Non-surgical Treatment for Adult Obesity

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Objectives

- **Definition, prevalence and cost of adult obesity**
- **Etiology of obesity**
- **Health risks associated with obesity**
- **Options for the treatment of adult obesity**
- **Non-surgical treatment including:**
  - **Diet and exercise**
  - **Behavior modification**
  - **Pharmacological treatment**

Definition of Obesity

BMI = Weight (kg)/Height (m²)

WHO Classification:	**BMI**
Underweight	< 18.5
Normal	18.5 – 24.9
Overweight	25 - 29.9
Obese Class 1	30 – 34.9
Obese Class 2	35 – 39.9
Obese Class 3	> 40 (Morbid obesity)

Definition of obesity

- **Waist circumference**
  - **may be used independently or in addition to BMI**

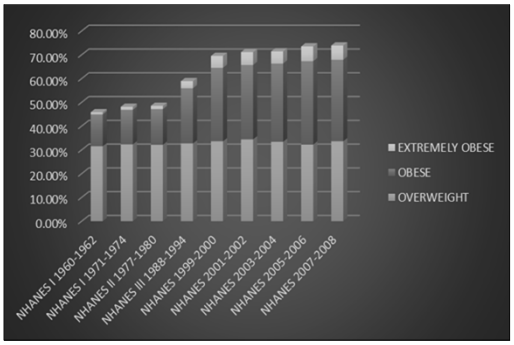
	Increased health risk	**Substantially increased health risk**
Women	≥ 80 cm	≥ 88 cm
Men	≥ 94 cm	≥ 102 cm

Prevalence of Obesity

- More than one-third (34.9% or 78.6 million) of U.S. adults are obese. [Journal of American Medicine (JAMA)]
- Among men, obesity prevalence is similar at all income levels
- Higher income women are less likely to be obese than low income women
- No trend between obesity and education among men
- Women with college degrees are less likely to be obese

NCHS data brief no 50. Huntsville, MD: National Center for Health Statistics. 2010

Prevalence of overweight, obesity and extreme obesity among U.S adults aged 20-74



NHANES is National Health Examination Survey; Pregnant females were excluded.

Prevalence* of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2011

*Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

15%–<20% 20%–<25% 25%–<30% 30%–<35% ≥35%

Prevalence* of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2013

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Cost of Obesity

- Cost of overweight and obesity estimated as high as $78.5 billion in 1998
- Half of this total financed by Medicare and Medicaid
- Estimates show that annual burden of obesity has risen to almost 10% of all medical spending
- $147 billion per year in 2008
- Across all payers, obese had medical spending that was $1,429 > spending for normal weight in 2006

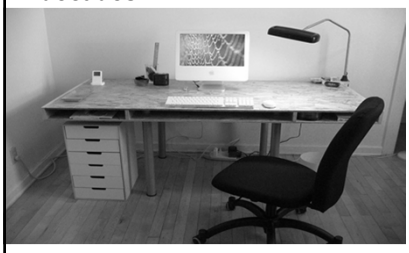
[Health Affairs 28, no. 5 (2009): w822–w831 (published online 27 July 2009; 10.1377/hlthaff.28.5.w822)]

Etiology of obesity

- Genetic components
- Behavioral
- Environmental
- Physiological
- Social
- Cultural

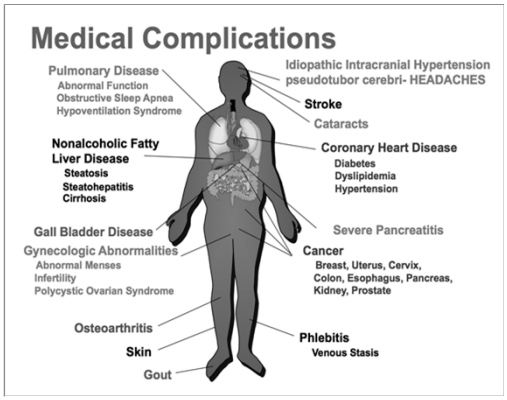
Etiology of obesity

- World Health Organization Consultation on Obesity concluded that behavioral and environmental factors are primarily responsible for dramatic increase in obesity during the past 2 decades



Author: Jordan Fischer

Health risks associated with obesity



http://mylivwell.org/ckfinder/userfiles/images/Screen

The AMA declared obesity a disease in 2013 at their annual meeting. This decision was supported by the American College of Cardiology and the American Association of Clinical Endocrinologists.

Non-surgical Treatment

- Goals of treatment are to achieve and then maintain clinically meaningful weight loss
- Reduce the risk for obesity-related diseases
- Weight losses of 5% to 10% in initial body weight produce health benefits
- Long term success
  - Maintenance of a 10% weight loss for at least 1 year

Non-surgical Treatment

- Should incorporate multiple approaches
  - Diet, exercise and behavioral strategies
- Options depend on
  - The degree of obesity
  - Presence of co-morbidities
  - Previous weight loss therapies utilized and success of each
  - Characteristics of the individual

Non-surgical treatment

- Dietary approaches
  - Success is dependent on a relative energy deficit not composition
  - May be very-low-calorie diets (VLCDs, <800 kcal/d) or low-calorie diets (LCDs, 800-15– kcal/d)
  - Produce clinically meaningful weight loss but maintenance is poor
  - 1200 kcal diets produce slower weight loss but can be followed for longer periods of time
  - Better adherence when food and beverage choices are limited and strictly controlled
  - No single approach shown to be effective for all people who are obese

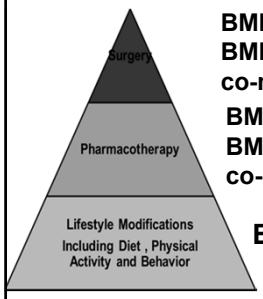
Exercise

- Does not produce considerable weight loss when used independently
- Important adjunct to weight reducing diet
- ↑ energy expenditure, ↑ loss of adipose tissue, and improves dietary adherence
- Physically active obese individuals have a lower risk for morbidity and mortality
- Goal is a minimum of 30 minutes of moderate-intensity activity 5 days/week

Behavior modification

- Target identifying stimuli that signal unhealthy behaviors
- Readiness in initiating positive behaviors
- Recognizing barriers to healthy pursuits
- Important components include:
  - Goal-setting
  - Self-monitoring
  - Frequent contact
  - Feedback
  - Continuous motivation and support

Obesity Treatment Pyramid



BMI ≥ 40
BMI = 35-39.9 with 1 obesity related co-morbidity

BMI ≥ 30
BMI ≥ 27 with 1 obesity related co-morbidity

BMI ≥ 25

Pharmacologic agents

- Use in conjunction with diet, exercise and behavioral strategies
- BMI of 30 kg/m² or greater OR
- BMI of 27 kg/m² with obesity related co-morbidity
- Safe and effective in producing modest but effective weight loss and amelioration of comorbid conditions
- Do not change the physiology of weight regulation in any permanent way
- Include short-term use (3 months) and chronic weight management medications

Pharmacologic agents

Short-term Medications

- Phentermine (Adipex)
- Diethylproprion (Tenuate)

Chronic Weight Loss Medications

- Orlistat (Xenical)
- Lorcaserin (Belviq)
- Phentermine/topiramate (Qsymia)
- Naltrexone/bupropriom (Contrave)
- Liraglutide (Saxenda)

Comparison of 1 year prospective, randomized, double-blind trials for lorcaserin (BLOOM and BLOSSOM) and phentermine-topiramate (EQUIP and CONQUER)

	BLOOM	BLOSSOM[a]	EQUIP[b]	CONQUER
Number of subjects	3182	4008	1230	2448
Age (yrs)	18–65	18–65	≥ 35	27–45
BMI (kg/m^2)	27–45	27–45	18–70	18–70
Comorbid conditions (cardiovascular and metabolic)	At least 1	At least 1	At least 1	≥ 2
Mean % weight loss compared to placebo	5.8% vs 2.2%	4.8% vs 2.8%	11% vs 1.6%	10.4% vs 1.8%
Placebo-subtracted weight loss (%)	3.6%	2.0%	9.4%	8.6%
Categorical change in 5% weight loss compared with placebo	47.5% vs 20.3%	47.2% vs 25%	67% vs 17%	70% vs 21%
Completion rate	55.4% lorcaserin; 45.1% placebo	55.5%	59.9%	

Pharmacologic agents Orlistat (Xenical, Alli)

- Approved by FDA in 1999 as first lipase inhibitor
- Approved as an OTC medication in 2007 at ½ the prescription dose
- 120 mg 3 x day with meals
- Blocks the digestion and absorption of ≈30% of dietary fat
- No systemic SEs
- Other SEs include:
- Oily spotting, flatus with discharge, fecal urgency, fatty/oily stool, increased defecation

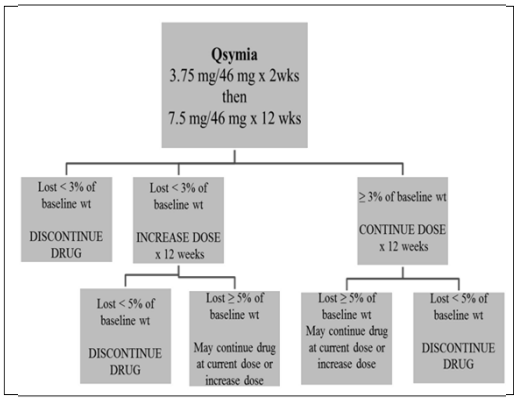
Pharmacologic agents Phentermine (Adipex, Adipex-p)

- Appetite suppressant
- Most commonly prescribed centrally acting adrenergic agent
- Schedule IV drug
- Approved for short term use (12 weeks) with 6 months off medication before re-start
- 37.5 mg once a day before breakfast
- Most common SEs include:
- Restlessness, insomnia, dry mouth, constipation, and increased BP and heart rate

Pharmacologic agents Phentermine-topiramate ER (Qsymia)

- FDA approved July 2012
- Catecholamine releaser (phentermine) and an anticonvulsant (topiramate)
- Pregnancy Category X.
- Increased risk of congenital fetal oral cleft formation
- Need for active birth control among child-bearing women
- Measure creatinine before/during treatment
- Common SEs include:
- Paresthesias, dry mouth, constipation, insomnia, taste alterations (particularly with carbonated beverages)

Qsymia Dose Flowsheet



Pharmacologic agents Lorcaserin (Belviq)

- Approved by the FDA in 2012
- Selective 5-HT2C receptor agonist
- Thought to decrease food intake through the pro-opiomelanocortin system of neurons
- 10 mg twice a day
- Should NOT be taken with MAOIs
- Caution with SSRIs
- Effect on cardiovascular morbidity and mortality has not been established
- Most frequent SEs include:
- Headache, dizziness, dry mouth, and nausea

Pharmacologic agents Naltrexone/buproprion (Contrave)

- FDA approved in 2014
- Tapered dose:

TIME	DOSE
Week 1	1 tablet QD x 7 days
Week 2	1 tablet BID x 7 days
Week 3	2 tablets QAM and 1 tablet QPM x 7 days
Week 4	2 tablets BID

Pharmacologic agents (Contrave)

- Reuptake inhibitor of dopamine and norepinephrine (buproprion) and opiod antagonist (naltrexone)
- Common SEs include: nausea, constipation, headache, vomiting, dizziness
- Contraindications
  - Uncontrolled hypertension
  - Seizure disorder
  - Drug or alcohol withdrawal
  - MAOIs

Pharmacologic agents Liraglutide (Saxenda)

- Liraglutide (Saxenda)
- Dosage: 3 mg injectable
- GLP-1 agonist
- FDA approved in 2014
- Common SEs include: nausea, vomiting, pancreatitis
- Contraindications
  - Medullary thyroid cancer history
  - Multiple endocrine neoplasia type 2 history

Personalized Risk Assessment

- BMI
- Sex. Race and WC
- Weight gain history, prior treatments
- Blood pressure
- Lipid panel
- FPG, A1C
- Liver function
- Medications
- Diabetes, HTN, CVD, gout, sleep apnea, GERD, NAFLD, PCOS, venous stasis
- Pain, mobility impairment, functional limitation
- Well-being and psychlogical symptoms

Example of medication use in obese patient

- Patient had visit with surgeon to discuss umbilical hernia repair on 6/2/14.
- Patient's weight was 278 lbs and BP was 163/71
- Surgeon recommended weight loss prior to hernia surgery and referred to weight management clinic
- Patient started on a chronic weight loss medication on 6/10/14 with monthly follow up appointments
- BP was too high for short-term medication

Example of medication use in obese patient

- Weight loss of 40 lbs in a little over 2 months
- Had successful hernia repair
- Continued weight loss of 100 lbs total in 1 year

APPOINTMENT	WEIGHT	WEIGHT LOSS
6/02/2014	278	
6/19/2014	266	12 LBS
7/10/2014	251	15 LBS
8/07/2014	238	13 LBS
Total		**40 LBS**

Conclusion

- Obesity is a chronic disease that predisposes people to numerous serious health disorders
- Efforts to reduce the escalating incidence of obesity are critical
- Treatment options are available and it is essential that these strategies are being recommended to patients
- A multidisciplinary approach is considered the most successful in combating the obesity epidemic

The Surgical Treatment of Obesity and Metabolic Disease

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National Institute of Health Criteria

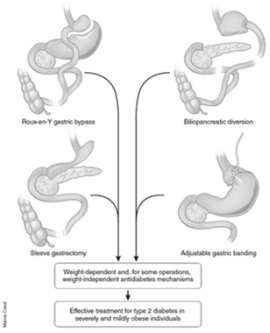
- BMI 35-40 in patients with high-risk co-morbidities or severe lifestyle limitations
- BMI > 40 if patient desires surgery and has failed "conventional" treatment modalities

Obesity is not created equal

- In the US our population is heterogeneous, yet we apply our BMI criteria to all without taking into account sex, age, or ethnic background.
- There are lower cutoff points for BMI and abdominal obesity metrics among Asians.
- China and Japan define overweight as a BMI of 24 or higher and obesity a BMI of 28 or higher;
- In India, overweight is defined as a BMI of 23 or higher, and obesity, a BMI of 27 or higher.
- The International Diabetes Federation now includes ethnic-specific criteria for the definition of abdominal obesity

Current Procedures

- There are still 4 main operations performed in the US
  - Gastric bypass
  - Sleeve gastrectomy
  - LAGB
  - Biliopancreatic diversion with or without DS



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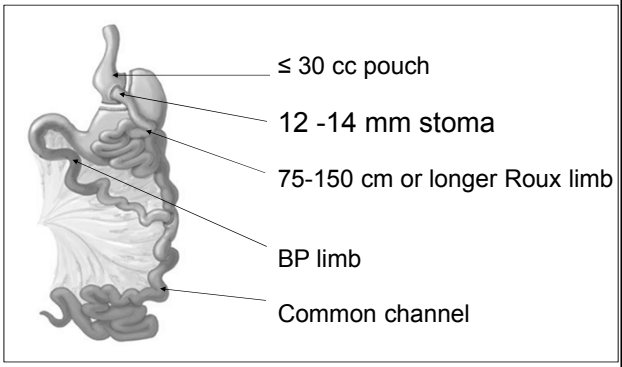
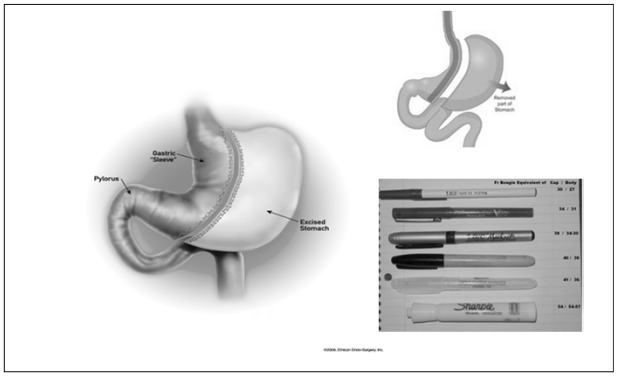
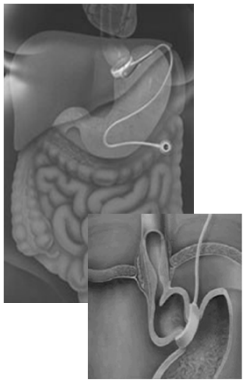
Roux-en-Y Gastric Bypass



Sleeve Gastrectomy

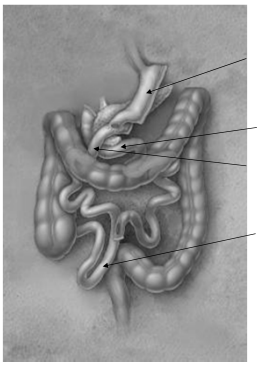


Adjustable Gastric Banding



- **<20 cc gastric "pouch"**
- **Adjustable "stoma"**
- **Normal GI anatomy and physiology**

Biliopancreatic diversion with Duodenal Switch



- **Sleeve (100-200ml)**
- **BP Limb (350ish cm)**
- **Alimentary Limb (250ish cm)**
- **Common channel (50-100 cm)**

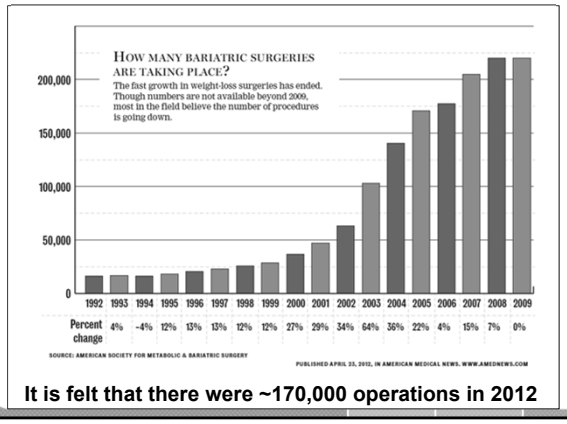
Comparison of Procedures

Gastric Bypass	Band	Sleeve
1-1.5 hours	<<1 hour	1-1.5 hours
2-3 days in hospital	Same day or 23 hour	2-3 days
2-6 week recovery	7-10 days	2-4 weeks
Fastest weight loss	Slower weight loss Need adjustments	Quick weight loss
Dumping	No dumping	No dumping
Vitamins mandatory	Recommended	Recommended (B12)
No NSAIDs	No steroids	No med restrictions
Regular food in ~2 wks	Regular in 2 weeks	Liquid-y for 1 month

Comparison of Complications

	Gastric Bypass	Band	Sleeve
Leak	++	0	+++
Bleeding	+	0	+
Internal hernia	++	0	0
Marginal Ulcer	+++	0	0
Slip/Erosion	0	+++	0
Failure	+	+++	++
Nutritional Abnormalities	++	0	+
GERD	+	+	++

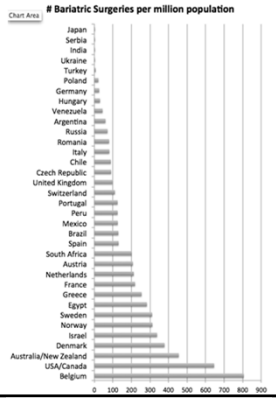
Overall bariatric procedure volume has plateaued



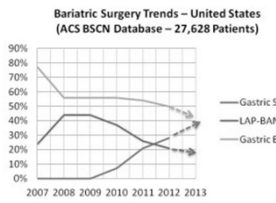
It is felt that there were ~170,000 operations in 2012

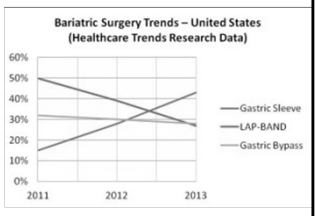
It is still a very common operation worldwide…

- It is one of the most commonly performed "elective" general surgery procedures in the US.



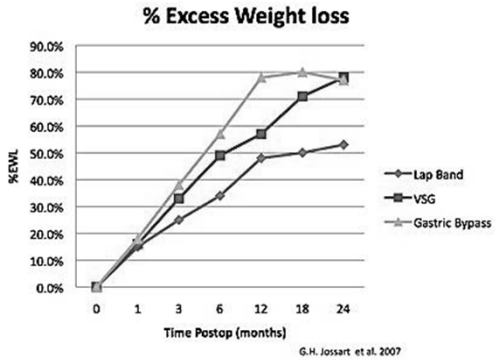
Trends



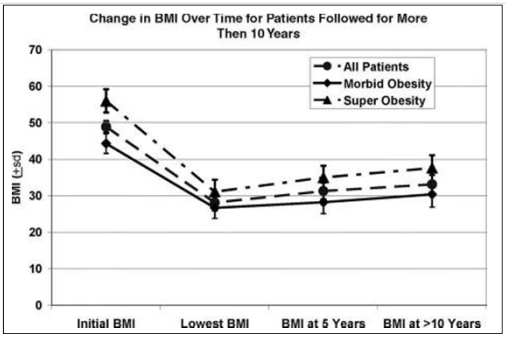


- Vertical Sleeves ↑
- Bands ↓ ↓
- Gastric Bypass ↓

Expected Weight Loss

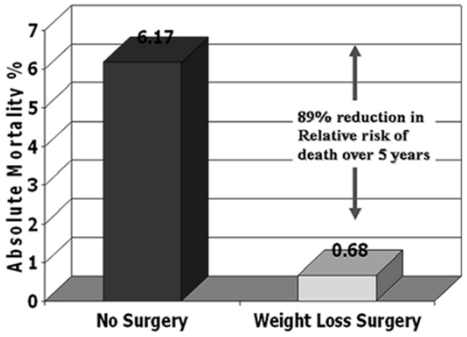


Weight loss curves



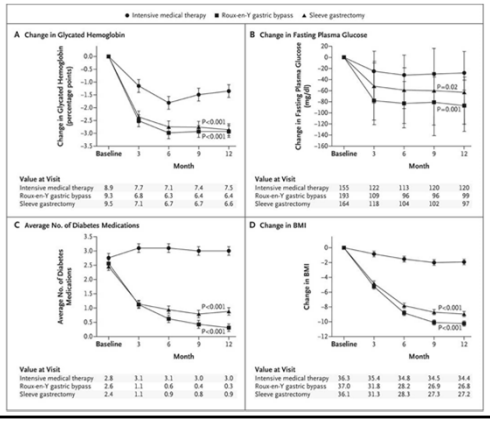
Nicolas V. Christou, MD, PhD, et.al. Ann Surg. 2006 November; 244(5): 734–740.

Bariatric Surgery and Change in Mortality



Nicolas V. Christou, MD, PhD, et.al. Ann Surg. 2006 November; 244(5): 734–740.

Bariatric Surgery and Diabetes



Bariatic Surgery is effective treatment for diabetes

Table 1. **Results of Different Types of Bariatric Surgery***

Result	Malabsorptive (BPD)	Restrictive (LAGB, VBG)	Combined (RYGB)
Excess weight loss, %	72	48–68	62
Resolution of comorbid conditions, %			
Type 2 diabetes	98	48–72	84
Hypertension	81	28–73	75
Dyslipidemia improved	100	71–81	94
Operative mortality rate, %	1.10	0.1	0.5

BPD = biliopancreatic diversion; LAGB = laparoscopic adjustable gastric banding; RYGB = Roux-en-Y gastric bypass; VBG = vertical banded gastroplasty.
* Mean values from a meta-analysis of 22 094 patients. Data from reference 7.

Buchwald H, Avidor Y, Braunwald E, Jensen MD, Pories W, Fahrbach K. et al. Bariatric surgery: a systematic review and meta-analysis. JAMA. 2004; 292:1724.-37

Resolution of Co-Morbidities: Hypertension

- All forms of weight loss = in reduction in BP
- Resolution of HTN in 62% with significant improvement 78.8% *
- In DM subset, 69% had resolution at 1yr., 66% at 7yr.**
- Gastric bypass is more effective than vertical banding

*Buchwald, et.al. *JAMA* 2004, **Sugarman, et.al. *Ann Surg* 2003

Resolution of Co-Morbidities Dyslipidemia

- Significant improvement in lipids in 70%
  - Gastric by-pass better than vertical bands
  - HDL improve significantly with vertical bands
- Swedish Obesity Study
  - 2 and 10 yrs, significant improvement in HDL and triglycerides
  - Total cholesterol was not changed

Buchwald, et.al. *JAMA* 2004, Sjostrom, et.al. *NEJM*

Resolution of Co-Morbidities OSA, NASH, Pseudotumor Cerebri

- NASH – decrease in severity
- OSA - 85.7-93% resolution
- Pseudotumor Cerebri – success rates are higher than results of shunt placement
  - No long term studies examining recurrence

Future

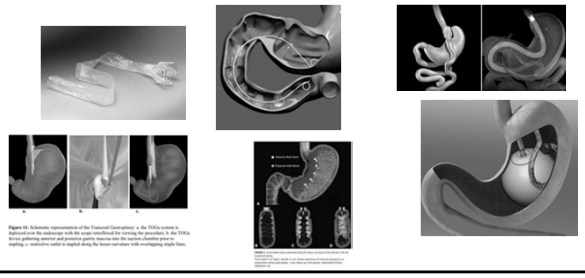
Endoluminal Procedures

Technique	Device	Author	No of patients	Fullow up (month)	% EWL(mean±SD)	BMI reduction (mean±SD)
Space occupying devices	BIB system	Genco et al	2515	6	33.9±18.7	4.9±12.7
		Göttig et al	109	9	-	8.7±5.1
		Genco et al	16	3	38.5±5.1	5.8±0.5
			16	3	33.6±4.9	5.1±0.6
		Okta et al	17	5	27±9	-
		Doldi et al	132	4	-	5.2
	Heliosphere Bag	Foristieri et al	10	6	-	5.2±13.1
		Shastri et al	59	7	-	2.38
		Mion et al	32	4	-	3.25
	Similed Balloon	Carvalho et al	14	6	46.5±36.7	3.9
Stapling/suturing	EndoCinch	Ryou et al	151	12	29.9	-
	Bard RS2	Thomson et al	18	6	30.4	-
	USGI IOP	Mullady et al	20	3	-	(8.8kg)
		Horgen et al	96	6	32	-
	StomaphyX	Mikami et al	39	12	20	-
	TOGA	Deviére et al	20	6	26.5	2.2
		Moreno et al	11	6	46	-
Prosthetic gastric sleeves	Valen Tx	Swain et al	12	3	46	-
	Endobarrier	Rodrigez-Grunert et al	12	3	23.6	-

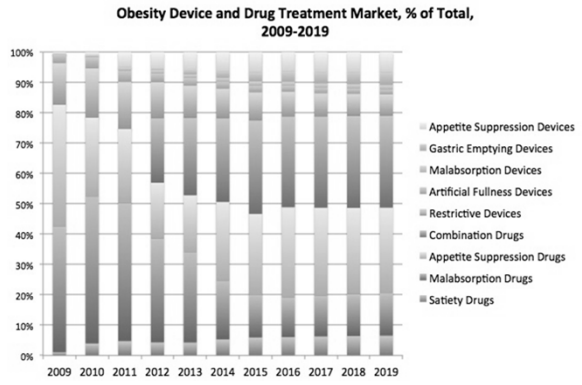
Table 2.
Excess weight loss and reduction of BMI after endoluminal therapies for obesity

FDA

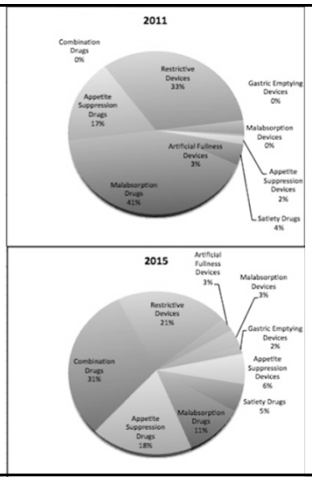
- **To get a medical device to market takes 4-6 years and $42 million**
- **Obesity Indication PMA 8-10 years and $90 million**



In the Future



Source: MedMarket Diligence Report #S835, "Products, Technologies and Markets Worldwide for the Clinical Management of Obesity, 2011-2019."



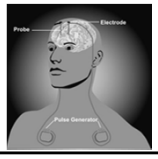
In the Future

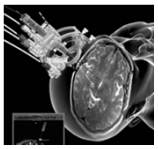
Source: MedMarket Diligence Report #S835, "Products, Technologies and Markets Worldwide for the Clinical Management of Obesity, 2011-2019."

Creating the future in obesity…

OSU Study Background: DBS of the behavioral and impulsivity target

- Research shows dysfunction and imbalances of the limbic cognitive circuits which leads to selective preference of impulsive choices vs. behavioral self control and regulation
  - Abnormally active impulsivity center
- Animal studies of DBS showed improvements
- Several studies have reported on the safety and efficacy of DBS for alcohol addiction and substance abuse





DBS of Behavioral Target for Obesity at OSU

- Study criteria
  - Age 22-60 years at time of enrollment
  - At least 24 months post Roux-en-Y gastric bypass surgery without evidence of a sustained improvement in BMI after gastric bypass surgery for at least 6 months
  - Anatomically intact bypass confirmed by endoscopy
  - Body mass index (BMI) > 40

We believe that DBS of the Behavioral brain target can improve decision-making, mood, anxiety and behavioral self-control. This study is for those who have not been able to control their body mass index (BMI) through other conventional methods, as well as Roux-en-Y (gastric bypass) surgery.

Left gastric artery embolization

- 5 patients (1 year follow up)
  - BMI >40 but <400#, age .> 22 years
- Primary Outcome Measures: Adverse Events
  - Safety outcomes involving the use of left gastric artery embolization for the purpose of weight loss.
- Secondary Outcome Measures: Change in BMI
  - Quality of life pre and post procedure to determine the changes of quality in life; everyday activities
  - Appetite hormone levels: Measuring changes in ghrelin, leptin, and CCK before and after left gastric embolization
  - Change in overall weight of subjects
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