



Highlights from the Summit

Presentation for UCLA Family
Medicine by Jessica A. Wang, MD,
MPH, PGY-3

Obesity is a CHRONIC DISEASE



World Obesity Federation¹

“... a **chronic, relapsing, progressive disease** process...[that needs] immediate action for prevention and control of this global pandemic”



US Food and Drug Administration²

“...a **chronic relapsing health risk** defined by excess body fat”

American Medical Association³

“...a **disease state with multiple pathophysiological aspects** requiring a range of interventions...”



European Medicines Agency⁴

“...the result of interactions of **genetic, metabolic, environmental, and behavioral factors...** associated with increases in morbidity and mortality”

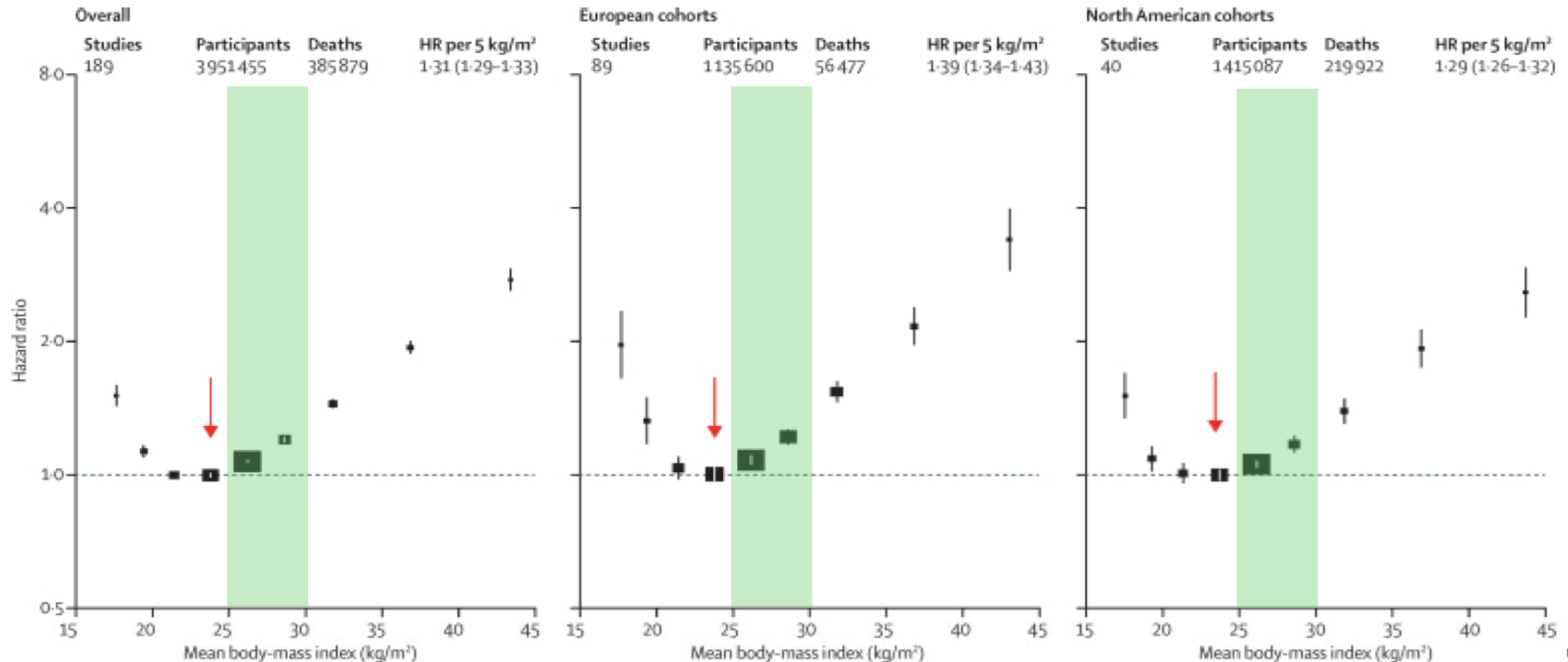


Canadian Medical Association⁵

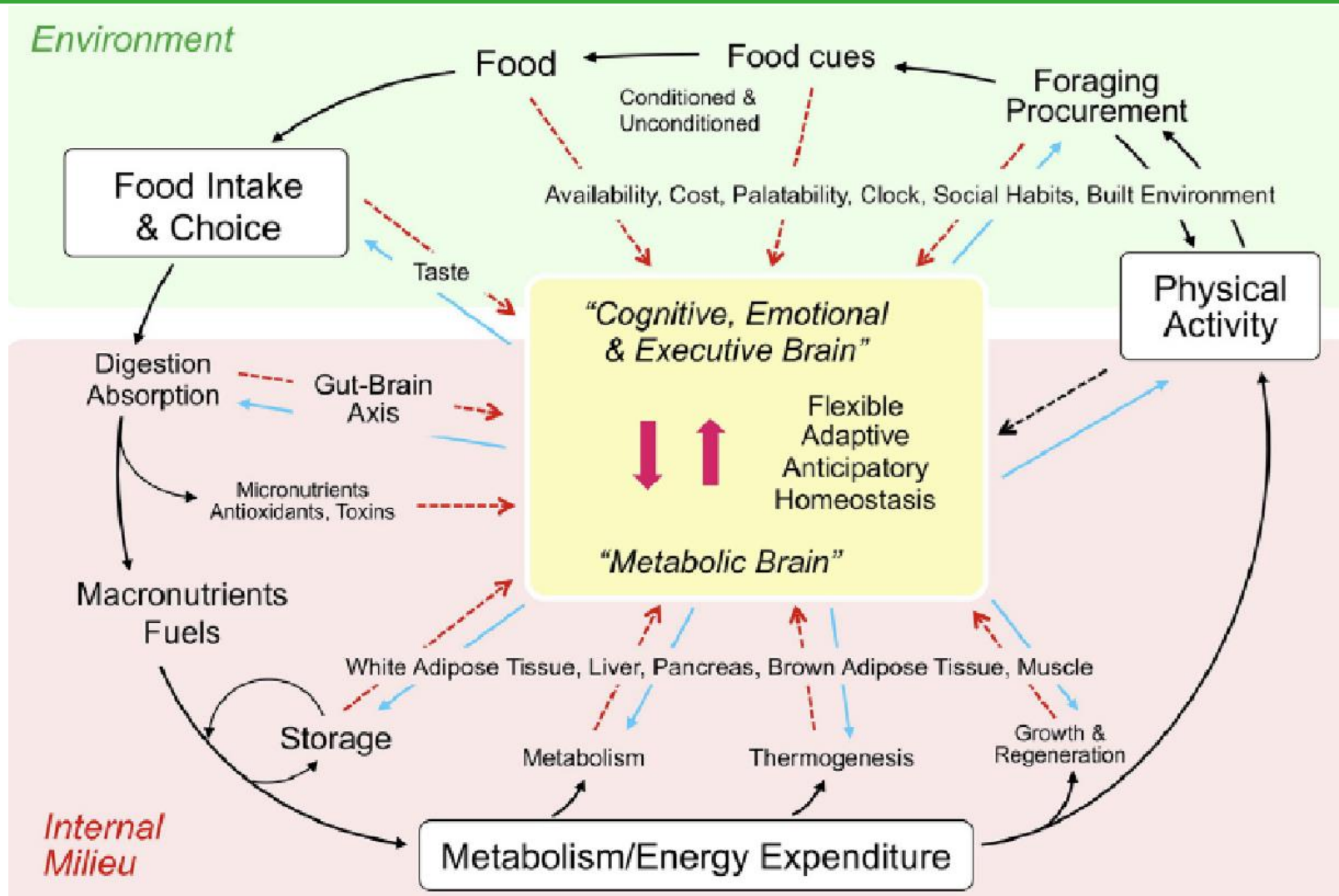
“...a **chronic medical disease** requiring enhanced research, treatment, and prevention efforts”

Pre-obesity and all-cause mortality

Association Between BMI and All-Cause Mortality Among Never-Smokers, by Region



The System That Regulates Eating Is Complex



The Hypothalamus Centrally Regulates Weight but is Influenced by Peripheral Signals

NPY and AgRP Neurons:

Increase Hunger
and Cravings

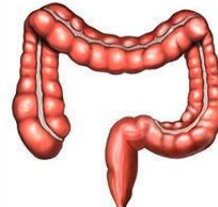
Promote Increase
in Feeding



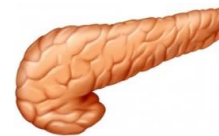
Stomach



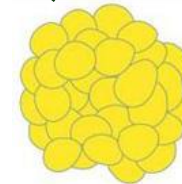
Small Intestine



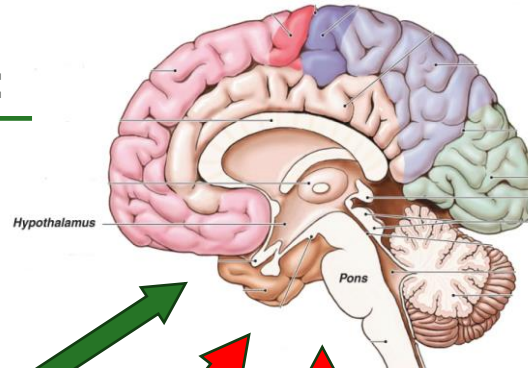
Large Intestine



Pancreas



Fat Cells



POMC and CART Neurons:

Reduce Hunger
and Cravings

Reduces
Feeding

AgRP = agouti-related peptide. CART = cocaine- and amphetamine-regulated transcript. NPY = neuropeptide Y. POMC = proopiomelanocortin.



Obesity...It's a Conspiracy

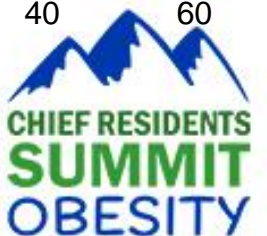
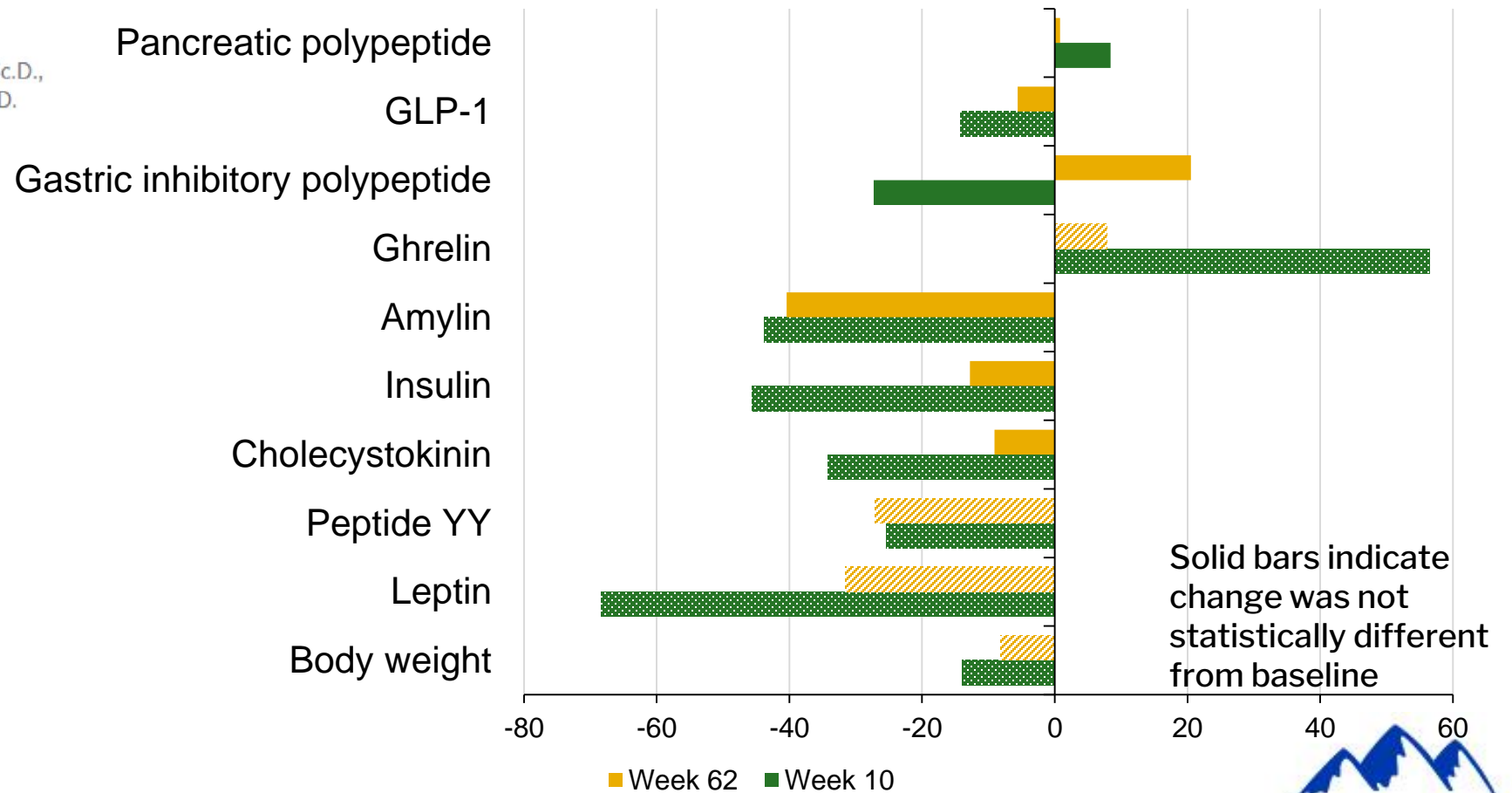
Long-Term Persistence of Hormonal Adaptations to Weight Loss

Priya Sumithran, M.B., B.S., Luke A. Prendergast, Ph.D., Elizabeth Delbridge, Ph.D., Katrina Purcell, B.Sc., Arthur Shulkes, Sc.D., Adamandia Kriketos, Ph.D., and Joseph Proietto, M.B., B.S., Ph.D.

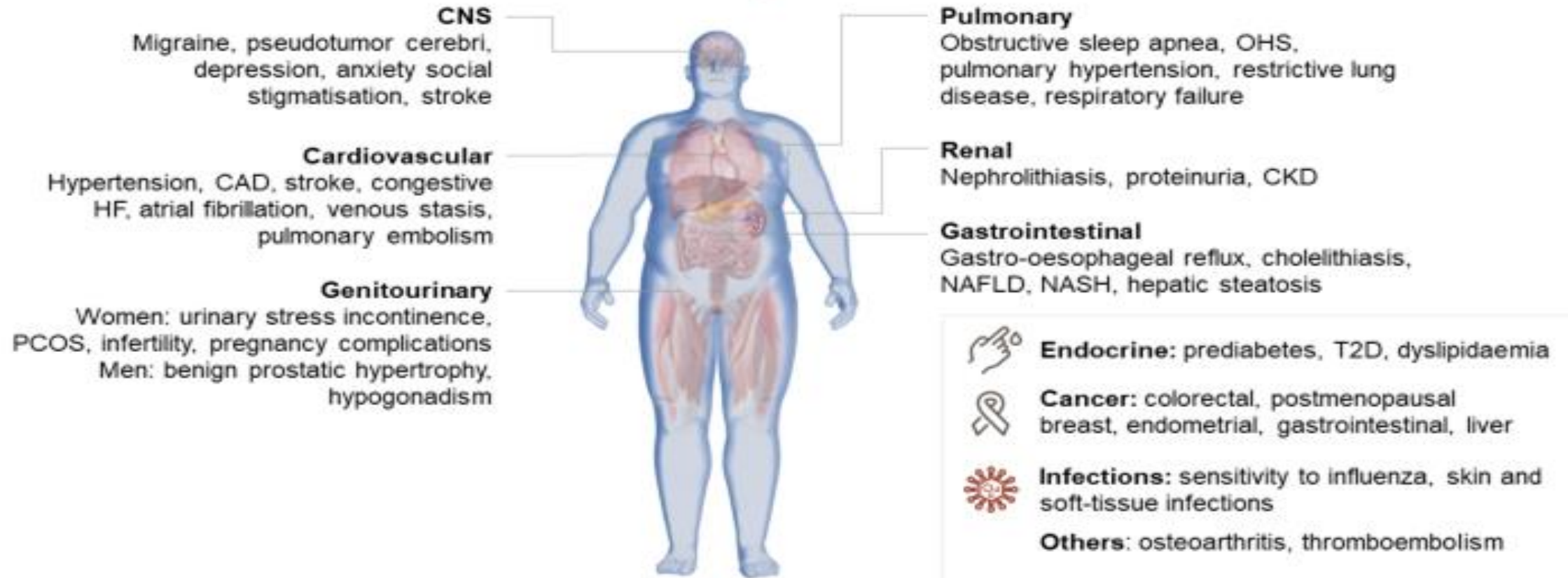
- 50 patients with overweight/obesity were treated with a very-low-energy diet for 10 weeks, then followed for 52 weeks
- 1 y after initial diet-induced weight reduction, levels of circulating mediators of appetite that promote weight regain did

Interpretation: The body acts to protect fat mass in persons with overweight/obesity

% Change in Endpoints from Baseline



Obesity is a **Multisystem Disease** associated with many complications (>100!) Doesn't it make sense to treat obesity to treat them all?

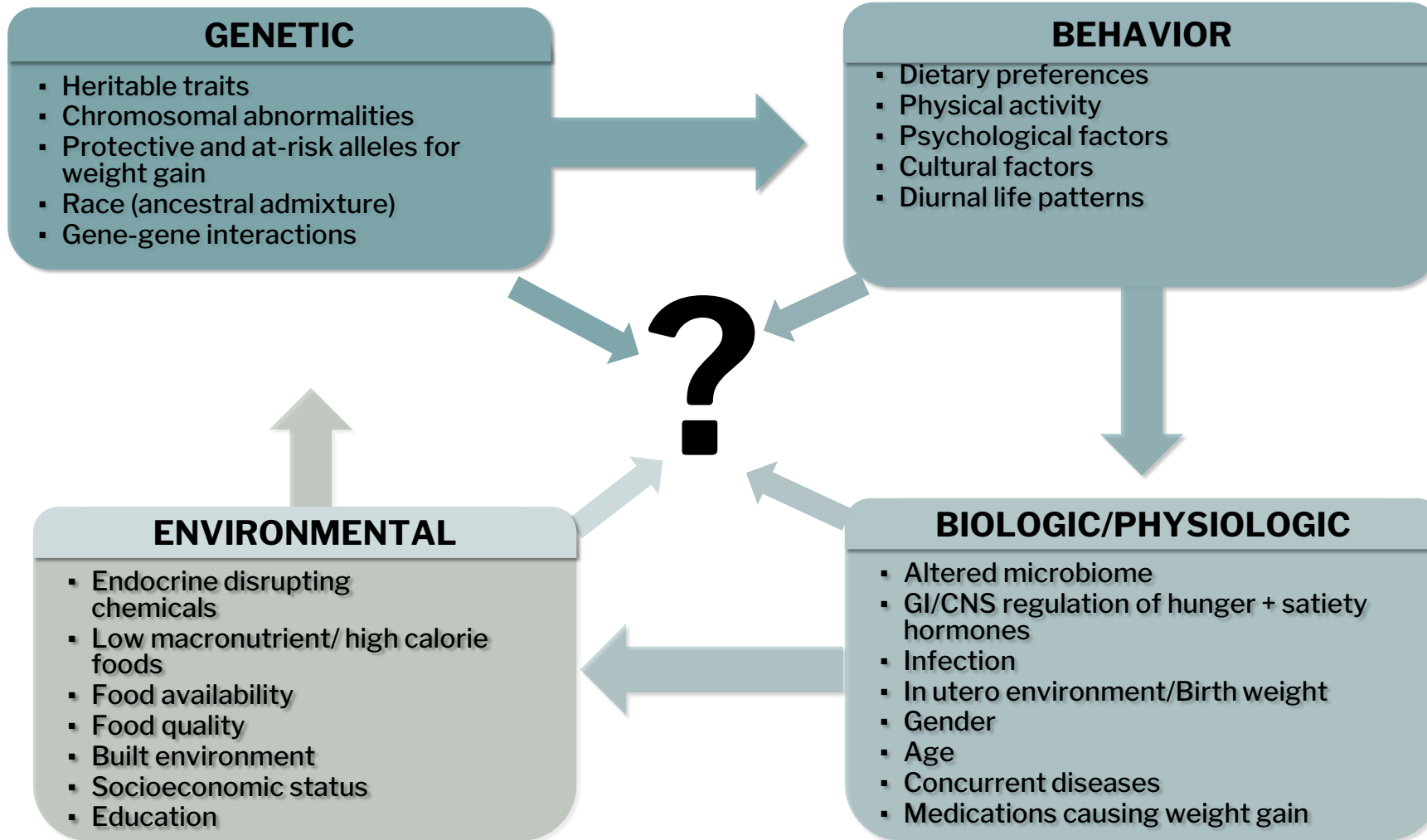


CAD, coronary artery disease; CKD, chronic kidney disease; HF, heart failure; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; OHS, obesity hypoventilation syndrome; PCOS, polycystic ovary syndrome; T2D, type 2 diabetes

Tsai AG, et al. *Ann Intern Med.* 2019;170(5):ITC33-ITC48; Sarma S, et al. *Diabetes Obes Metab.* 2021;23(suppl 1):3-

16.

Multifactorial Etiology



What is Weight Bias?

- Negative attitudes toward individuals with obesity
- Stereotypes leading to:
 - Stigma
 - Rejection
 - Prejudice
 - Discrimination
 - Verbal, physical, relational, cyber
 - Subtle and overt

Why Understanding Weight Bias is Important

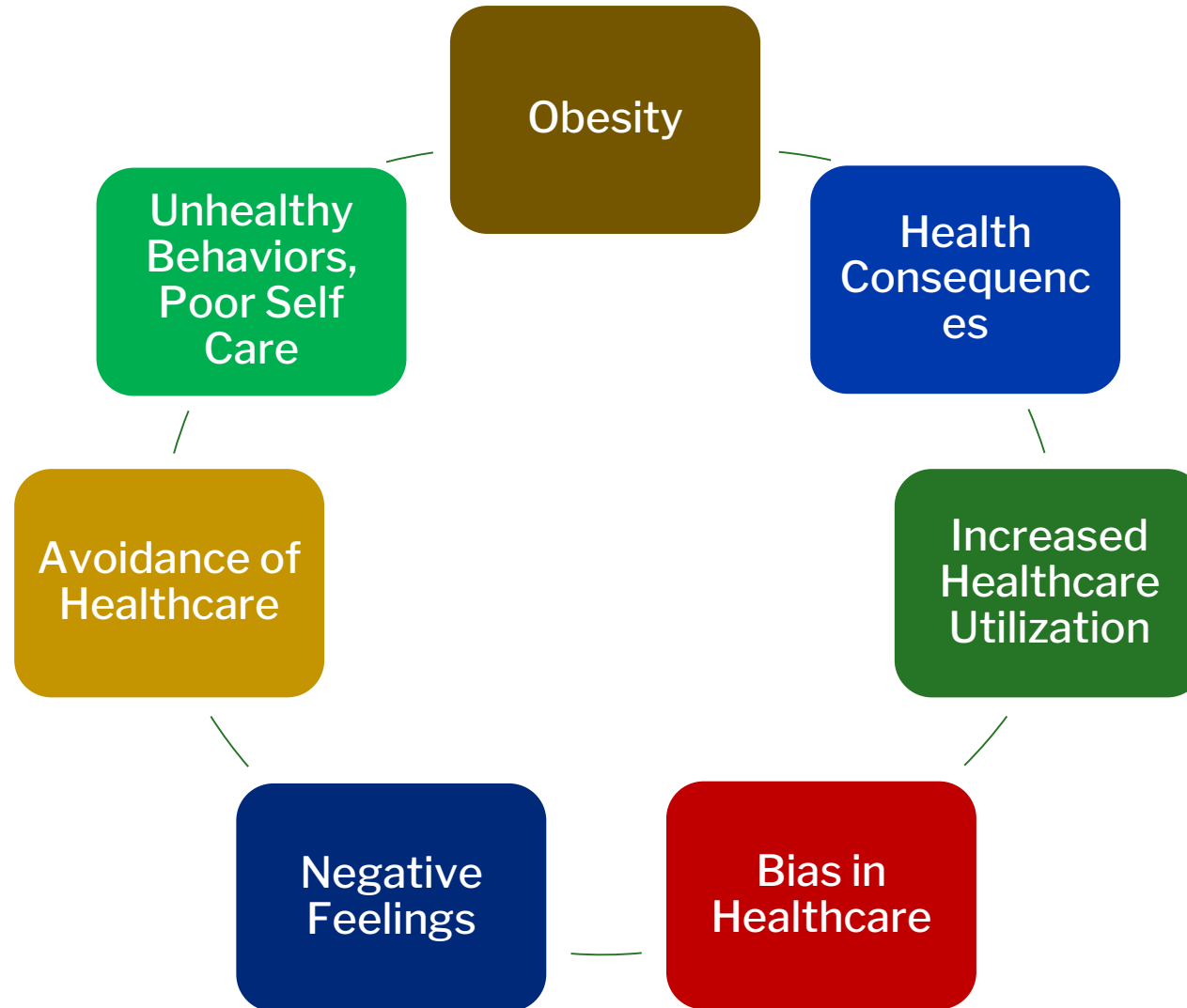
In OAC's opinion, weight bias:

- Keeps patients affected by obesity from seeking help and professionals from offering it.
- Is the last socially acceptable form of discrimination.
- Hampers our nation's efforts to effectively combat the obesity epidemic.
- Is a primary driver around the current limitations of access to treatment.

Recognizing and combatting bias, both your own and in the community, is an important step in addressing obesity.



Cycle of Bias and Obesity



Clinicians View Patients with Obesity as:¹⁻³

- Non-compliant
- Lazy
- Lacking self-control
- Awkward
- Sloppy
- Unsuccessful
- Unintelligent
- Dishonest
- More annoying

Strategies to Reduce Clinician Weight Bias

Consider the
patient's
experience

Reflect on
your own
bias

Use
supportive
language

Use
preferred
weight terms

Conversational Scripts: Improve Patient Communication

Can I talk about your health and how your lifestyle is affecting it? Can we talk about your weight?

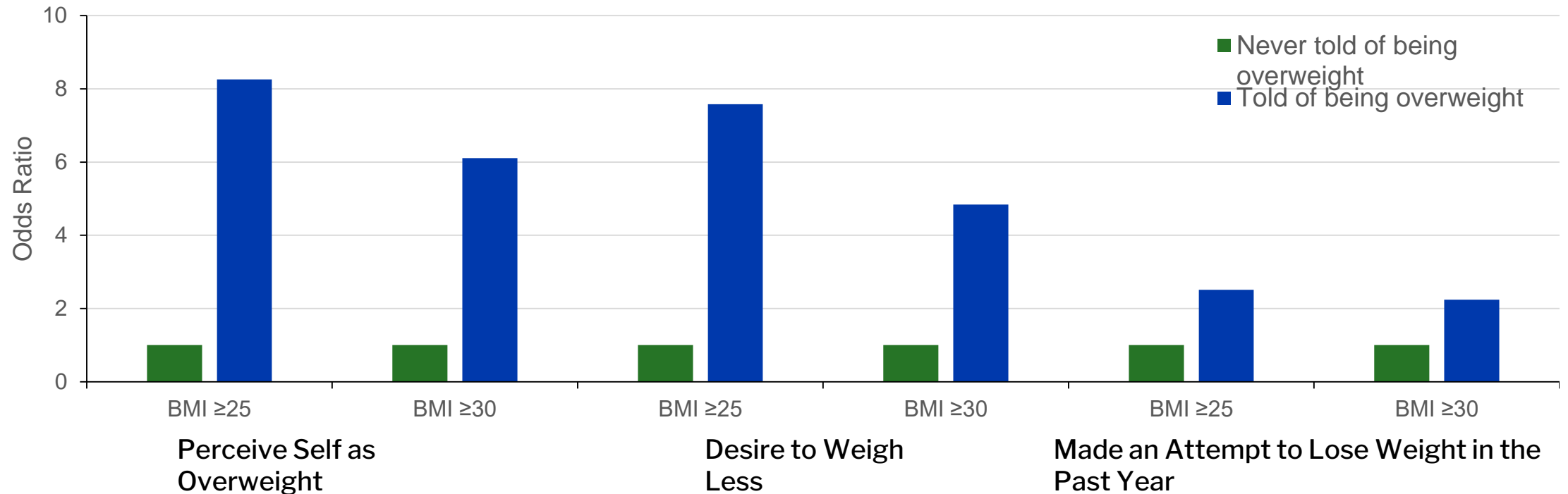
NO... "The single best thing you can do to improve your health is to make some changes in your diet and other lifestyle factors. Let's talk about this at the end of the next visit."

YES... "Great. The single best thing you can do to improve your health is to make some changes in your diet and other lifestyle factors. Let's see what might work to help you do this."



Benefits of Simply Discussing Weight

Logistic Regression Analysis of Reports of Being Told of Weight Status



Having the conversation makes a difference!



Consider Your Office Environment: Does This Look Familiar?



In-Office Measures of Weight

Classification	Children/ Adolescents	Adult BMI	Disease Risk* Relative to Normal Weight and Waist Circumference (WC)	
			Men WC ≤40 inches (102 cm)	Men WC >40 inches (102 cm)
			Women WC ≤35 inches (88 cm)	Women WC >35 inches (88 cm)
Underweight	<5 th percentile	<18.5	–	–
Healthy Weight	5 th to <85 th percentile	18.5 to 24.9	–	–
Overweight	85 th to <95 th percentile	25.0 to 29.9	Increased	High
Obese/Class 1	≥95 th percentile	30.0 to 34.9	High	Very high
Obese/Class 2		35.0 to 39.9	Very high	Very high
Obese/Class 3		≥40	Extremely high	Extremely high

*Disease risk for type 2 diabetes, hypertension, cardiovascular disease



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on of

Sensitive Weighing Procedures

- Ask patients for permission to weigh
- Weigh in private location
- Check in advance to be sure that appropriate equipment is available
- Record weight silently, free of judgment or commentary
- Consider weighing less often if requested by person



Key Issues to Include in Patient Assessment

History

- Assess risk for obesity-related comorbidities....
- How is this patient feeling and perception of personal health
- Weight history, onset obesity, emotional triggers past/present
- Previous weight loss attempts
 - What worked? Didn't work?

Physical Examination

- Height, weight, calculated BMI
- Vital Signs
- Waist circumference
 - Adds no risk information if BMI ≥ 35 kg/m²
- Comprehensive Physical Exam
 - Essential to Touch these patients
- Depression and Sleep apnea screen

BMI, body mass index

Appropriate Documentation of Visit

Which is preferred?

- A 36-year-old obese female presents with increased urination and thirst

OR

- A 36-year-old female with moderate class II obesity, BMI 32.3 kg/m² and upper body fat distribution (waist circumference of 37 inches), presents with increased urination and thirst. ...

Treatment Goals for Weight Optimization

Overall goals

- Improve health and quality of life
- Prevent progressive weight gain
- Achieve weight loss to prevent complications
- Reduce risk of cardiovascular and other obesity-related diseases

Patient-specific goals

- Weight loss targets
 - 3-5% weight loss can lower risk of complications
 - **ACC/AHA/TOS: 5-10% weight loss within 6 months recommended as initial goal**
- Reduced calorie diet
 - 1200 to 1500 kcal/d for women and 1500 to 1800 kcal/d for men
- Increase quality and duration of physical activity
 - ≥150 minutes of moderate aerobic physical activity if appropriate
- Behavioral strategies for long-term adherence to lifestyle changes

AHA, American Heart Association; ACC, American College of Cardiology; TOS, The Obesity Society

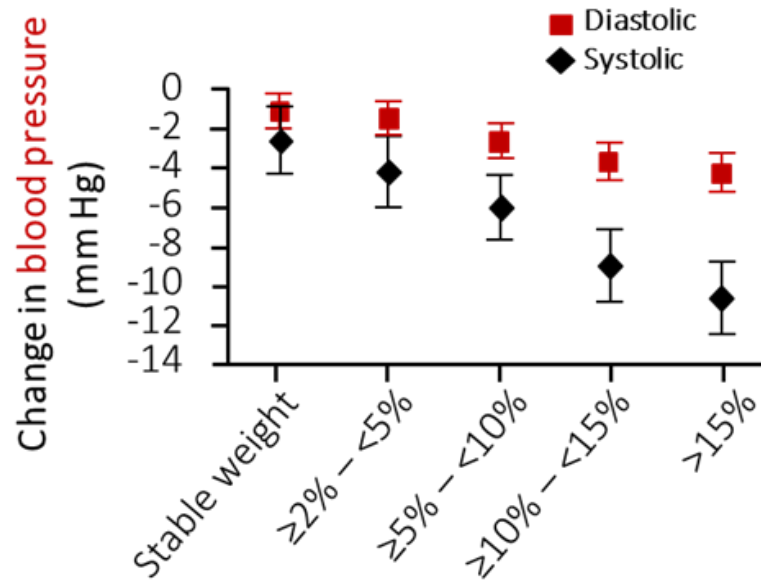
Jensen MD, et al. *Circulation*. 2014;129(25 Suppl 2):S102-S138; Garvey WT, et al. *Endocr Pract*. 2016;22(Suppl 3):1-203.



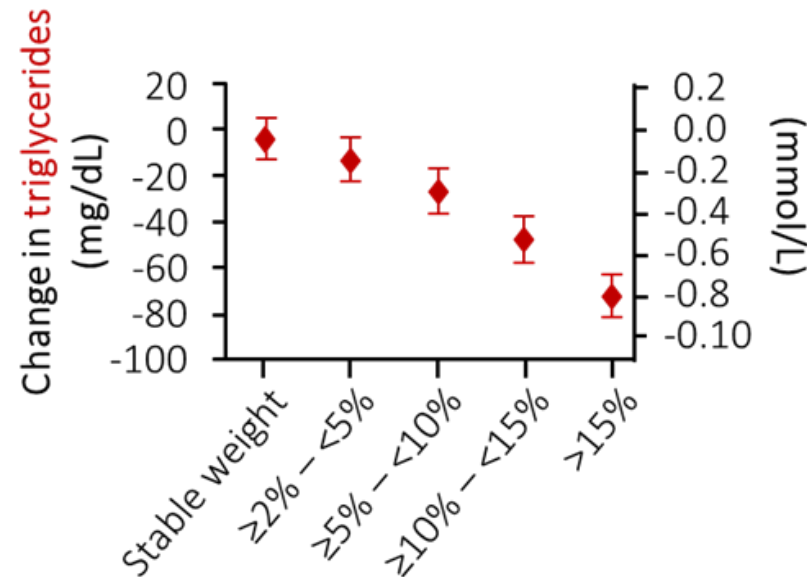
Guidelines - Key Treatment Considerations

2013 AHA/ACC/TOS ¹	2015 ENDO ²	2016 AACE/ACE ³	2022 AGA ⁴
<ul style="list-style-type: none"> • Not necessary to achieve normal weight; health improvement begins with modest weight loss • There is no magic diet • Lifestyle-intervention counseling conducted face-to-face in 14 or more sessions over 6 months is the gold standard for weight loss • Bariatric surgery should be discussed with patients who meet criteria and would benefit from it; refer if appropriate 	<ul style="list-style-type: none"> • Weight-centric prescribing should be done for chronic diseases (avoid medications that promote weight gain when possible) • Medications are useful adjuncts to diet and exercise, when prescribed appropriately • Choosing which medication to use is a shared decision of clinician and patient 	<ul style="list-style-type: none"> • Weight-related complications should direct intensity of treatment and urgency of treatment • Medications for chronic weight management may be used initially as an adjunct to lifestyle measures for patients with more severe disease manifestations • Individuals without comorbidities or risk factors are stage 0 and no medical intervention is required 	<ul style="list-style-type: none"> • Adults with obesity or overweight with weight-related complications who have had an inadequate response to lifestyle interventions should receive pharmacological agents to lifestyle interventions over continuing lifestyle interventions alone

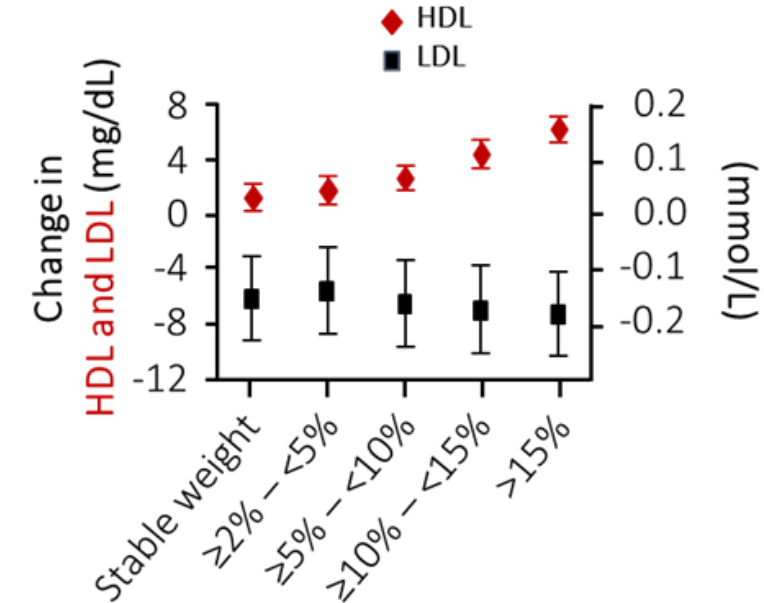
Look AHEAD 1-year Data: Modest Weight Loss (5%–10%) Improved CVD Markers



Weight loss category



Weight loss category



Weight loss category

LDL, $P=0.3614$

Data presented as adjusted least square means and 95% CIs. Stable weight defined as $\pm 2\%$ of baseline weight. $P < 0.0001$ vs baseline for all weight categories, unless specified otherwise.

HDL, high-density lipoprotein; LDL, low-density lipoprotein



What else do you need to know before developing an individualized weight loss plan?

- What has worked (or not) in the past?
- What has triggered weight gain in the past?
- What are the health and weight goals...
 - From the patient's perspective?
 - From a health perspective?
- Dietary preferences and cultural influences?
- How much effort is the patient willing to invest now? Long-term?
- Other patient experiences, expectations, concerns, barriers?

Primary Care Clinician Role

- Collaborate with the patient to develop and implement an individualized treatment plan based on the chronic disease model of care
 - Identify achievable short- and long-term goals
 - Identify barriers to achieving goals
 - Identify and implement strategies to overcome barriers
 - Understand values and beliefs
- Support the patient to achieve and maintain weight loss goals
- Modify treatment as needed
- Provide holistic management of obesity-related diseases
- Involve other healthcare professionals as appropriate

The Multidisciplinary Care Team



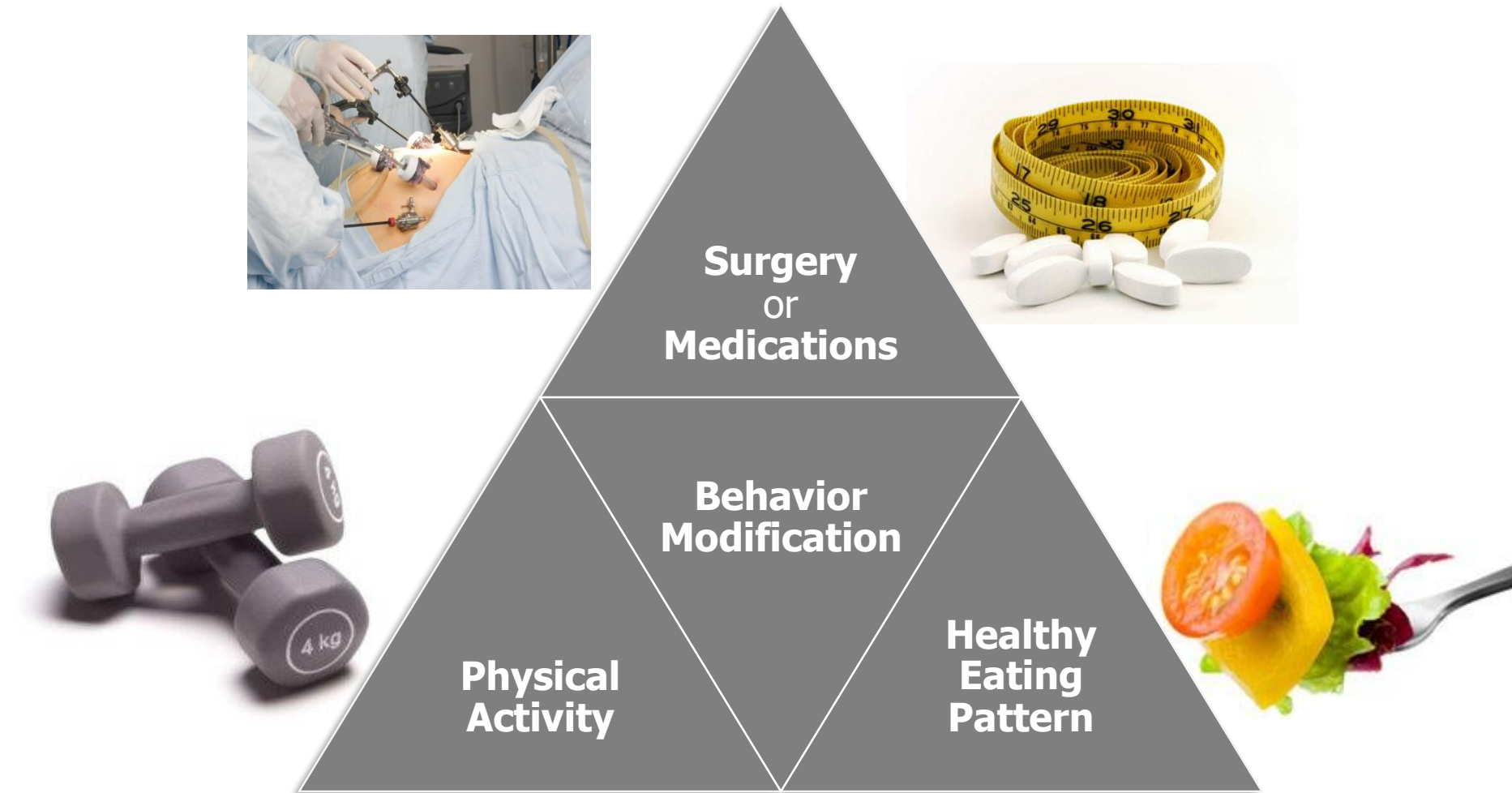
- Ongoing education/reinforcement
 - Nutrition, physical activity, cognitive behavioral
- Comorbidities
- Psychological therapy
- Pharmacological, surgical therapies
- Treatment adherence

Choice of Initial Treatment

- The greater the weight-related health risks, the greater the urgency to treat and the more justification for higher treatment intensity
- Weight management history informs the treatment plan
 - **History of struggling with weight loss (even when not under clinician observation) should be enough justification to add adjunctive treatment, e.g., pharmacotherapy**
- Because the goal of weight loss is improvement in health and quality of life, the targeted health goal should guide treatment approach/intensity, as well as to assess treatment success



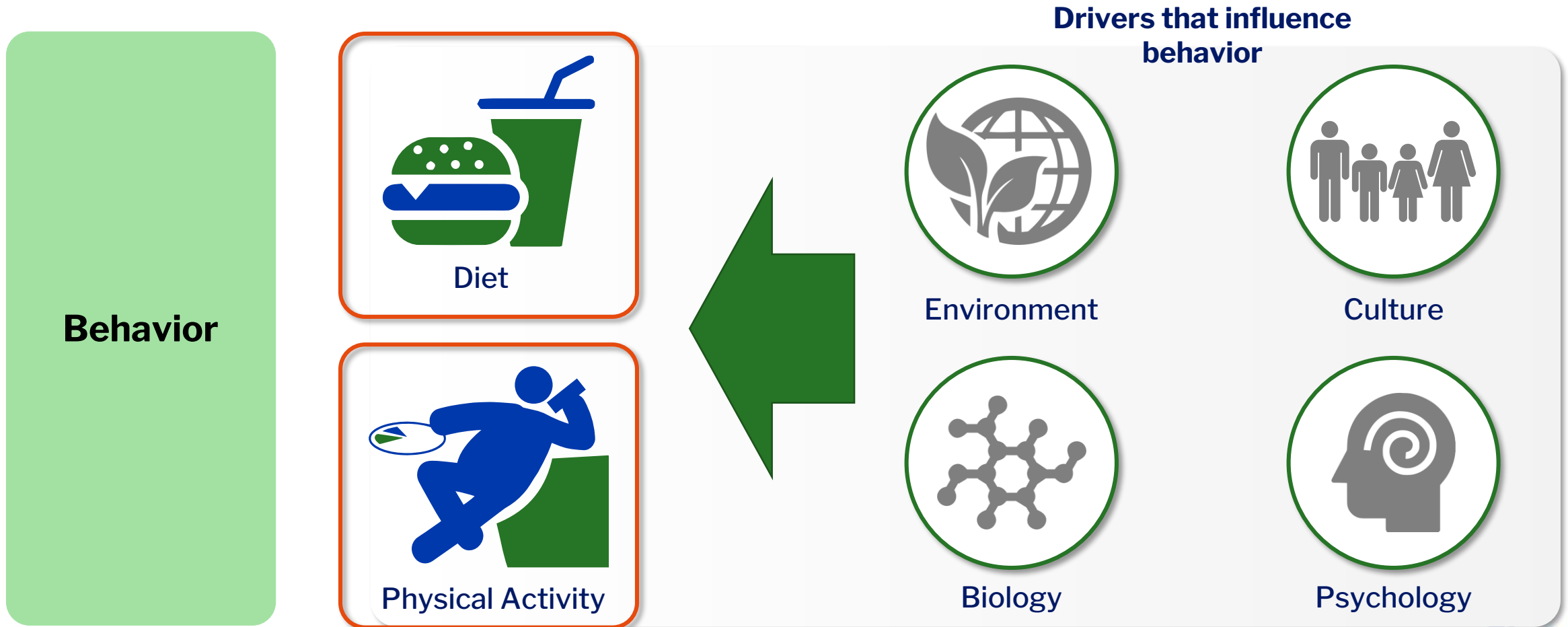
Components of an Effective Obesity Management Program



Overview of Treatment Options for Weight Loss

Method	Description	Criteria (BMI kg/m ²)	Average Weight Loss at 1 Year
Lifestyle Intervention	<ul style="list-style-type: none"> Diet Physical activity Behavioral therapy 	≥25	3% to 10%
Medications	<ul style="list-style-type: none"> Liraglutide 3mg or Semaglutide 2.4 mg Naltrexone/bupropion ER Orlistat Phentermine/topiramate ER 	≥27 with comorbidity or ≥30	3% to 12%
Devices	<ul style="list-style-type: none"> Palate space occupying device Intragastric balloons Ingested, transient, space occupying device Laparoscopic adjustable gastric band 	Varies	10% to 20%
Surgery	<ul style="list-style-type: none"> Gastric sleeve Roux-en-Y gastric bypass Biliopancreatic diversion (with/without duodenal switch) 	≥35 with comorbidity or ≥40	20% to 40%

Eating and moving do not occur in a vacuum

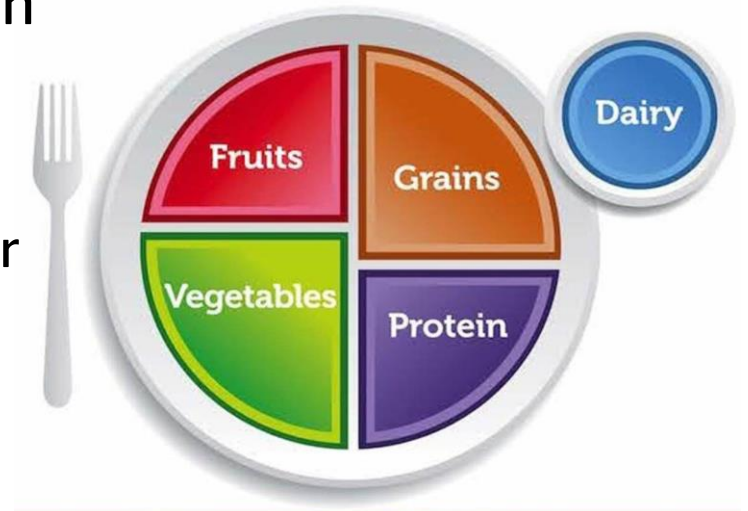


Dietary Intervention: Which One Is Best?

(cont)

2013 American Heart Association (AHA)/American College of Cardiology (ACC)/The Obesity Society (TOS) Guidelines¹

- Systematic review of 17 dietary patterns: none was superior in ability to produce and sustain weight loss
- Negative energy balance is the key objective
 - 1200-1500 kcal/d for women and 1500-1800 kcal/d for men, or
 - 500 kcal/d or 750 kcal/d energy deficit from baseline diet



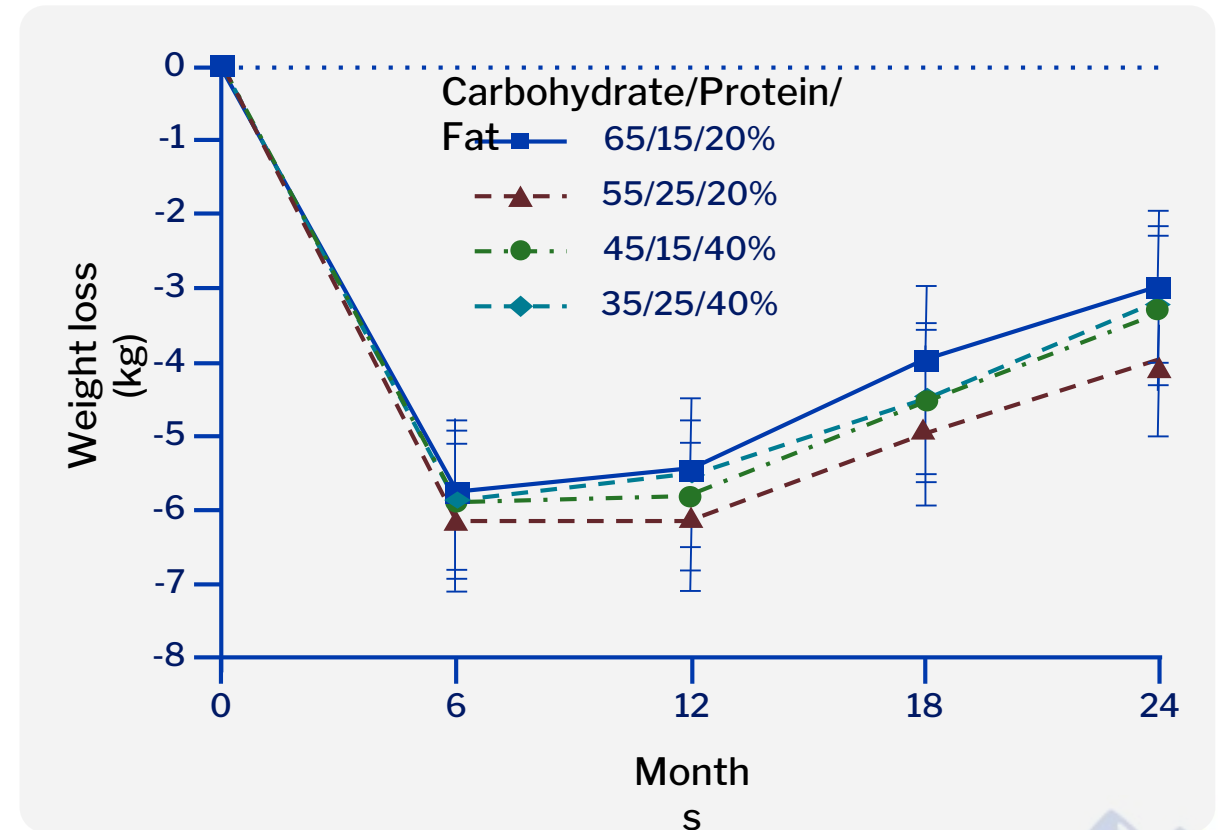
The best dietary intervention is the one to which the patient adheres²

- Assessing patient preference is critical



Caloric Reduction is the Key for Weight Loss

- Overweight patients (N=811) were assigned to 1 of 4 dietary groups
 - Offered group and individual instruction
- After 2 years, there were no significant difference in weight loss among the 4 groups
- Regardless of macronutrient composition, reduced calorie diets result in weight loss



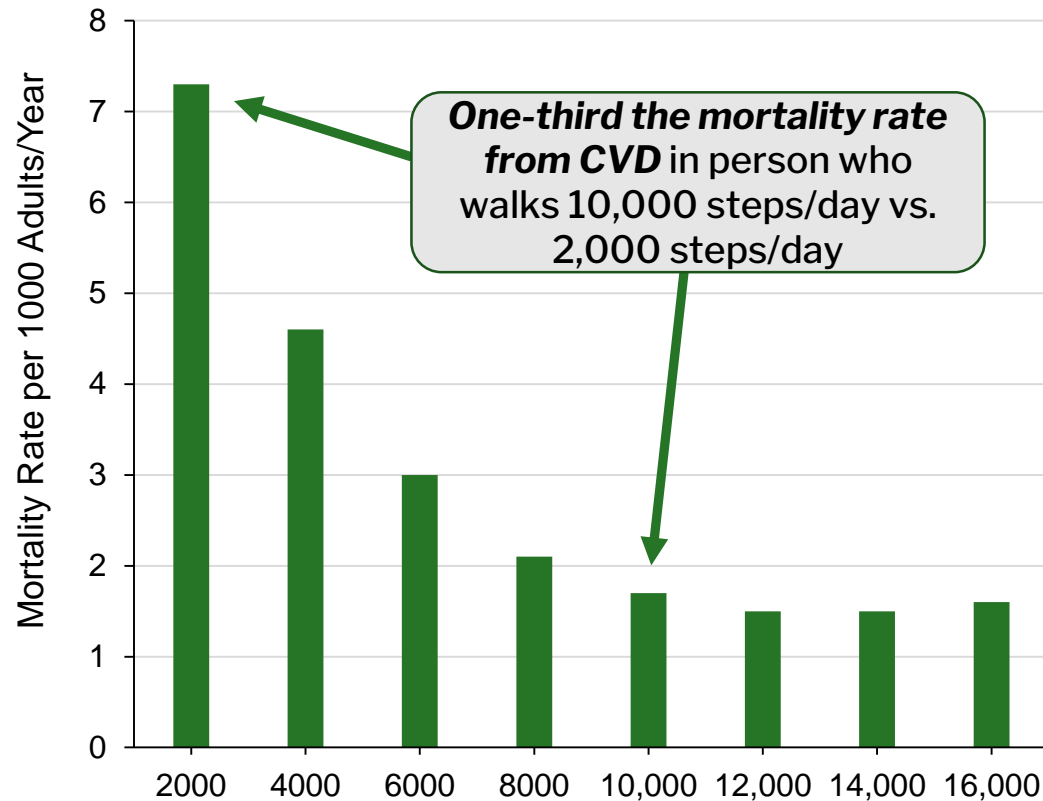
Aerobic Physical Activity and Expected Weight Loss

Expected initial weight loss and possibility of clinically significant weight loss from different types of exercise training programs¹

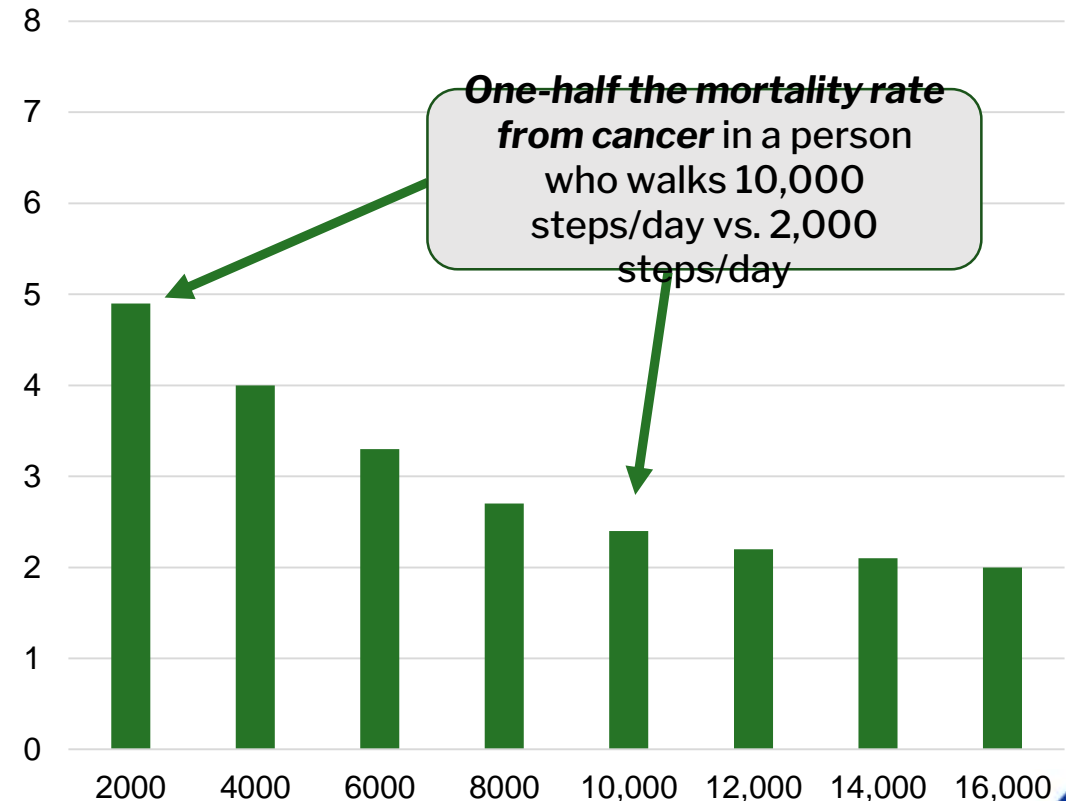
Exercise type	Range of expected weight loss	Chance of clinically significant weight loss
Aerobic exercise training only	0-3%	Possible with high exercise volumes
Resistance training only	0-1%	Possible with high exercise volumes
Aerobic and resistance training	0-3%	More likely than either aerobic or resistance training alone
Caloric restriction combined with aerobic exercise training	5-15%	Possible
Aerobic physical activity amount	Weight loss amount ²	
<150 min per week	No weight loss or minimal weight loss	
150-225 min per week	Weight loss of 2-3 kg	
225-420 min per week	Weight loss of 5-7.5 kg	
200-300 min per week	Weight maintenance after weight loss	

More Steps per day Results in Greater Benefits

Cardiovascular Disease



Cancer

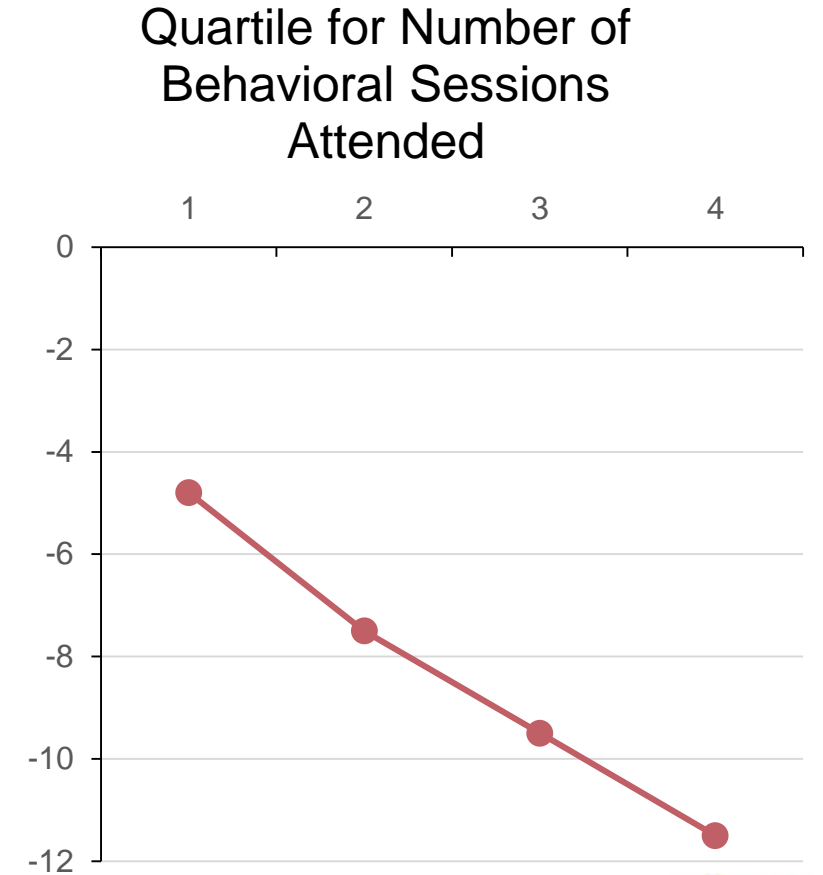
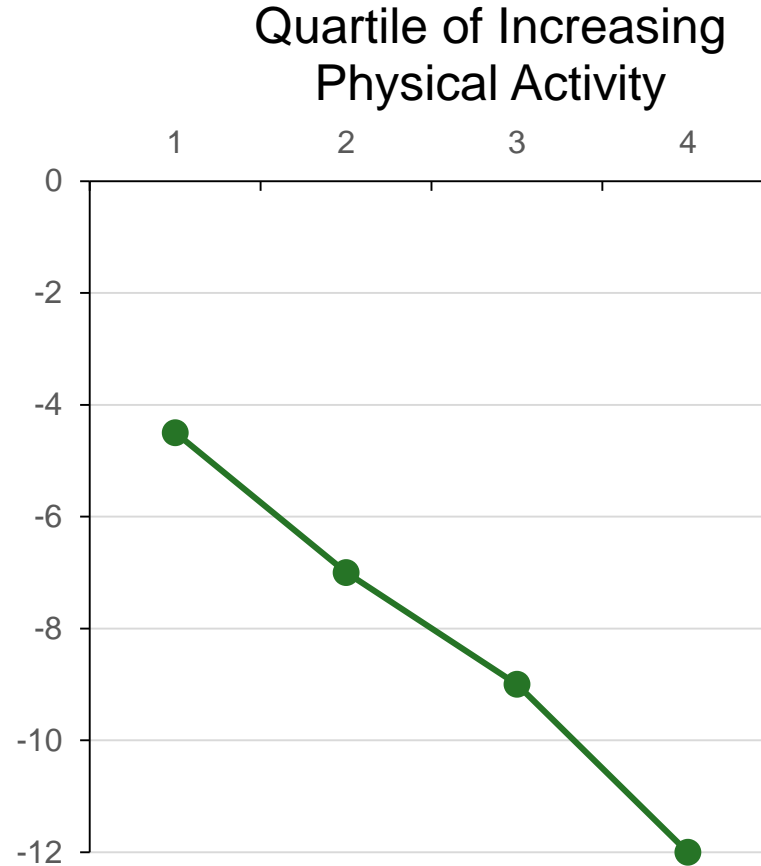
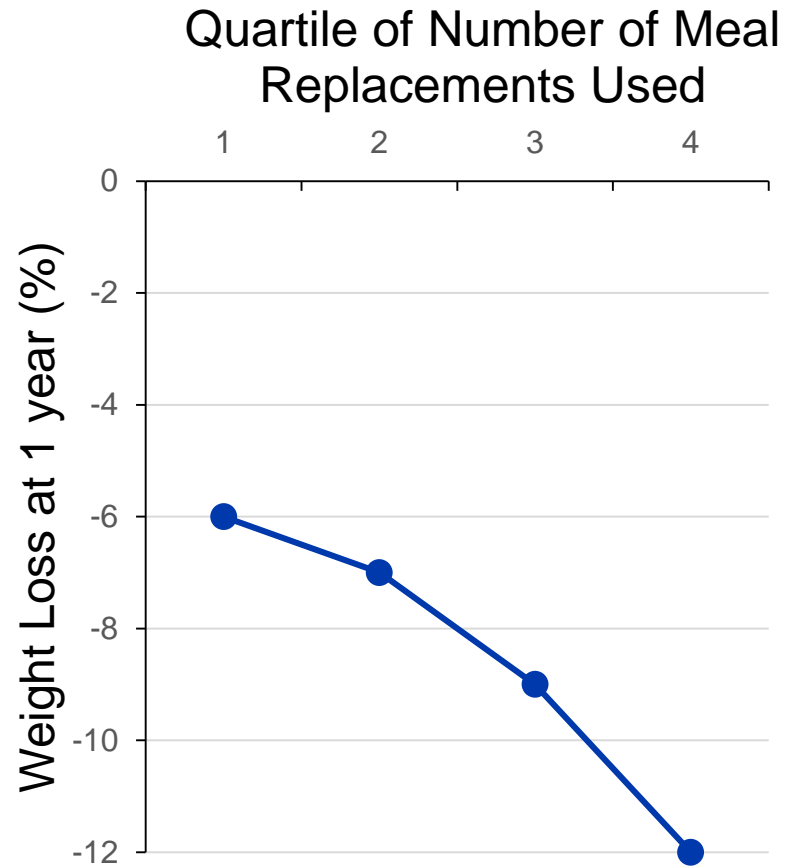


CVD, cardiovascular disease

Saint-Maurice PF, et al. *JAMA*. 2020;323(12):1151-1160.



Intensity and Frequency of Lifestyle Modification Impacts Weight Loss



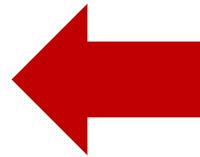
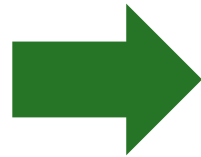
Will Behavior Change Take Place?

Behavior change is almost never easy.
It depends on the balance of two opposing forces:

Ambivalence/Distress

Motivation

(Desire to
change)



Resistance

(Barriers to
change)

Clinicians need to find the leverage point to
facilitate behavior change

The OARS Motivational Interviewing Strategy

O Open-ended questions	Ask open-ended questions that encourage thought-provoking responses and engage a 2-way dialogue. This is an important first step to understanding a patient's barriers and expectations.
A Affirmative statements	Recognize and support your patient's personal strengths, successes, and efforts to change. This will help promote a collaborative relationship.
R Reflections	Use reflective listening and respond thoughtfully by paraphrasing. Confirm that the patient has been heard and validate his or her point of view.
S Summary statements	The statements that recount and clarify the patient's statements and identify specific points to act upon.



Developing Goals: Be SMART

S

Specific: Choose one specific behavior modifier per goal to work on

M

Measurable: Can you measure this against a baseline?

A

Achievable or Action Based behavior: Is the goal attainable?

R

Realistic: Do you have honest and realistic expectations of yourself?

T

Timed: Is the time allotted reasonable and manageable for you right now?





Coverage for Behavioral Therapy for Obesity

- For patients with BMI ≥ 30 kg/m²
- Intensive behavioral therapy consists of:
 - Screening using BMI
 - Nutritional assessment
- Goal is to promote sustained weight loss through high intensity interventions on diet and exercise
- Should be consistent with the 5 A's
- Coverage for face-to-face visits
 - every week x 1 month
 - every other week for months 2-6
 - every month for months 7-12 if ≥ 3 kg weight loss over first 6 months
- If < 3 kg weight loss achieved over first 6 months, readiness to change and BMI is required for additional 6 months



Indications for Pharmacologic Therapy

- **BMI \geq 30 kg/m²**
- **BMI \geq 27 kg/m² with hypertension, dyslipidemia, type 2 diabetes, or obstructive sleep apnea**

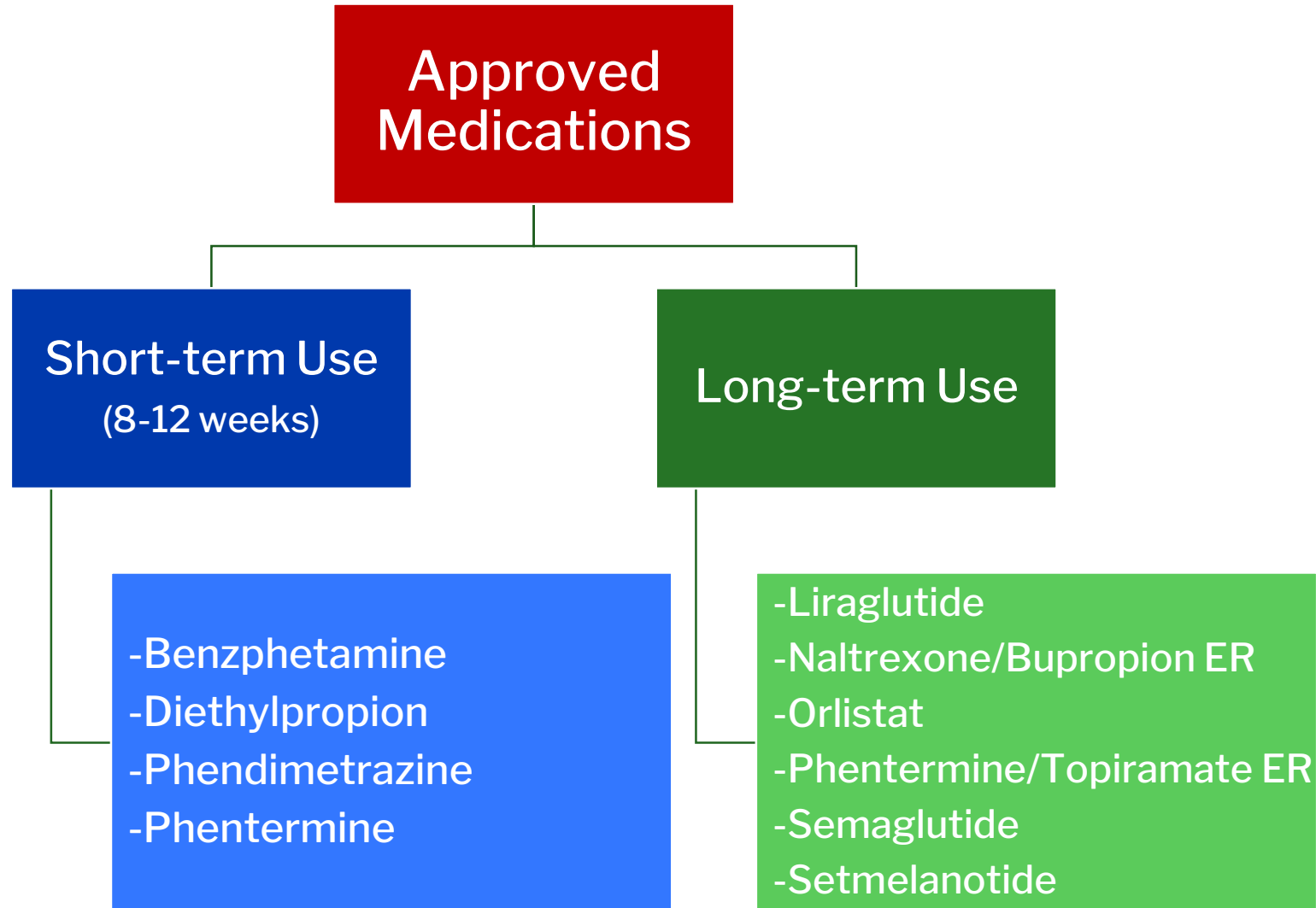
Especially consider for patients who have not achieved weight loss goals (\geq 5% weight loss in 3-6 months)

Weight loss medication should be re-evaluated at 3 months if no noticeable weight loss is observed

- Reassess medication options

If weight loss goals have been achieved after 3-6 months, continue weight loss medication if tolerating

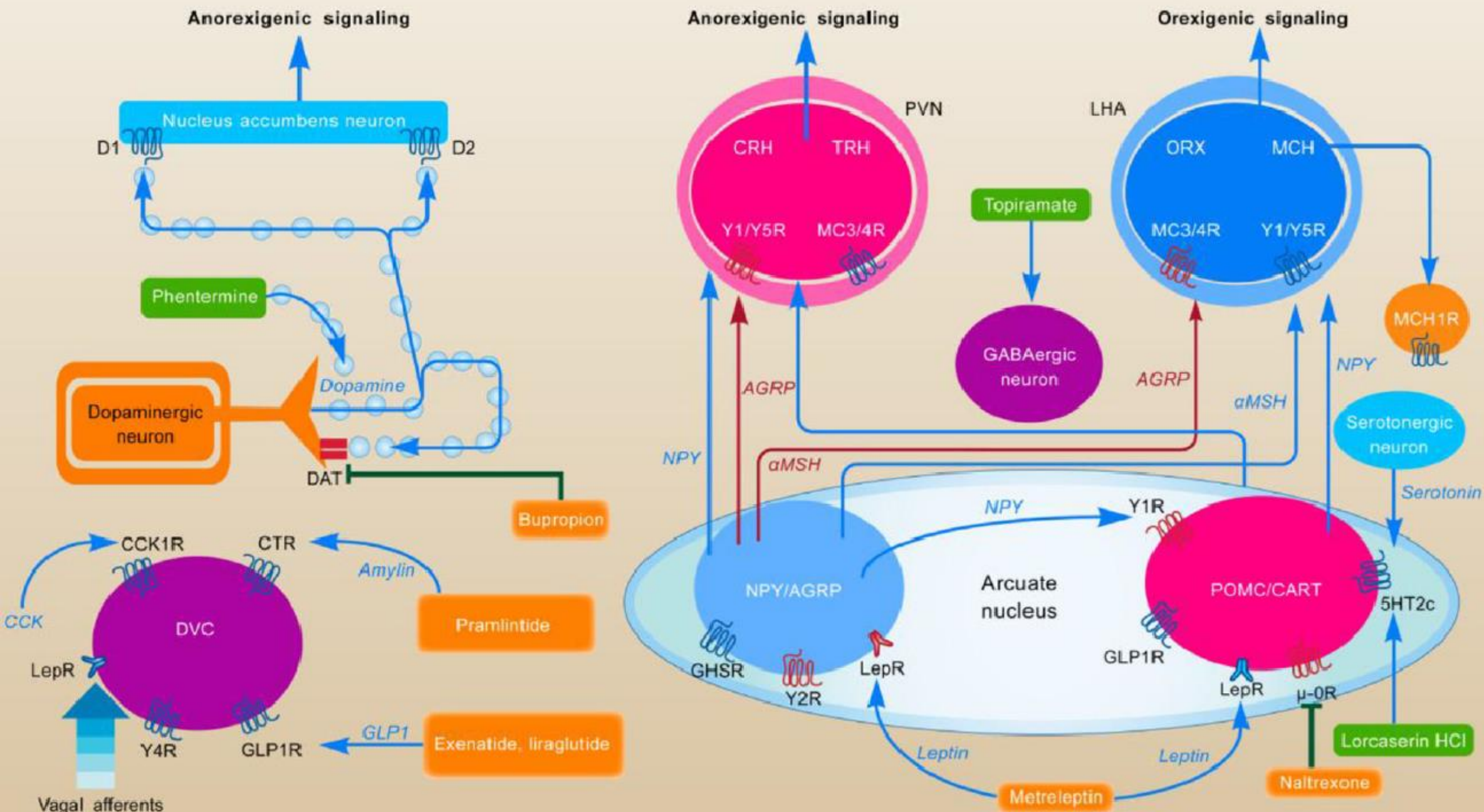
Medications Approved for Weight Loss



Pathophysiologic Targets

Receptors:  Stimulating  Inhibitory

Note: drugs shown in figure do not reflect FDA-approved obesity drugs



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Medications Approved for Long-term Use

Medication	Mechanism of Action	Mean Weight Loss at 1 Year*	Schedule
Liraglutide	GLP-1 receptor agonist	3 mg QD: 5.4%	–
Naltrexone/Bupropion ER	Opioid antagonist/reuptake inhibitor of dopamine and norepinephrine	16/180 mg BID: 4.8%	–
Orlistat	Reversible inhibitor of GI lipases	60 mg TID: 2.5% 120 mg TID: 3.4%	–
Phentermine/Topiramate ER	Sympathomimetic amine anorectic/GABA receptor modulator	7.5/46 mg QD: 6.7% 15/92 mg QD: 8.9%	CIV
Semaglutide injection	GLP-1 receptor agonist	2.4 mg QW: 6.2% to 12.4%**	–
Setmelanotide	Melanocortin 4 receptor agonist***	% Achieving ≥10% wt loss at 1 y: POMC/PCSK1 deficiency: 80% LEPR deficiency: 46%	–

GI, gastrointestinal; GABA, gamma-amino-butyric acid; LEPR, leptin receptor; PCSK1, proprotein convertase subtilisin/kexin type 1; POMC, proopiomelanocortin; GLP-1, glucagon-like peptide-1

*Placebo-subtracted

**At 68 weeks

***Indicated for POMC, PCSK1, or LEPR deficiency; not polygenic

Medications Approved for Long-term Use: Dosing

Medication	Route of Administration	Maintenance Dose	Comments
Liraglutide ¹	SC	3 mg QD	Initiate at 0.6 mg/d x 1 wk; increase by 0.6 mg weekly to 3 mg/d
Naltrexone/ Bupropion ER ²	PO	2 tablets BID	1 tablet (8 mg/90 mg) qAM x 1 wk; 1 tablet morning and evening x 1 wk; 2 tablets morning and 1 tablet evening x 1 wk; then 2 tablets morning and 2 tablets evening
Orlistat ³	PO	120 mg TID	Take with meals containing fat; distribute fat, protein, carbohydrate intake over 3 main meals
Phentermine/ Topiramate ER ⁴	PO	7.5 mg/46 mg qAM	Initiate at 3.75/23 mg qAM x 14 d then increase to 7.5 mg/46 mg daily x 12 wks. If <3% wt loss after 12 wks on 7.5 mg/46 mg, discontinue or increase to 11.25 mg/69 mg daily x 14 d, then increase to 15 mg/92 mg daily. Do not exceed 7.5 mg/46 mg if moderate/severe renal impairment or moderate hepatic impairment
Semaglutide ⁵	SC	2.4 mg QW	0.25 mg QW x 4 wks, then 0.5 mg QW x 4 wks, then 1 mg QW x 4 wks, then 1.7 mg QW x 4 wks, then 2.4 mg QW

1. Saxenda [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; December 2020. 2. Contrave [package insert]. Morristown, NJ: Nalpropion Pharmaceuticals LLC; March 2021. 3. Xenical [package insert]. Montgomery, AL: H2-Pharma, LLC; November 2020. 4. Qsymia [package insert]. Campbell, CA: VIVUS, Inc.; October 2020. 5. Wegovy [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; June 2021.

Medications Approved for Long-term Use: Assessing Treatment Response

Medication	Comments
Liraglutide ¹	<ul style="list-style-type: none"> • Pediatrics: Discontinue if BMI reduction <1% after 12 weeks on maintenance dose • Adults: Discontinue if weight loss <4% after 16 weeks
Naltrexone/ Bupropion ER ²	<ul style="list-style-type: none"> • Discontinue if weight loss <5% after 12 weeks on maintenance dose
Orlistat ³	–
Phentermine/ Topiramate ER ⁴	<ul style="list-style-type: none"> • Discontinue or titrate dose to 15 mg/92 mg if weight loss <3% after 12 weeks on 7.5 mg/46 mg dose • Discontinue if weight loss <5% 12 weeks after escalation to 15 mg/92 mg dose
Semaglutide injection ⁵	–

1. Saxenda [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; December 2020. 2. Contrave [package insert]. Morristown, NJ: Nalpropion Pharmaceuticals LLC; March 2021. 3. Xenical [package insert]. Montgomery, AL: H2-Pharma, LLC; November 2020. 4. Qsymia [package insert]. Campbell, CA: VIVUS, Inc.; October 2020. 5. Wegovy [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; June 2021.

Liraglutide: Clinical Pearls

- Useful in patients with type 2 diabetes/diabetes
- Non-stimulating (non-cardiovascular disease) and useful in patients with
 - Improvement in blood glucose
 - Improvement in lipids
- Tachycardia side effect
- Useful for weight loss

Advise about acute pancreatitis, gallbladder disease

Risk of C-cell tumors

Monitor HR, depression

If T2DM, monitor blood glucose before prescribing and during

T2DM, type 2 diabetes; HR, heart rate

Saxenda [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; December 2020.

Naltrexone/Bupropion ER: Clinical Pearls

- May have benefit in patients with obesity and depression
Monitor HR, BP
- Be cautious combining with other depression meds (potential interaction)
- Has potential to work on “cravings” and binge eating
Numerous drug interactions
- Recommend starting low due to nausea
Risk for seizures, hepatotoxicity, glaucoma
- May not need highest dose, in clinical practice many patients respond on lower doses

BP, blood pressure

Orlistat

Indications and Dose

- Approved in adolescents
- Indication: BMI ≥ 30 kg/m² or BMI ≥ 27 kg/m² with other risk factors
- Dosing:
 - Rx: 120 mg TID with each meal
 - OTC: 60 mg TID with each meal
- Advise patients:
 - Nutritionally balanced, low-calorie diet; avoid excess of calories from fat
 - Take a multivitamin with fat-soluble vitamins

Advise a moderate fat diet

Recommend a multivitamin

Contraindications and Warnings

Contraindications

- Pregnancy, malabsorption, cholestasis

Advise about bowel effects

Warnings:

- Decreased exposure to other drugs; liver injury, increased levels of urinary oxalate

Side Effects

- Oily spotting, flatus with discharge, fecal urgency, fatty/oily stool, oily evacuation, increased defecation and fecal incontinence

Phentermine/Topiramate: Clinical Pearls

- Very potent weight loss agent
 - Positive studies for weight loss (topiramate)
 - Significant number of adverse events (sets of potential AEs)
 - REMS program potential for teratogenicity, cleft lip and cleft palate
 - Sleep disorders (topiramate)
 - Glaucoma (topiramate)
 - Acute angle-closure glaucoma (topiramate)
 - Hypertension and blood pressure (phentermine)
- Dose titration required*
- Discuss paresthesias and taste disturbance*
- Obtain pregnancy test before prescribing and monthly*
- Rare, serious side effects*

AE, adverse events; REMS, Risk Evaluation and Mitigation Strategy

Qsymia [package insert]. Campbell, CA: VIVUS, Inc.; October 2020.

Semaglutide: Clinical Pearls

- Useful in patients with
- Non-stimulating (non-cardiovascular diseases

Advise about acute pancreatitis, gallbladder disease

Risk of C-cell tumors

Monitor HR, depression, suicidal thoughts

- T
 - I
- GI side effects are common
pat
weight on their own

Monitor blood glucose before prescribing and during

Monitor kidney function before prescribing or escalating

ready lost

Principles of Using Medications Approved for Long-Term Use To Treat Obesity

- Use as part of a comprehensive lifestyle change program
- Establish appropriate expectations
- Provide ongoing patient education and support
- Individualize treatment and modify as needed
- Non-responders: Discontinue in absence of weight loss
- Use medications with “chronic use indications” for long term
- Tailor dietary instructions to medication



Emerging Therapy – Tirzepatide

- GIP and GLP-1 receptor agonist
- Approved in 2022 for T2DM
- Is being studied for use in obesity – **not currently FDA-approved for obesity**
 - SURMOUNT-1: complete
 - SURMOUNT-2: estimated completion April 2023 (NCT04657003)

October 6, 2022:

Lilly receives U.S. FDA Fast Track designation for tirzepatide for the treatment of adults with obesity, or overweight with weight-related comorbidities

GIP, glucose-dependent insulinotropic polypeptide

Mounjaro [package insert]. Indianapolis, IN: Eli Lilly and Company; May 2022; Eli Lilly and Company. Published October 6, 2022. Accessed October 15, 2022. <https://investor.lilly.com/news-releases/news-release-details/lilly-receives-us-fda-fast-track-designation-tirzepatide>

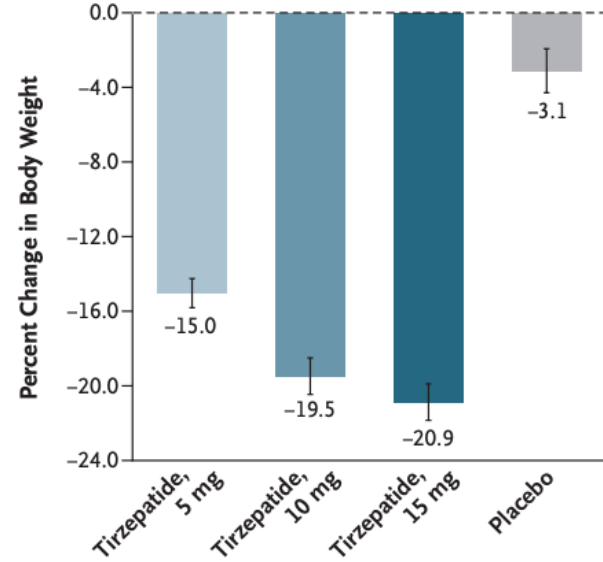


Tirzepatide: SURMOUNT-1

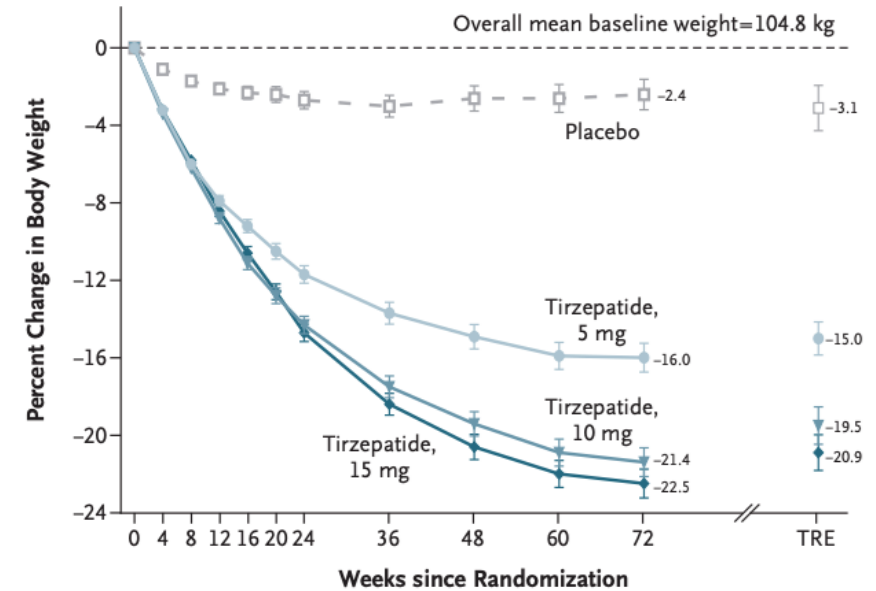
- 72-week trial
- N=2539
- P <.001 for all comparisons with placebo

■ Tirzepatide, 5 mg ■ Tirzepatide, 10 mg ■ Tirzepatide, 15 mg ■ Placebo

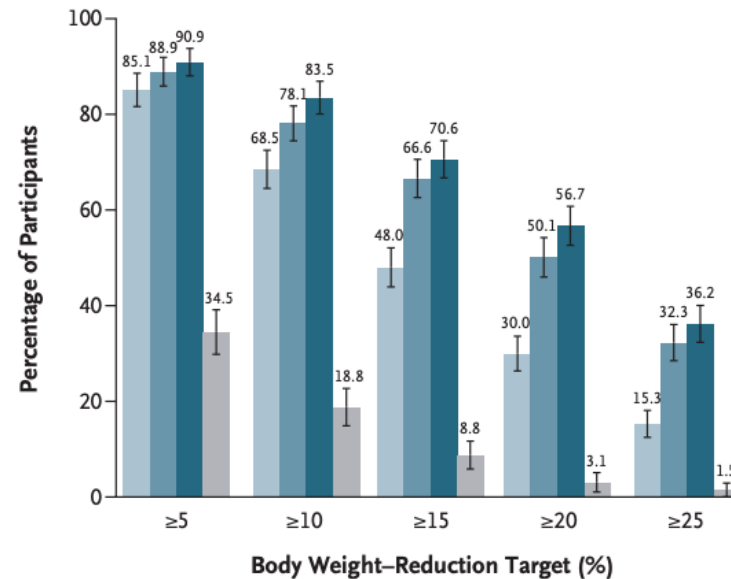
A Overall Percent Change in Body Weight from Baseline (treatment-regimen estimand)



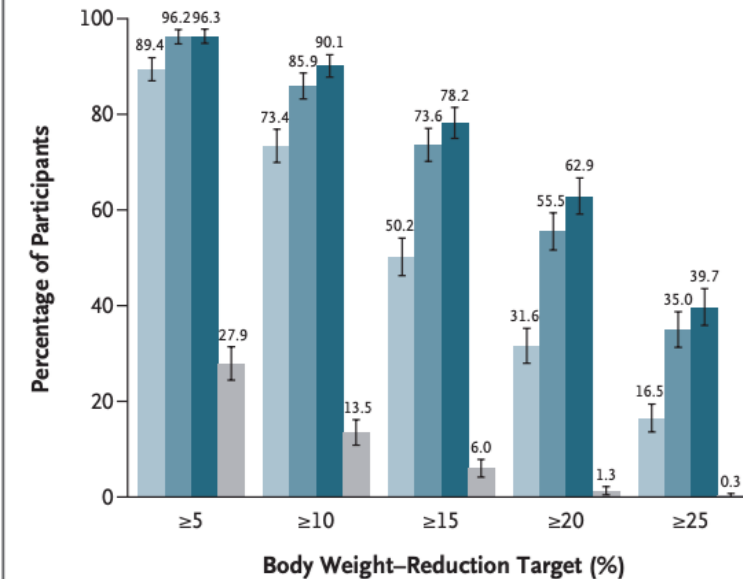
B Percent Change in Body Weight by Week (efficacy estimand)



C Participants Who Met Weight-Reduction Targets (treatment-regimen estimand)



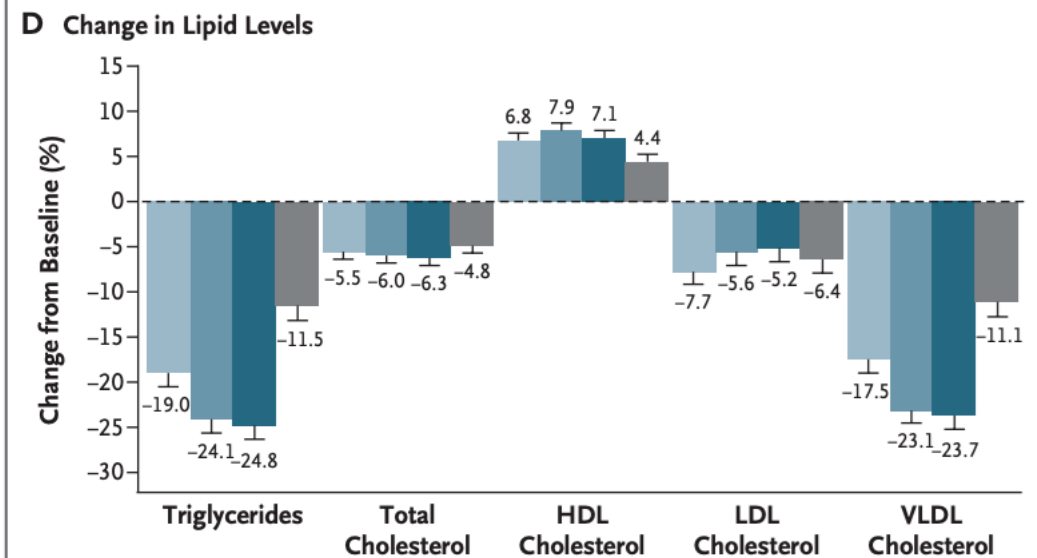
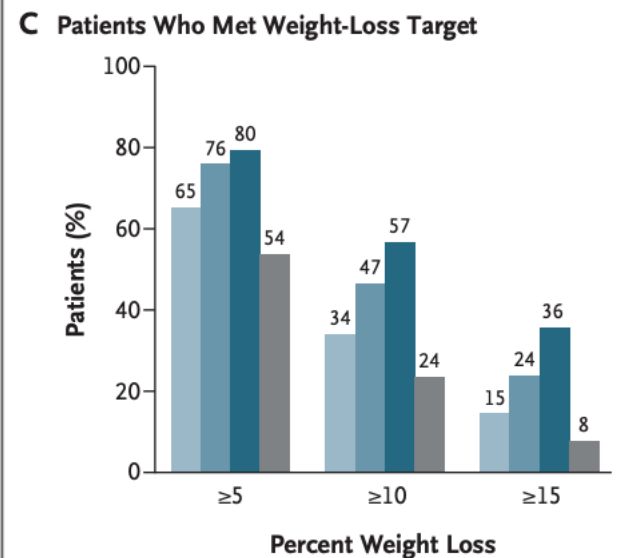
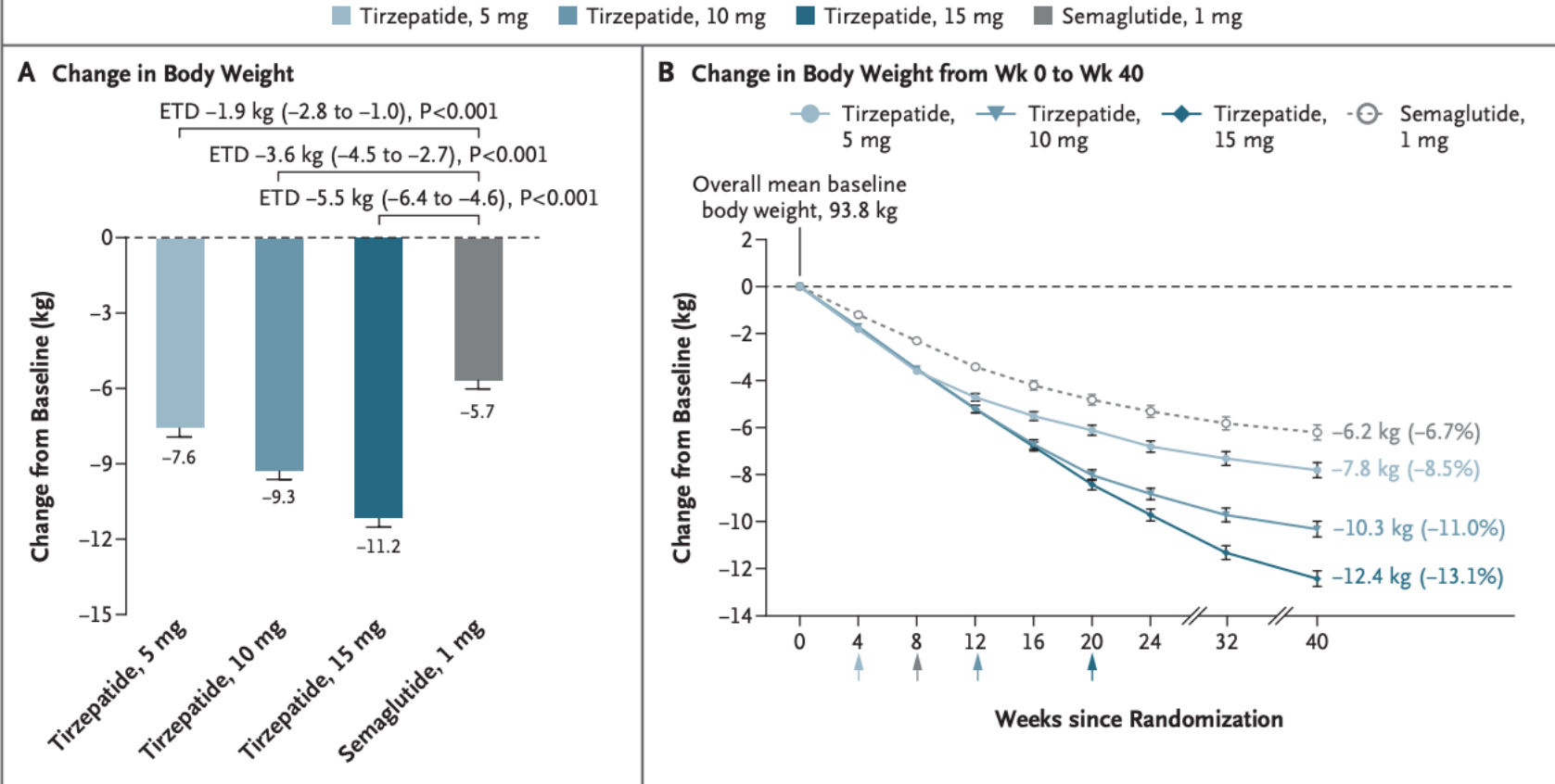
D Participants Who Met Weight-Reduction Targets (efficacy estimand)



From the New England Journal of Medicine, Jastreboff AM, Aronne LJ, Ahmad NN, et al., Tirzepatide Once Weekly for the Treatment of Obesity, 387:201-216. Copyright © 2022 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

Tirzepatide vs. Semaglutide

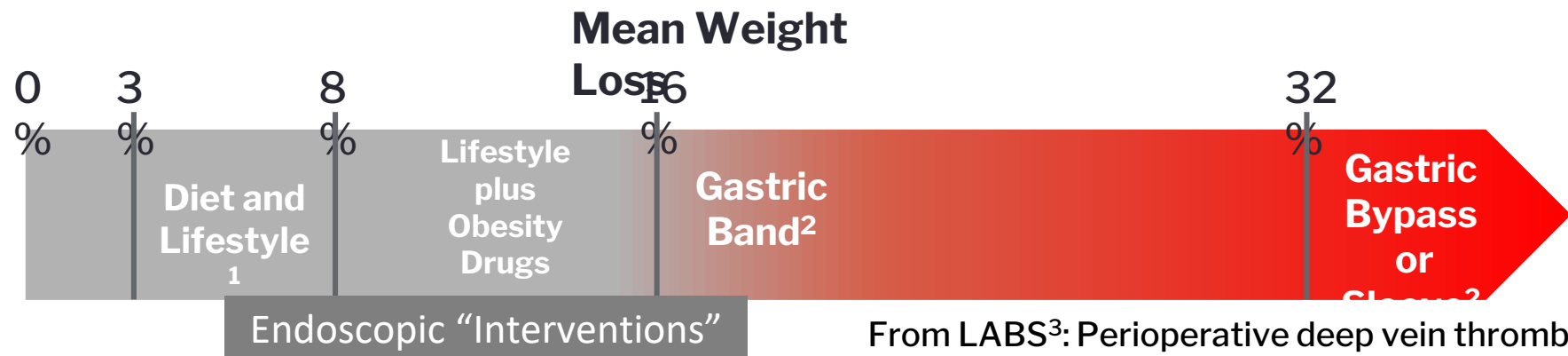
- 40-week trial
- N=1879
- P <.001 for all body weight comparisons



From the New England Journal of Medicine, Frías JP, Davies MJ, Rosenstock J, et al., Tirzepatide versus Semaglutide Once Weekly in Patients with Type 2 Diabetes, 385:503-515. Copyright © 2021 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

Weight Management Intensification Options

- Patients with low risk should have lower intensity, less risk approaches.
- Higher risk approaches are justified when patients have more complicated obesity.



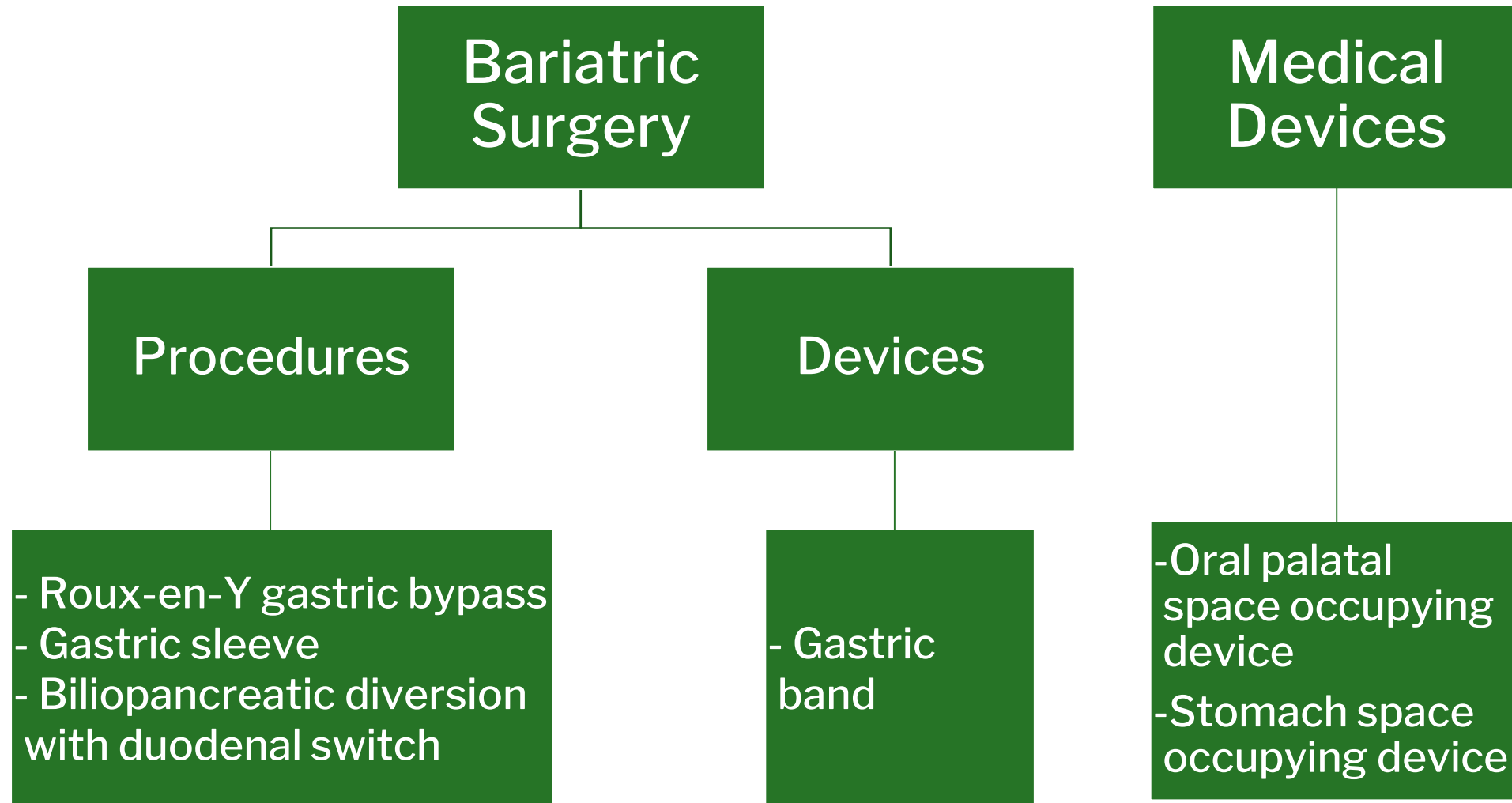
From LABS³: Perioperative deep vein thrombosis, thromboembolism, or death 1% for gastric band 5% for bypass

LABS, longitudinal assessment of bariatric surgery

1. Jensen MD, et al. *Circulation*. 2014;129(25 Suppl 2):S102-S138. 2. Courcoulas AP, et al. *JAMA*. 2013;310(22):2416-2425. 3. Longitudinal Assessment of Bariatric Surgery (LABS) Consortium, et al. *N Engl J Med*. 2009;361(5):445-454.



Surgery and Devices for Weight Loss & Management



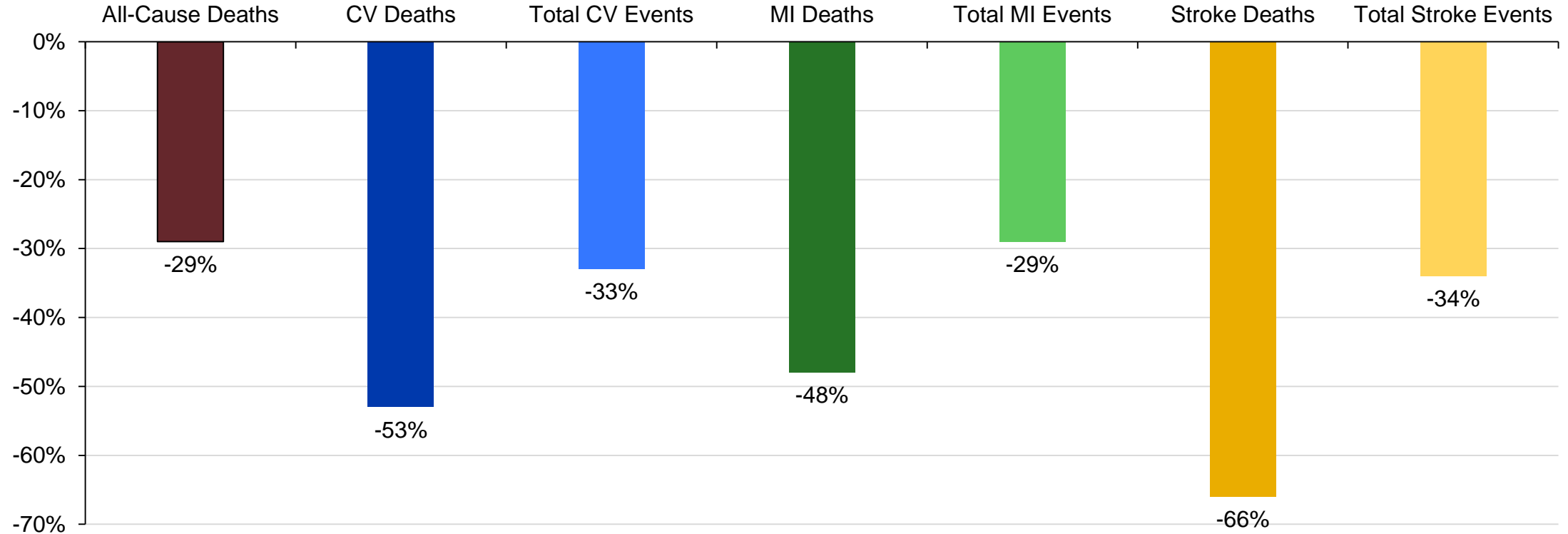
Considerations and Benefits for Surgical Treatment

- Indicated for patients with¹:
 - BMI 35-39.9 kg/m² and ≥1 obesity-related comorbidity
 - BMI ≥40 kg/m²
 - BMI 30-34.9 kg/m²: can consider to treat type 2 diabetes²
- Complications can lead to reoperation³
- Nutritional deficiencies are common with gastric bypass⁴
- Long-term reduction in¹:
 - Body weight
 - Cardiovascular biomarkers, events
 - Other weight-related complications
- Need for ongoing support and intervention



Bariatric Surgery Outcomes: Swedish Obese Subjects Study

Reduction in Events with Bariatric Surgery vs. Control Group



N=2010 who underwent bariatric surgery (baseline BMI 42.4 kg/m²) vs N=2037 who received conventional treatment (baseline BMI 40.1 kg/m²)

Bariatric surgery (gastric bypass 13.2%; banding 18.7%; vertical banded gastroplasty (68.1%))

Median follow-up was 10.9 y for all-cause deaths and 14.7 y for all other outcomes

Mean change in body weight at 10 y was -17% in bariatric surgery group vs +1% in conventional treatment group

CV, cardiovascular;
MI, myocardial
infarction



Why does bariatric surgery work so well?

Food Intake

- Changes in hunger and fullness via enhanced satiety leading to decrease in calorie intake
- Mean caloric intake 600-700 one month postop to 1000-1800 after first year
- Average reduction of 1800 kcal per day from pre-op intake sustained for several years

Potential Mediators of Decreased Food Intake

- Increased transit of food into mid-gut through gastric pouch

Mediators for Food Preferences

- Taste function domains
- Sensory-discriminative (*stimulus identification*)
- Hedonic (*ingestive motivation*)
altered brain responsiveness to high calorie food cues
- Physiological (*digestive preparation*)

Hormonal

- GLP-1 and PYY increase
- Ghrelin decreases

Change in Gut Microbiota

- Short chain fatty acids – calorie extraction/signals

Energy Expenditure

- Increase/Decreased basal metabolic rate after bariatric surgery – in gut?

Food Preferences Change

- Dumping syndrome?
- Conditioned food avoidance?

Calorie Malabsorption

- Exclusion of 10% of the bowel after RYGB unlikely to result in malabsorption

Neural

- Vagal and partial vagal transection

Change in Bile Acids

- Partly responsible for intestinal hypertrophy, anorexigenic hormone secretion and alterations in gut microbiota; activation of FXR signaling



General Recommendations for Bariatric Surgery Follow-up Care

- Monitor weight and evidence of complications
- Assess adherence to lifestyle interventions
- Assess cardiovascular fitness, sleep, mood, substance use, social engagement
- Chemistry, CBC/platelets, lipids
- Avoid NSAIDs
- Adjust medications as needed
- Consider gout, gallstone prophylaxis
- Assess need for antihypertensive therapy
- Vitamin, trace element supplementation
- Consider support groups

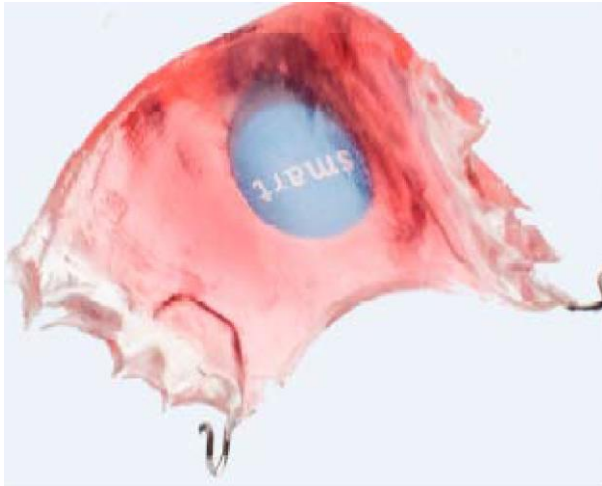
CBC, complete blood count; NSAIDs, nonsteroidal anti-inflammatory drugs

Stomach Space Occupying Devices: Pros and Cons

	Target Weight Loss	Favorable Aspects	Unfavorable Aspects
Intragastric Balloon	10-12%	<ul style="list-style-type: none"> • Endoscopic or swallowed • Good safety profile 	<ul style="list-style-type: none"> • Temporary (6 mos) • Temporary N/V, pain • Early removal rate 10-19%
Ingested, transient, space occupying device	6%	<ul style="list-style-type: none"> • Swallowed, noninvasive • Not absorbed • No major AEs • Increased fullness 	<ul style="list-style-type: none"> • Minor GI AEs • Only 24-wk trial; no long-term data



Oral Palatal Space Occupying Medical Device*



- Device worn only at mealtime to limit bite size and slow food intake
- Embedded temperature recording sensor allows monitoring of device usage
- Use results in ~2% weight loss at 16 wks
- Indicated for weight management (not weight loss) in combination with behavioral therapy in patients with BMI 27-35 kg/m²

*Self Monitored Alimentary Restriction Therapy (SMART) device

Access and Affordability: Helpful Apps and Programs

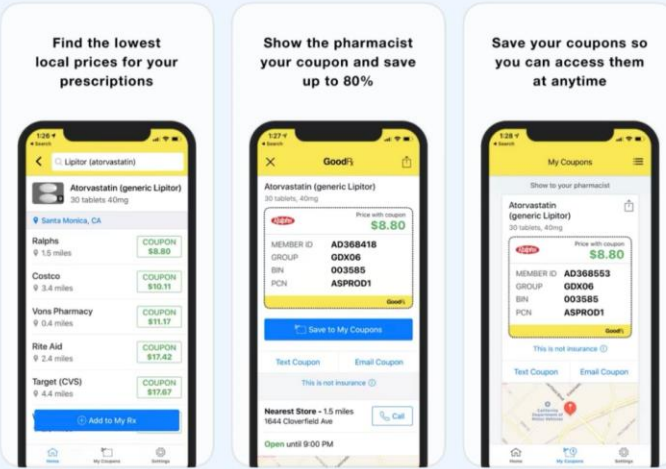
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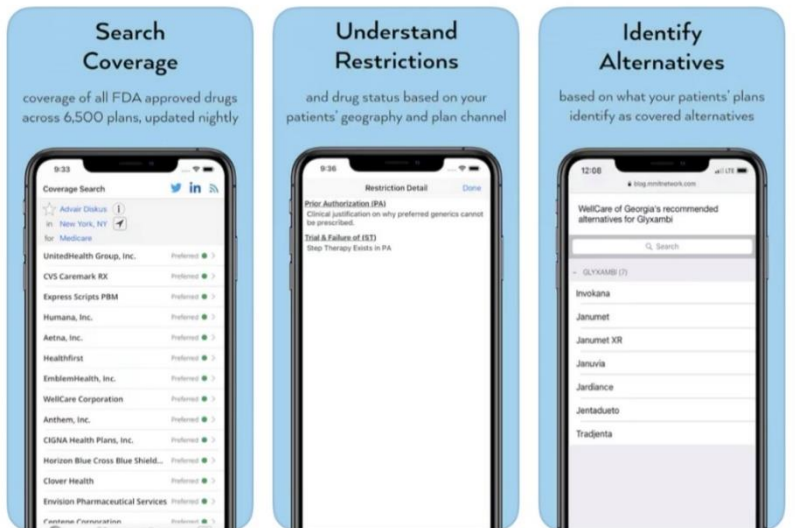
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Search Coverage coverage of all FDA approved drugs across 6,500 plans, updated nightly

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Identify Alternatives based on what your patients' plans identify as covered alternatives



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Resident Name
