

“Eat Less, Move More”— We Know it’s Not that Simple: Finding Your Evidence-based Approach

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July 18, 2020

Disclosures:

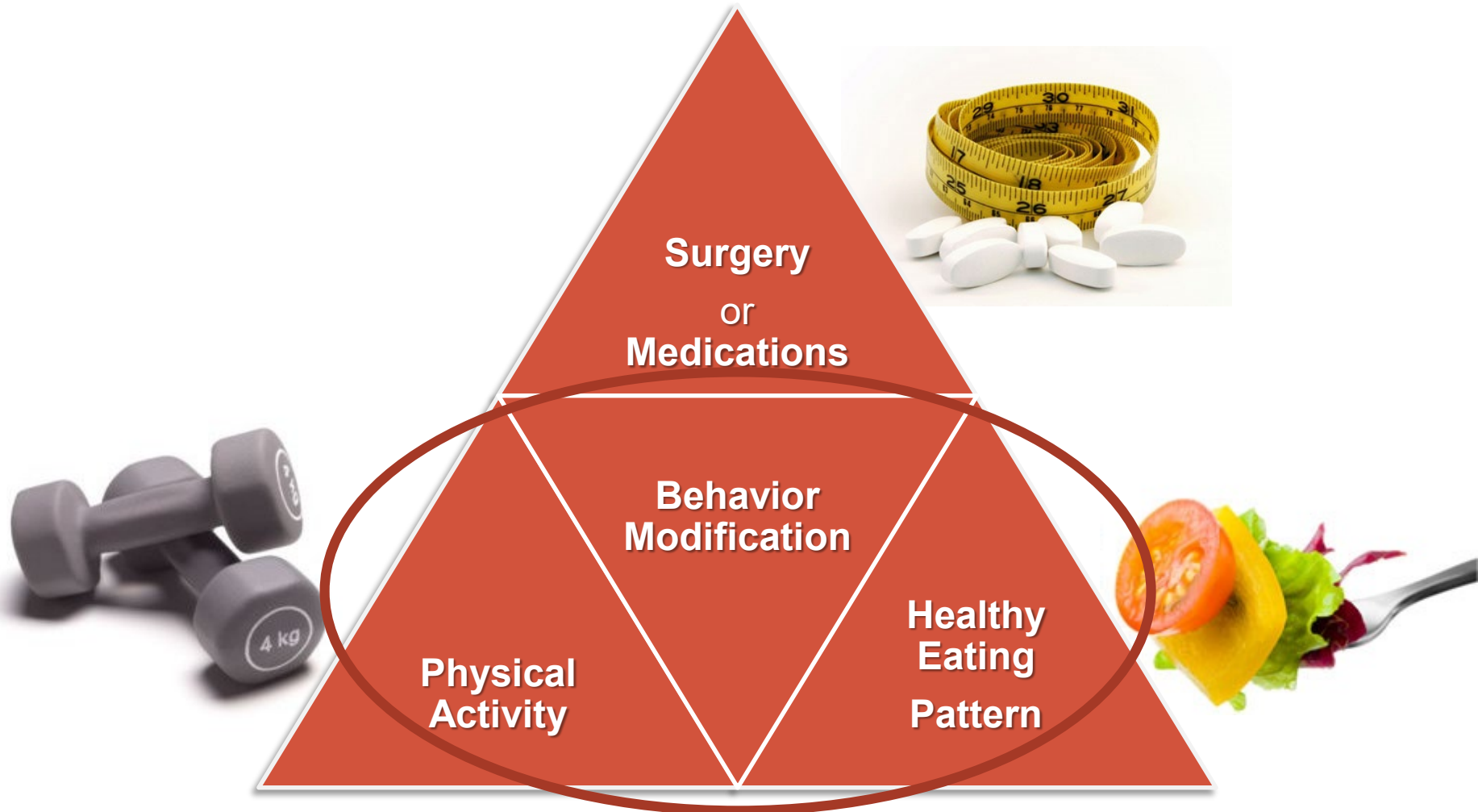
Speaker Bureau/Consultant

- Novo Nordisk

Investigator-initiated Research

- Ethicon-Endosurgery

Components of an Effective Obesity Management Program



Benefits of Modest Weight Loss

Greater Benefits with Greater Weight Loss

Measures of glycemia¹

Triglycerides¹

-3%

HDL cholesterol¹

Systolic and diastolic blood pressure

Hepatic steatosis measured by MRS²

Measures of feeling and function:

Symptoms of urinary stress incontinence³

Measures of sexual function^{4,5}

Quality of life measures(IWQOL)⁶

-5%

NASH Activity Score measured on biopsy⁷

Apnea-hypopnea index⁸

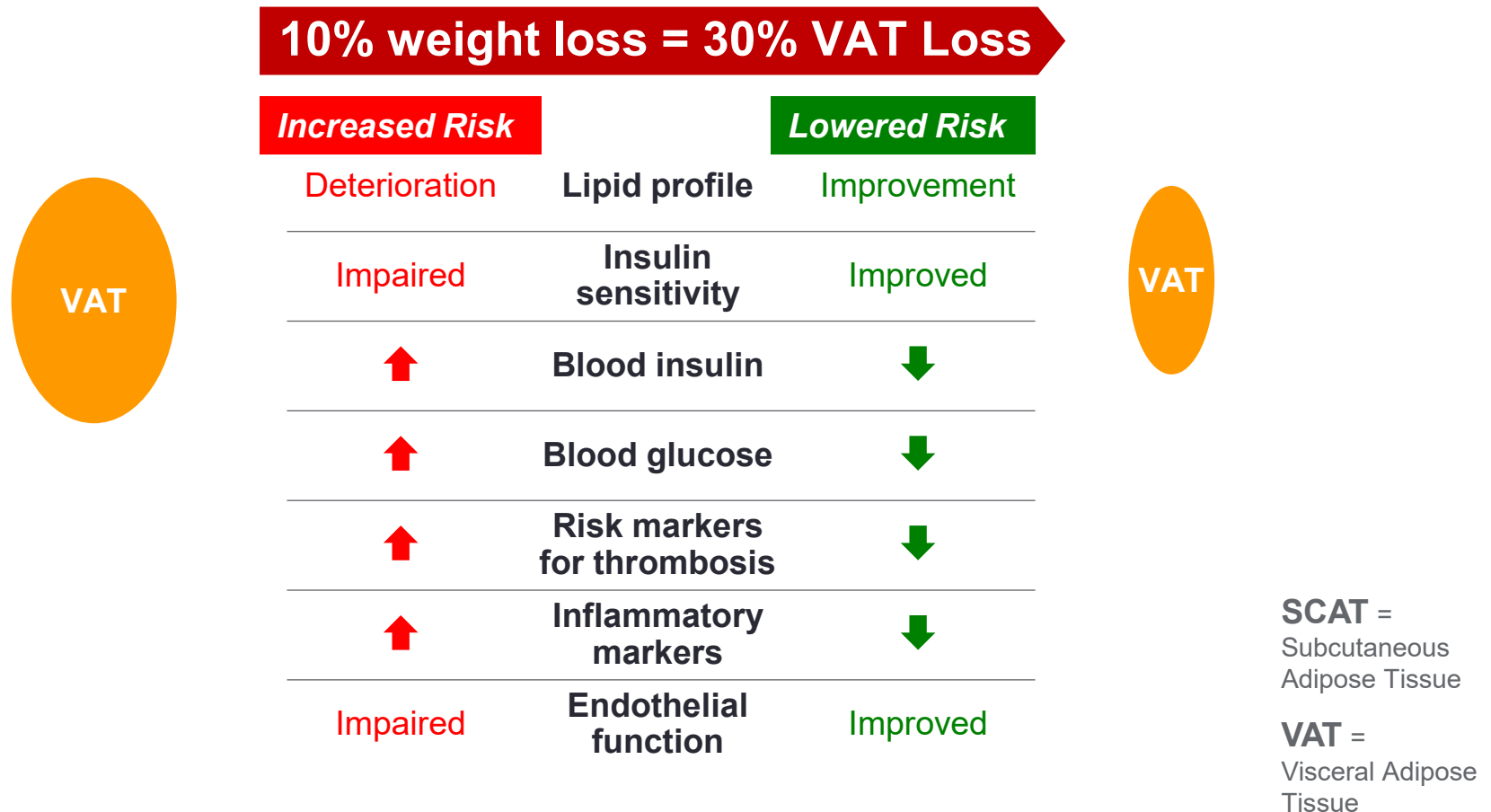
-10%

Reduction in CV events, mortality, remission of T2DM

-15%

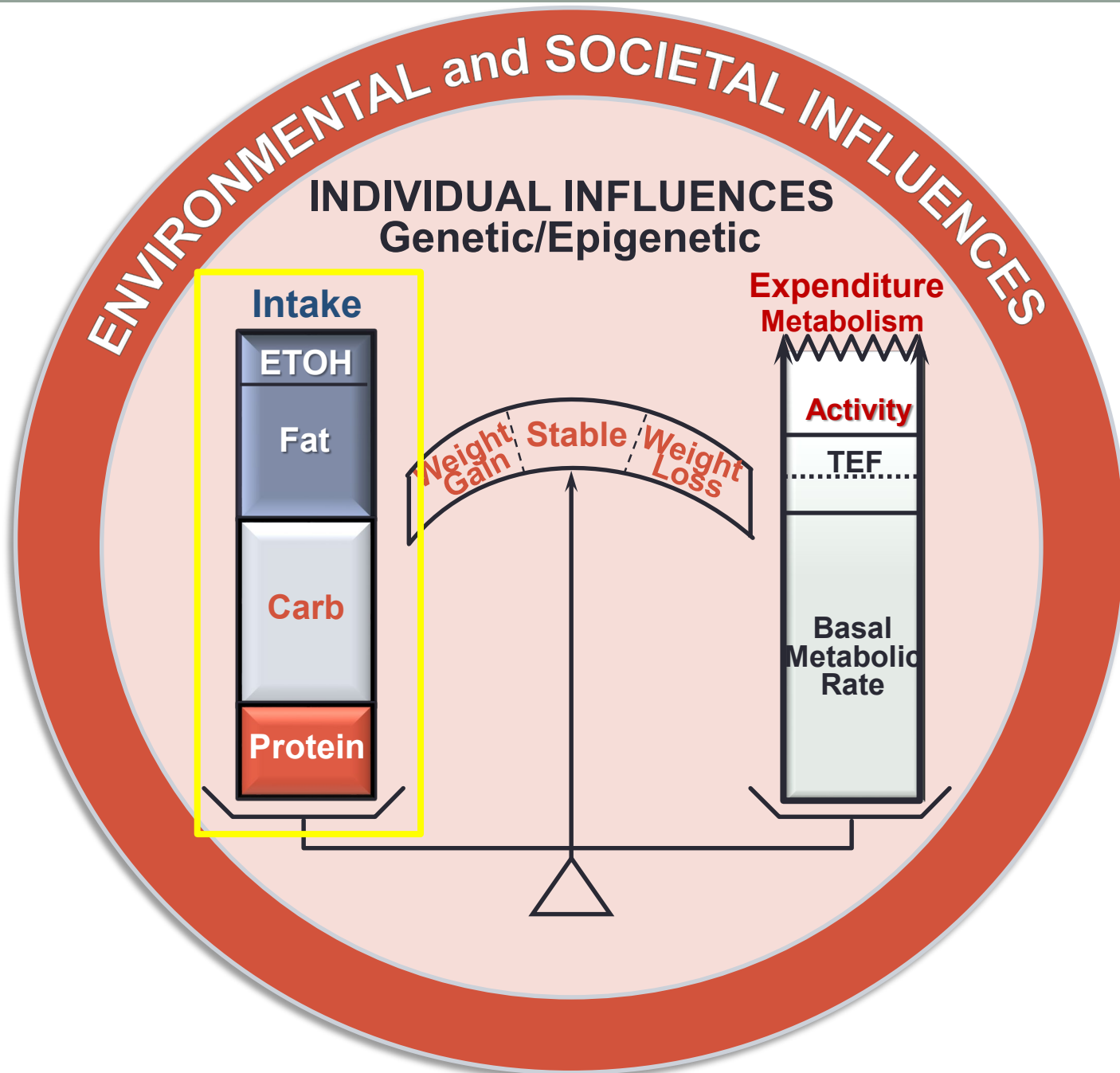
1. Wing et al. Diabetes Care 2011;34:81-1486. 2. Lazo et al. Diabetes Care 2010;33:2156-63. 3. Phelan et al. Urol. 2012;187:939-44. 4. Wing et al. Diab Care 2013;36:2937-44. 5. Wing et al. Journal of Sexual Medicine 2010 ; 7:156-65. 6. Crosby, Manual for the IWQOL-LITE Measure. 7. Promrat et al. Hepatology 2010;51:121-29. 8. Foster et al. Arch Intern Med 2009;169:1619-26.

Why is modest weight loss beneficial?





Diet and Physical Activity



What is the BEST DIET for Weight Loss?

3-Hour Diet
8-Minutes
The Abs Diet
Age-Defying Diet
Atkins
BMIQ
Beck Diet Solution
The Best Life Diet
The Biggest Loser
The Blood Type Diet
Body-For-Life
Cabbage Soup
Curves
DASH
Dr. Phil
E-Diets
Eat Clean Diet

Fat Flush Plan
Fat Smash Diet
Flat Belly Diet
The Flavor Point Diet
French Women Don't Get Fat
The G.I. Diet
Grapefruit
The Hamptons Diet
Japanese Women
Jenny Craig
Master Cleanse
The Mediterranean Diet
NutriSystem
Ornish
The Perfect Body Diet
Picture Perfect
Pritikin

Scarsdale
Slim-Fast
Snack Factor Diet
South Beach
The Step Diet
Structure House
Sugar Busters
Suzanne Somers
The Skinny
The Solution
Ten Years Thinner
The Thrive Diet
Weight Watchers
You on a Diet
The Zone

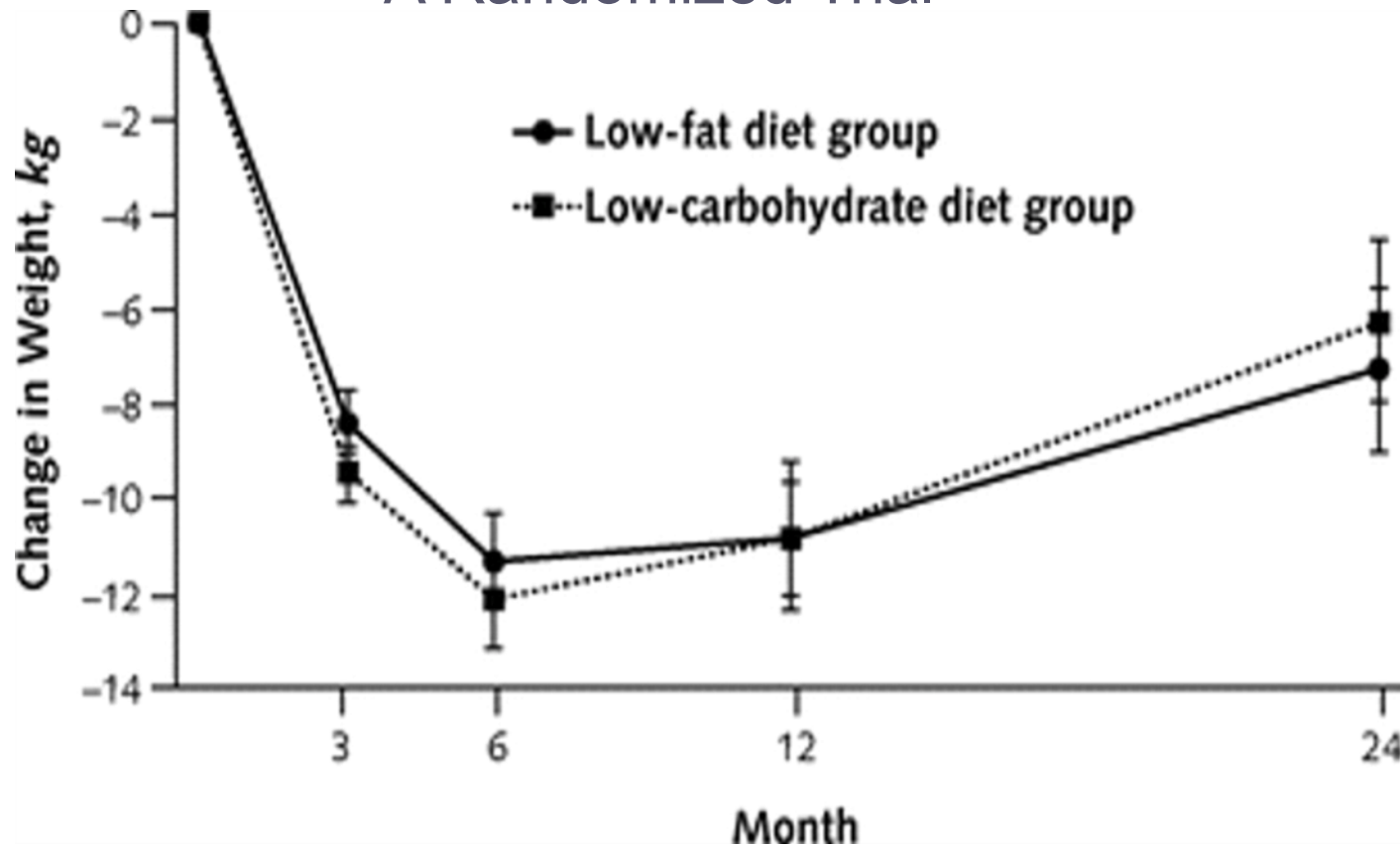


BEST WEIGHT LOSS
#1 Weight Watchers

BEST OVERALL
#1 Mediterranean

Weight and Metabolic Outcomes After Two Years on Low CHO vs Low-Fat Diet

A Randomized Trial



Predicted absolute mean change in body weight for participants in the low-fat and low-carbohydrate diet groups, based on a random-effects linear model. Error bars represent 95% CIs.

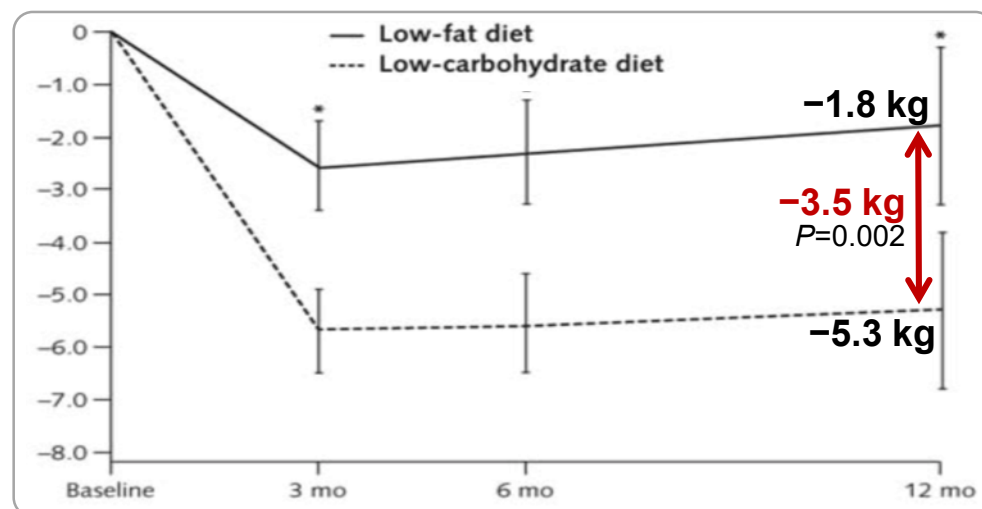
Effects of Low-Carbohydrate and Low-Fat Diets

Randomized trial, 119 completers, 12 months

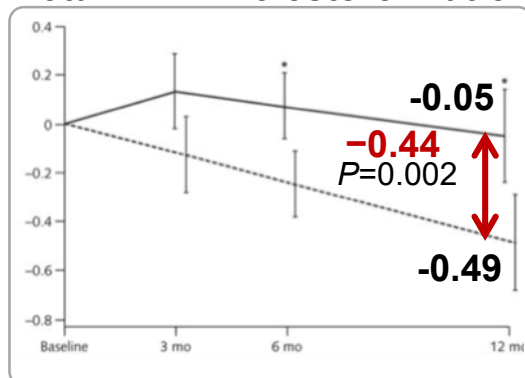
Conclusion:

Low-carbohydrate diet was more effective for weight loss and cardiovascular risk factor reduction vs low-fat diet

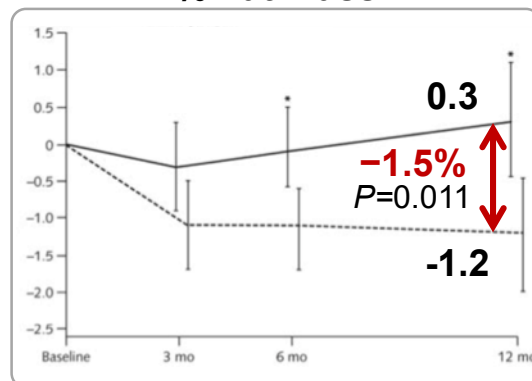
- n= 60/82; low-fat group <30% fat daily (<7% sat fat) 55% from carbs
- n=59/79; low-carb group <40 gm/day



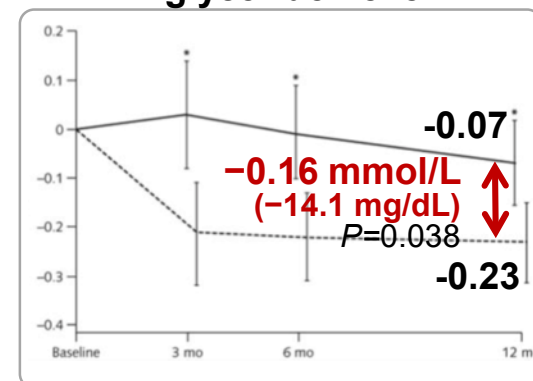
Total HDL Cholesterol Ratio



% Fat Mass



Triglyceride Level



Online Programs



Internet-delivered Programs

Most successful internet programs, that provide weekly email feedback to participants, will induce weight losses of **~2/3** the size of those achieved by traditional on-site behavioral programs



How many calories per day are
realistic for weight loss???



2013 Obesity Guidelines

Evidence Statement 1.

To achieve weight loss, an energy deficit is required. The techniques for reducing dietary energy intake include the following:

Specification of an energy intake target that is less than that required for energy balance, usually:

- **1,200 to 1,500 kcal/day for women**
- **1,500 to 1,800 kcal/day for men**

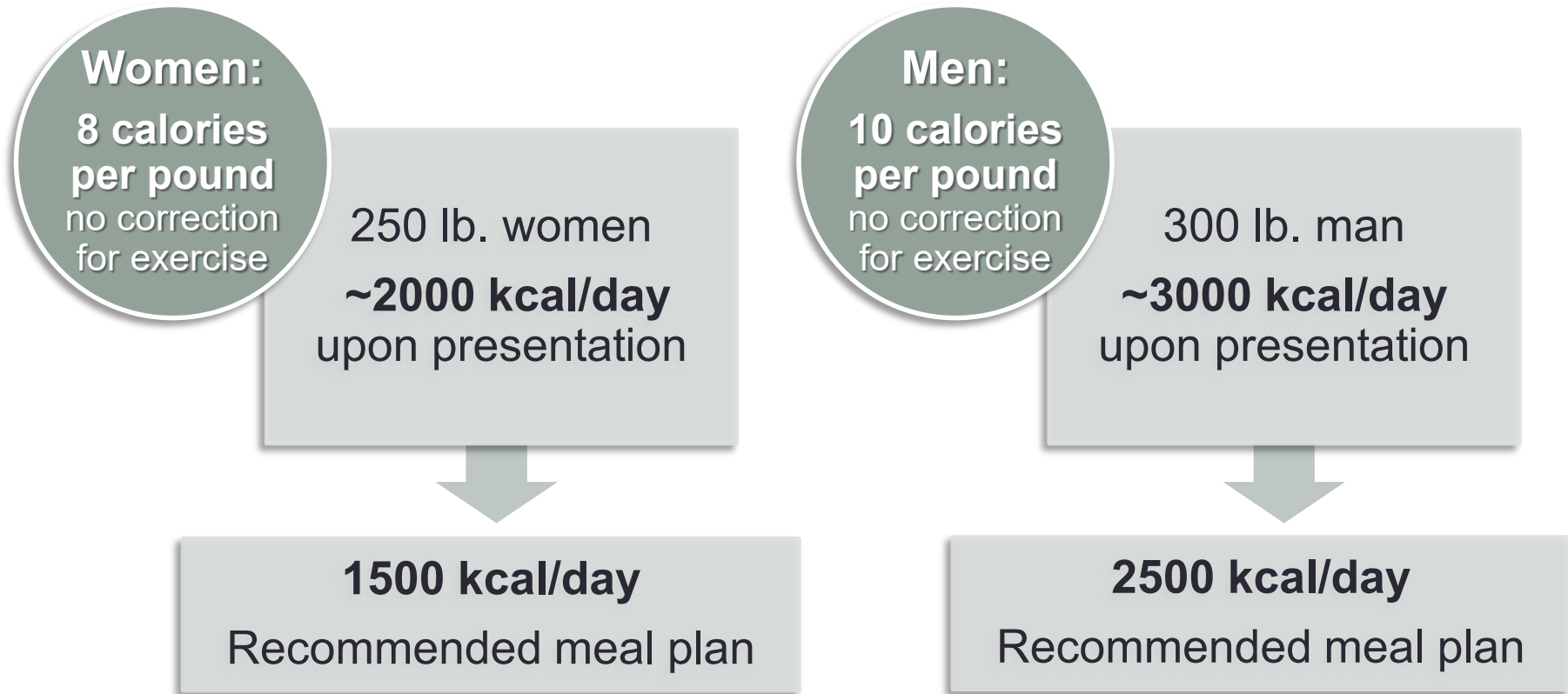
(kcal levels are usually adjusted for the individual's body weight and physical activity levels')

Estimation of individual energy requirements according to expert guidelines and prescription of an energy deficit of:

- **500 kcal/day or**
- **750 kcal/day or**
- **30% of energy**

Ad libitum approaches where a formal energy deficit target is not prescribed, but lower calorie intake is achieved by restriction or **elimination of particular food groups or provision of prescribed foods**

Calculating Caloric Needs: Rule of Thumb



The Bottom line on Diets

Reduce calories by ~500 kcal/day

Stick with it!!

The Power of Monitoring and Accountability



Self-monitoring

FOOD DIARY

Date

Time	Food	Feelings

Summary for Tue, Nov 18

Budget	Food	Exercise	Net	Under
1,911	785	-243	542	1,370

Breakfast: 330

- Cereal, corn flakes** 110 >
1 Cup
- Milk, 1%** 110 >
1 Cup
- Juice, orange** 110 >
8 Fluid ounces

Lunch: 455

- Sandwich, turkey** 360 >
1 Each
- Apples, fresh** 95 >
1 Each

Exercise: 243

- Stationary Bicycle** 243 >
Moderate — 30 Min

Navigation: My Day, Log, Goals, More

Frequent Weigh-Ins



Water Intake

AVOID:

- Regular sodas
- Fruit juices
- Caloric beverages

National Academy of Sciences

Recommendations:

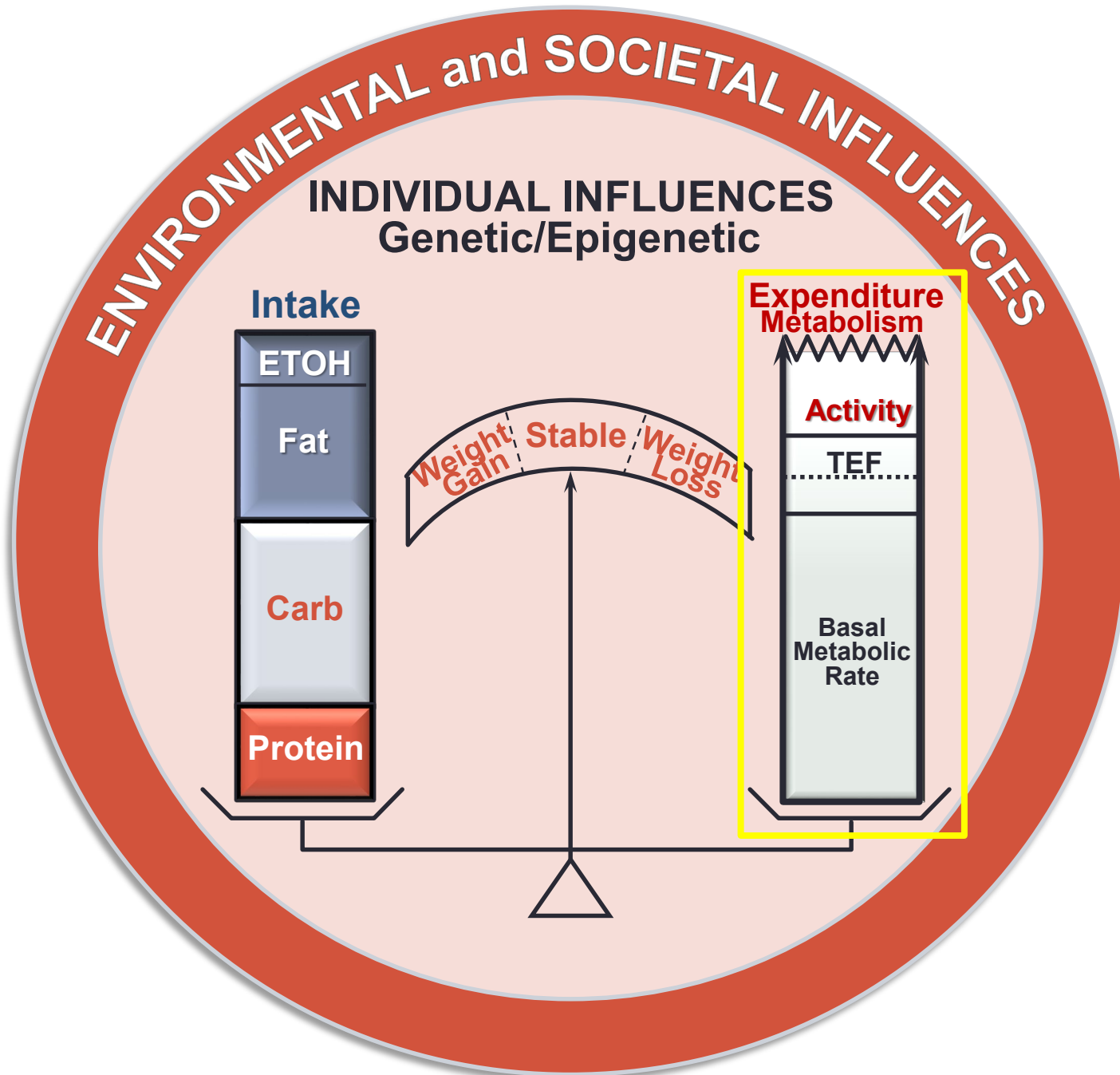
- **Men: at least 125 ounces of water per day**
- **Women: at least 91 ounces**

Although daily fluid intake can come from food and beverages, plain drinking water is one good way of getting fluids as it has zero calories



Physical Activity...





Increase Physical Activity

For substantial health benefits, adults should do at least :

Moderate-intensity

150-300 minutes (2.5 to 5 hours) per week

Vigorous-intensity Aerobic

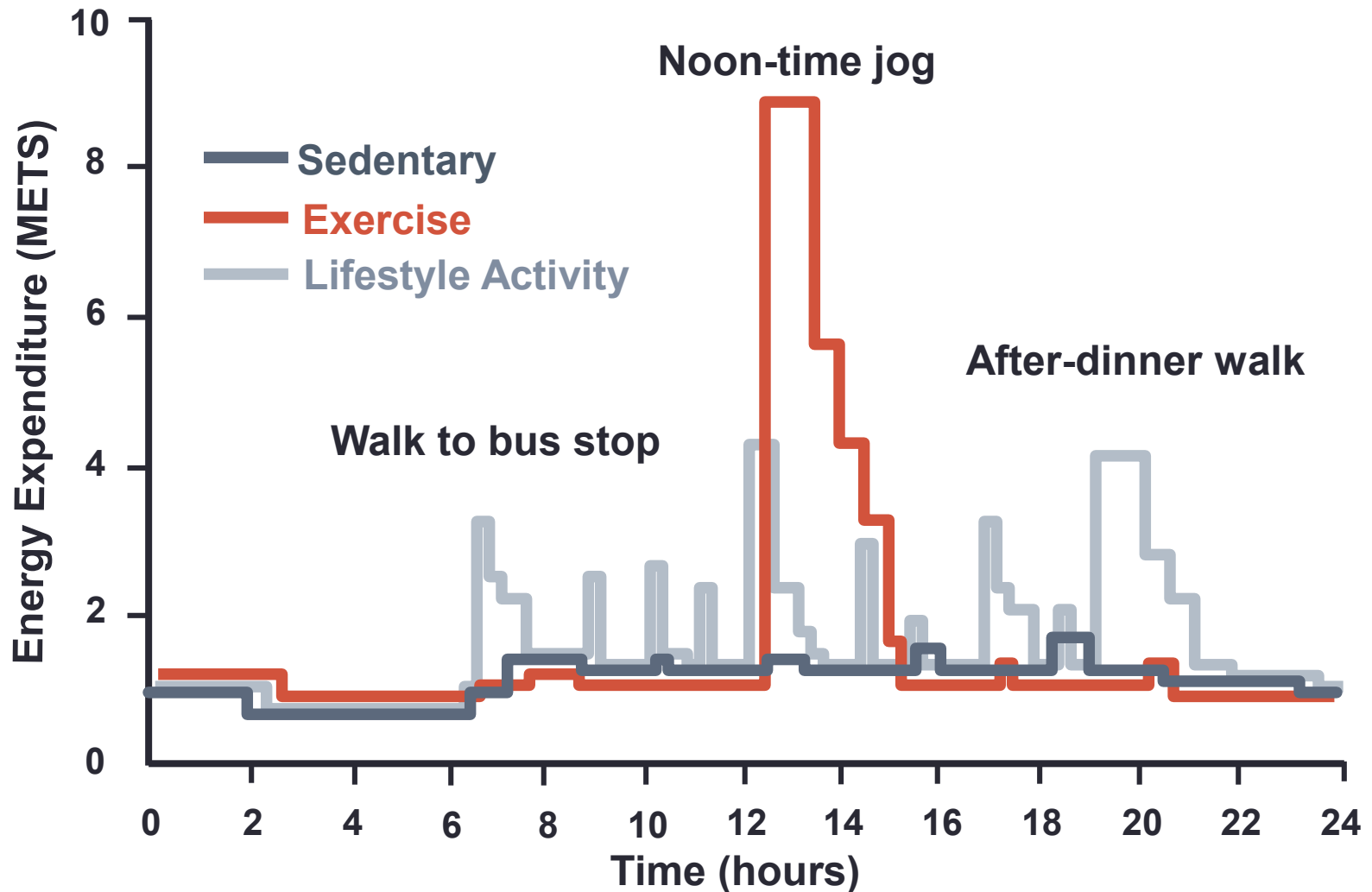
75-150 minutes (1.25 to 2.5 hours) per week

**Muscle-strengthening of moderate or greater intensity
and that involve all major muscle groups**

2 or more days a week



The Lifestyle Approach



Tracking Physical Activity



Nike FUEL



JawBone



Accellerometer



Fitbug



BodyMedia



Fitbit



Pharmacotherapy

Weight Effects of Medications

Category	Drugs That May Cause Weight Gain	Possible Alternatives
<i>Neuroleptics</i>	Thioridazine, haloperidol, olanzapine, quetiapine, risperidone, clozapine	Ziprasidone, aripiprazole
<i>Antidiabetic agents</i>	Insulin, sulfonylureas, thiazolidinediones	AGIs, DPP-4i, SGLT2i, GLP-1 RAs, metformin
<i>Steroid hormones</i>	Contraceptives, glucocorticoids, progestational steroids	Barrier methods, NSAIDs
<i>Tricyclics (ADs)</i>	Amitriptyline, nortriptyline, imipramine, doxepin	Protriptyline, bupropion, nefazodone
<i>MAOIs (ADs)</i>	Phenelzine	
<i>SSRIs (ADs)</i>	Paroxetine	Fluoxetine, sertraline
<i>Other (ADs)</i>	Mirtazapine, duloxetine	Bupropion
<i>Anticonvulsants</i>	Valproate, carbamazepine, gabapentin, pregabalin, vigabatrin	Topiramate, lamotrigine, zonisamide, felbamate
<i>Antihistamines</i>	Cyproheptadine	Inhalers, decongestants
<i>β- and α-adrenergic blockers</i>	Propranolol, doxazosin	ACEIs, CCBs



Pharmacotherapy

Criteria by BMI

BMI ≥ 27 kg/m²
with ≥ 1 comorbidity

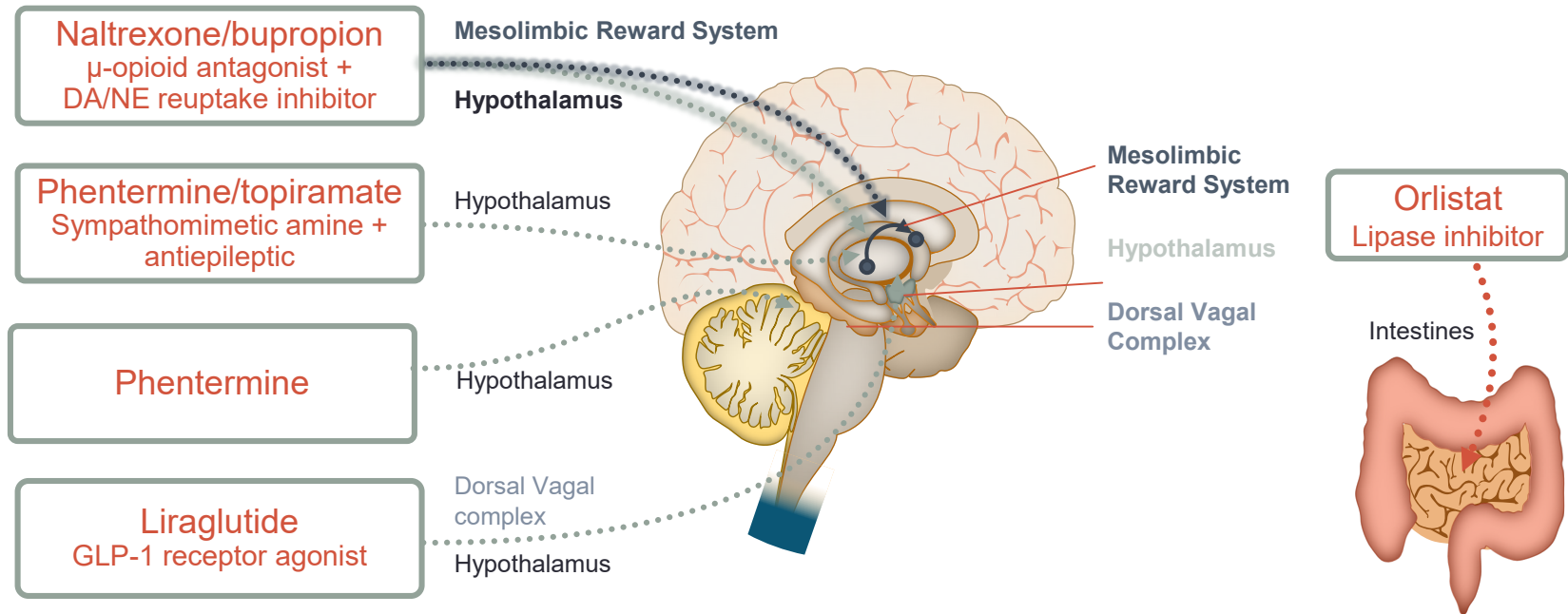
OR

BMI ≥ 30 kg/m²
with no comorbidities

Obesity Pharmacotherapy

- Few providers prescribe pharmacotherapy
- Few patients use pharmacotherapy
- Pharmacotherapy can be extremely effective but also misused, overused, or underused
- Patients respond differently to each medication
- Combining therapeutic options significantly improves weight loss and other outcomes
- Pharmacotherapy can be effective for weight maintenance, not just weight loss

Current Obesity Pharmacotherapy for Use¹⁻⁴



5-HT_{2c}=serotonin; DA=dopamine; GLP-1=glucagon-like peptide-1; MOA=mechanism of action; NE=norepinephrine.

1. Yanovski SZ et al. *JAMA*. 2014;311:74-86. 2. Apovian CM et al. *J Clin Endocrinol Metab*. 2015;100:342-362. 3. Kim GW et al. *Clin Pharmacol Ther*. 2014;95:53-66. 4. Dietrich MO et al. *Nat Rev Drug Discov*. 2012;11:675-691.

Phentermine

- Sympathomimetic amine, NE release
- Blunts appetite
- Approved in 1959 for short-term use, schedule IV
- Dosing: 8-37.5 mg qAM; use lowest effective dose
- Contraindications: pregnancy, nursing, MAOIs, glaucoma, drug abuse history, hyperthyroidism
- Relative contraindications: uncontrolled HTN, tachycardia, history of CAD, CHF, stroke, arrhythmia
- Warnings: primary pulmonary hypertension, valvular heart disease, tolerance, risk of abuse, concomitant use with alcohol

Orlistat

- Lipase inhibitor, decreases fat absorption
- Approved 1999; long-term use
- Not scheduled
- Not centrally acting in the satiety center of the brain
- 120 mg TID with meals (Rx) or 60 mg TID (OTC)
- Use MVI with fat-soluble vitamins at bedtime
- Contraindications: pregnancy, chronic malabsorption syndrome, cholestasis
- Possible gastrointestinal adverse events

MVI = multivitamin; OTC = over-the-counter; Rx = prescription; TID = 3 times per day.

Orlistat [package insert]. South San Francisco, CA: Genentech; 2012; Orlistat [package insert]. Moon Township, PA: GlaxoSmithKline; 2011.

Phentermine/Topiramate ER



- Phentermine: sympathomimetic amine; blunts appetite
- Topiramate: increases GABA activity, carbonic anhydrase inhibitor, other actions; prolongs satiety
- Approved in 2012 for long-term use; schedule IV
- Treatment (“recommended” dose): 7.5/46 mg qAM; max dose: 15/92 mg
- Contraindications: pregnancy, glaucoma, MAOIs, hyperthyroidism
- Warnings: **fetal toxicity**, increased HR, suicidal thoughts, mood disorders, sleep disorders, cognitive impairment, metabolic acidosis, creatinine elevations, hypoglycemia with some diabetic medications

Bupropion SR/Naltrexone SR

- Approved by FDA September 10, 2014
- Bupropion: dopamine/noradrenaline reuptake inhibitor; activates POMC neurons in the hypothalamus, leading to decreased appetite
- Naltrexone: opioid receptor antagonist; blocks autoinhibition of POMC neurons and amplifies the effect of bupropion
- Dosing:
 - Week 1: 1 tab (8mg/90mg) in AM
 - Week 2: 1 tab BID
 - Week 3: 2 tabs in AM; 1 in PM
 - Week 4+: 2 tabs BID
- Consider discontinuation if <5% weight loss after 12 weeks








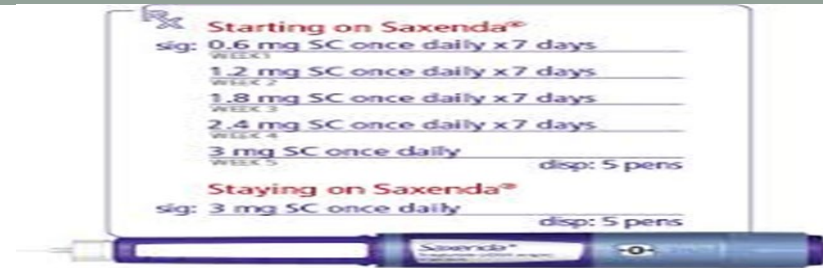
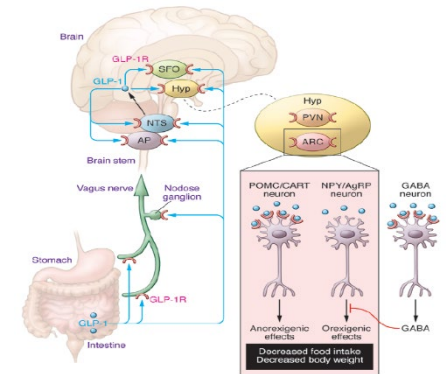
HOW TO TAKE CONTRAVE		
	 Morning dose	 Evening dose
Starting: Week 1		
Week 2		
Week 3		
Week 4-onward		

Image not of actual tablets.

Liraglutide 3.0 mg



- Glucagon-like peptide 1 (GLP-1) receptor agonist
- Multiple actions; effect on weight is primarily via POMC neurons
- Liraglutide 1.8 mg FDA-approved in 2010 for T2DM
- Liraglutide 3.0 mg FDA-approved for primary indication of obesity in December 2014
- Not a controlled substance
- Dosing: weekly escalation by 0.6 mg SC
- Discontinue if <4% weight loss at 16 weeks
- Contraindications: Medullary Thyroid Carcinoma



Acute Pancreatitis

T2DM = type 2 diabetes mellitus; REMs = Risk Evaluation and Mitigation Strategies; SC = subcutaneous.
Saxenda (liraglutide 3.0 mg) prescribing information. <http://novo-pi.nnitest.com/saxenda.pdf>.

Choosing Among Options

Drug factors

- Contraindications
- Dual benefits
- Studied populations

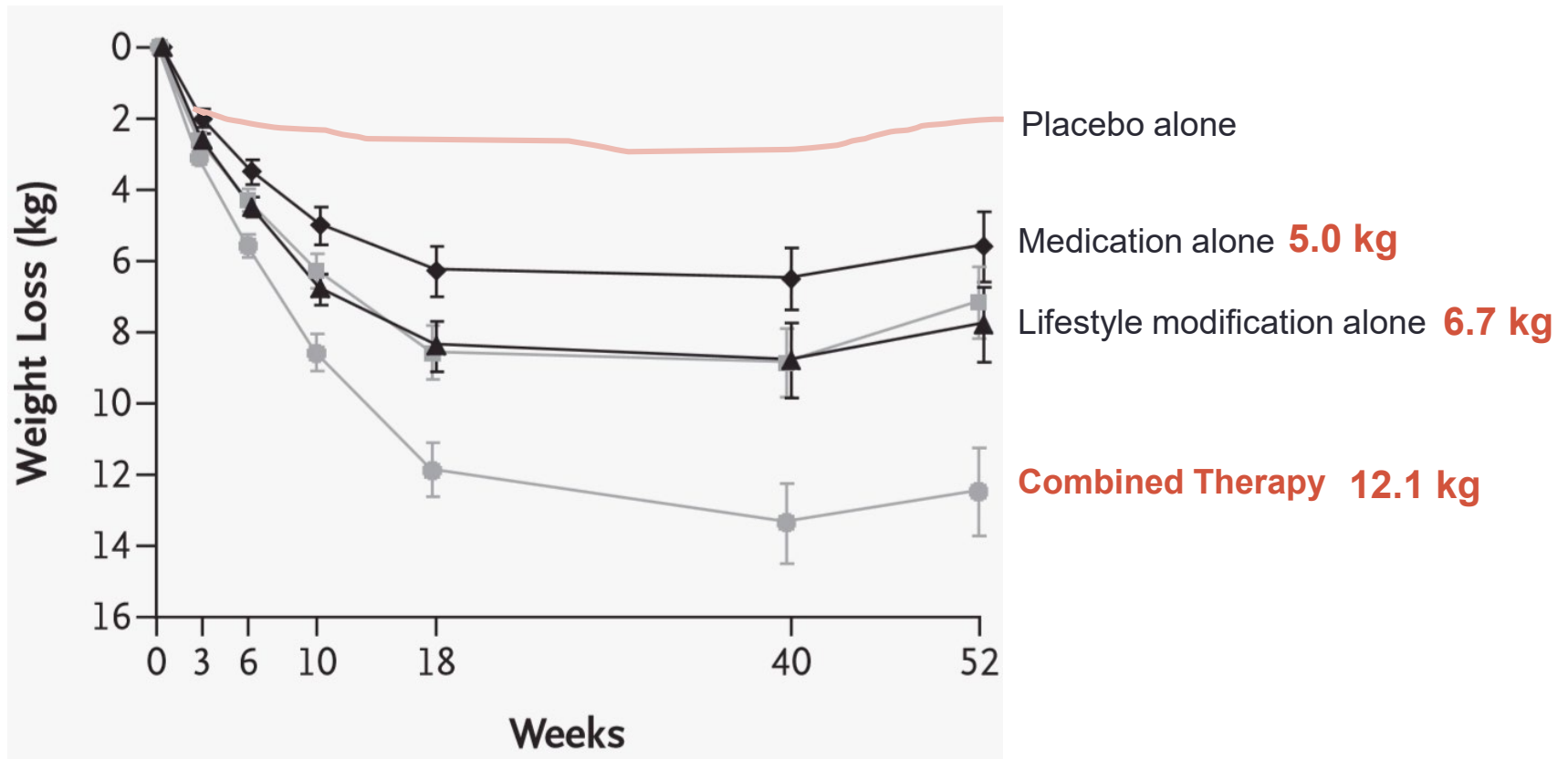
Patient factors

- Patient preferences
- Adverse events
- Prior experiences
- Access

Physician factors

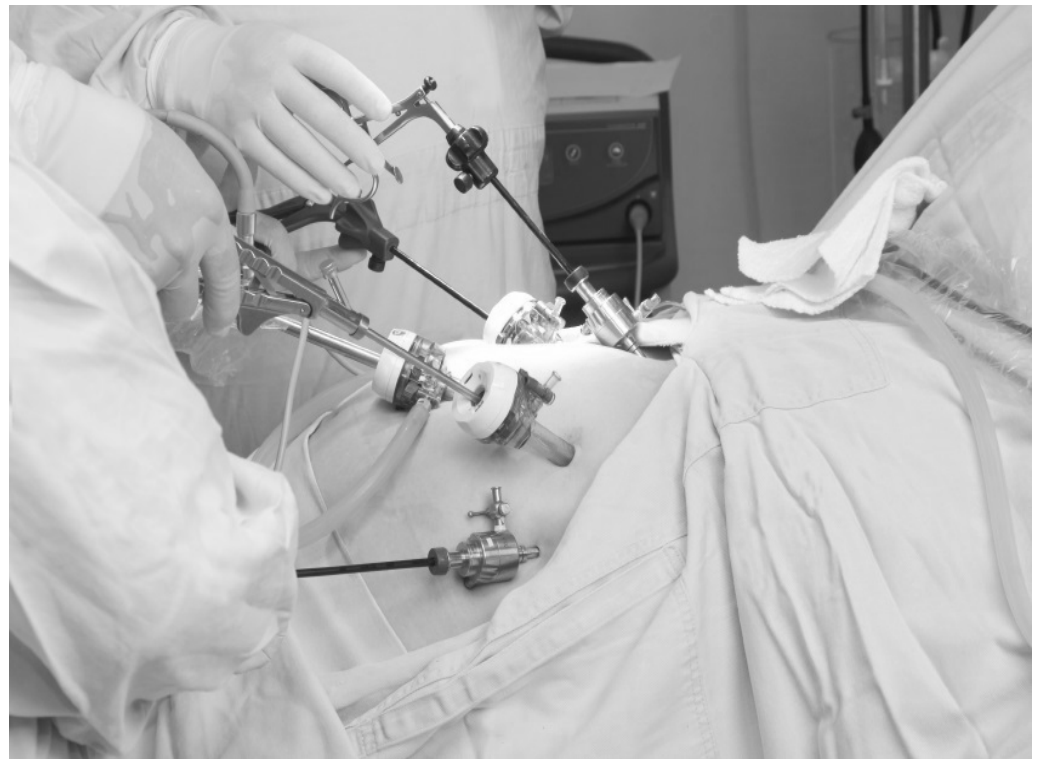
- Provider knowledge/comfort

Combination Therapy





Bariatric Surgery



Bariatric Surgery Criteria

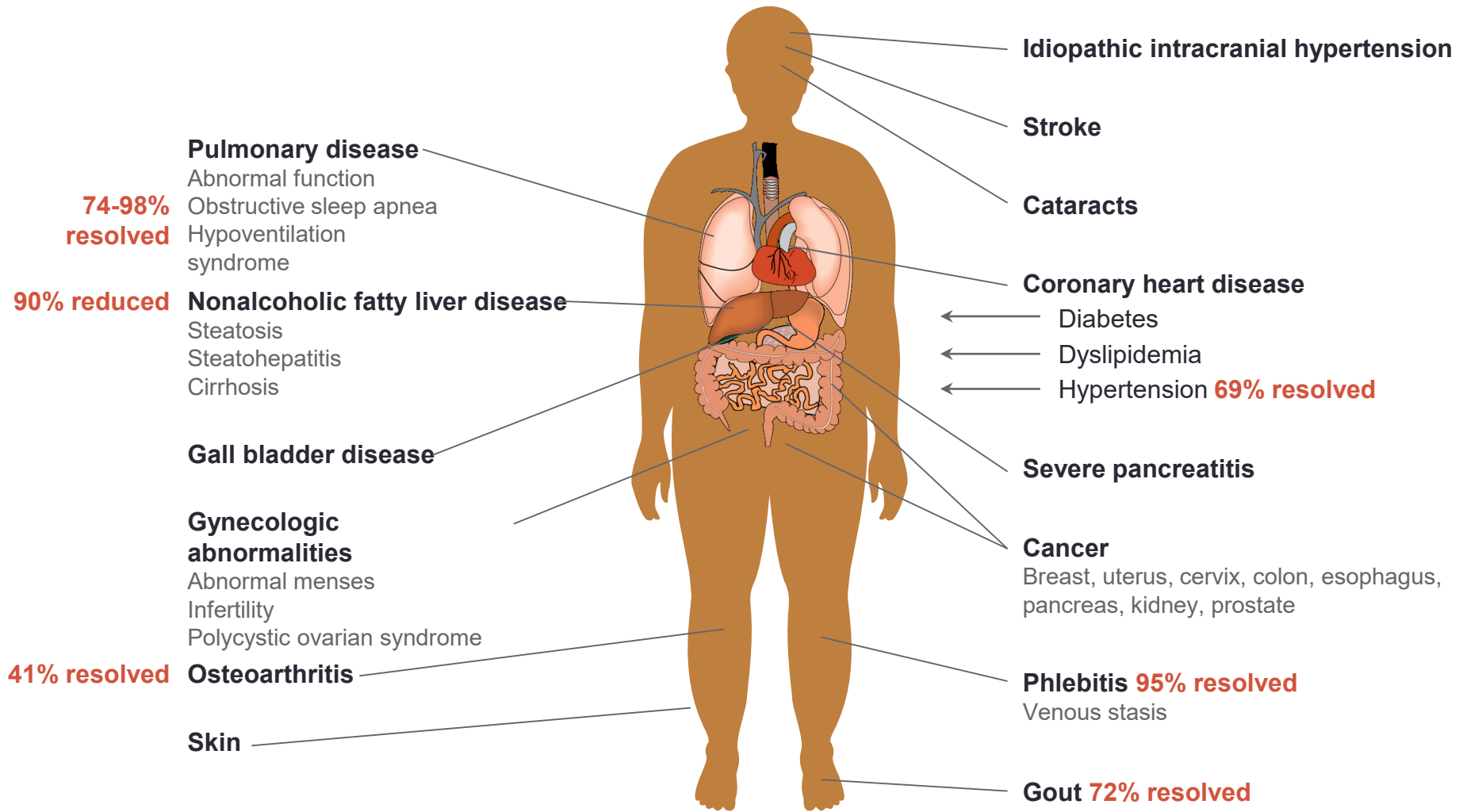
BMI: <18.5	18.5-24.9	25.0-29.9	30.0-34.9	≥35	>40
				With ≥1 severe obesity-associated comorbidity (eg, diabetes or OSA)	With no comorbidities

http://www.cdc.gov/healthyweight/assessing/bmi/adult_bmi.

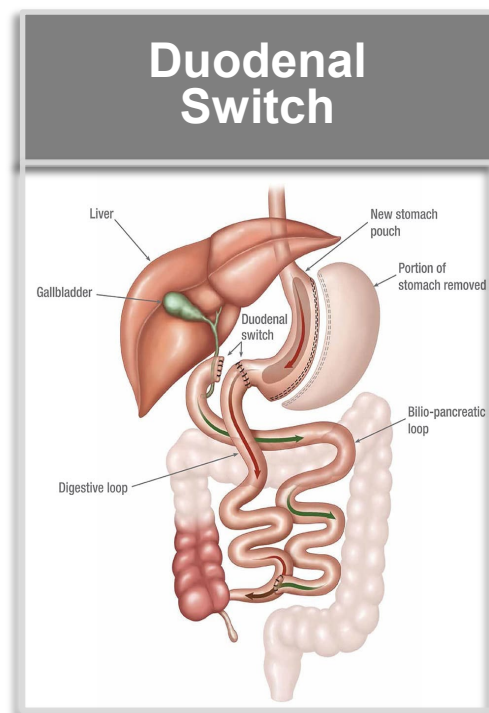
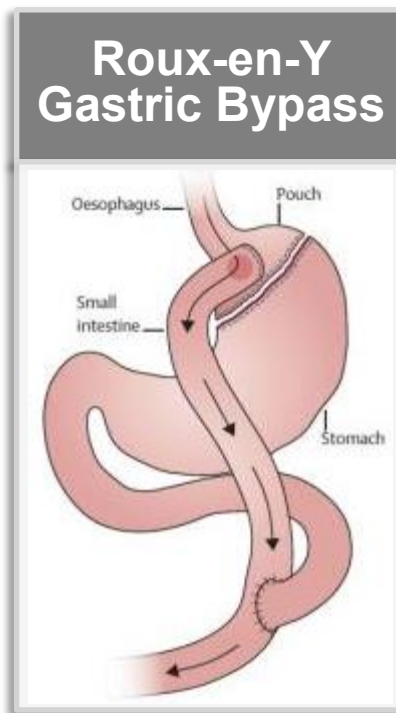
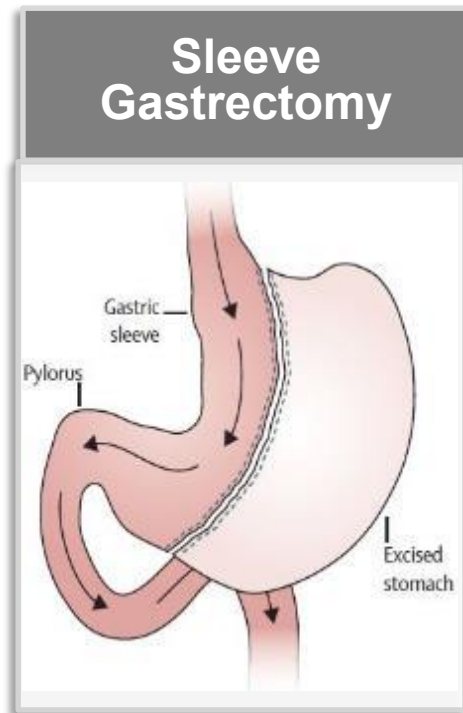
AACE/ACE Comprehensive Clinical Practice Guidelines for Medical Care of Patients with Obesity.

https://www.aace.com/sites/all/files/Obesity_Guidelines_Algorithm_slides_FINAL_2016.pdf

Resolution of Comorbidities



Most Common Bariatric Procedures



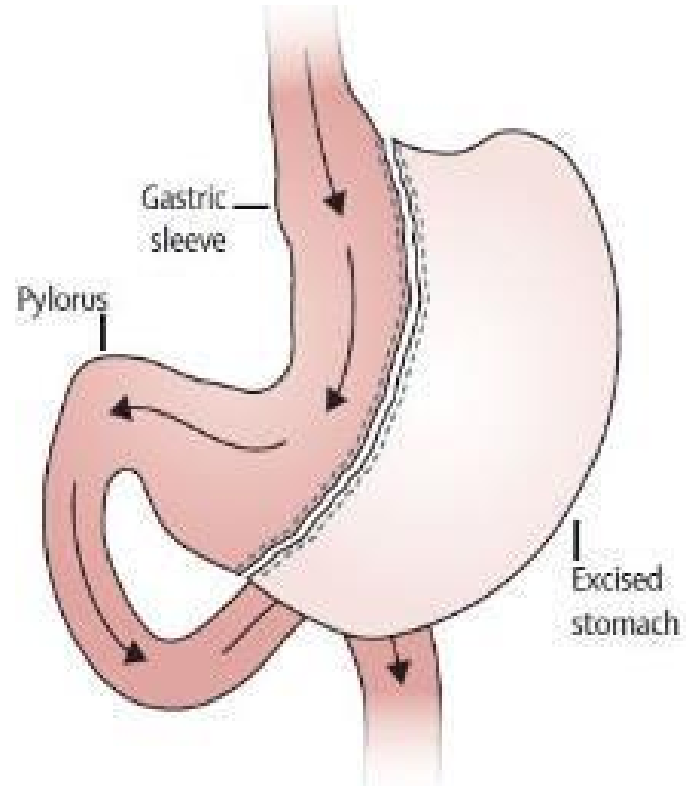
96% performed laparoscopically
Average length of stay – 1.2 days

Madsbad S, et al. *Lancet Diabetes Endocrinol.* 2014;2(2):152-64.

ASMBS. Estimate of Bariatric Surgery Numbers, 2011-2017. <http://asmbs.org/resources/estimate-of-bariatric-surgery-numbers>. Accessed Sept 17, 2018.

Sleeve Gastrectomy

- Bariatric procedure originally as part of BPDDS, now used as a first stage or stand alone if patient loses enough weight
- Remove part of stomach, creating a sleeve from esophagus to antrum
- A 36Fr bougie is used to size the sleeve



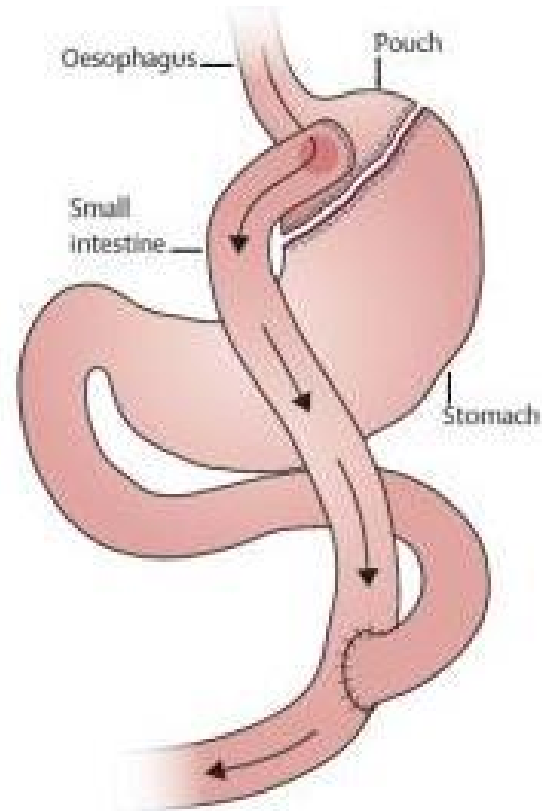
Roux-en-Y gastric bypass (RYGB)

↓ Ghrelin

↑ GLP-1

↑ PYY

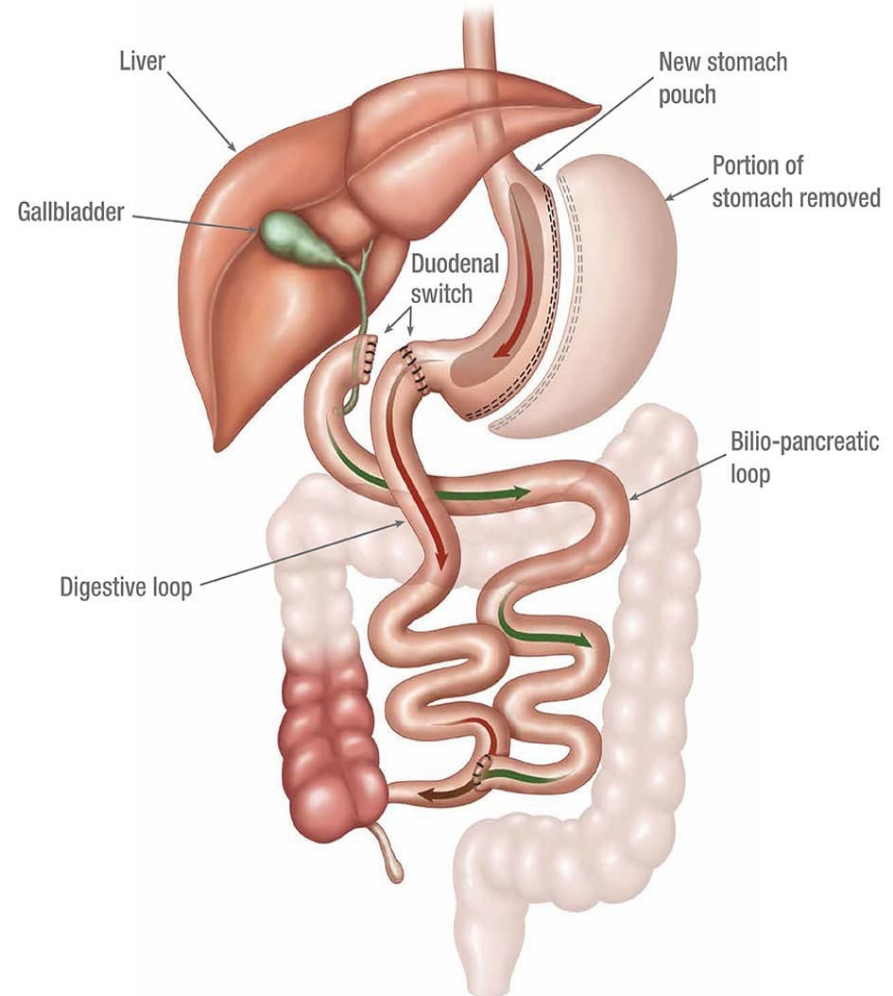
↑ Insulin



Excess Weight Loss is ~65-70%*

Duodenal Switch

- Combination operation
 - Sleeve
 - Biliopancreatic Diversion
 - Neurohormonal – decreased Ghrelin and increased GLP1
- Highest remission rate for type 2 diabetes
- ~85% Excess Weight Loss
- Significant risk of malabsorption of nutrients
- Usually performed on patients with a BMI > 60 kg/m²



Nutritional and Metabolic Deficiencies After Bariatric Surgery

- **Gastric restrictive procedures**
 - Iron deficiency 32%
 - Thiamine deficiency
- **Roux-en Y gastric bypass**
 - Calcium (50% to 60%) and vitamin D (20% to 60%)
 - Iron deficiency 15% to 50% (49% to 52% with BMI >50)
 - Decreased acidification and proximal small bowel absorption
 - B12 deficiency 10% to 70% 1 to 9 years after* (half-life 400 d)
 - Decreased liberation of B₁₂ from protein foods
 - Decreased intrinsic factor production
 - Decreased ileal absorption
 - Requirement = 2 mcg/day; stores = 3000 to 5000 mcg
 - Thiamin deficiency
 - Folic acid deficiency 10% to 35% due to low intake and ↓ gastric acid
 - Protein deficiency (<1% to 4.7%)¹

* Earlier if B12 deficiency occurs preoperatively.

1. Faintuch J, et al. *Obes Surg*. 2004;14(2):175-81.

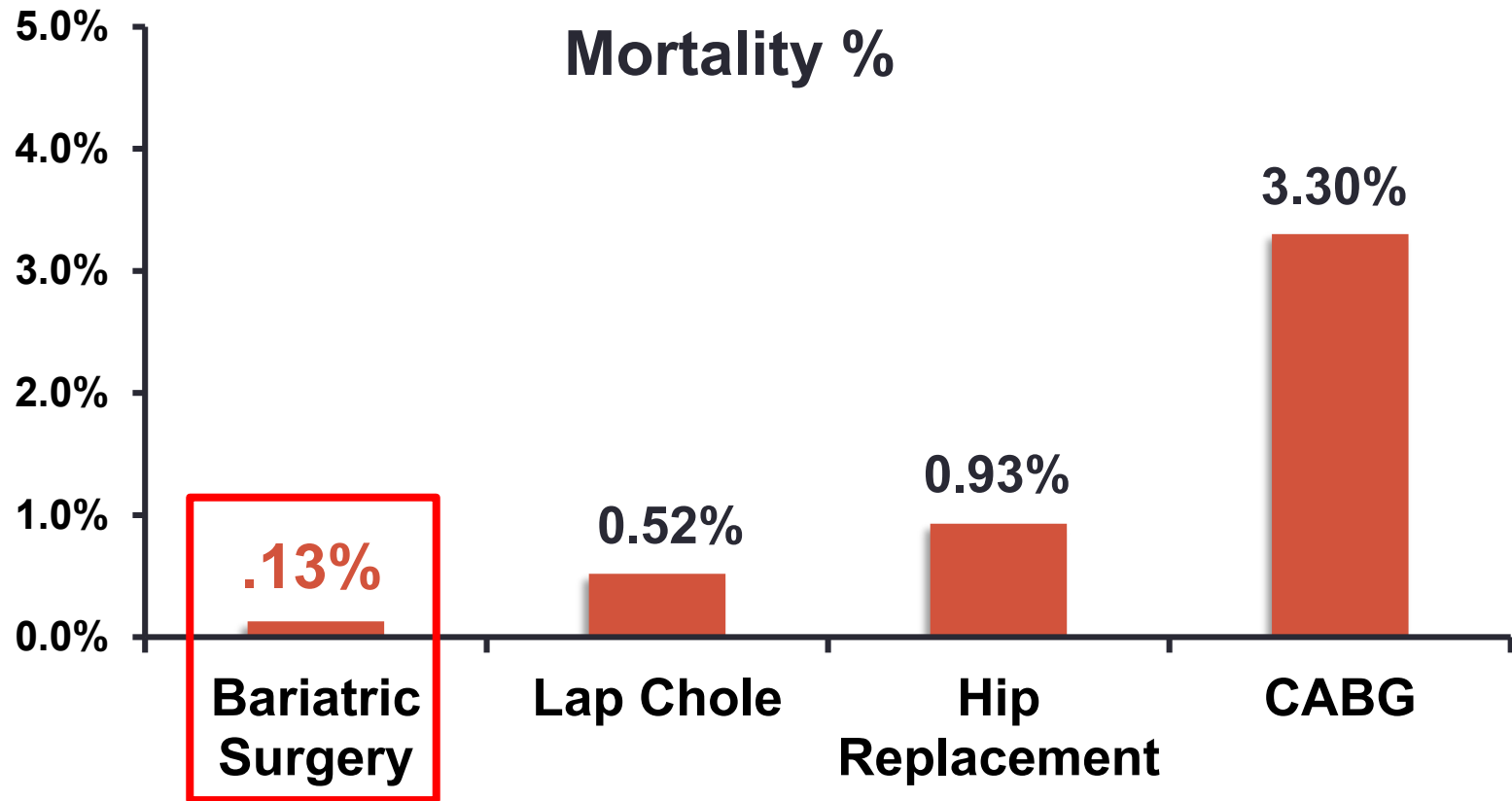
Routine Vitamin and Mineral Supplementation for RYGB Patients

Supplement	Dosage
Multivitamin	1 to 2 daily
Calcium citrate with vitamin D	1200 to 2000 mg/day + 3000 U/day vitamin D
Elemental iron	40 to 65 mg/day
Vitamin B12	5000 µg/day orally <i>OR</i> 1000 µg/month IM <i>OR</i> 500 µg weekly intranasal

RYGB = Roux-en-Y gastric bypass

Bariatric Surgery - Low Mortality

0.13% mortality, n=5,365 bariatric surgery patients, 1998 and June 2006



When performed at a bariatric surgery center of excellence.

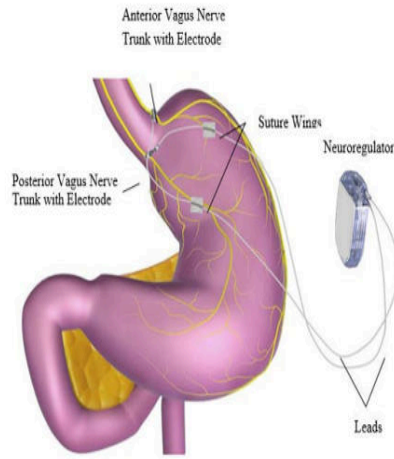
CABG = coronary artery bypass grafting; lap chole = laparoscopic cholecystectomy.

Ballantyne GH, et al. *Obes Surg*. 2008;18(6):660-7.

ASMBS. Bariatric Surgery Misconceptions. <http://asmbs.org/patients/bariatric-surgery-misconceptions>.

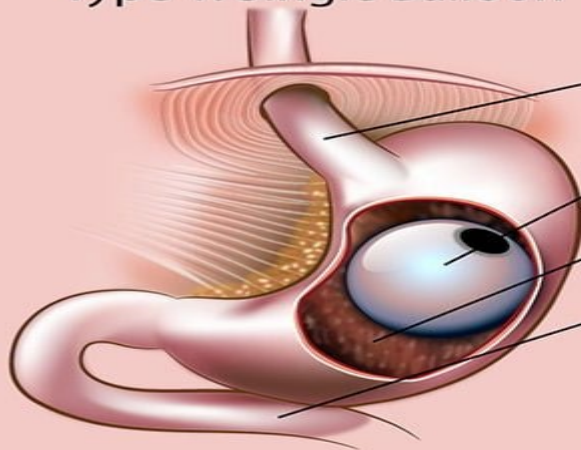
Devices

Devices

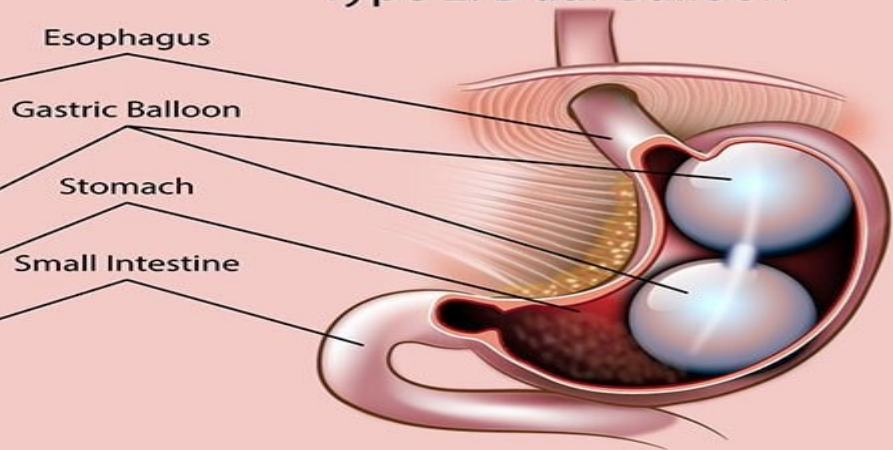


Intragastric Balloon: 2 Types

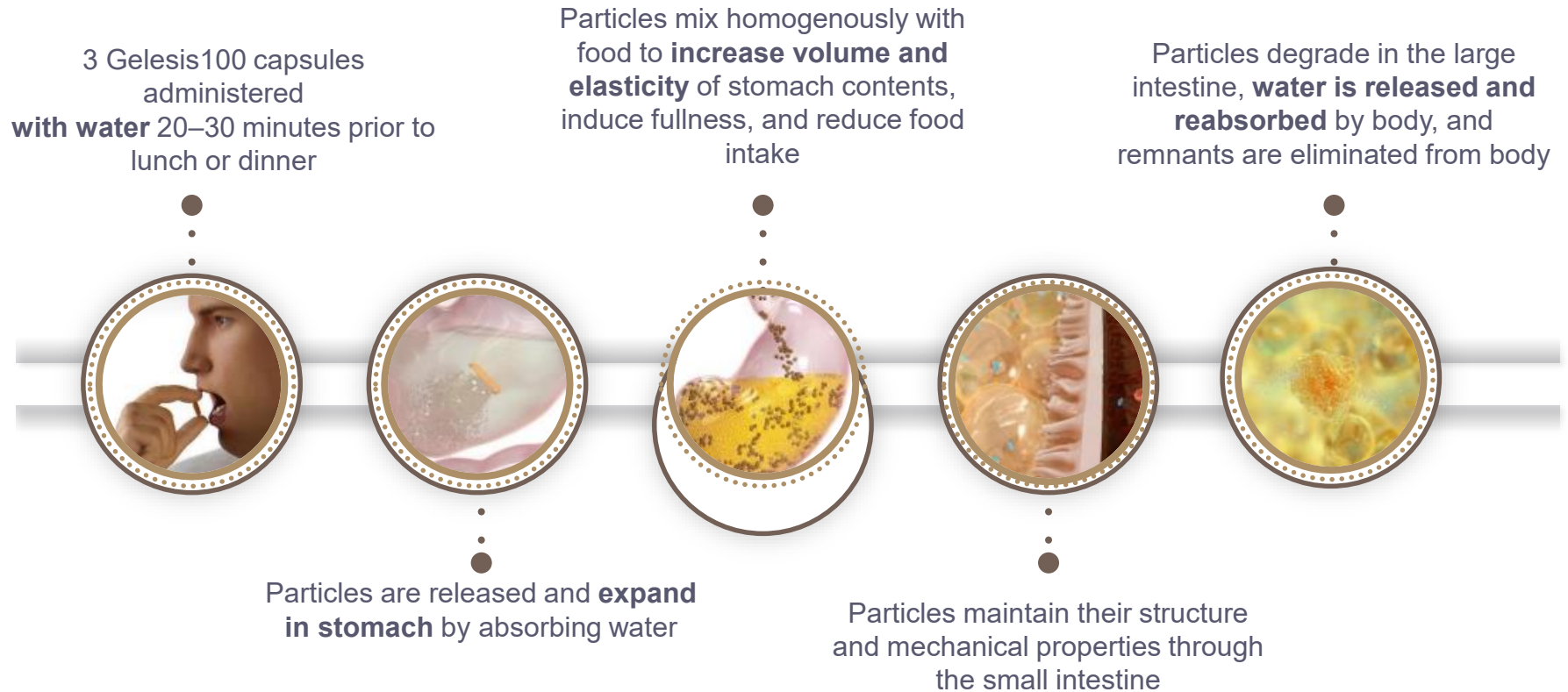
Type 1: Single Balloon



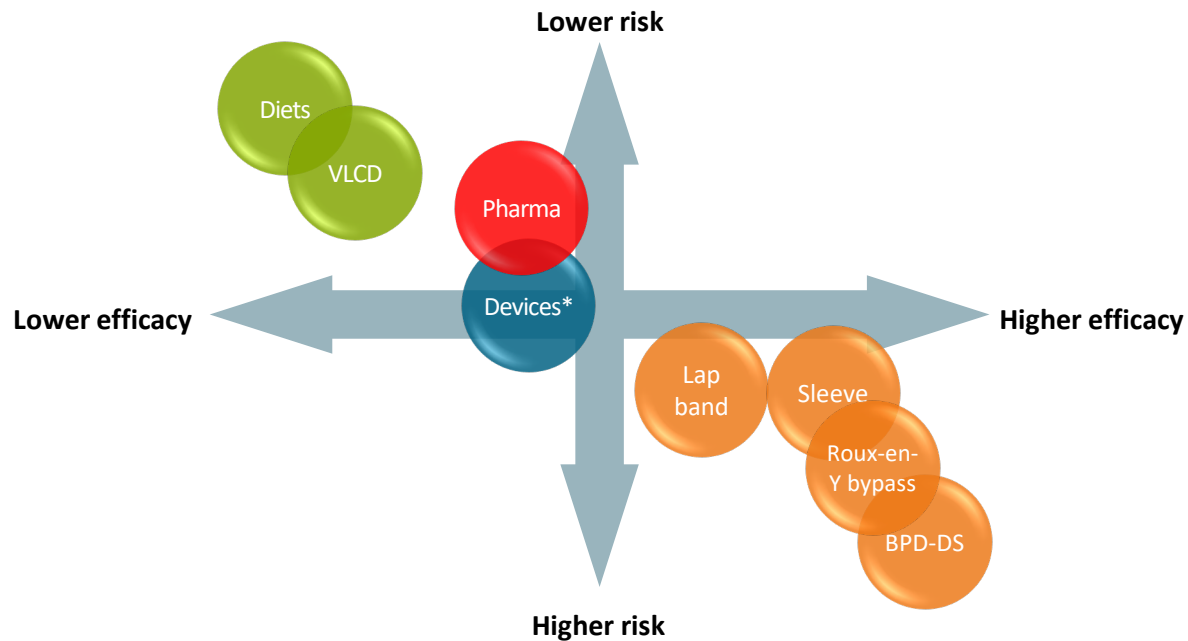
Type 2: Dual-Balloon



Gelesis100 Hydrogel in the Gastrointestinal Tract



Currently Available Treatments: Risks and Efficacy



*Gastric sleeve and vagal stimulator under phase 3 study

•SVLCD: very low calorie diet

Jensen MD, Ryan DH, et al. *J Am Coll Cardiol*. 2013;pii:S0735-1097(13)06030-0. <http://formularyjournal.modernmedicine.com/print/368664>. Accessed May 12, 2014.

Final Thoughts.....

- Diet and Exercise remains the cornerstone of any treatment
- Continuum of care
 - Pharmacotherapy
 - Devices
 - Bariatric surgery
- “GPS MODEL OF CARE”
- Work with your provider to side best option(s) for you!
- More innovation is happening – “Exciting time for treatment”