



Comprehensive Management of Overweight/Obesity

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Disclosures

Dr. Yancy has the following disclosures:

- FoodMinds (consultant)



What if there was a treatment for our patients that:

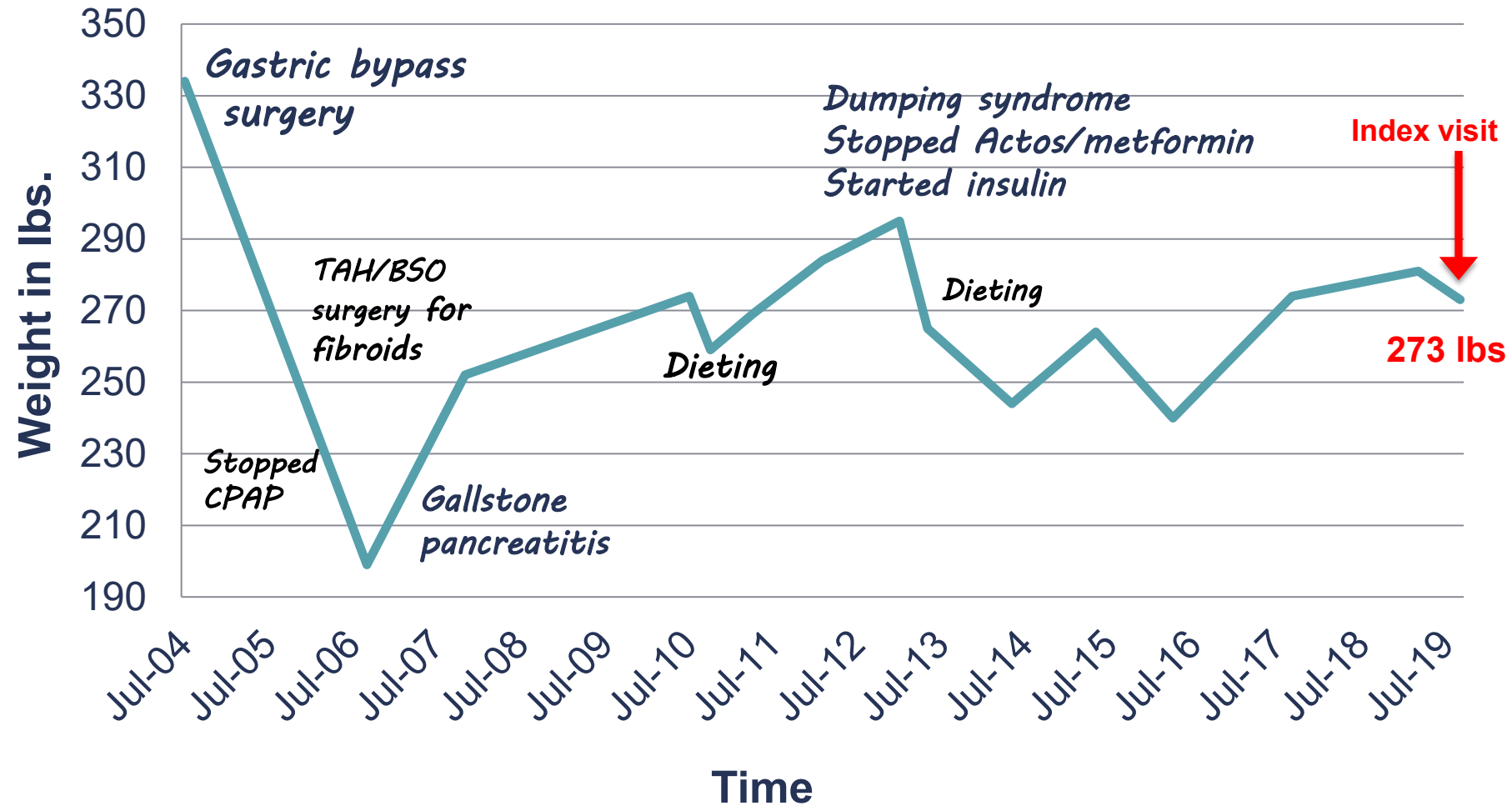
1. Reduced HbA1c by 0.5-1.6% while diabetes medications were reduced or eliminated
2. Reduced blood pressure
3. Lowered triglycerides and raised HDL cholesterol
4. Was renal protective – decreasing albuminuria
5. Improved sleep apnea
6. Decreased pain and improved mobility
7. Reduced urinary incontinence
8. Improved quality of life

These are the effects of weight loss!

Look AHEAD study. Phase 3 trials for weight loss meds.

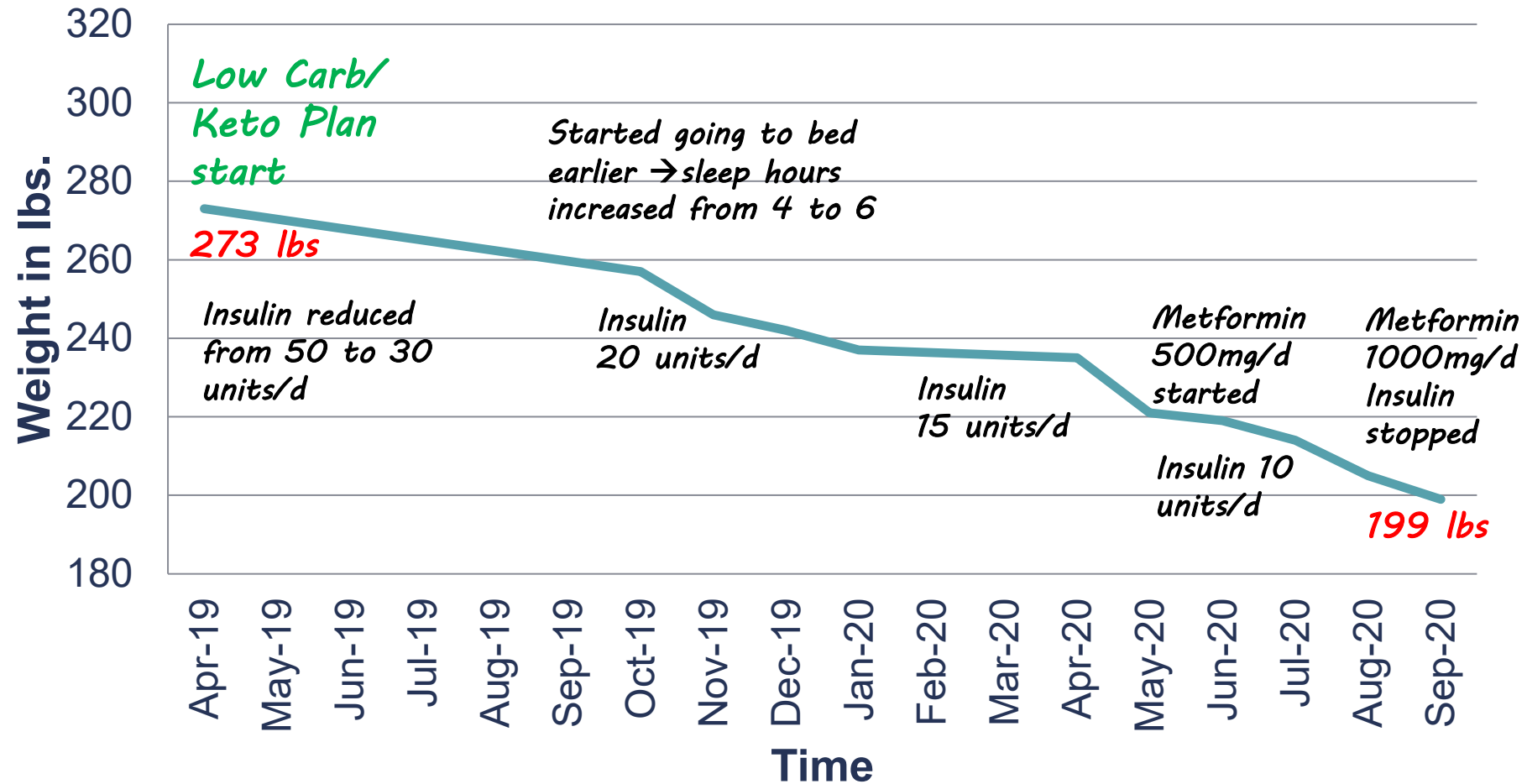


Weight history graph before





Weight history graph after



Walking: 1.5 mi 2x/wk
 A1c: 10.9%

5 mi/d on incline
 6.6%

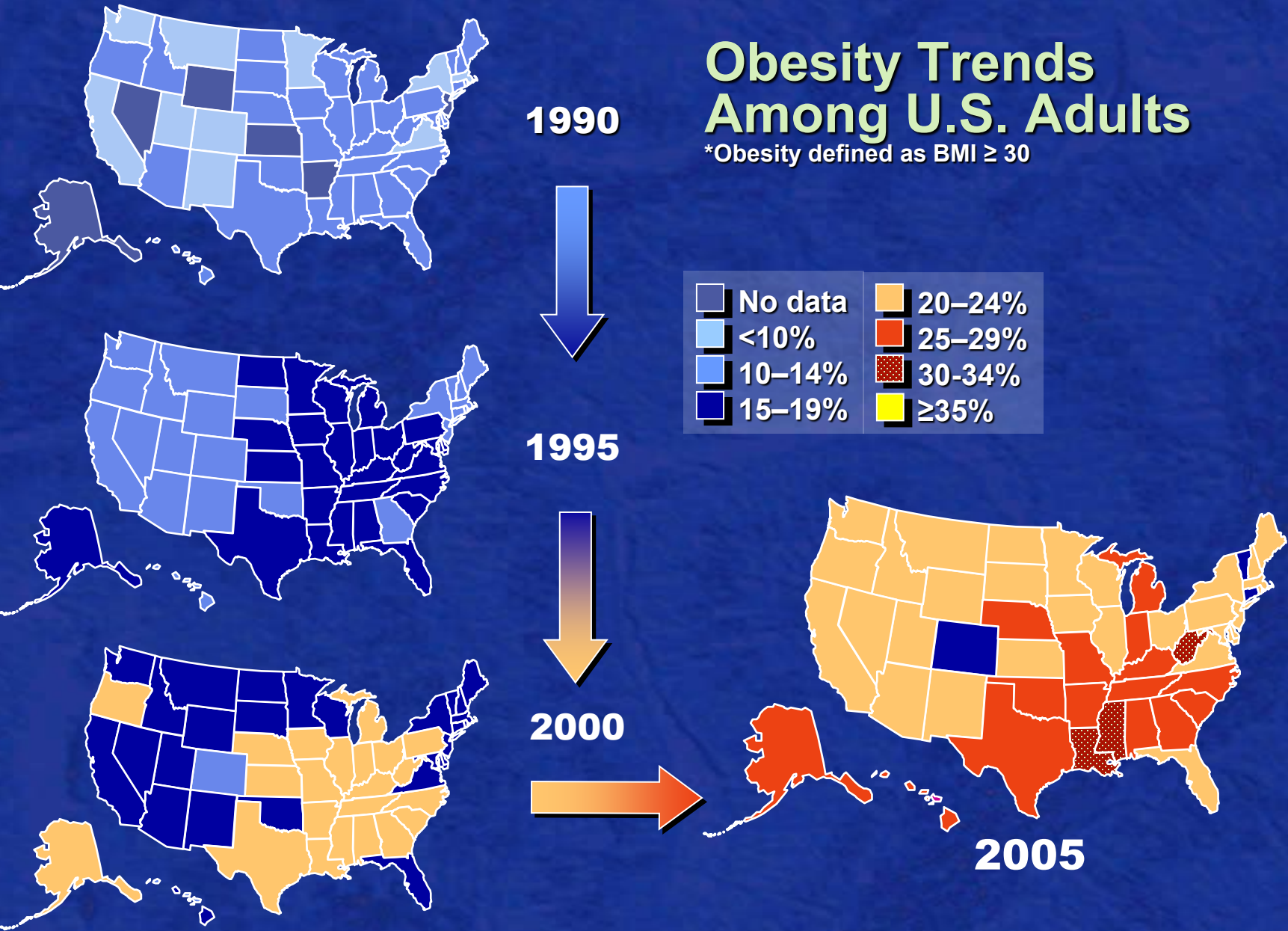


Comprehensive Management of Overweight/Obesity

- How to Assess and Manage Obesity
- Why and How to Treat Obesity with a Low Carbohydrate/Keto Diet
- How to Treat Obesity with Weight Loss Medications and Surgery

Obesity Trends Among U.S. Adults

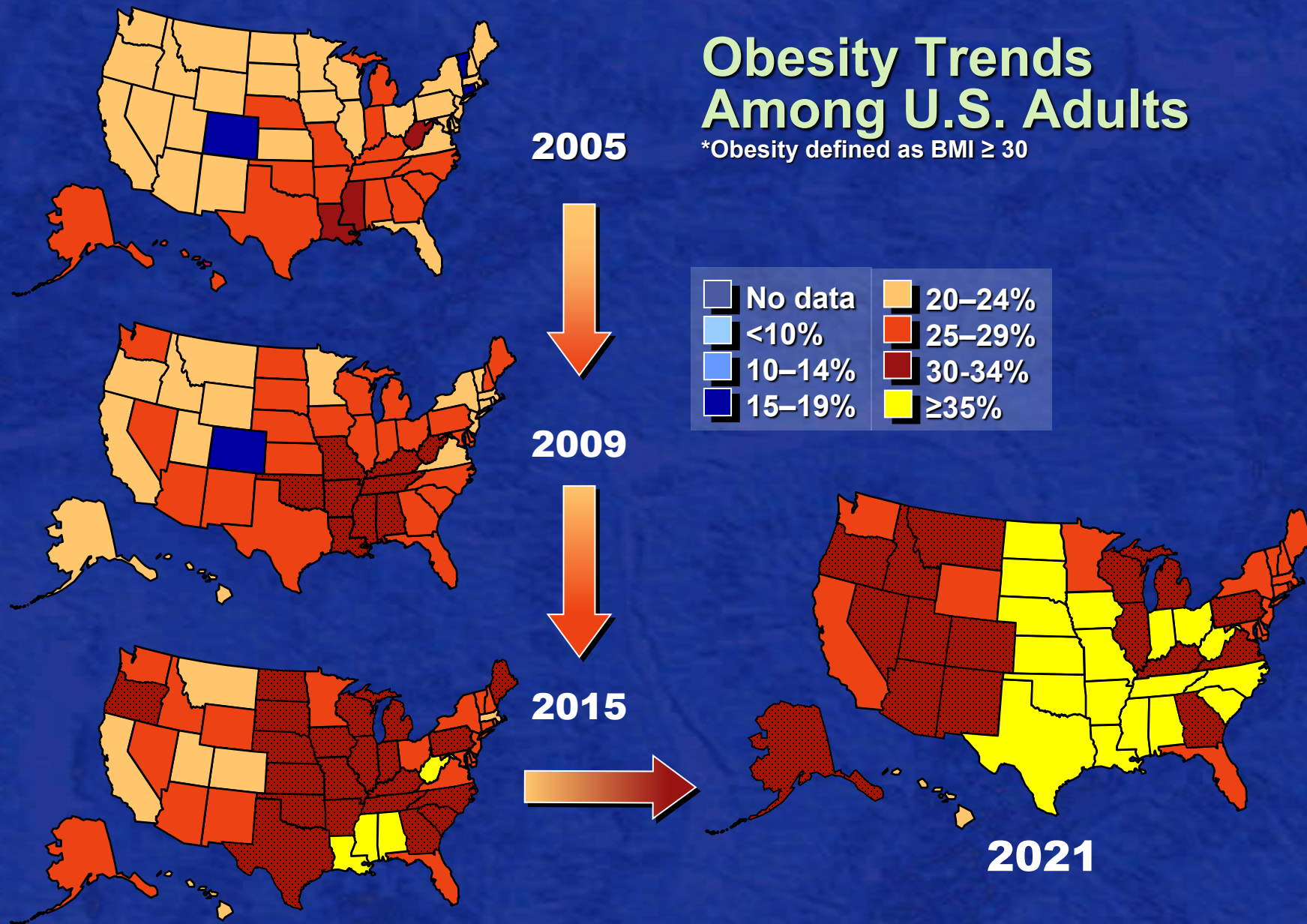
*Obesity defined as BMI ≥ 30



BRFSS, CDC; Mokdad AH, JAMA, 1999, 2001, 2003; MMWR 2006:55:36

Obesity Trends Among U.S. Adults

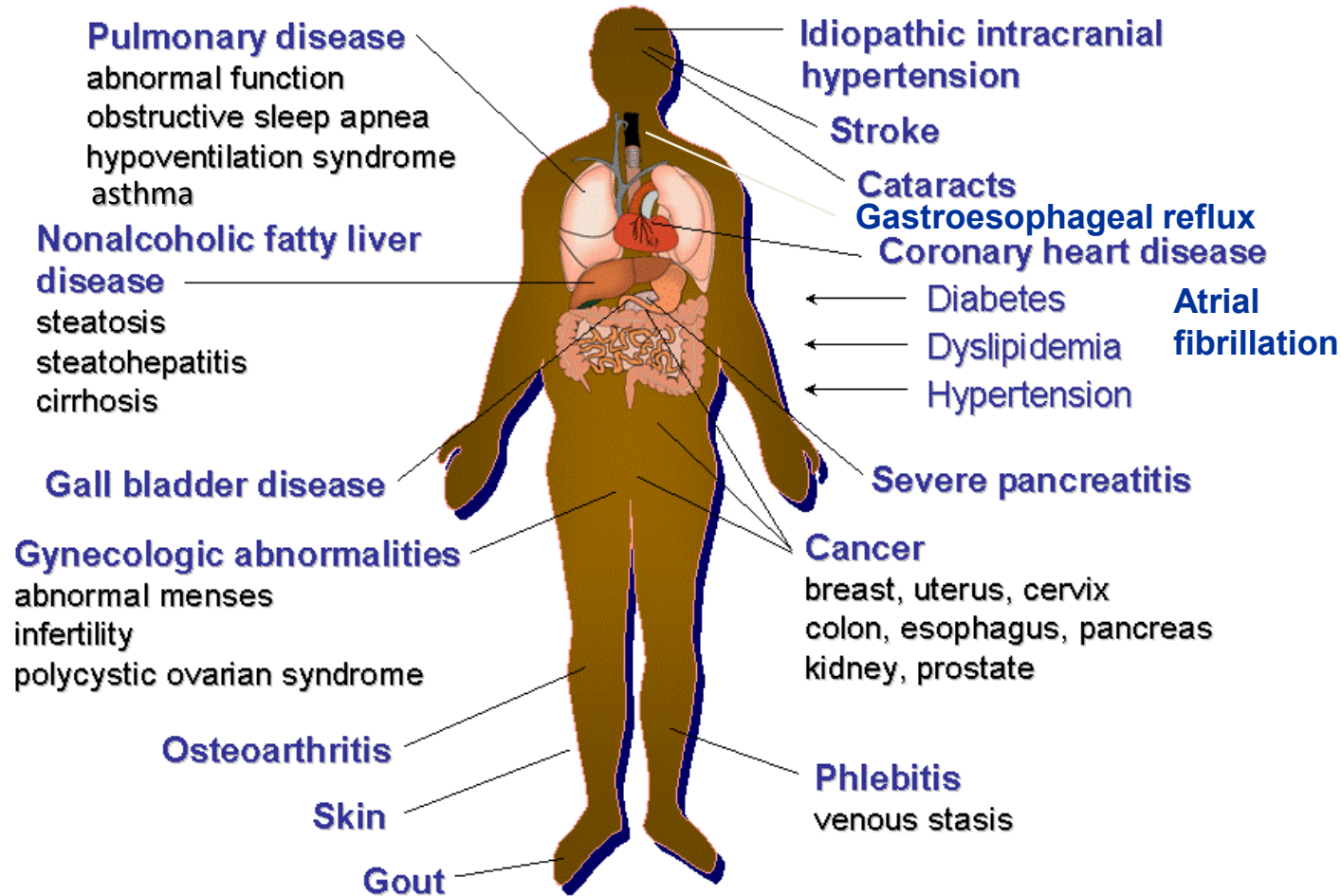
*Obesity defined as BMI ≥ 30



BRFSS, CDC; Mokdad AH, JAMA, 1999, 2001, 2003; MMWR 2006:55:36



Medical Complications of Obesity





Recent Developments Regarding Obesity

- American Board of Obesity Medicine established in 2011
- Payment for weight management services increasingly covered by payers, including...
 - **Medicare coverage of intensive behavioral therapy (IBT) for obesity in primary care in 2012**
 - **Medicare coverage of Diabetes Prevention Program in YMCAs in 2016**
- AMA recognized obesity as a disease in 2013
- 5 new weight loss medications approved by FDA since 2012 (**none between 1999-2012!**)
- Less invasive procedures / devices entering clinical care



What to Assess?

HPI:

- Weight history, highest/lowest adult weight
- Contributing factors to weight gain
- Previous strategies/therapies and results
- Eating habits and disorders
- Physical activity

ROS:

- Daytime somnolence, snoring, gasping/stopping breathing while asleep, AM headaches → **sleep apnea**
- Polydipsia, polyuria → **T2DM**
- Irregular menses, infertility → **PCOS**
- Chest pain, dyspnea on exertion, joint pain, weakness, falls → **barriers to activity**



What to Assess?

Measurements:

- Weight
- Body mass index (BMI)
- Waist and neck circumference
 - Waist is a better marker of risk if BMI 25 - 30 kg/m²
 - Cutoffs: Men >40 in. and Women >35 in.
- Bioelectrical impedance (BIA)

Physical exam:

- Moon facies, buffalo hump, truncal obesity, purple striae → **Cushing's**
- Skin tags, acanthosis nigricans, intertrigonal candida → **insulin resistance, hyperglycemia**
- Facial hair (women) → **PCOS or Cushing's**
- Leg swelling → **Venous stasis/edema, lymphedema or lipedema**
- Mobility limitations → **barrier to activity**



24-hour Dietary Recall

- *Breakfast*
 - *Smoothie with banana, frozen berries, low-fat vanilla yogurt, 1% milk*
 - *Special K breakfast bar*
 - *OJ and Latte*
- *Lunch*
 - *Chick fil A grilled chicken sandwich with mac-n-cheese*
 - *Diet Coke*
- *Dinner*
 - *Spaghetti with marinara sauce, green salad, roll*
 - *Iced tea with Splenda/sugar*
- *Snacks*
 - *Sun Chips or popcorn*



Screening for Secondary Causes of Obesity

- Hypothyroidism – TSH
- Depression - Depressed mood, anhedonia
- Medications
- Eating disorders
 - Binge eating
 - Consume large amounts in short period with feeling of loss of control and subsequent guilt
 - No compensatory behaviors (emesis, laxatives, diuretics)
 - Night-eating
 - More than half of daily food intake at evening/night
 - Morning/day anorexia



Assess Possible Secondary Causes of Obesity

- Cushing's syndrome
 - Weakness, easy bruising, irregular menses, ED
 - High BP, truncal obesity, moon facies, buffalo hump, purple striae, acne, hirsutism
 - **Screening: 24-hr urinary cortisol/creatinine, low-dose dexamethasone suppression test or late night salivary cortisol**
- Polycystic ovary syndrome
 - Hirsutism, acne, irregular menses (late-onset, erratic or heavy/frequent), infertility
 - **Screening: 8 AM total or free testosterone**

Medications Related to Weight Change



Medication Classes	Marked Weight Gain	Mild-Moderate Weight Gain	No Weight Change or Weight Loss (↓)
Antidepressants	Clomipramine Doxepin Imipramine Amitriptyline	Desipramine Mirtazapine Nortriptyline Paroxetine Phenelzine Protriptyline	Bupropion (↓) Fluvoxamine Citalopram Nefazodone Desvenlafaxine Sertraline Duloxetine Venlafaxine Escitalopram Vilazodone Fluoxetine (↓) Vortioxetine
Mood stabilizers/ anticonvulsants	Valproate Gabapentin	Carbamazepine Lithium	Lamotrigine Topiramate (↓) Zonisamide (↓)
Antipsychotics	Chlorpromazine Clozapine Olanzapine Perphenazine Thioridazine Trifluoperazine	Aripiprazole Molindone Flupentixol Quetiapine Fluphenazine Haloperidol	Pimozide Risperidone Cariprazine Lurasidone Ziprasidone
Antihistamines	Cyproheptadine? Diphenhydramine?	–	Steroid inhalers? Decongestants

Domecq JP, J Clin Endocrinol Metab, 2015; Apovian CM, J Clin Endocrinol Metab, 2015.

Medications Related to Weight Change



Medication Classes	Marked Weight Gain	Mild-Moderate Weight Gain	No Weight Change or Weight Loss (↓)
Antihypertensives	Propranolol Terazosin	Doxazosin Prazosin	ACE Inhibitors Calcium channel blockers
Anti-diabetics	Insulin Sulfonylureas Thiazolidinediones Repaglinide Nateglinide	Sitagliptin	Acarbose ↓ Liraglutide ↓ Canagliflozin ↓ Miglitol ↓ Dapagliflozin ↓ Pramlintide ↓ Exenatide ↓ Nateglinide Metformin ↓ Semaglutide ↓ Tirzepatide ↓
Contraceptives	-	Depomedroxy- progesterone acetate (DMPA) Letrozole Megesterol Tamoxifen	Other contraceptives
Corticosteroids	All oral steroids	-	-
Bladder stabilizers	-	Fesoterodine	-

Domecq JP, J Clin Endocrinol Metab, 2015; Apovian CM, J Clin Endocrinol Metab, 2015.



Obesity Algorithm[®]

2023

Important Principles For The Effective Treatment Of Patients With Obesity.



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OMA Obesity Algorithm VIII – January 2023

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Primary Care Tools for Weight Management

- **5 A's**
 - Ask permission to discuss weight
 - Assess BMI, waist; drivers; complications
 - Advise on health risks, benefits of wt loss, tx options
 - Agree on behavior change goals, treatments
 - Assist by addressing barriers; offering resources; f/u
- **SMART Behavioral Goals**
 - Specific
 - Measurable
 - Attainable
 - Relevant
 - Time-bound

Sherson EA, Family Practice, 2014.



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Low Carb / High Fat Diet Rationale: The Carbohydrate-Insulin Model

- Dietary carbohydrate (sugar or starch) raises blood glucose and insulin
- A carbohydrate restricted (high fat) diet reduces the diet contribution to blood glucose, which then lowers insulin levels
- **Insulin is a potent stimulator of lipogenesis (fat storage) and a potent inhibitor of lipolysis (fat burning)**
- Lowering insulin levels leads to burning of stored body fat, raising blood ketones and lowering body weight



Low Carbohydrate Ketogenic Eating Plan

- Initially, < 20 g carbohydrate/day
- Calories **not restricted**
- Carbohydrate intake slowly increased as weight goal approached
- Daily multivitamin, copious liquids, broth





Meta-Analysis: Low Carb vs Low Fat

Variable	No. of Trials	Net Difference Low Carb – Low Fat	95% CI
Weight, kg	22	-1.0	-2.2, 0.2
Systolic BP, mmHg	18	-1.0	-3.5, 1.5
Diastolic BP, mmHg	18	-0.7	-1.6, 0.2
TG, mg/dL	20	-14.0*	-19.4, -8.7
HDL-C, mg/dL	19	3.3*	1.9, 4.7
LDL-C, mg/dL	19	3.7*	1.0, 6.4

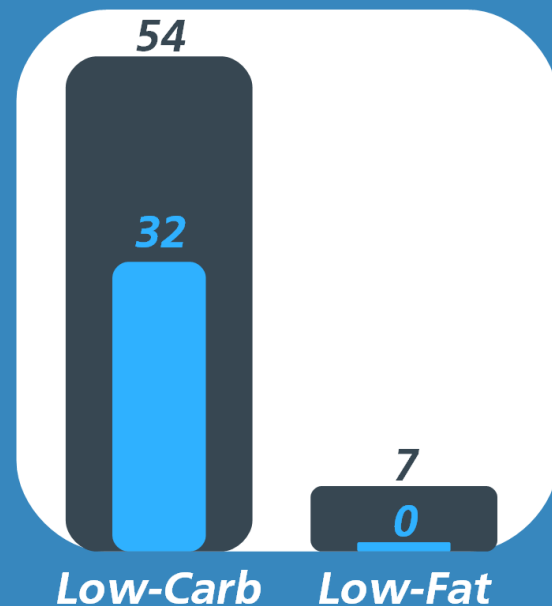
* $p \leq 0.05$ for net change.

Hu T, Am J Epidemiol, 2012.



RCTs Comparing LC vs LF Diets

Weight Loss Results From Published Randomised Controlled Trials (RCTs) Between Low-Carb & Low-Fat Diets



*63 RCTs In Total
(2 Are Equal)*



Greater Weight Loss

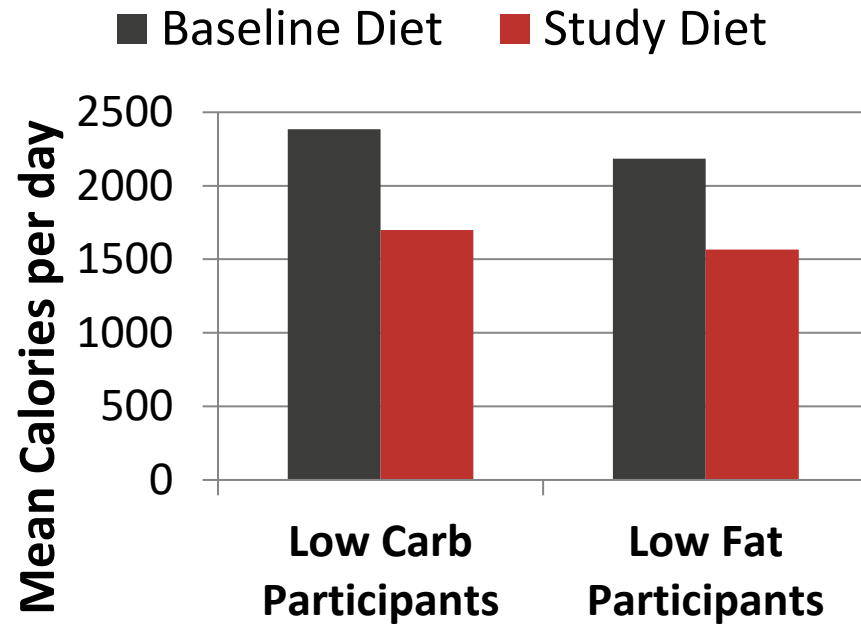


Significantly Greater Weight Loss Between Groups

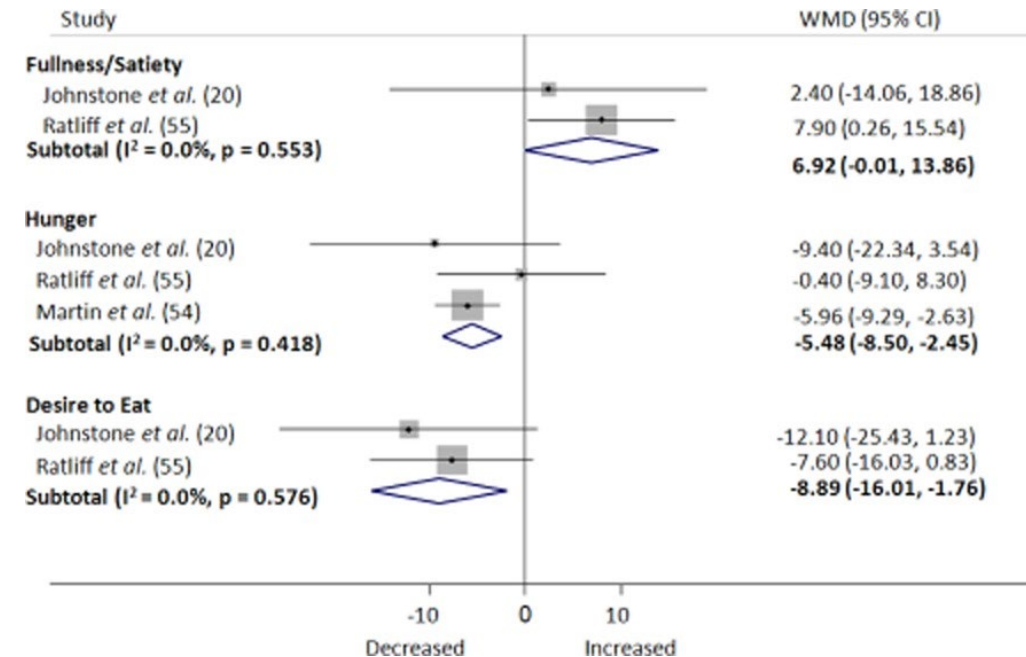
*Public Health Collaboration. RCT search up to November 2019.
Find out more at: www.PHCuk.org/RCTs. Accessed 5/14/20.*



How Weight Loss Occurs: Calories are Reduced because Hunger is Less



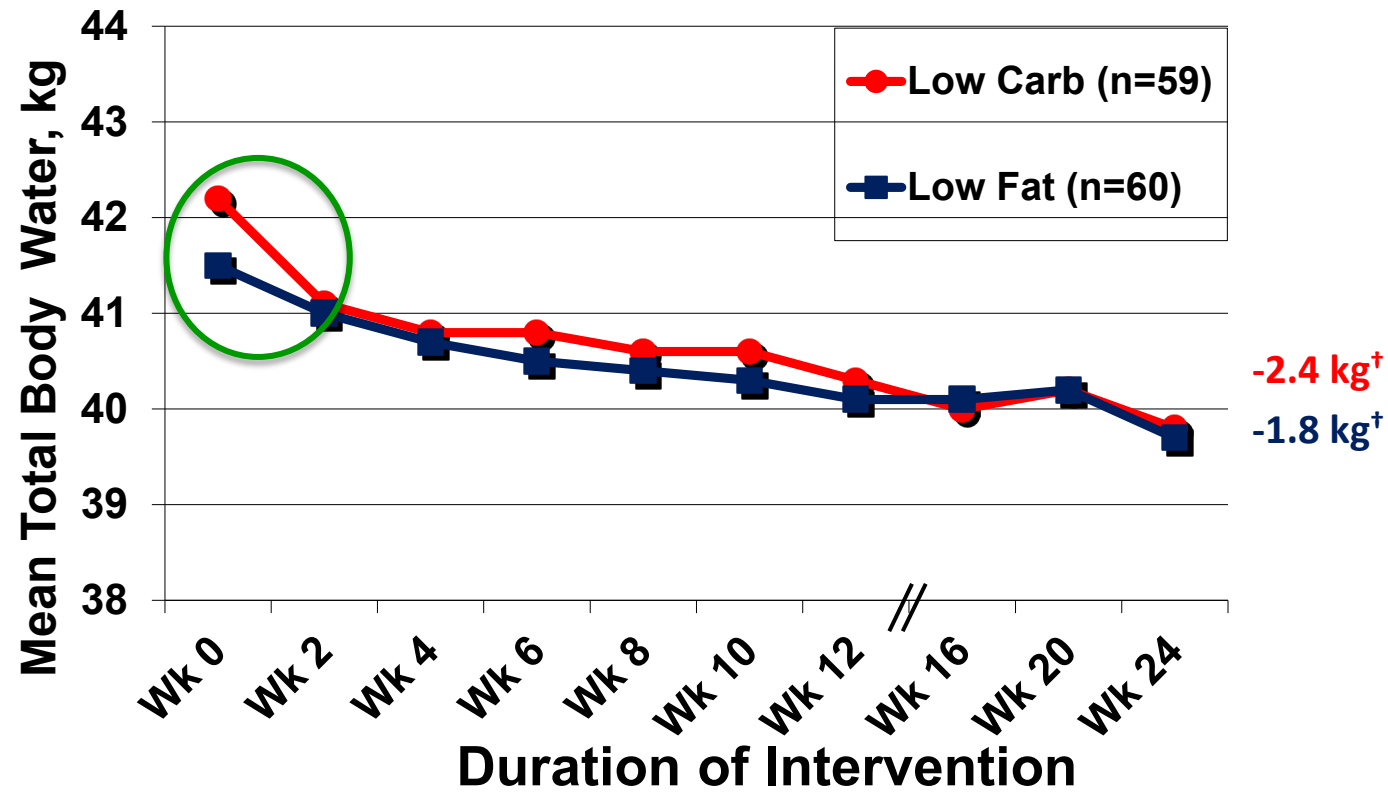
Yancy WS, Arch Intern Med, 2010.



Gibson AA, Obes Rev, 2015.



How Weight Loss Occurs: A Little Bit of Water Loss

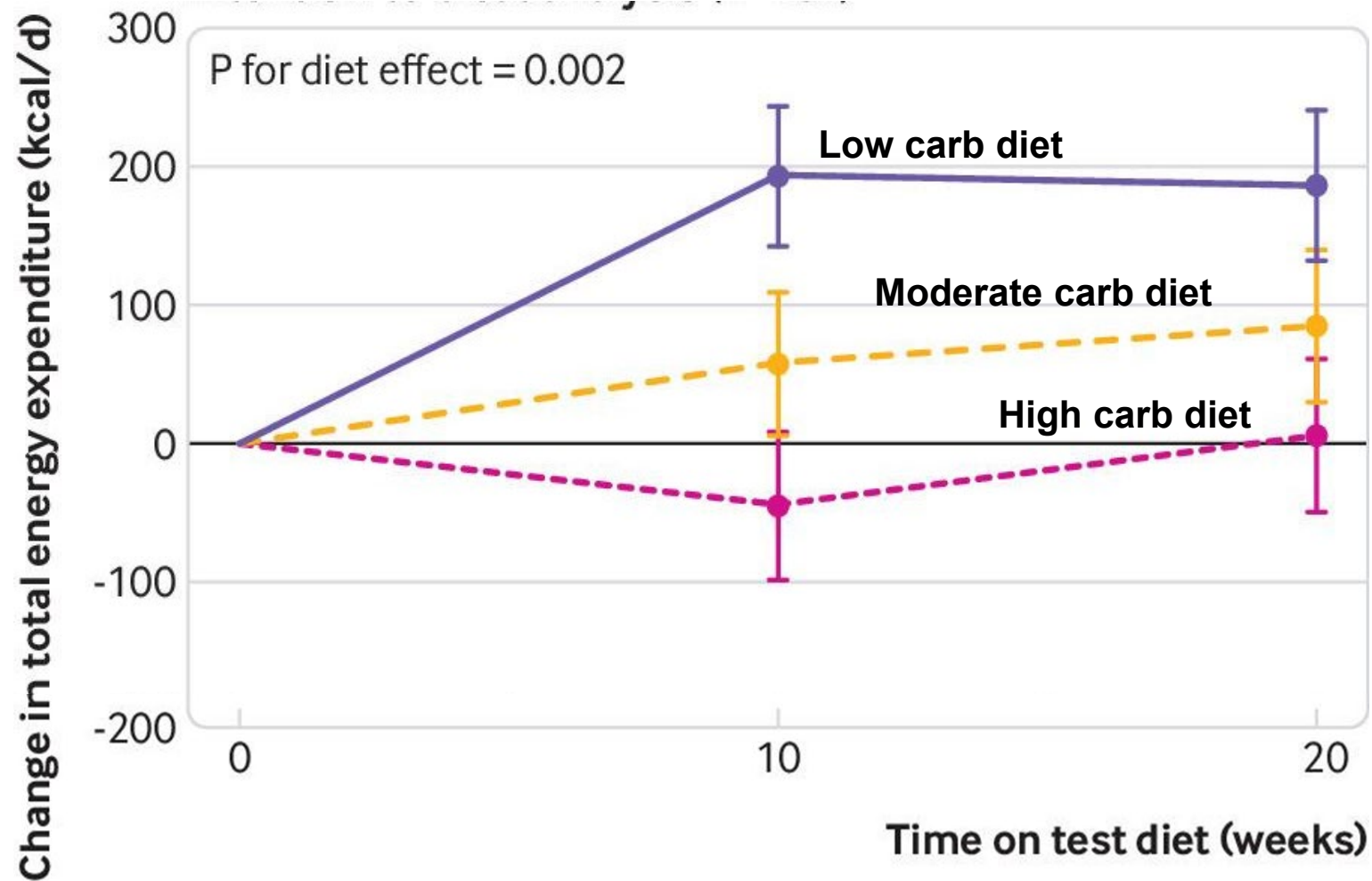


† p = 0.05, for comparison between diet groups.

Yancy WS, *Ann Intern Med*, 2004.



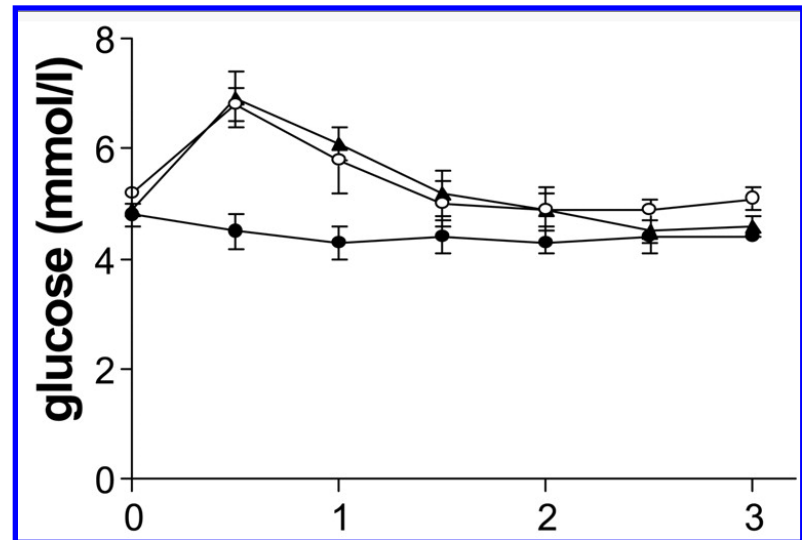
How Weight Loss Occurs: What About Metabolism?



Ebbeling CB, BMJ, 2018.



Glucose and Insulin Response to 300 kcal Meal After 10 days on Diet

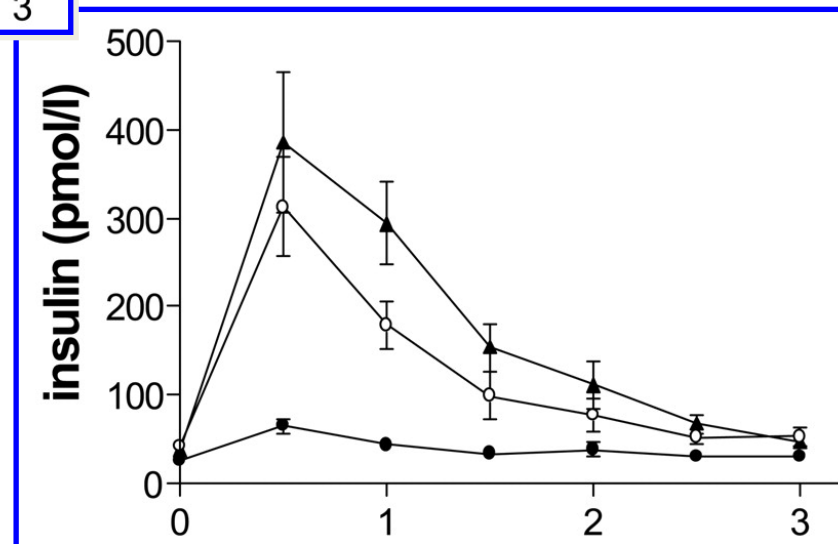


▲ High-carb diet
○ Intermediate-carb diet
● Low-carb diet
(n = 6)

*Glucose AUC lowest for low-carb diet (p = .001).

*Insulin AUC different for each diet (p = .001)

Bisschop, J Clin Endocrinol Metab, 2003.





How to Avoid Side Effects

- Maintain hydration
 - Drink adequate no-calorie fluids
 - Reduce diuretics proactively
- Adequate sodium intake
 - Broth/bouillon is an efficient source
 - **Use caution if CHF, uncontrolled BP, edema**
- Eat adequate vegetables
- Reduce antiglycemic agents proactively
 - Insulin and sulfonylureas to prevent hypoglycemia
 - SGLT2 inhibitors to prevent euglycemic DKA



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Weight Loss Medications: General Principles

- Eligibility
 - BMI >30 kg/m² OR
 - BMI 27-30 kg/m² with obesity-related comorbidity
- Most effective when paired with lifestyle change
- If 4-5% weight loss not achieved in initial 3-4 months, long-term response is unlikely so medication should be stopped
- Coverage by health insurance is variable but improving
- Weight regain occurs on average after stopping medication
 - Parallels effects of medications for HTN, DM, hyperlipidemia

FDA-Approved Weight Loss Rx



Generic name	Phentermine
Trade name (Manufacturer)	Adipex-P , Suprenza (multiple)
How it works	Amphetamine-like; suppresses appetite
Available doses	15, 30, 37.5 mg
Frequency	Once a day (before breakfast or 1-2 hours after)
Cost for 30 day GoodRx.com	\$15
Weight loss (above placebo)	17 lbs
Cautions	See Contraindications
Contraindications	-Pregnancy -Heart disease/stroke -Uncontrolled high blood pressure -Pulmonary hypertension -Overactive thyroid -Glaucoma -Drug or alcohol abuse -MAO inhibitors past 14 days
Drug interactions	
Possible side effects	Increased heart rate and blood pressure, nervousness, insomnia, tremors, dry mouth , constipation
Notes	-Schedule IV controlled substance -Approved for only up to 12-16 weeks -Decrease high doses gradually before stopping



Generic name	Phentermine/Topiramate	
Trade name (Manufacturer)	Qsymia (Vivus, 2012)	
How it works	See phentermine; uncertain for topiramate	
Available doses	7.5/45 mg, 15/92 mg (3.75/23 mg, 11.25/69 mg for titration)	
Frequency	Once a day	
Cost for 30 day GoodRx.com	\$210	
Weight loss (above placebo)	15 lbs (7.5/45 mg)	19-23.5 lbs (15/92 mg)
Cautions	-May cause birth defects → Risk Evaluation and Mitigation Strategy: Pregnancy test monthly	
Contraindications	-Pregnancy -Overactive thyroid	-Glaucoma -MAO inhibitors past 14 days
Drug interactions	-Lowers blood K+ with thiazide; Topiramate level decreased by phenytoin or carbamazepine; Increases alcohol, sedatives' effect	
Possible side effects	Nervousness, insomnia, dry mouth, constipation, numbness/tingling, abnormal taste, decreased concentration/ memory , dizziness	
Notes	-Schedule IV controlled substance -Take 3.75/23 mg x 14d, then 7.5/46 mg; if <3% weight loss at 12 wks, increase to 11.25/69 mg for 14d, then 15/92 mg -7.5/46 mg max if mod. kidney/liver disease -Seizures can occur if stopped abruptly!	



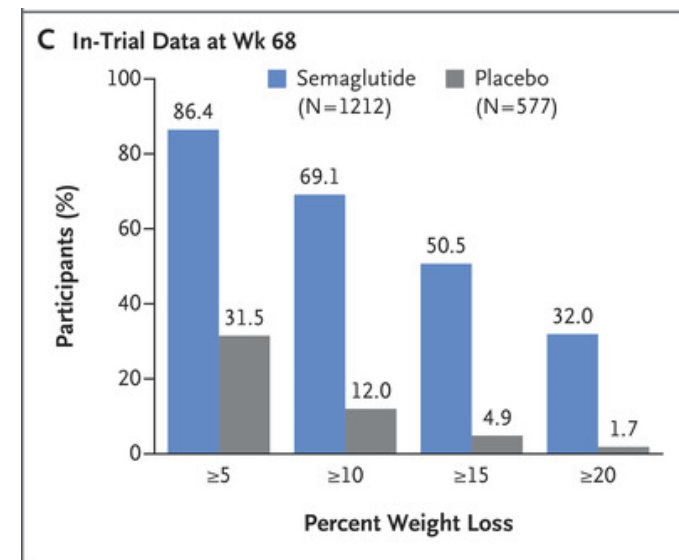
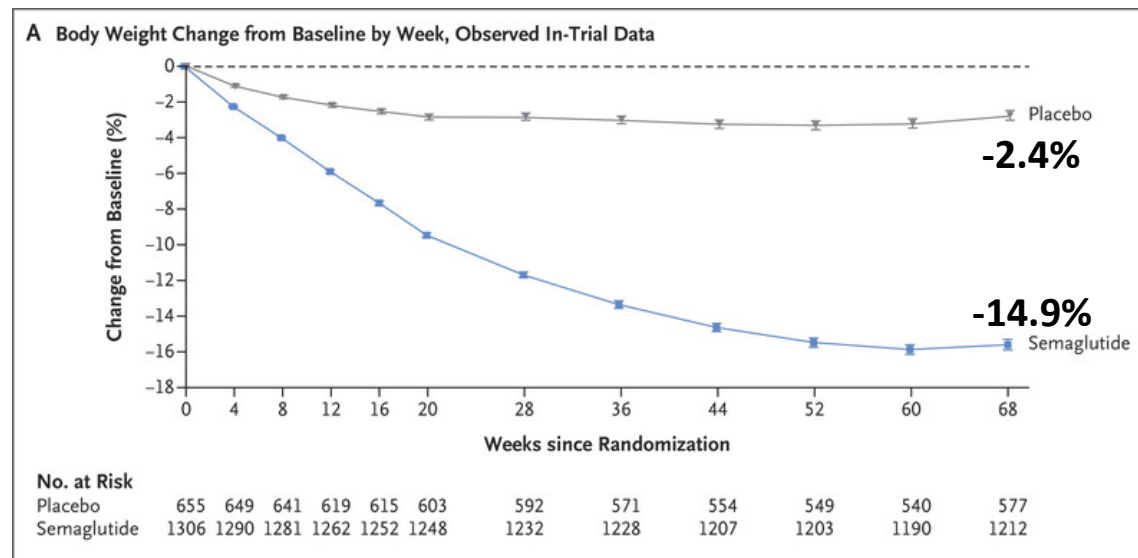


Generic name	Liraglutide	Semaglutide	Tirzepatide
Trade name (Mfr)	Saxenda (Novo Nordisk) (Victoza for DM)	Wegovy (Novo Nordisk) (Ozempic for DM)	Mounjaro (Lilly)
How it works	GLP-1 agonist		GIP/GLP-1 agonist
Available doses	0.6 - 3.0mg	0.25 - 2.4mg	2.5 - 15mg
Frequency	Once daily, SC inj.	Once weekly, SC inj.	Once weekly, SC inj.
Cost for 30 day	\$1400		\$900
Weight loss (above placebo)	12-13 lbs	32 lbs	50 lbs.
Cautions	May cause gallbladder attack or pancreatitis May increase risk of thyroid cancer Semaglutide may increase risk of DM retinopathy		
Contraindications	History (or family history) of medullary thyroid carcinoma or multiple endocrine neoplasia (MEN) type 2		
Drug interactions	Insulin, hypoglycemic agents		
Possible side effects	-Nausea, vomiting, diarrhea, constipation, low blood sugar if taking diabetes medication		
Notes	-Discontinue if less than 4% weight loss at 16 weeks		



Semaglutide (Wegovy) STEP-1 Trial

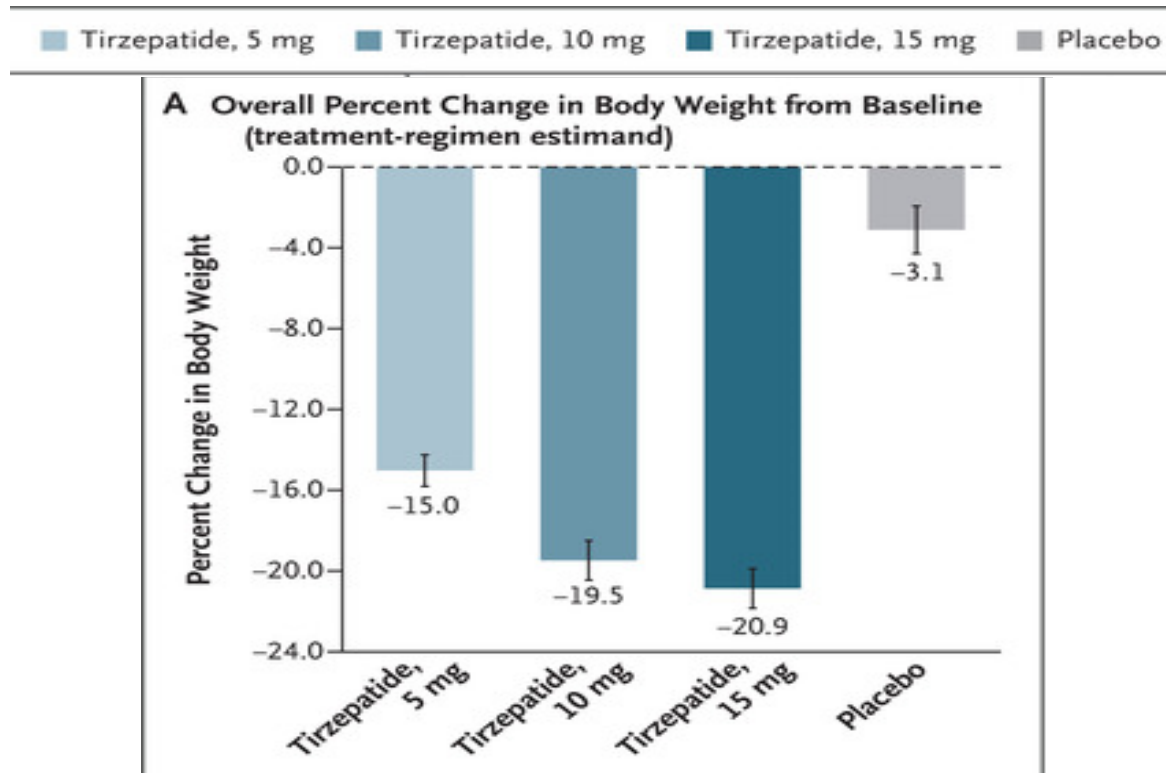
- Semaglutide 2.4 mg weekly vs placebo
- BMI ≥ 30 or ≥ 27 with comorbidity, **without DM**
- GI side effects:
 - Rate: 74% with semaglutide, 48% with placebo
 - Discontinued study: 4.5% with semaglutide, 0.8% with placebo



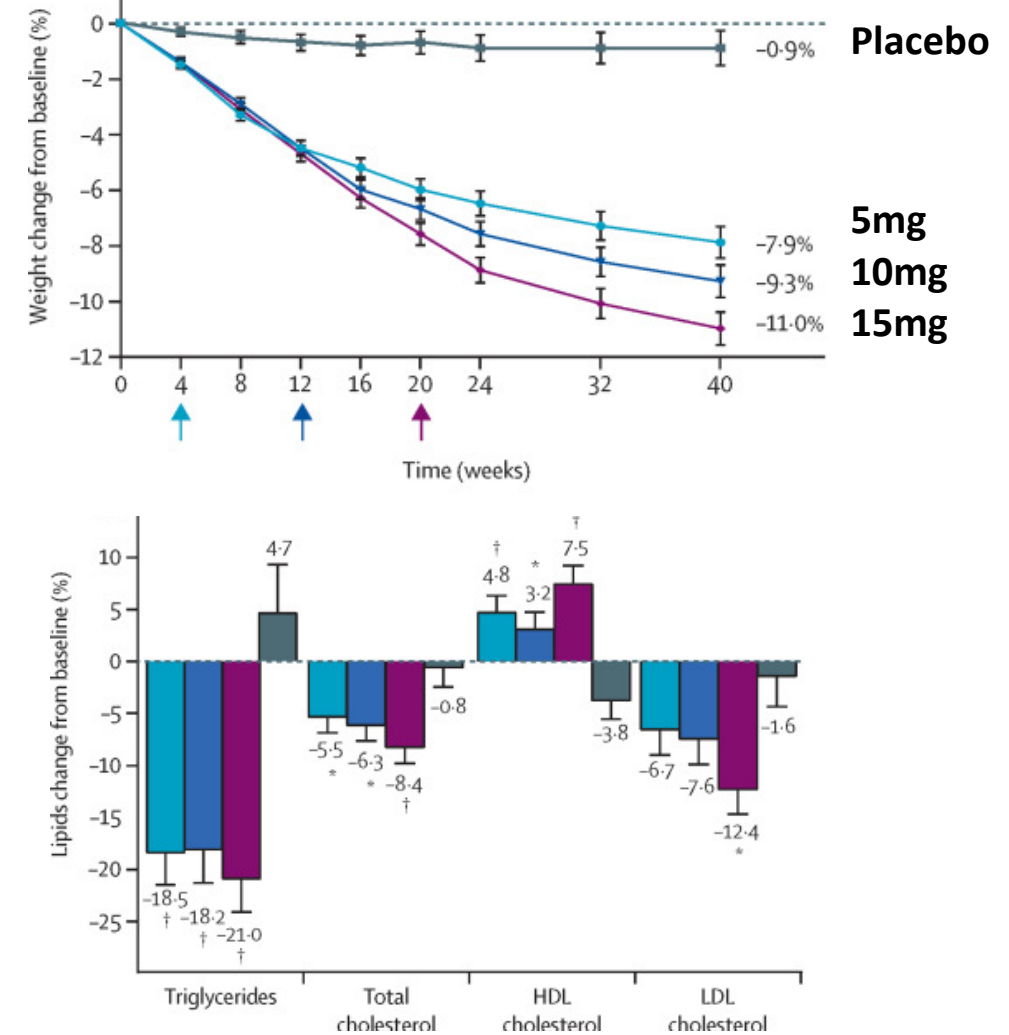
Wilding JPH, NEJM, 2021.



Tirzepatide (Dual GIP and GLP1RA)



SURMOUNT-1 Trial: Jastreboff AM, NEJM 2022.
N=2539, BMI ≥ 30 or ≥ 27 with comorbidity, **without DM**



SURPASS-1: Rosenstock J, Lancet, 2021.
N=478 pts **with Type 2 DM**



Bariatric Surgery

- Utilization: Approx 252,000 procedures yearly

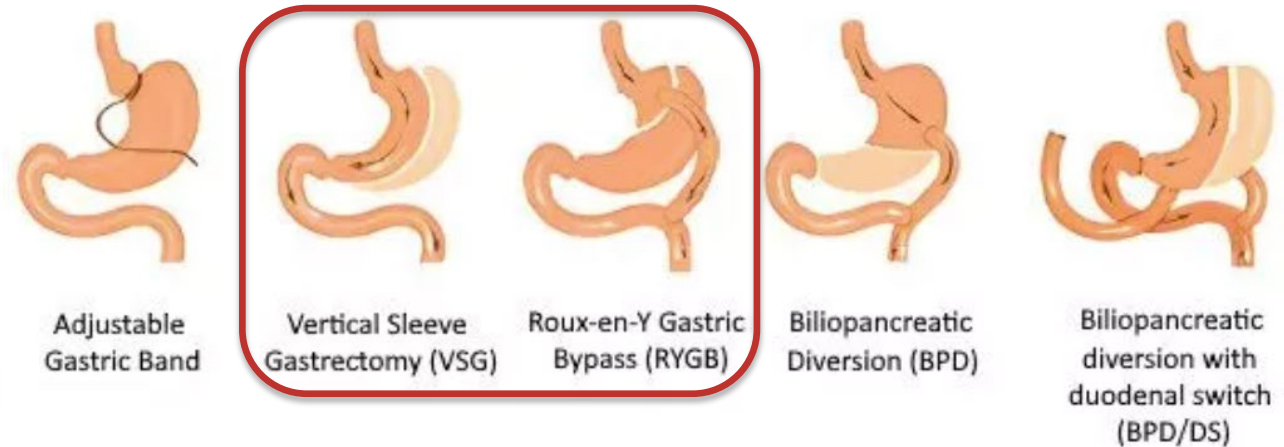
- 61% sleeve gastrectomy
- 17% Roux-en-Y gastric bypass
- 15% revisions
- 7% other types

- Eligibility

- BMI >40 kg/m² OR
- BMI 35-40 kg/m² with obesity-related comorbidity

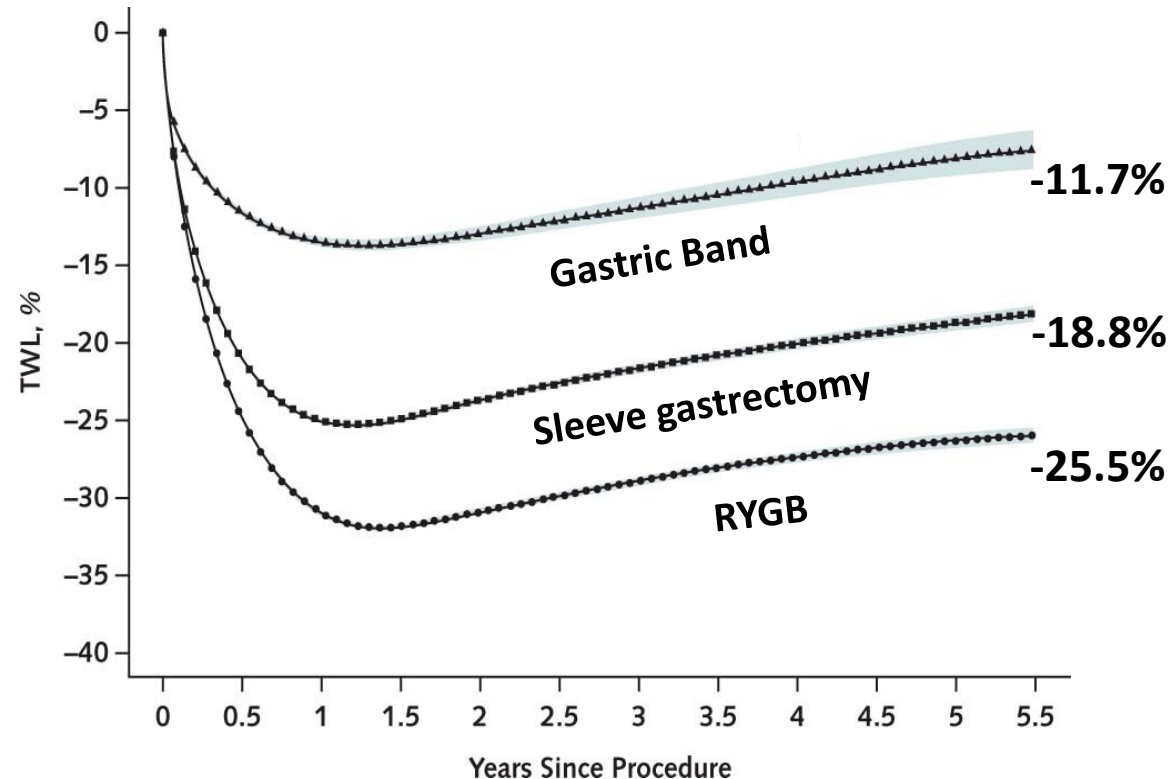
- Contraindications

- Severe heart failure, coronary disease, lung disease, cirrhosis
- Active cancer, Crohn's disease
- Drug/alcohol dependency, impaired intellectual capacity
- Current or planned pregnancy within the next 1 to 2 years





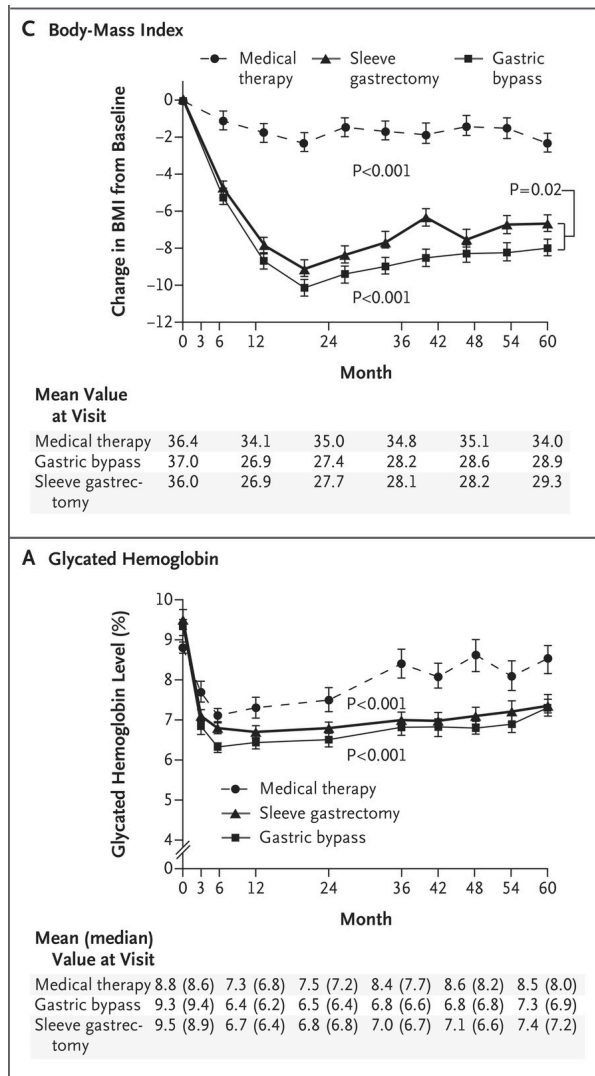
Bariatric Surgery Effects on Weight – PCORNET



- Weight loss similar (or better) for RYGB vs sleeve
 - Both better than gastric band
- Max weight loss at ~1.5 years
- Major Adverse events
 - 5% RYGB
 - 2.6% Sleeve
 - 2.9% Gastric band



Bariatric Surgery Effects on Type 2 Diabetes – STAMPEDE as an example



- Diabetes remission (A1c <6.5%, no DM Rx)
 - 0% of medical therapy
 - 23% of sleeve gastrectomy (P=0.003)
 - 31% of RYGB (P=0.002)
- In this and other studies of surgery
 - Greater reductions in...
 - DM medications
 - Micro- and macrovascular complications
 - Benefits similar if BMI <35 (vs ≥35)
 - Benefits similar for sleeve (vs RYGB)
 - **BUT** remission prevalence decreases over time

Schauer PR, N Engl J Med, 2017; Arterburn DE, JAMA, 2020; Müller-Stich BP. Ann Surg, 2015.



Other Benefits of Bariatric Surgery

- Mortality
 - 2.7% (RYGB) vs 4.1% (non-surgical) at 7 years in Utah patients
 - 13.8% (RYGB) vs 23.9% (non-surgical) at 10 years in VA patients
- Hypertension
 - 43-83% remission at 1 year
- Sleep apnea
 - AHI reduced from 39.3 to 12.5 events per hour
 - Epworth Sleepiness Scale reduced from 11.1 to 5.6
- Urinary incontinence
 - Reduced prevalence in women from 49% (baseline) to 25% (3 years)



Complications of Bariatric Surgery

- Perioperative mortality: 0.03% to 0.2%
- 30-day risk of serious adverse events (reoperation, prolonged hospitalization, DVT/PE)
 - 0.8% to 5.6% for Sleeve
 - 1.4% to 9.4% for RYGB
- Long-term reoperation rates: 5% to 22.1%
 - RYGB higher than Sleeve in several studies
 - Gastric band similarly high (bands are often removed nowadays)



Summary

- Obesity prevalence has increased markedly, causing major health problems
- Assessing weight should be done systematically to detect underlying causes or associated disease
- Low carbohydrate diets are another viable option for weight loss and metabolic management
- More and a greater variety of effective weight loss medications are available
- Surgeries, particularly RYGB and sleeve gastrectomy, have increasing evidence for long-term benefit