# The Obesity Epidemic

## Todd Eibes MD FACS Medical Director Obesity Surgery Iowa Weight Loss

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# **Qualifications & Experience**

### Todd Eibes, MD, FACS

- Bariatrics since 2001
- Exclusively bariatrics since 2006
  - **500** Roux en Y Gastric Bypasses
  - **650** Lap Bands
  - **1600** Sleeve Gastrectomies
- MBSAQIP Center of Excellence
- Blue Distinction Center of Excellence
- United/Optum Center of Excellence IOWA WEIGHT | SPECIALISTS

- N.N. 43 yo Female
  - Allergies Metformin
  - Medications
    - Januvia 100mg/day
    - Levemir 80U SQ/day
    - Humalog 20U SQ/TID with meals
    - Lisinopril 5mg/day
    - Atorvastatin 20mg/day
    - Gabapentin 300mg/TID
    - Topiramate 150mg/day



- Past Medical History
  - Diabetes Mellitus (type II)
  - Hypertension
  - High Cholesterol
  - Low Back Pain
  - Polycystic Ovarian Syndrome
- Past Surgical History
  - Laminectomy



- Tobacco use: Never
- Alcohol use: 1-2 drinks/year
- Substance abuse:

1-2 drinks/yea Never

- Married/5 children
- Exercise
  - Walks daily limited by back pain



### Diet History

- Body by Vi:
- Exercise/low calorie
- Lowest Adult Weight:
- Highest Adult Weight:
- 1 year prior to consult:

- 5 months -20lbs
- 9 months -80lbs
- 1990 225 lbs (age 18) 2013 – 412 lbs 338 lbs



### Diet

- 24 hour recall
  - Breakfast Protein shake or skips
  - Lunch: Out with husband (Applebees/Mexican)
  - Dinner: Meat/Veg/Rice or Bread
  - Eat out: 2-3 times/week
- Daily

■ Fluid:

Snack:

- 2-4 cans diet Coke/20 ounces water
- Skinny popcorn/Almonds



- Height 5'7"
- Weight 366 lbs
- BMI 57.5

### Estimate – basal calorie needs 2300 kcal/day



- Medical Weight Loss
  - Short term goals
    - Decrease soda to 2 cans/day
    - Increase Water to 48 ounces/day
    - Food Journal (will set calorie goals next visits)
    - Exercise



- Long term goals (set by patient)
  - Get off insulin
  - Weight under 300 lbs
  - Be able to fit on rides at Adventureland
  - Be able to fit on rides at Disney World
  - Be able to ride on airplane without seatbelt extender
  - Be able to walk on vacation with kids



### Patient effort

- Met with team for 6 months
- Worked with psychiatric provider
- Worked with exercise specialist
- Joined local gym
  - Stationary bike/swim: 3-5 days/week
- Increased water intake 48 ounces/day



### Results

- Pre medical: Weight-366 lbs BMI-57.5Post 6 months: Weight-330 lbs BMI-51.6
- Meds unchanged
- Continued Diabetes/Hypertension/High Cholesterol

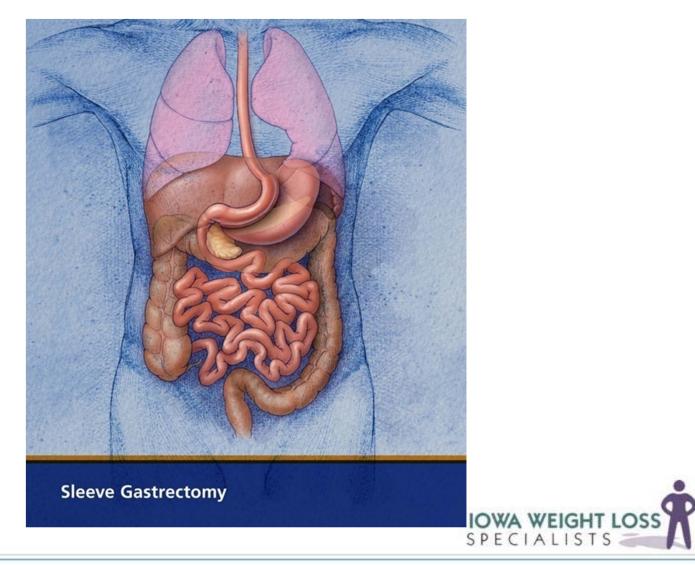






- Lap Sleeve Gastrectomy
  - 36 French Lighted Bougie
  - UGI day following surgery
  - Began liquid diet day following surgery
  - Discharged home 36 hours postop
  - Home Meds
    - Omeprazole/Lovenox(2 weeks)
  - Diet
    - 64 ounces fluid/60-80g protein daily
    - 2 weeks full liquid/2 weeks pureed IOWA WEIGHT LOSS





#### Results

	Pre	1wk	6wk	3mo	6mo	9mo	1yr
Wt(lbs)	330	310	296	272	244	223	207
Wt loss(lbs)		-18	-33	-67	-85	-106	-122
BMI	51.5	48.6	46.3	42.6	38.2	34.9	32.4
MM (lbs)	70	66	65	58	56	53	52
FM (lbs)	185	175	158	144	118	98	84
BF%	56	56	53.5	53	48.6	44	40



### Final Results

- 1 year post surgery
  - Total Weight loss 168 lbs
    - Medical: -36 lbs Surgical: -122 lbs
  - Starting Excess Weight 207 lbs
  - Percent Excess Weight loss 81%
- Exercise
  - Walking/stationary bike/swim (goal 3-5days/wk)
    - Had foot surgery at 9 mos postop limited exercise
- Diet

■ 3 meals/occasional 1 snack



### Final results

Diabetes

Immediately after surgery – sliding scale only

■ 8 weeks postop – off all insulin

Hemoglobin A1C – 5.9 off meds at 3 months postop

#### Hypertension

Off lisinopril – 9 months postop

Cholesterol

Continues on Statins





# **Obesity Definition**

Normal Weight
Overweight
Severe Obesity
Class I
Class II

■ Class III

Morbid Obesity

BMI 20.0 – 24.9 BMI 25.0 – 29.9

BMI 30.0 – 34.9 BMI 35.0 – 39.9

BMI > 40

BMI >40 or 100 lbs overweight



# **Obesity Epidemic**

- 68% Americans are overweight or obese
- 2013 National Study
   BMI > 40
   26 million Americans
  - **B**MI 30-40

60 million Americans



### **Obesity Epidemic** National Health and Nutrition Exam Survey (NHANES)

Adult Obesity Rates 1962 - 2014 40.00% 35.00% 30.00% 25.00% 20.00% -Adult Obesity Rates 15.00% 1962 - 2014 10.00% 5.00% 0.00%1960-62 1774 1976-80 98-94 1999-02 000-0007-10 12124 **IOWA WEIGHT** SPECIALIS

# **Adolescent Obesity**

- Childhood obesity epidemic
  - 80% obese kids become obese adults
  - Eating patterns form at young age
  - Deposition of fat cells in youth
  - Health is affected
    - Diabetes
    - **Sleep apnea** (22% of obese children)
    - Fatty liver (38% of obese children)
  - Weight bias and discrimination
  - Bullying



# **Obesity - Impact**

- Increasing mortality rate as weight increases
  - BMI>40:

■ BMI>40 and diabetic:

2x mortality rate5x mortality rate

- Mortality
  - 300,000 deaths yearly
  - Decreased life expectancy (5-15 years)



# Morbid Obesity Risks

Disease Relative Risk Source

Type 2 DM	3.4 times	NHANES survey
CAD	1.69 times	(meta analysis 31 studies/389,239 pts)
CHF	2.12 times	Framingham Heart Study
Breast Cancer	1.5 times	Int Jour Cancer, Vol 111(2004): 762-771
Ovarian Cancer	3.2 times	BMC Pub Health, Vol 9(2009) #88



### Diabetes Mellitus

■ 7<sup>th</sup> Leading Cause of Death in United States

■ 90% Type 2 cases related to obesity



#### **Diabetes Mellitus** (National Data 6/2014 CDC/NIH)

- Prevalence
  - 29.1 Million Cases (9.3% of US population)
    - 1.25 Million Type I
    - 27.85 Million Type II
- New Cases
  - 1.4 Million yearly
- Prediabetes
  - US 2010 79 Million
  - US 2012 86 Million



### Diabetes Mellitus

- Diabetes Cost
  - Total Cost of diagnosed cases 245 billion dollars
  - Direct Medical Cost 176 billion dollars
  - Reduced Productivity Cost 69 billion dollars
- Associated Disease
  - Diagnosed diabetics >18 years old
    - 71% Hypertension
    - 65% LDL>100 or on cholesterol lowering meds



- Cardiovascular Disease
  - Risk of heart attack directly related to amount excess weight
  - Morbid obesity causes heart strain
     10% of patients have congestive failure
- Hypertension
  - Directly related to heart and vascular disease
  - Occurs in 50% patients with morbid obesity



- Cancer
  - Obesity causes up to 90,000 cancer deaths/year
  - Overall death rate from any form of cancer
    - Men increases by 52%
    - Women increases by 62%
  - CDC estimates 2030 500,000 cancer death/year
- Respiratory
  - Sleep apnea occurs in over 70% of morbidly obese
  - Asthma occurs in over 25% of morbidly obese



# **Preop Risk Factors**

### IA Specialty (4/15 – present)

Mean BMI 46.5
Diabetes 19.4%
Hypertension 42.3%
Sleep Apnea 32.4%
Hyperlipidemia 26.6%
GERD 35.6%



## Surgeon General Report 2003

#### Health Crisis

■ Fastest-growing cause of disease/death in U.S.

■ Nearly 2/3 Americans are overweight or obese

1/8 deaths in America are caused by an illness directly related to overweight & obesity!



**Psychological Factors** 

- Discrimination By Society
  - Viewed as less intelligent
  - Disease is your fault
- 90% of morbidly obese clinically depressed
  - Repeated failed diets feeling hopeless
  - Constant reminders that you are obese
    - Clothes/airline seats/limited mobility
    - Affects relationships and self-worth



# Why Is Weight Increasing

### Food Supply

- Increased calories/less nutrition
- High carbohydrate processed foods
- 1970 to 2014 avg American 300cal/day more

### Physical Activity

- Decreased at home TV/video games/computer
- Decreased at work Knowledge based/less labor



# Appetite Control What causes hunger?

### Hormones

- Stomach Ghrelin
- Pancreas Polypeptide YY
- Small Intestine Incretins
- Fat Cells Leptin
- Gut microbiota variable ability to utilize calories



# **Appetite Control**

### Leptin

- Produced by fat cells
- Increased when cells full decreases appetite
- Not released by meal patterns
- Chronic elevated calories induces leptin resistance
   Fructose induces leptin resistance



## **Appetite Control**

#### Cortisol

- Produced by adrenal glands
- Increased by stress or lack of sleep
- Increases abdominal fat
- Increases appetite



## **Appetite Control**

- Neuropeptide Y
  - Produced by hypothalmus
    - Inhibited by Leptin/Insulin decrease appetite
    - Stimulated by Ghrelin/Cortisol increases appetite



## **Appetite Control**

- **Ghrelin** stomach increases appetite
- Incretins ileum (GLP1) suppress ghrelin
- Cholecystekinin duodenum decrease appetite
- Peptide YY ileum/colon
  - Peak 1-2 hours after meal
  - Highest level after fatty meal
  - Decrease appetite/slow gastric emptying
  - Elevated after sleeve or bypass



#### Metabolism

#### Pancreas

#### Insulin

- Produced by increased blood glucose
- Stores excess calories as fat
- Chronic elevation downregulates recptors
  - Insulin resistance / Diabetes
- Glucagon
  - Produced by low blood glucose
  - Mobilizes fat for energy / increases blood sugar

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### **Insulin Stimulation**

# Types of calories important Pancreas insulin response Fat None Protein Minimal Carbs Large

Increasing evidence – carbs are harmful



#### Initial Treatment

- Dieting and exercise (<u>Document</u>)
  - Diet trial for few months
  - Physician or dietitian supervision
  - Lifestyle change
    - Decrease calories
    - Increase physical activity
  - Change type of calories (lower carb)



## **Medical Weight Loss**

- Medical Provider
  - Optimize current meds (eliminate weight promoting)
  - Possible use of meds (appetite suppression)
  - Set goals (realistic and attainable)
- Dietitians
  - Meal planning
  - Education of types of calories
  - Vitamin deficiencies and supplements



# **Medical Weight Loss**

- Psychiatric provider
  - Trauma history
    - High rates of history of sexual abuse
  - Eating as coping mechanism
  - Eating for pleasure
  - Discrimination history due to weight
  - Treatment plans
    - EMDR
    - Counseling
    - Group Therapy



# **Dieting Results**

- Weight loss if morbidly obese
  - Diet 1 year
    - **7%** excess weight loss
  - Diet and Drugs for 1 year(Qsymia, Belvique, Contrave, Phentermine)
     10-15% excess weight loss
  - Surgery results at 1 year
    - 65% excess weight loss
- Chance of losing 50% excess weight
  - Diet 1%
  - Surgery 90%

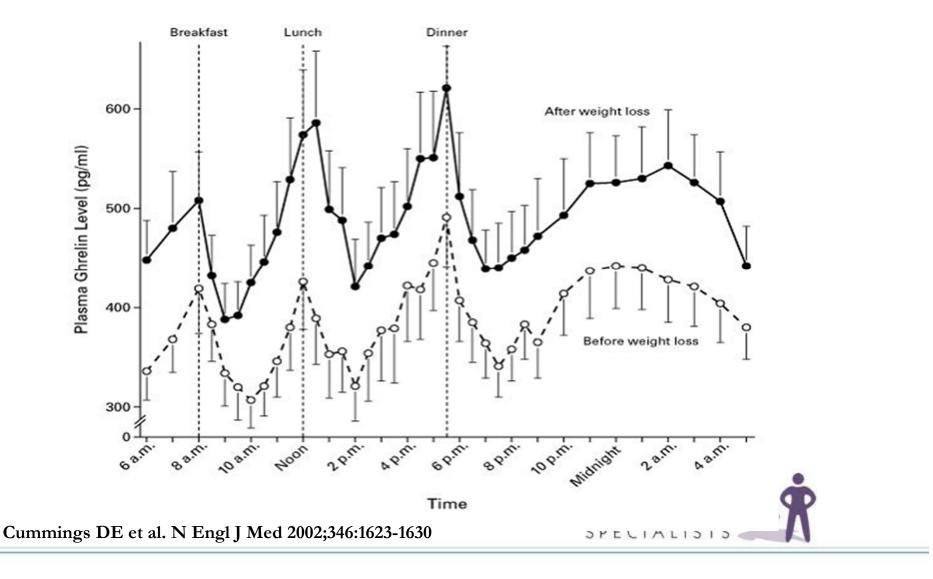


## National Institute of Health

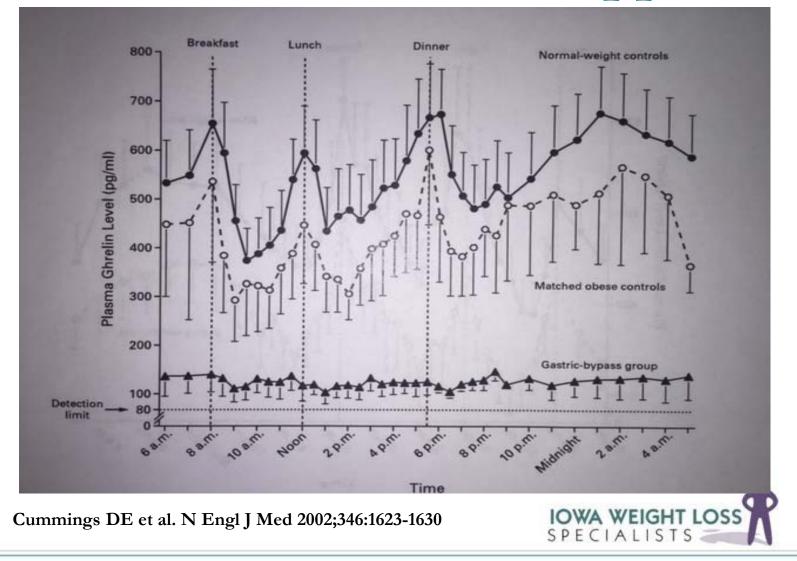
- 1991 Consensus Statement on treatment of morbid obesity
  - Dieting is ineffective
  - Bariatric Surgery Indications
    - BMI > 40
    - **B**MI 35-40
      - Diabetes
      - Hypertension
      - Sleep Apnea



#### Hormone Control of Appetite



### Hormone Control of Appetite



### **Postop Sleeve Results**

#### Ghrelin Reduction

■ 12 patients – prospective trial – 5 years

	Preop	1 Year	5 Year
Ghrelin	593 +-52	219 +-23	257+-23
Decrease	e Ghrelin	63%	57%

Bohdjalan et al. Obes Surg, May 2010;20:535-40.



# Weight Loss Surgery

- Restrictive not metabolic
  - Laparoscopic Adjustable Gastric Banding
  - Vertical Banded Gastroplasty
- Metabolic Procedures
  - Vertical Sleeve Gastrectomy
  - Roux-en-Y Gastric Bypass
    - Open/Laparoscopic/ Robotic assisted
- Malabsorptive
  - Bileopancreatic Diversion



#### **Roux-en-Y Gastric Bypass**

#### How Does RYGB Work?

#### Mechanical

Small pouch holds less food Dumping syndrome if too many sweets

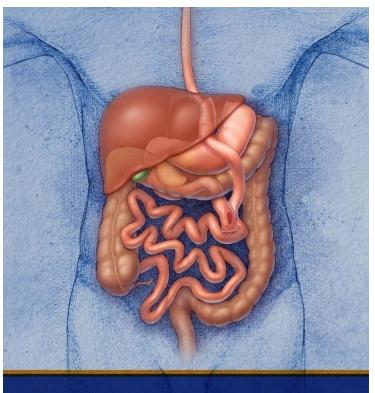
Malabsorption

Bypassed bowel (reduced calories absorbed)

Metabolic

#### Hormonal changes

Decreased hunger (decreased Ghrelin) Increased insulin activity (modulated through neuropeptide Y-food in ileum)



**Roux-en-Y Gastric Bypass** 



## Roux-en-Y Gastric Bypass

#### Advantages

- Long history of proven effectiveness
- Good weight loss 70% excess weight at 1 year
- Suppresses hormones and controls portions

#### Disadvantages

- Most invasive bariatric surgery
- More difficult surgery and increased challenge as weight increases
- Highest rate of complications
- Complications more severe and can happen years later
- Vitamin deficiencies
- Dumping syndrome
- Bowel Obstructions



# Surgical Risks Roux-en-Y

- Anastamotic Leak: 1-2%
- DVT/PE
- Bleeding
- Stricture
- Pneumonia
- Ulcer (smoking)
- Wound Infection
- Hernia
- Nutrient Deficiency
  - Geisinger database(2000 patients) 10% iron def with Hb<8 at 8 year postop
- **Bowel Obstruction:** 2-3%
- Death

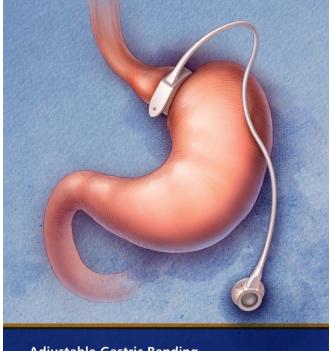


#### Adjustable Gastric Banding

#### How Does Lap-Band Work?

Mechanical Pressure on vagus nerve Feeling of satiety Limit portions Slow eating

Hormonal **No effect** 



Adjustable Gastric Banding



## Lap-Band

- Disadvantages
  - Least weight loss 30-40% at 2 years
  - No regulation of appetite hormonesInadequate appetite suppression
  - Highest rate of mechanical problems
     Slips or esophageal dilation
  - Highest rate of reoperations (10-20% removal rate)
  - Most unnatural eating food sticking/spitting up IOWA WEIGHT LOSS SPECIALISTS

## Lap Band

- 1996-2007 France 1 hospital
  897 bands placed
- Mechanical failure or weight loss<25%</li>
   <u>2 year</u> <u>10 year</u> <u>15 year</u>
   18.4% 43% 70%

Arapis et al. Obes Surg 6/2016



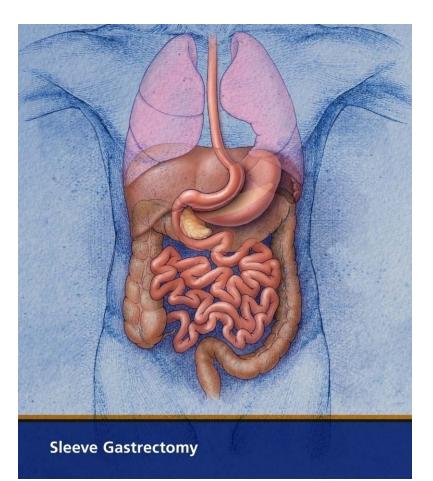
#### **Vertical Sleeve Gastrectomy**

#### How Does Sleeve Work?

#### Metabolic

Hormone control Decreased Ghrelin

Mechanical Limits portion size





## Lap Sleeve Gastrectomy

- Advantages
  - Good weight loss 65% at 1 year
  - Technically easier surgery no rerouting
  - Suppressed hormones and controls portions
  - Much less vitamin deficiency
  - Eat more naturally (rare dumping or sticking)
  - No rerouting options for future (meds)
  - Rapid recovery
  - Much easier long-term care (bariatric surgeon)



# Lap Sleeve Gastrectomy

#### Advantages

- Compared to Band
  - No foreign body
  - No adjustments
  - Better appetite suppression
  - Much lower risk of reoperation
  - Much lower risk of spitting up food
- Compared to Gastric Bypass
  - Much lower surgical and long-term risk
  - Much faster recovery
  - Much lower risk vitamin deficiency
  - Weight loss nearly identical to bypass



## Lap Sleeve Gastrectomy

- Disadvantages
  - Not reversible
  - Sleeve could stretch
  - Long-term data limited (past 8 years)



#### Surgical Risks Sleeve Gastrectomy

Iowa Weight Loss Data – 1200 Patients

Gastric leak	0.1%
DVT/PE	0.1%
Portal Vein Thrombosis	0.2%
Bleeding	1%
Hernia	0.2%
Stricture	0.1%



#### Long Term Sleeve Weight Loss

Author	Patients	Follow up (yrs)	<u>Weight Loss (est.)</u>
Himpens et al.	41	6	53%
Bohdjalian et al.	26	5	55%
Sarela et al.	20	8-9	69%
D' Hondt et al.	23	6	56%



### Long Term Sleeve Results

- 185 Patients had sleeve 2006-2008
- **148** Patients followed up at **6** years after surgery
- **37** Patients followed up at **7** years after surgery
- Excess Weight Loss 6 years 67.3%
- Excess Weight Loss 7 years 65.7%



## Long Term Sleeve Results

<u>Preop</u>	<u>Number</u>	<u>Resolution</u>	<u>Improved</u>
Diabetes	31	83%	12%
Htn	67	60%	39%
Sleep Apnea	37	75%	21%

G. Cassela et al. Surg Obes Rel Dis 2016;12:757-762



#### Sleeve vs Gastric Bypass

#### Randomized trial

	6 months	12 months
Lap Sleeve	50%	60%
Lap Gastric Bypass	55%	67%

Ann Surg. 2008 Mar;247(3):401-7.



## Bariatric Surgery in U.S.

Michigan Bariatric Surgery Collaborative Database
43,732 patients (2006-2013)

	2008	<u>2012</u>
Lap Band	34%	4%
Lap Gastric Bypass	58%	27%
Lap Sleeve	6%	67%

2013 – Lap Sleeve most common surgery



## **Bariatric Surgery United States**

#### ASMBS database

	2012	2013	2014	2015	2016
Cases(thousands)	173	179	193	196	210
Morbid obesity		18 Million		24 Mil	26 Mil
(CDC data 2016)					

# Surgical Risks

#### Surgery vs. Morbid Obesity

- Surgery carries much less risk than obesity
- Morbid obesity
  - Diabetes
  - High blood pressure
  - Heart disease
  - Sleep apnea
  - Cancer
  - Decreased life expectancy
  - Decreased quality of life



# Weight Loss Surgery Results

- Utah Adams study
  - Surgery patients (n=7925)
  - Matched Controls (n=7925)
  - Follow up of 7.1 years
- Death Rate after surgery
  - All Causes: Decreased 40%
  - Diabetes: Decreased 92%
  - Heart disease:
  - Cancer:

Decreased 56% Decreased 60%



N Engl J Med 2007; 357:753-61

## Weight Loss Surgery Risks

- ASMBS National Database
   60,000 patients
  - 30 day mortality 0.06%
    (Less than for gallbladder surgery)
  - Major Complication Rate (Leak/Abscess/Bleed/DVT/PE/Death)
    - Sleeve Gastrectomy 1-1.5%
    - Gastric Bypass 2-3%



## **Personal Accountability**

- Appetite Suppression
- Portion Control
- Accountability
  - Good food choices
  - Avoid snacking and liquid calories
  - Exercise
    - Most that exercise regularly lose 80% excess weight



## **Surgery for Diabetes**

#### Literature review

- 621 studies
- 135,247 patients
- Diabetes
  - Improved and decreased meds, 85%
  - Remission and off all meds, 60-70% (1 year)



# **Surgery for Diabetes**

- Stampede Trial (Cleveland Clinic)
  - 150 patients prospective and randomized
    - 50 each to intensive medical care/Bypass/Sleeve
    - Med group follow up visits
      - Every 3 months first 2 years
      - Every 6 months last 3 years
  - BMI range 27-43 (all type 2 diabetics)
  - Trial duration 5 years
  - Primary outcome HbA1C < 6.0 on or off meds



Schauer et al. N Engl J Med. 2017;376(7):641-51.

#### **Surgery for Diabetes**

	A1C<6	A1C<6 no med	Wt Loss(Kg)
Med(38 pts)	2 (5%)	0	-5.3
Bypass(49pts)	14(29%)	11(22.4%)	-23.2
Sleeve(47pts)	11(23%)	7(14.9%)	-18.6

Schauer et al. N Engl J Med. 2017;376(7):641-51



#### **Diabetes Mellitus**

- 3<sup>rd</sup> World Congress Consensus Conference (2016)
  - International Diabetes Federation Recommendations
  - Surgery for those not achieving treatment targets with dieting
  - Surgery acceptable for BMI > 35
  - Surgery is cost effective
  - Surgery is very low risk (similar to gallbladder)



#### **Economic Impact of Diabetes**

- Lifetime cost of diabetes in the United States
  - Diagnosed at age 50 \$100,000
  - Diagnosed at age 30 \$200,000
- Insurance companies decreasing presurgery requirements
  - Diet visits (monthly)
    - Cigna 1
    - Blue Cross 2
    - United/Optum 0
    - Medicaid 6
    - Medicare 6



#### Surgery for Sleep Apnea

- Weight loss highly effective at producing remission
- Numerous studies
   Remission rate is 80% at 6 months after surgery



# Surgery for Cardiovascular Disease

- Hypertension
  - Improved or resolved in over 30-40%
- Congestive heart failure
  - Significant improvements in heart function
  - Decreased heart strain and hypertrophy as weight decreases



#### Pregnancy

- Morbid Obesity
  - Infertility
  - Pre-eclampsia
  - Gestational Diabetes
- Sleeve gastrectomy
  - Recommend wait 1 year after surgery
  - Decreased risk to baby and mother
  - Improved fertility



#### **Orthopedic Surgery**

#### Knee Replacement

- BMI 40-50: 6 times higher risk
- BMI >50: 18 times higher risk
- Spinal Surgery
- Hip Replacement



#### Surgery Cost Savings

Study by George Washington University

Individual Annual Cost of Obesity

- Men \$6,518 yearly
- Women \$8,365 yearly

Costs 15 times higher overall compared to BMI<30



# Surgery Cost Savings

Scandinavian Obesity Surgery Registry

■ Lifetime results per patient

- Direct Cost Savings 8408 euros
- Added Life Years 0.8 years
- Added Quality Adjusted Life Years 4.1 years
- Overall Cohort Savings 66 million euros

Obesity Surgery, Sept 2015;25:1559-68.



# Long Term Results

- Bariatric Surgery
  - Safe
  - Effective
  - Durable results
  - Only effective treatment for morbid obesity



#### **Results of Weight Loss Surgery**

- Bariatric surgery long term weight loss
  - 90% patients maintain over 50% excess weight loss
- Bariatric surgery is **safe** 
  - 60,000 patients and risk of dying was 0.06%
- Bariatric surgery is effective
  - 78% resolution of diabetes
  - 90% resolution of sleep apnea
  - Average weight loss is 60% of excess
- Only effective tool for long-term weight control if morbidly obese
  IOWA WEIGHT LOS

### **Results of Weight Loss Surgery**

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Laparoscopic Vertical Sleeve Gastrectomy

Starting Weight: 303

4 years post-op: 165

Total weight loss: 138

Lost 92% of excess weight





Laparoscopic Vertical Sleeve Gastrectomy

Starting Weight: 323

7 months post-op: 220

Total weight loss: 103

Lost 100% of excess weight





Laparoscopic Vertical Sleeve Gastrectomy (Failed Lap Band Prior)

Starting Weight: 297

1 year post-op: 196

Total weight loss: 101

Lost 73% of excess weight





Vertical Sleeve Gastrectomy Starting Weight: 290 9 months post-op: 200 *Total weight loss: 90 Lost 70*% of excess weight

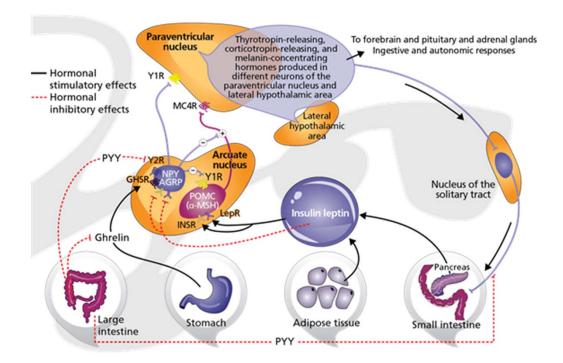


# Medical Weight Loss

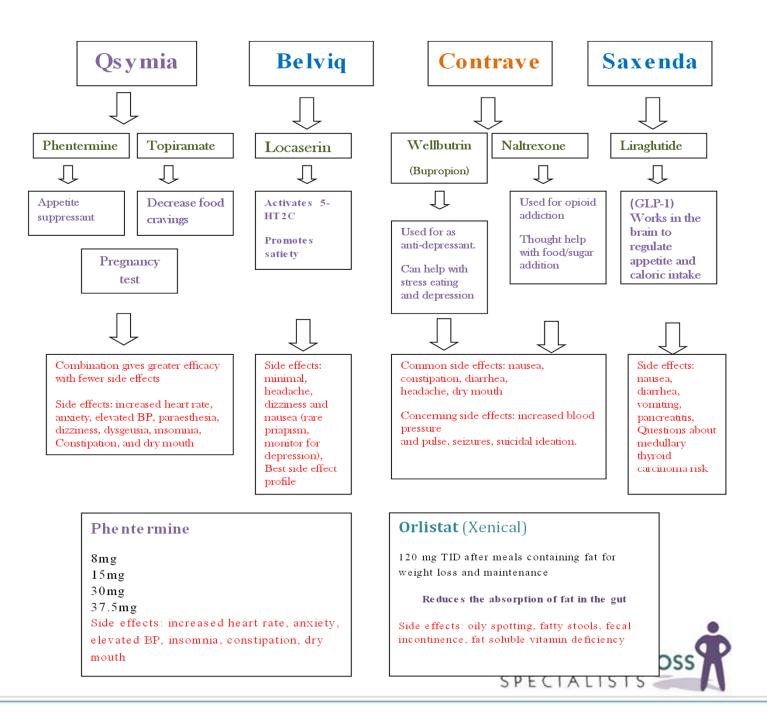
- Comprehensive team approach
- -Mental health
- -Dietitians
- -Exercise
- -Medications
- -Possible surgery referral



#### Why Use Weight Loss Medications?



AGRP: agouti-related peptide; α-MSH: α-melanocyte-stimulating hormone; GHSR: growth hormone secretagogue receptor; INSR: insulin receptor; LepR: leptin receptor; MC4R: melanocortin-4 receptor; NPY: neuropeptide Y; POMC: proopiomelanocortin; PYY: peptide YY; Y1R; neuropeptide Y1 receptor; Y2R: neuropeptide Y2 receptor. Apovian CM, Aronne LJ, Bessesen D et al. *J Clin Endocrinol Metab.* 2015;100:342-362.



# Things to remember

- Obesity is a disease!
  - Much more complicated than eat less exercise more
  - What may be easy for you may seem impossible for someone else
- If you have an interest in treating your patients obesity get educated!
  - If not, refer to obesity specialist
- BE KIND!
  - Patients are shamed by medical providers regularly
  - Obese patients are at higher risk for depression and hx of physical and sexual abuse
     IOWA WEIGHT LOSS

#### **References:**

- Arapis et al. Obes Surg 6/2016
- AGRP: agouti-related peptide; α-MSH: α-melanocyte-stimulating hormone; GHSR: growth hormone secretagogue receptor; INSR: insulin receptor; LepR: leptin receptor; MC4R: melanocortin-4 receptor; NPY: neuropeptide Y; POMC: proopiomelanocortin; PYY: peptide YY; Y1R; neuropeptide Y1 receptor; Y2R: neuropeptide Y2 receptor. Apovian CM, Aronne LJ, Bessesen D et al. *J Clin Endocrinol Metab.* 2015;100:342-362.
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