthermore, 25 U of BTX were injected into the 4 separate quadrants of pyloric area. The authors concluded that their initial experience revealed that endoscopic TTS clips and intra-pyloric BTX injection was technically feasible, safe and effective in patients with leaks following primary LSG, whereas OTSC was suggested for revisional cases.

Noninvasive Testing in Nonalcoholic Fatty Liver Disease (NAFLD)

In an UpToDate review entitled “Management of nonalcoholic fatty liver disease in adults”, Chopra and Lai (2021) noted the following: Nonalcoholic fatty liver disease “NAFLD ranges from the more benign condition of nonalcoholic fatty liver (NAFL) to nonalcoholic steatohepatitis (NASH), which is at the more severe end of the spectrum. In NAFL, hepatic steatosis is present without evidence of inflammation, whereas in NASH, hepatic steatosis is associated with lobular inflammation and apoptosis that can lead to fibrosis and cirrhosis.”

In an UpToDate review entitled “Epidemiology, clinical features, and diagnosis of nonalcoholic fatty liver disease in adults”, Sheth and Chopra (2021) provide a distinction between nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH). They note that “NAFLD is subdivided into nonalcoholic fatty liver (NAFL) and nonalcoholic steatohepatitis (NASH). In NAFL, hepatic steatosis is present without evidence of significant inflammation, whereas in NASH, hepatic steatosis is associated with hepatic inflammation that may be histologically indistinguishable from alcoholic steatohepatitis.” The only method to definitively confirm or exclude a diagnosis of NASH and to assess disease severity is via a liver biopsy. Furthermore, the histologic diagnosis of NASH is based on the presence of hepatic steatosis in relation to hepatocyte ballooning degeneration and hepatic lobular inflammation (usually in acinar zone 3)." Although fibrosis may be visible, it is not a required diagnostic feature for NASH.

In "The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Associiation for the study of liver diseases", Chalasani, et al.(2018) note the utility of serum biomarkers (e.g., Enhanced Liver Fibrosis [ELF] panel, Fibrometer, FibroTest, and Hepascore) and imaging (e.g., transient elastography [TE], magnetic resonance elastography [MRE], acoustic radiation force impulse imaging, and supersonic shear wave elastography) as noninvasive assessment of advanced fibrosis in patients with NAFLD.

Castera and colleagues (2019) note key issues in NAFLD patients as the differentiation of NASH from simple steatosis and indentification of advanced hepatic fibrosis. Although liver biopsy remains the gold standard for identification of NASH and advanced hepatic fibrosis in patients with NAFLD, the procedure has inherent limitations (i.e.,

invasiveness, poor acceptability, sampling variability, cost). The emergence of noninvasive testing has become important in determination of the two previously mentioned end points in NAFLD patients. The most accurate and validated methods that were noted for the identification of advanced fibrosis included magnetic resonance elaastography (MRE), transient elastography (TE), fibrosis-4 index (FIB-4), and nonalcoholic fatty liver disease fibrosis score (NFS). Additonally, FIB-4 and NFS show best application as first-line tools in the primary health care setting to conclusively exclude advanced fibrosis. TE and MRE are better suited for referral centers to choose patients who require a liver biopsy.

Appendix

Calculation of BMI

** BMI is calculated by dividing the patient's weight (in kilograms) by height (in meters) squared:

BMI = weight (kg) * [height (m)]^2

Note: To convert pounds to kilograms, multiply pounds by 0.45. To convert inches to meters, multiply inches by 0.0254; *or*

For a simple and rapid calculation of BMI, please click below and it will take you to the Obesity Education Initiative.

** BMI = weight (kg) * [height (m)]2 (https://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm)

Table: American Society of Anesthesiologists Physical Status Classification

Class	Description
I	Healthy patient
II	Mild systemic disease, no functional limitation
III	Severe systemic disease, definite functional limitation

IV	Severe systemic disease that is a constant threat to life
V	Moribund patient unlikely to survive 24 hours with or without operation
E	Emergency status: In addition to indicating underlying ASA status (I - V), any patient undergoing an emergency procedure is indicated by the suffix "E". For example, a fundamentally healthy patient undergoing an emergency procedure is classified as I-E. If the patient is undergoing an elective procedure, the "E" designation is not used.

Source: Adapted from Miller RD, Principles and Practice of Anesthesia, 2nd ed., New York, NY: Churchill Livingstone; 1986.

Criteria for the Diagnosis of Diabetes

- Hemoglobin A1C > 6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the Diabetes Control and Complications Trial (DCCT) assay ***; or
- Fasting plasma glucose (FPG) >126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 hours ***; or
- 2-hour plasma glucose (PG) >200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test (OGTT). The test should be performed as described by the World Health Organization (WHO), using a glucose load containing the equivalent of 75 grams anhydrous glucose dissolved in water ***; or
- In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose >200 mg/dL (11.1 mmol/L).

*** In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing.

Source: ADA; 2015.

Laparoscopic Adjustable Silicone Gastric Band Adjustments

The Lap-Band labeling provides the following regarding the medically necessary frequency and indications for band adjustments:

I. The initial post-operative adjustment should occur at 6 weeks or more after placement, when usually 3 to 4 cc of normal saline would be added.
II. The patient should be reviewed regularly (every 4 to 6weeks), depending on patient need, with weight and clinical status measured. If the weight loss has averaged less than 1 lb/week over the period and the patient indicates there is no excessive restriction to eating, a further increment of fluid should be added.
III. Normally, additional fluid would not be added if average weight loss has been greater than 2 lbs/week between visits.
IV. If the weight loss averaged between 1 and 2 lbs/week, additional fluid would be indicated if the patient felt he/she could eat too freely or found it difficult to comply with the dietary rules.
V. Fluid would be removed from the system if there were symptoms of excessive restriction or obstruction, including excessive sense of fullness, heartburn, regurgitation and vomiting. If symptoms are not relieved by removal of the fluid, barium meal should be used to evaluate the anatomy.

Prior to doing an adjustment to decrease the stoma, review the patient's chart for total band volume and recent adjustments. If recent adjustments have not been effective in increasing restriction and the patient has been compliant with nutritional guidelines, the patient may have a leaking band system, pouch enlargement or esophageal dilatation due to stomal obstruction, band slippage or over-restriction.

Lap-Band System patency can be confirmed by injecting saline into the band system, then immediately withdrawing it. An absence or decrease in fluid volume indicates that a leak in the system may exist. The band may be evaluated for a leak using a radiopaque solution, such as Hypaque or Conray-43, flushing it from the band system after the evaluation. If pouch enlargement or band/stomach slippage is suspected, a limited upper GI with a small amount of barium or gastrografin can be used to evaluate the size of the pouch, the gastric stoma and the position of the band.

Caution: Insufficient weight loss may be a symptom of inadequate restriction (band too loose), pouch or esophageal enlargement, and may be accompanied by other symptoms, such as heartburn, regurgitation or vomiting. If this is the case, inflation of the band would not be appropriate.

Excessive restriction may result in a closed stoma. Because of the possible complications that can occur with excessive restriction, a doctor familiar with the adjustment procedure must be available for several days post-adjustment to adjust the stoma in case of an emergency. Deflation (an increase in stoma size) is considered if the patient experiences frequent episodes of vomiting, is unable to swallow liquids or appropriate foods, or if there are medical indications for increasing nutrient intake. Elective deflation of the band is advisable in the following situations:

- Pregnancy
- Significant concurrent illness
- General anesthesia
- Remote Travel
- Travel to areas where food or water contamination is endemic.

Warning: Esophageal distension or dilatation has been reported and may be associated with stoma obstruction due to incorrect band placement or over-restriction from excessive band inflation. Patients should not expect to lose weight as fast as gastric bypass patients, and band inflation should proceed in small increments. Deflation of the band is recommended if esophageal dilatation develops. If esophageal dilatation is present, then steps should be taken to identify and resolve the cause(s). Deflation of the band may resolve dilatations that are entirely due to over-restriction. Dietary evaluation and appropriate nutritional counseling regarding correct eating behavior should follow band deflation and precede subsequent gradual re-inflations. Re-inflation of the band should be conducted gradually in small increments over several months. Dietary counseling should be ongoing, and repeat upper GI exams should be done at each band adjustment. Band deflation may not resolve the dilatation if the stoma obstruction is due to a significant gastric slippage or if the band is incorrectly placed around the esophagus. Band repositioning or removal may be necessary if band deflation does not resolve the dilatation.

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