Staying in the Solution: How Do We Implement Evidence in Obesity Care?

Provided by
HME
Haymarket Medical Education

Supported by an educational grant from **Lilly**

Pre-test

- Please be sure to scan the QR code at your table to complete the activity pre-test before we begin.

A hard copy is available if needed.

Faculty

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Learning Objectives

- **Apply** the most recent evidence-based guidelines and emerging data for the diagnosis and management of obesity as a chronic, treatable disease
- **Review** recent efficacy and safety outcomes of clinical trials of available and emerging anti-obesity medications (AOMs) and the implications for real-world practice
- **Employ** holistic care plans for patients with obesity that incorporate education and principles of shared decision-making (SDM) while avoiding the perception of stigma or bias

Accreditation Statements

In support of improving patient care, this activity has been planned and implemented by Haymarket Medical Education. Haymarket Medical Education is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

AAFP

The AAFP has reviewed *Staying in the Solution: How Do We Implement Evidence in Obesity Care?,* and deemed it acceptable for AAFP credit. Term of approval is from 06/21/2024 to 06/21/2025. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

This session is approved for 1.0 Live AAFP Prescribed.

Credit Designation Statements

PHYSICIANS:

Haymarket Medical Education designates this live activity for a maximum of 1.00 *AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

AAFP

AMA/AAFP Equivalency:

AAFP Prescribed credit is accepted by the American Medical Association as equivalent to *AMA PRA Category 1 credit(s)*™ toward the AMA Physician's Recognition Award. When applying for the AMA PRA, Prescribed credit earned must be reported as Prescribed, not as Category 1.

Faculty Disclosures

- Dr. Bade Horn is a consultant for Gelesis, Lilly, and Novo Nordisk, Inc. She is an advisor for Lilly and Novo Nordisk, Inc., and is also on the speakers' bureau for Novo Nordisk, Inc.
- Dr. Vega is a consultant for Boehringer Ingelheim and GlaxoSmithKline.

ACCREDITED PROVIDER DISCLOSURE

None of the planners, reviewers, Haymarket Medical Education, and the Hypersomnia Foundation staff for this educational activity have relevant financial relationship(s) with ineligible companies to disclose.

All of the relevant financial relationships listed for these individuals have been mitigated.

PART 1

Meeting the Unmet Challenges in Obesity Care

Obesity:
Scope of the Problem

Obesity Is a Chronic Disease

- Obesity is defined by the World Health Organization (WHO) as *excess abnormal body fat, which may impair health*
- Body mass index (BMI) is a good population measure of body fat and an imperfect measure in individuals

For Europids:

Overweight BMI >25 kg/m^2

Obesity BMI >30 kg/m^2

Waist circumference: 35 inches for women & 40 inches for men

Jensen MD, et al. *Obesity.* 2014;22(S2):S1-S410.

For Asians:

Overweight BMI >23 kg/m^2

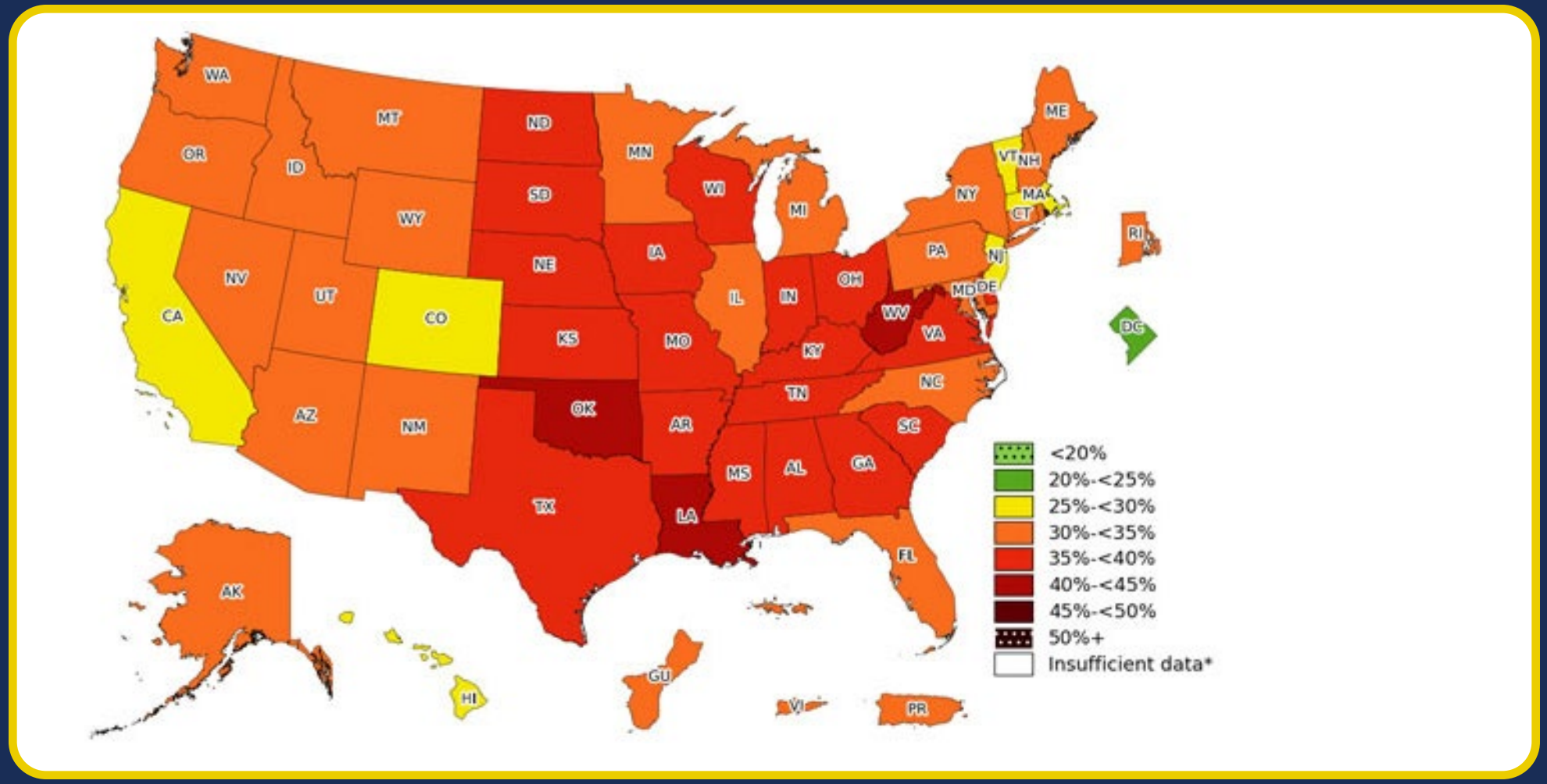
Obesity BMI >25 kg/m^2

Waist circumference: 31.5 inches for women & 35 inches for men

WHO/IASO/IOTF, 2000.

(http://www.idi.org.au/obesity_report.htm)

Geographical Disparities in the United States



https://www.cdc.gov/obesity/data/prevalence-maps.html

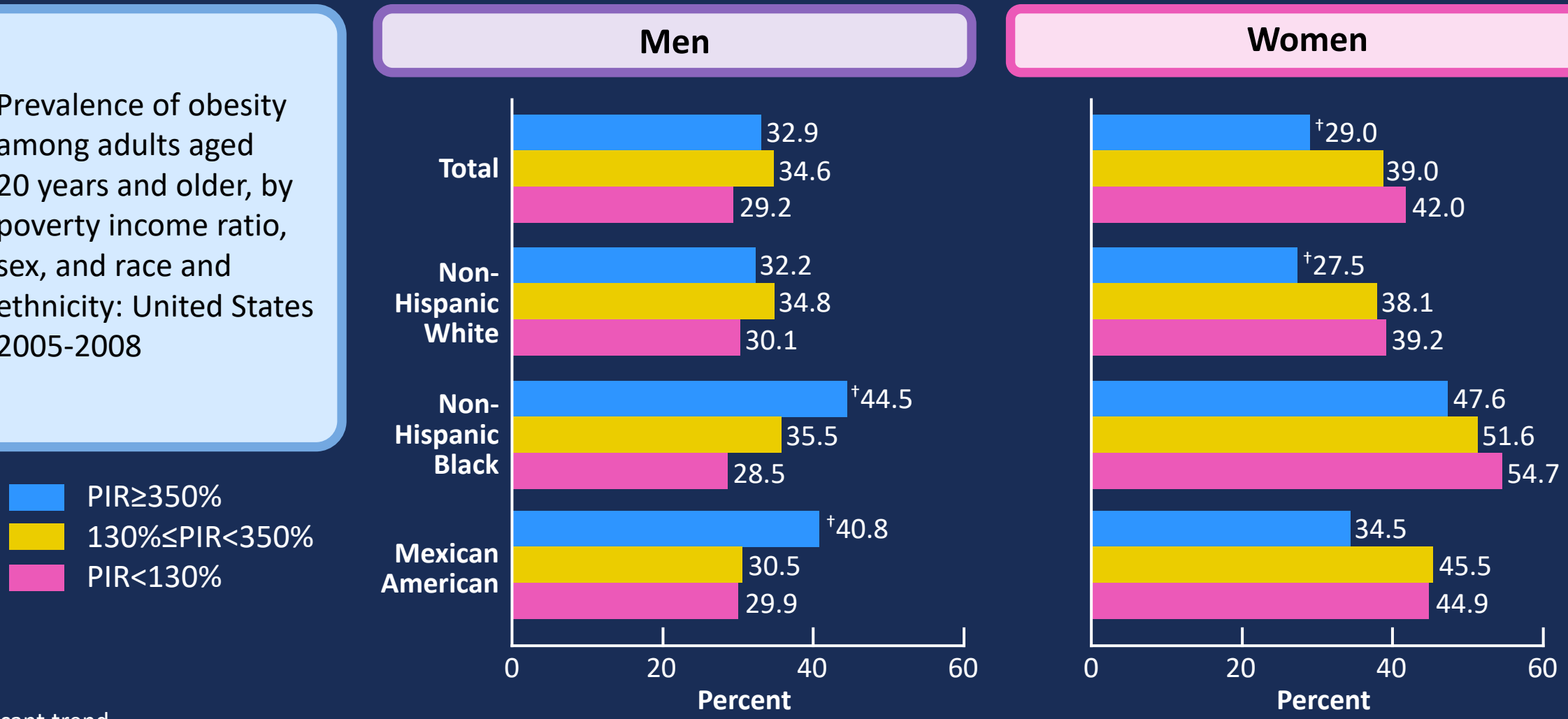
Obesity Rates for Adults in the United States in 2022, By Race/Ethnicity

- Black adults had the highest obesity rates of any race or ethnicity in the United States, followed by American Indians/Alaska Natives, and Hispanics
  - As of that time, approximately 44% of all Black adults had obesity
- Obesity rates for Asian women (14.8%) and men (10.1%) are much lower than the rates for the other racial/ethnic groups

https://www.statista.com/statistics/207436/overweight-and-obesity-rates-for-adults-by-ethnicity/

Obesity and Socioeconomic Status Among U.S. Adults

Prevalence of obesity among adults aged 20 years and older, by poverty income ratio, sex, and race and ethnicity: United States 2005-2008



†Significant trend.

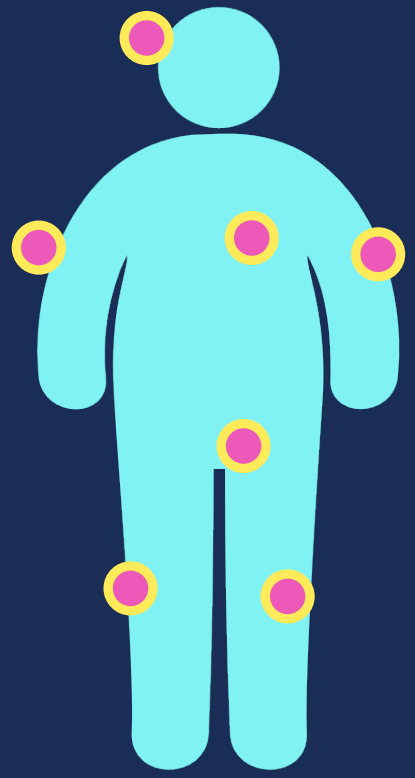
PIR, poverty income ratio. Persons of other race and ethnicity included in total.

SOURCE: CDC/NCHS, National Health and Nutrition Examination Survey, 2005-2008.

Comorbidities of Obesity

Complications associated with obesity include:

- Type 2 diabetes
- Heart/Cardiovascular Disease
- Cancer
- Arthritis
- Urinary incontinence
- Infertility
- Depression
- Anxiety
- Obstructive sleep apnea
- MASLD



Overweight and obesity are defined as abnormal or excessive fat accumulation that presents a risk to health

Despite this, healthcare systems focus on treating the **complications vs the cause**

https://obesityopen.org/content/uploads/2020/07/Clinical-Obesity.pdf

How Does Obesity Drive Comorbidities?

- Burden of excess fat – biomechanical effects
  - Knee arthritis
  - Obstructive sleep apnea
  - GERD
  - Urinary incontinence
  - Others
- Products of excess abnormal fat
  - Prothrombotic effects
  - Proinflammatory effects
  - Immune function effects
  - Promote blood pressure elevation
  - Promote insulin resistance
  - Promote angiogenesis
  - Others

Coelho M, et al. *Arch Med Sci*. 2013;9(2):191-200.

Diagnosis/Staging

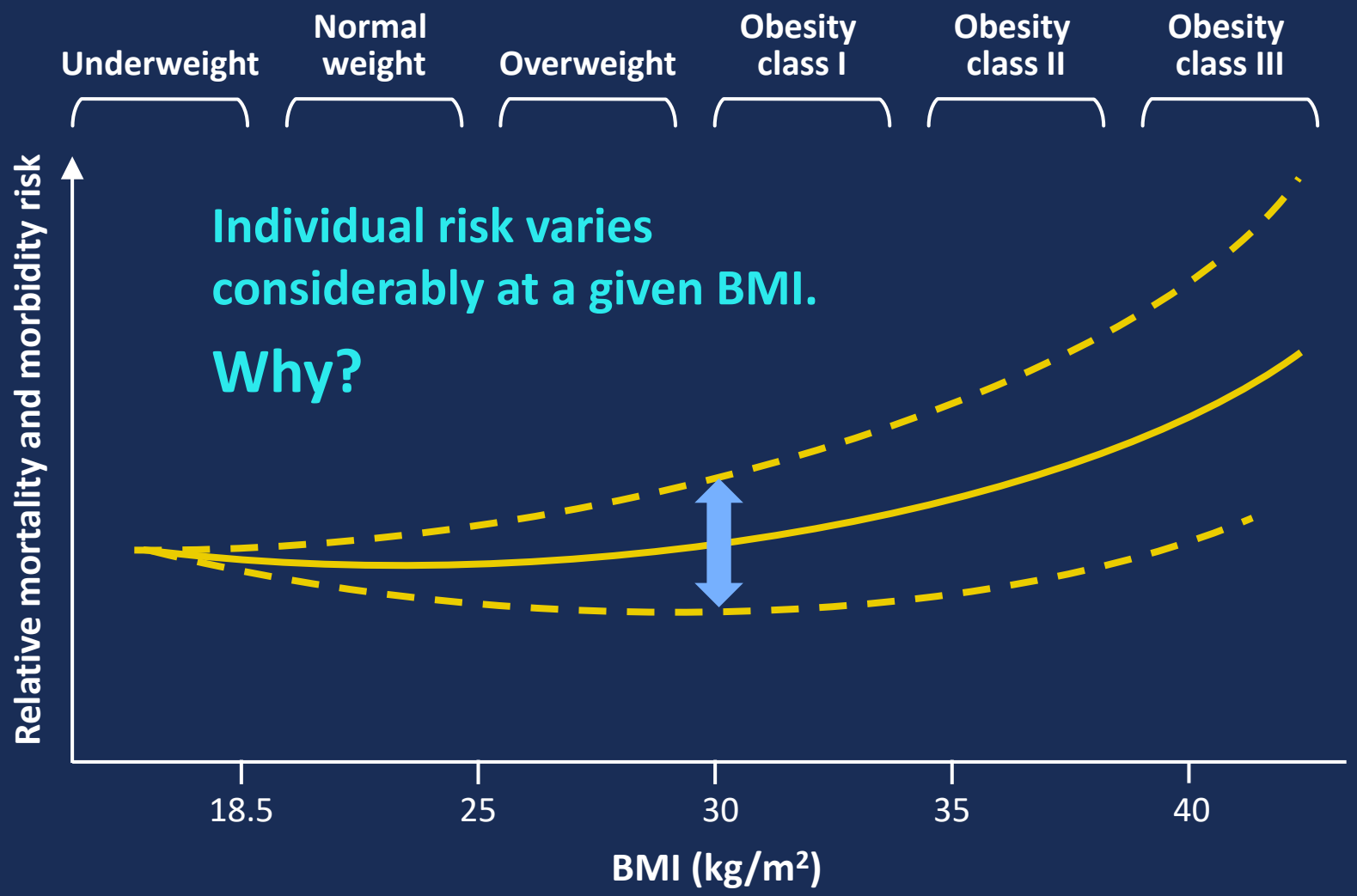
How Do You Make a Clinical Diagnosis of Obesity?

- Body mass index (BMI) is easy to measure and inexpensive
- It also has standardized cutoff points for overweight and obesity and is strongly correlated with body fat levels as measured by the most accurate methods

However, BMI is an imperfect measure because it does not directly assess body fat and is misleading about the effects of body fat mass on mortality rates

https://www.ama-assn.org/delivering-care/public-health/ama-use-bmi-alone-imperfect-clinical-measure

Limitations of the BMI



AMA June 14, 2023

Body mass index (BMI) is easy to measure and inexpensive. But BMI is an imperfect measure because it does not directly assess body fat. Thus, the AMA suggests that it be used in conjunction with other valid measures of risk such as, but not limited to, measurements of visceral fat, body adiposity index, body composition, relative fat mass, waist circumference, and genetic/metabolic factors.

Gonzalez-Muniesa P, et al. *Nat Rev Dis Primers*. 2017;3:17034.

Edmonton Obesity Staging System

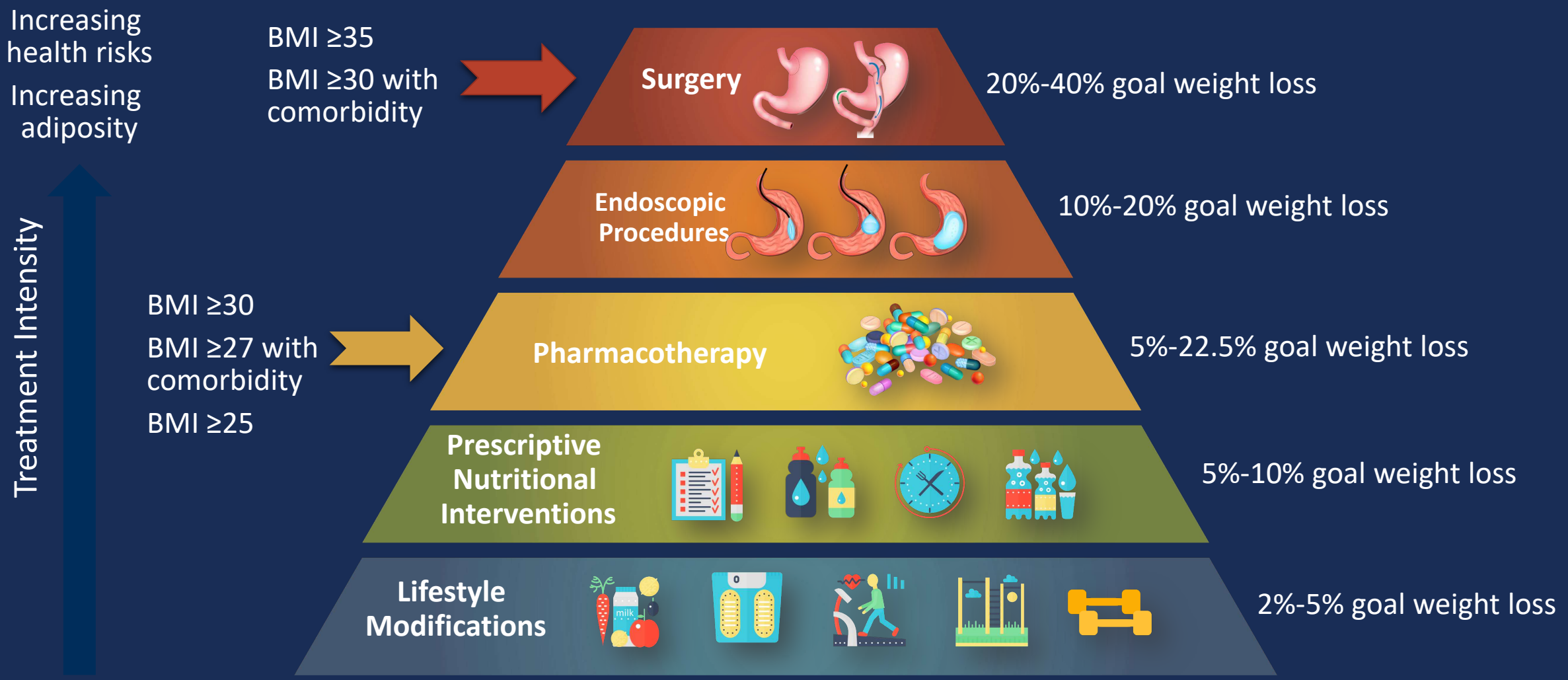
Stage	Severity	Characteristics
0		No obesity-related risk factors, physical symptoms, psychopathology, or functional limitations
1	Mild	• BP ≥130/85 mmHg or ≤125/75 mmHg with T2D • FPG 100-124 mg/dL • Total cholesterol 200–240 mg/dL; triglycerides 150/199 mg/dL; HDL-C <60 mg/dL • Shortness of breath during physical activity
2	Moderate	• Diagnosed/treated hypertension; untreated BP ≥140/90 mmHg or ≥130/80 wit T2D • T2D or untreated FPG ≥125 mg/dL • Diagnosed hypercholesterolemia; untreated total cholesterol ≥240 mg/dL, triglycerides ≥200 mg/dL, HDL-C <40 mg/dL • Gout, depression, fatigue, urinary leakage, low back pain, joint stiffness • Reported emotional outlook of “generally sad” or “fair” self-reported health
3	Severe	• Chest pain, MI, calf pain during exercise, stroke, shortness of breath when sitting or sleeping cardiomegaly • Psychological/psychiatric counseling • Reported emotional outlook of “often depressed” or “poor” self-reported health

BP, blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; MI, myocardial infarction; T2D, type 2 diabetes.

Sharma AM, Kushing RF. *Int J Obes (Lond)*. 2009;33(3):289-95.

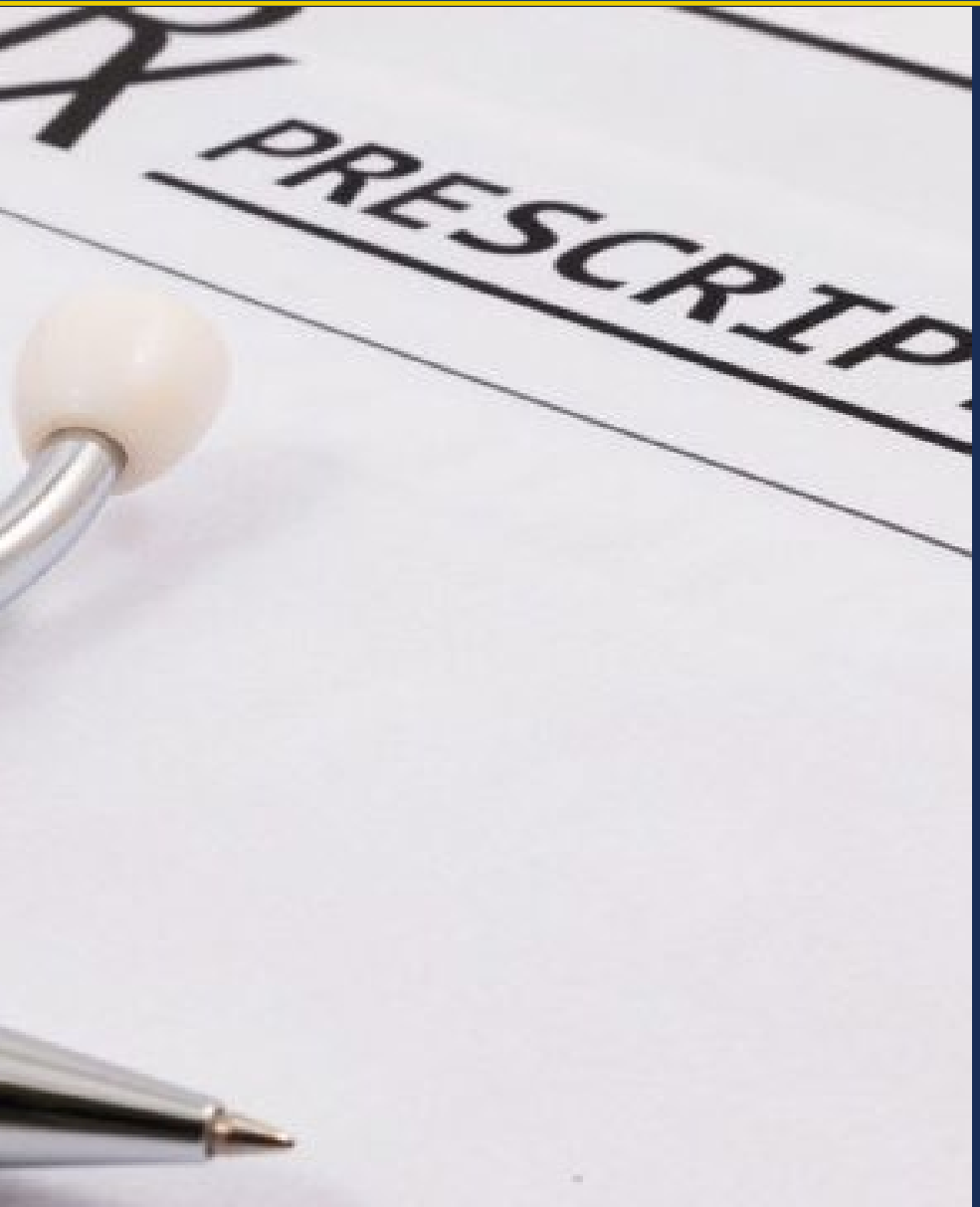
Treatment Strategies

Obesity Treatment Pyramid



Slide courtesy of Angela Fitch, 2020.

Anti-Obesity Medications
FDA Criteria



- For patients with BMI ≥30
- For patients with BMI ≥27 or above at least 1 comorbidity (hypertension, dyslipidemia, CHD, type 2 diabetes, sleep apnea)
- In conjunction with lifestyle interventions
- Semaglutide 2.4 mg indicated in people with overweight or obesity at risk for recurrent cardiovascular event

A Multitudes of Organizations Recommend Treating Obesity Via Pharmacotherapy

- American Academy of Pediatrics
- American Association of Clinical Endocrinology
- American College of Cardiology
- American College of Endocrinology
- American Diabetes Association
- American Gastroenterological Association
- American Heart Association
- American Society for Metabolic and Bariatric Surgery
- Endocrine Society
- Obesity Medicine Association
- The Obesity Society
- Veterans Health Administration's (VHA) Office of VA/DoD Health Affairs

Medications for Chronic Weight Management

Agent	Mechanism of action	Effect	Approval
Phentermine (US Only)*	▪ Sympathomimetic	Appetite regulation	1959
Orlistat (Xenical, Alli)	▪ Pancreatic lipase inhibition	Reduced fat absorption	1999
Phentermine/ topiramate ER (Qsymia)	▪ Sympathomimetic ▪ Anticonvulsant (GABA receptor modulation, carbonic anhydrase inhibition, glutamate antagonism)	Appetite regulation	2012
Naltrexone/bupropion SR (Contrave/Mysimba)	▪ Opioid receptor antagonist ▪ Dopamine/noradrenaline reuptake inhibitor	Appetite regulation	2014
Liraglutide (Saxenda)	▪ GLP-1 receptor agonist	Appetite regulation	2014
Semaglutide (Wegovy)	▪ GLP-1 receptor agonist	Appetite regulation	2021
Tirzepatide (Zepbound)	▪ GIP/GLP-1 receptor co-agonist	Appetite regulation	2023
Setmelanotide (Imcivree)	▪ Melanocortin-4 receptor agonist	Appetite suppression	Approved 2020 (rare genetic conditions; deficiency of POMC, PCSK1, or LEPR)
Metreleptin (Myalept)	▪ Recombinant human leptin analog	Management of lipodystrophy	2014 (leptin deficiency only)

* Off-label for chronic weight management.
ER, extended release; GABA, gamma-aminobutyric acid; SR, sustained release

Third-generation Anti-Obesity Medications

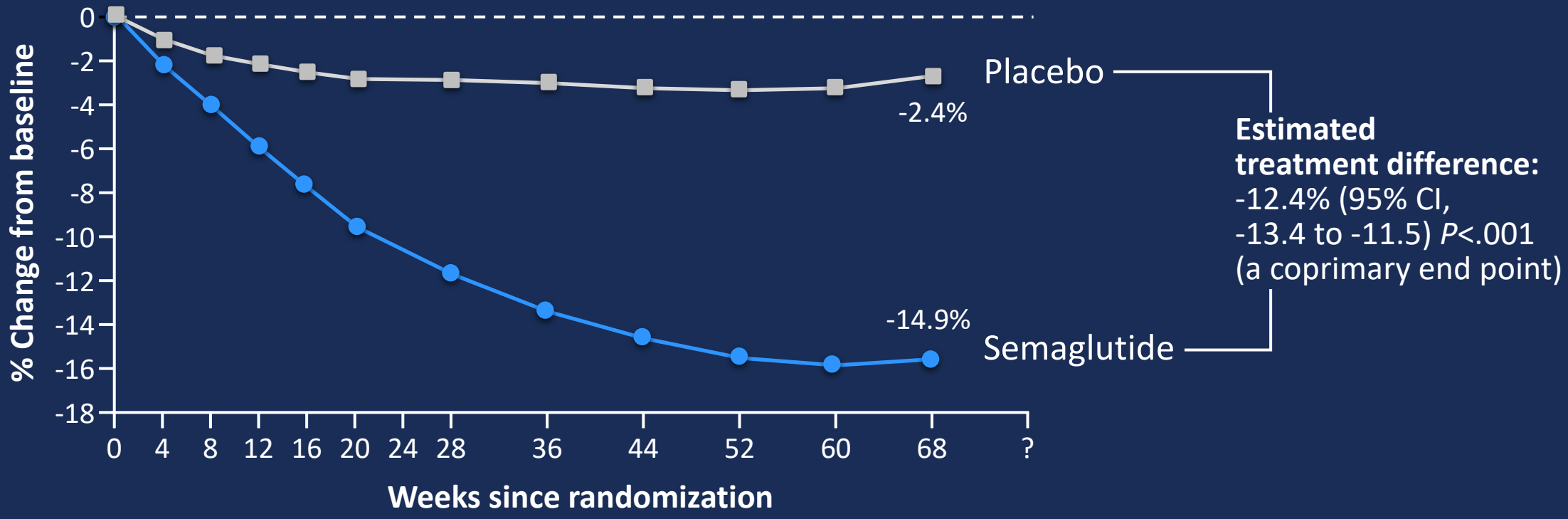
Tirzepatide
(Dual GIP/GLP-1 receptor co-agonist)

Semaglutide
(GLP-1 RA)

Semaglutide 2.4 mg Weekly

GLP-1 Receptor Agonist:

- Common SE: GI – nausea, vomiting, diarrhea, constipation
- Avg. weight loss of 34 lbs = 14.9% weight loss in the total trial population
- 16.9% weight loss compared with 2.4% in subjects who completed the trial and stayed on medication



Wilding JPH, et al. *N Engl J Med*. 2021;18;384(11):989-1002.

SELECT Trial (Semaglutide)

SELECT Trial: primary and confirmatory secondary endpoints

Beneficial effects of semaglutide 2.4 mg on cardiovascular risk vs. placebo

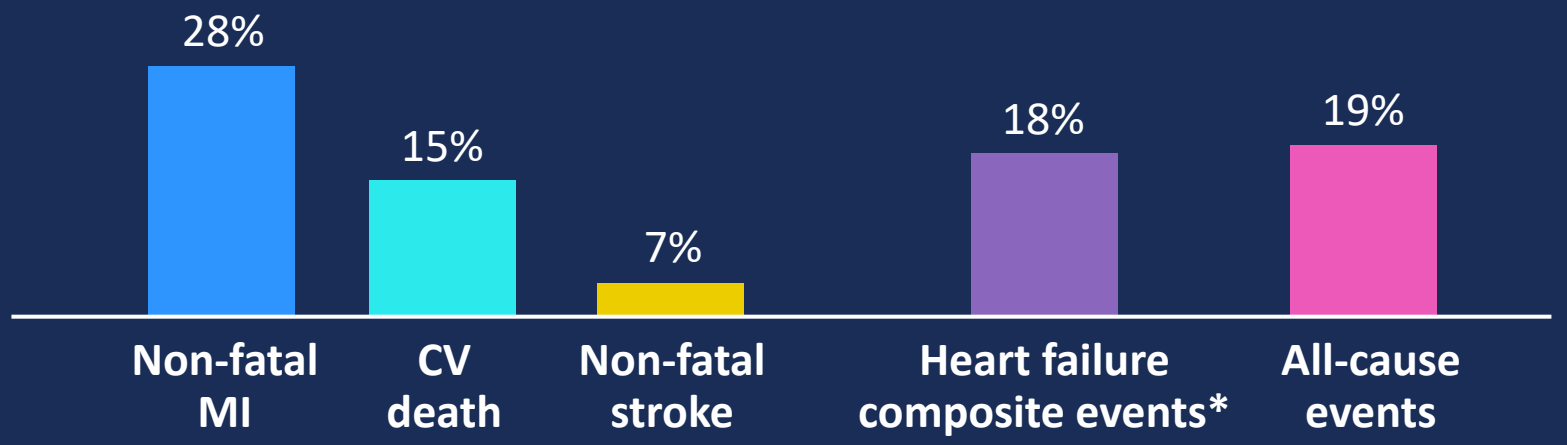
Primary endpoint
(top-line readout, 8 Aug, 2023)

20%

Relative risk reduction in MACE-3 events
(statistically significant)

MACE-3 components
(relative risk reduction)

Confirmatory secondary endpoints
(relative risk reduction)



Statistical significance achieved over length of trial

Since CV death, the first confirmatory secondary endpoint, missed statistical significance, the remaining secondary confirmatory endpoints were not tested for superiority due to hierarchical testing

*Including cardiovascular death, urgent heart failure visits and hospitalizations.

Lincoff A, Brown-Frandsen K, Colhoun H, et al. Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes. *N Engl J Med.*

March 2024

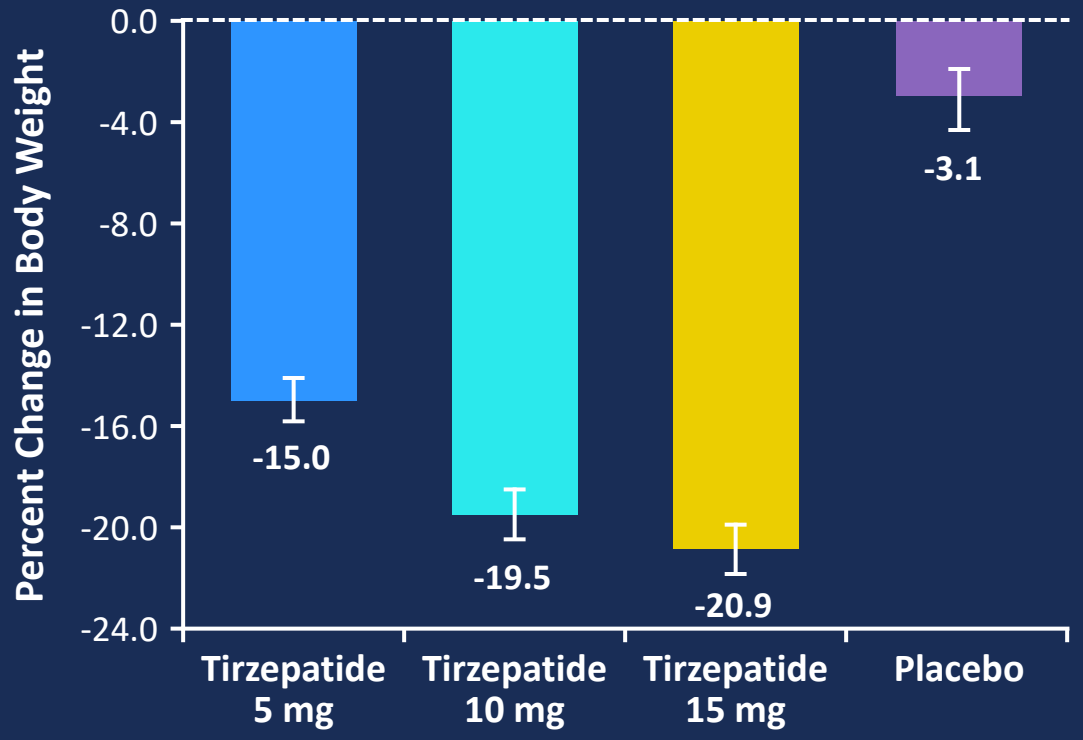
- U.S. Food and Drug Administration approved a new indication for use for semaglutide 2.4 mg injection to reduce the risk of cardiovascular death, heart attack and stroke in adults with cardiovascular disease and either obesity or overweight
  - "… (semaglutide) should be used in addition to a reduced calorie diet and increased physical activity"

https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-reduce-risk-serious-heart-problems-specifically-adults-obesity-or

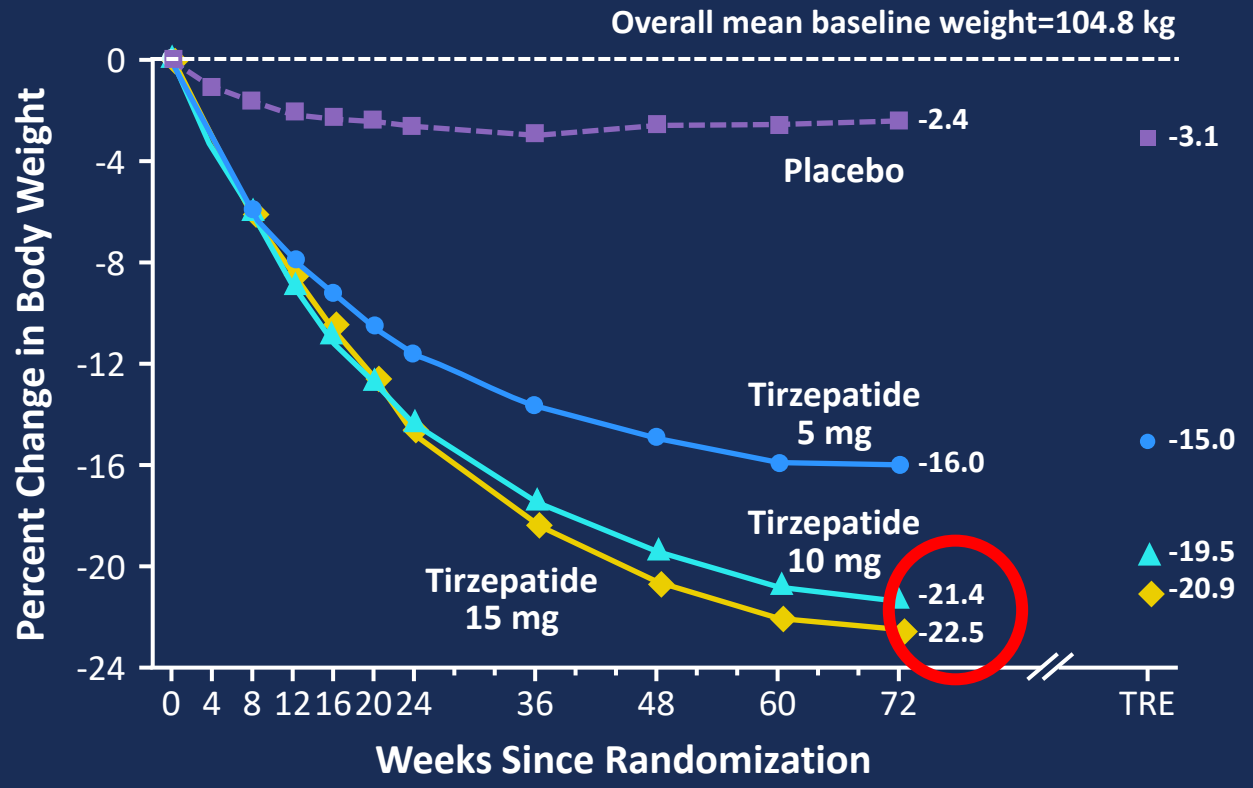
SURMOUNT-1 (Tirzepatide)

Tirzepatide 5 mg Tirzepatide 10 mg Tirzepatide 15 mg Placebo

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



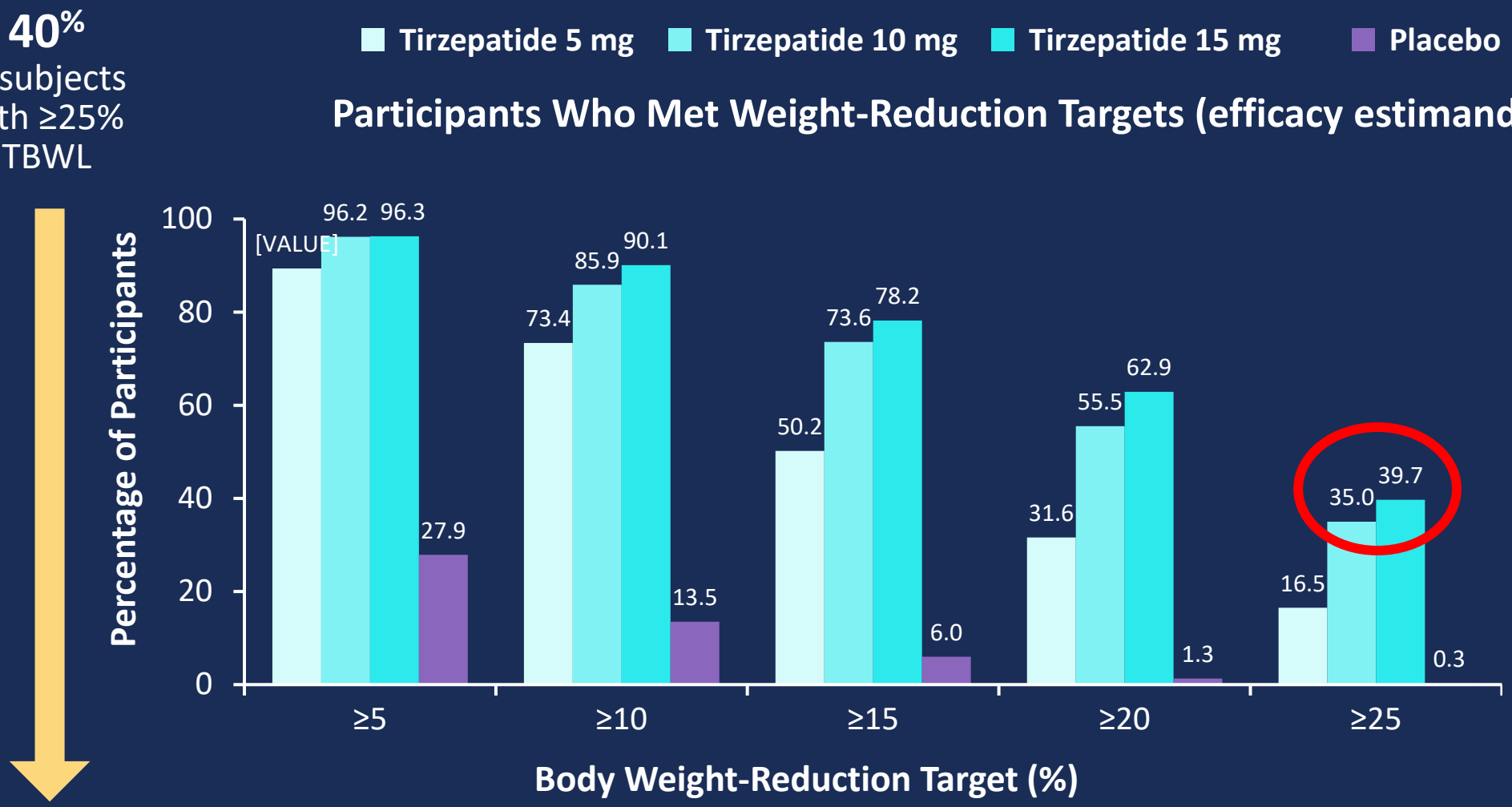
Percent Change in Body Weight By Week
(efficacy estimand)



Jastreboff AM, et al. *N Engl J Med*. 2022;387(3):205-216.

SURMOUNT-1 (Tirzepatide; *cont'd*)

40% of subjects with ≥25% TBWL



GLP-1/GIP: Tirzepatide

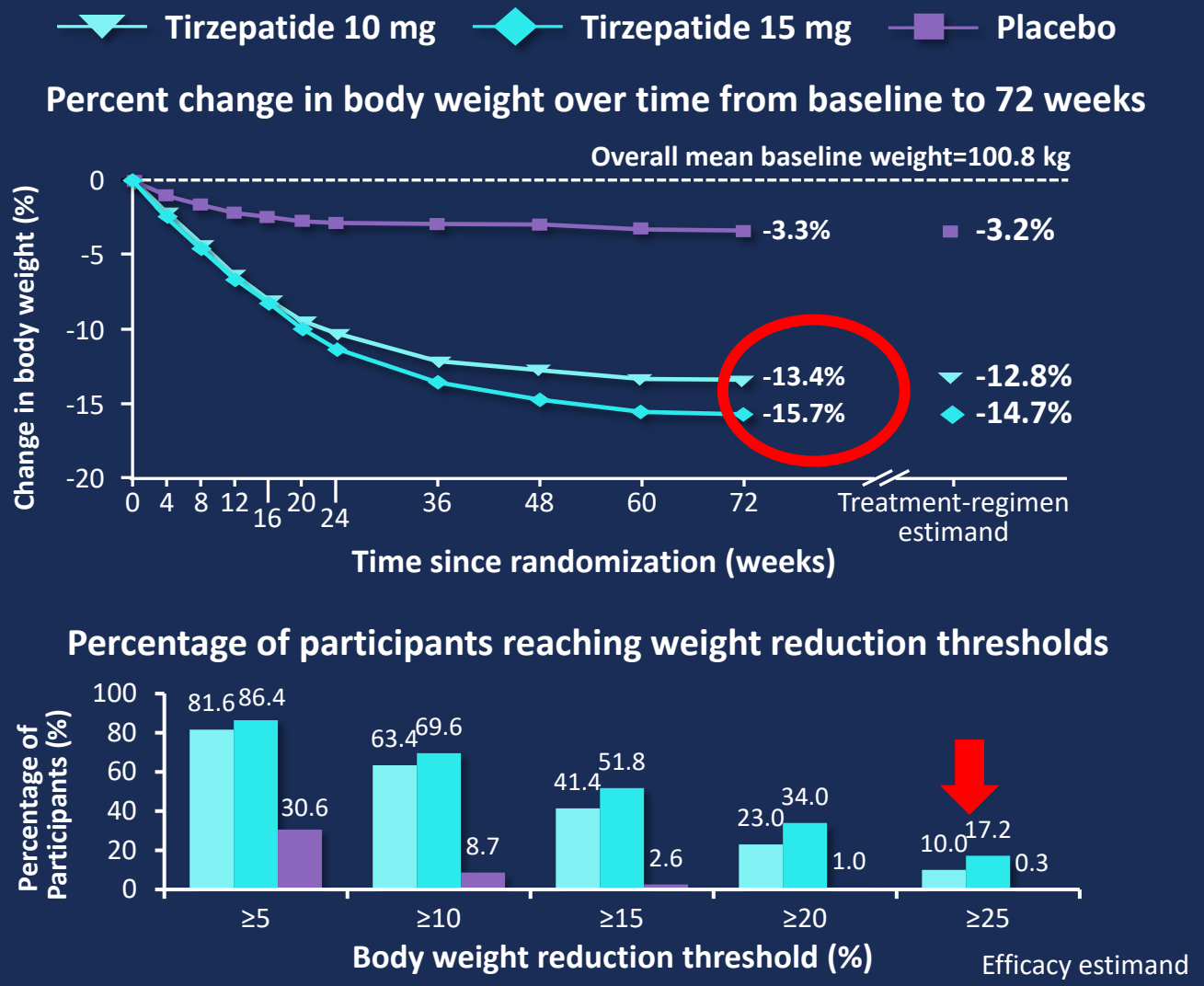
- 40% of subjects lost 25% or more of their total body weight
  - Ex 1: 300 lb 25% TBWL = 75 lb; new weight = 225 lb
  - Ex 2: 250 lb 25% TBWL = 62.5 lb; new weight = 187.5 lb

TBWL, total body weight loss.

Jastreboff AM, et al. *N Engl J Med*. 2022;387(3):205-216.

SURMOUNT-2 DATA (Tirzepatide)

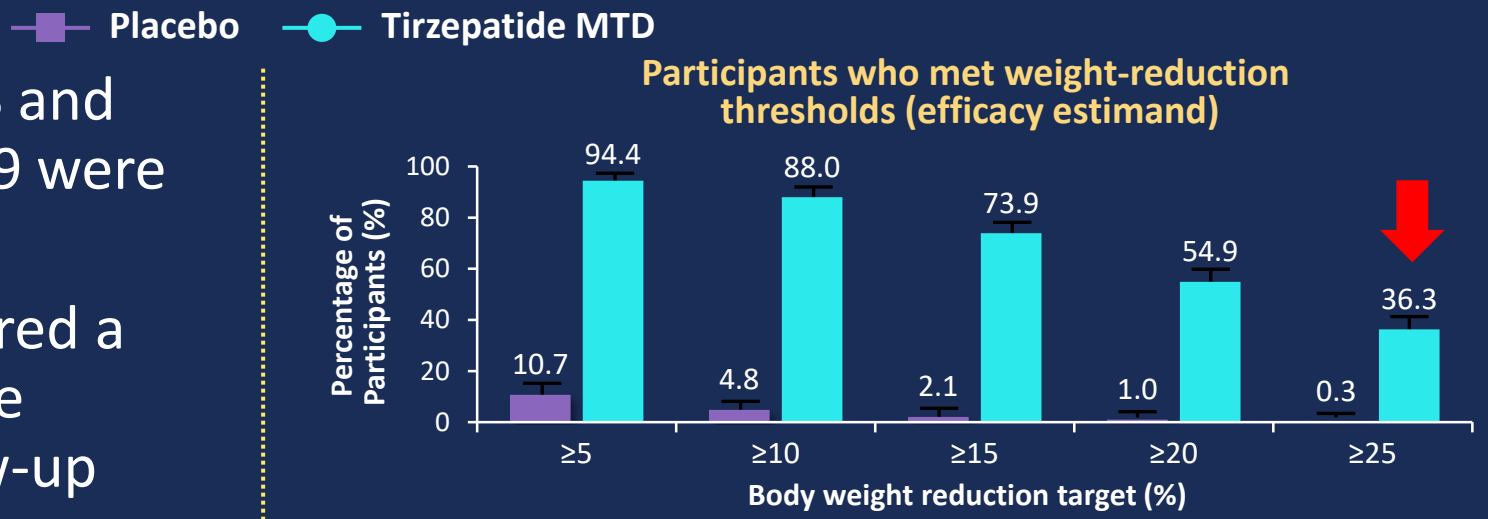
- 938 subjects with OW or obesity WITH diabetes
- 15.7% TBWL
- First time double-digit weight loss has been demonstrated in subjects with obesity and diabetes

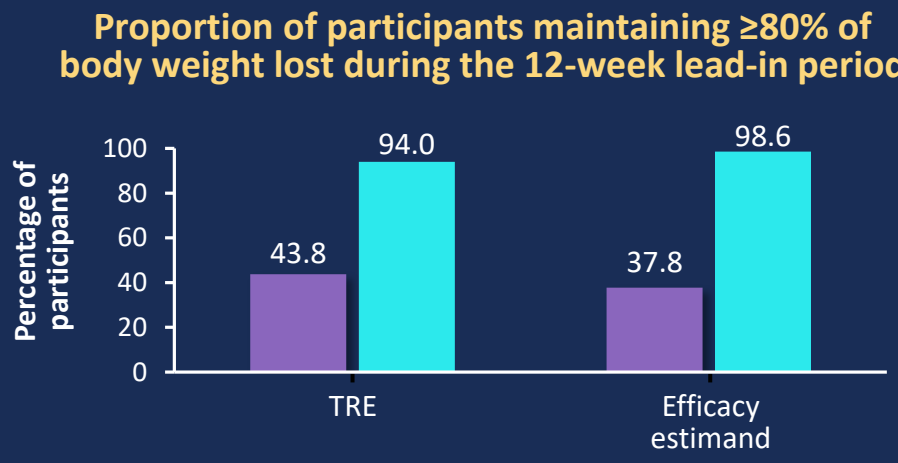


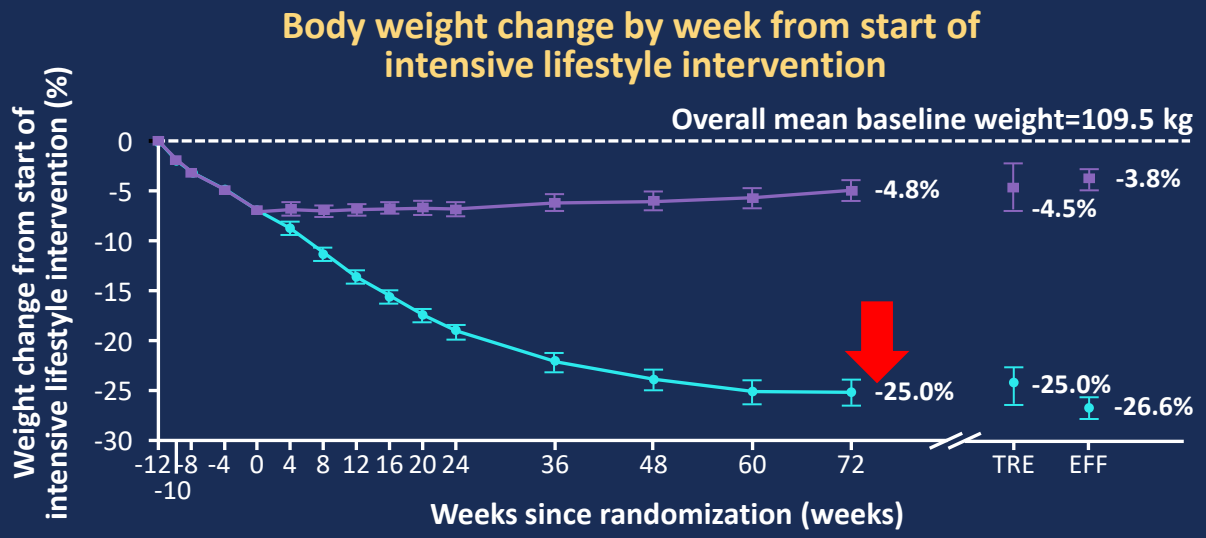
Garvey WT, et al. *Lancet*. 2023;402: 613-626.

SURMOUNT-3 Data (Tirzepatide)

- 806 subjects with OW or OB and no diabetes started trial, 579 were randomized
- 12-week ILI run which required a 5% weight loss in order to be randomized. 72-week follow-up







ILI, intensive lifestyle intervention; MTD, maximum tolerated dose.

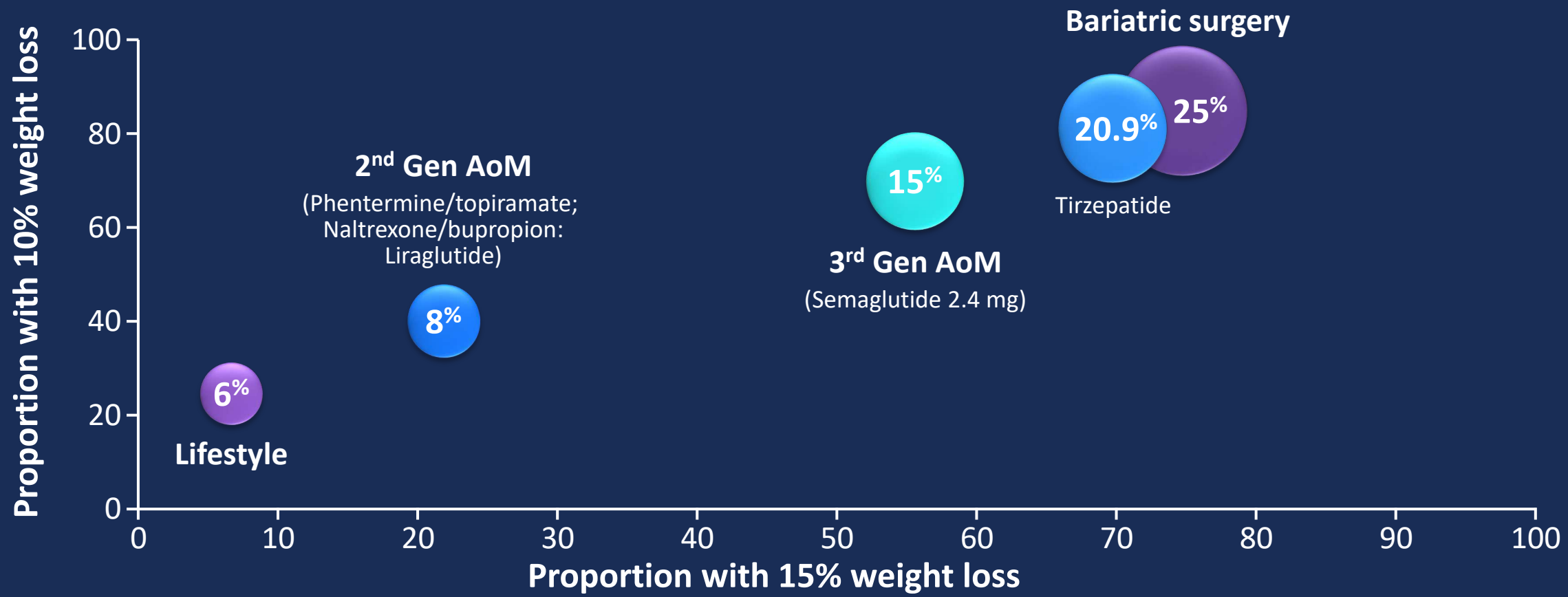
Wadden TA, et al. *Nat Med*. 2023;29:2909-2918.

SURMOUNT MMO: TIRZEPATIDE Maximally Tolerated Dose in Adults With Obesity Effect on Mortality and Morbidity

- 15,000 patients BMI ≥27 kg/m^2, without diabetes
  - ≥40 years of age with established cardiovascular disease, or
  - women 55 to 69 years of age or men 50 to 64 years of age with at least 3 risk factors like tobacco use, dyslipidemia, hypertension at screening, or
  - women ≥70 years of age or men ≥65 years of age with at least 2 risk factors at screening
- Primary Outcome: Time to first occurrence of any component event of composite of . . .
  - All-Cause Death, Nonfatal Myocardial Infarction (MI), Nonfatal Stroke, Coronary Revascularization, or Heart Failure Events
- Results expected in 2027

https://classic.clinicaltrials.gov/ct2/show/NCT05556512. September 15, 2023

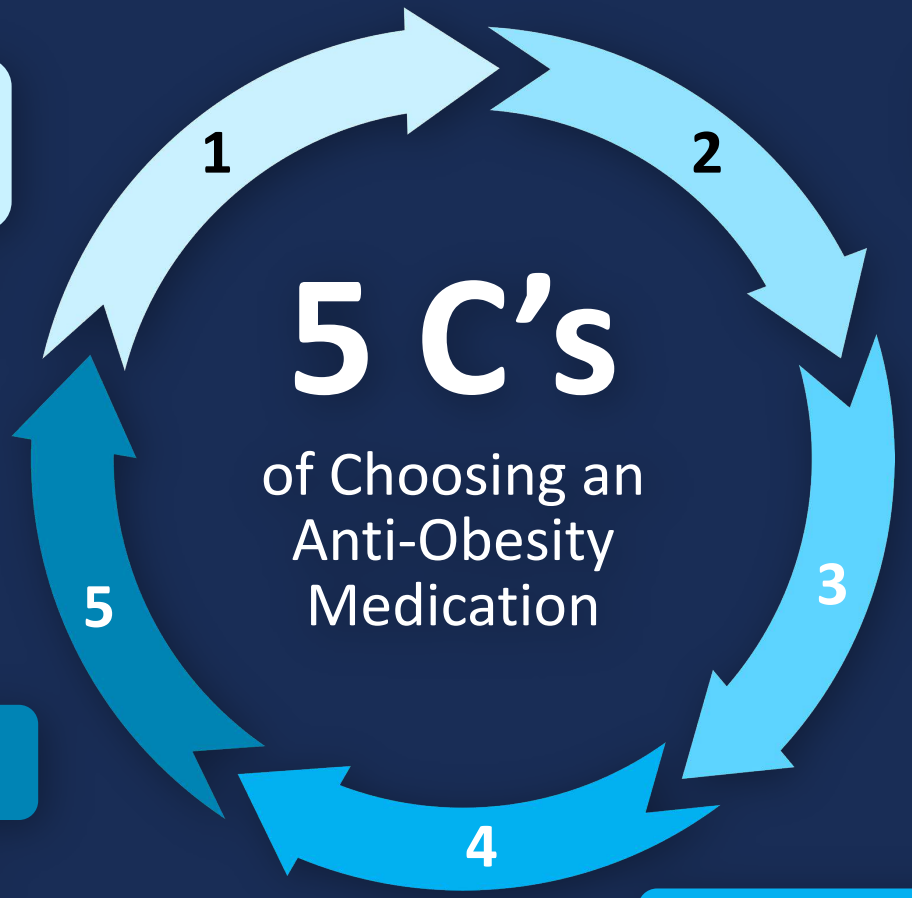
Efficacy of Existing Obesity Interventions



Allison DB, et al. *Obesity*. 2012;20:330-342. [EQUIP]; Gadde KM, et al. *Lancet.* 2011;37:1341-1352. [CONQER]; Greenway FL, et al. *Lancet.* 2010;376:595-605. [COR-I]; Apovian CM, et al. *Obesity*. 2013;21:935-943. [COR-II]; Wadden TA, et al. *Obesity*. 2011;19(1):110-120. [COR-BMOD]; Pi-Sunyer X, et al. *N Engl J Med.* 2015;373(1):11-22. [SCALE]; Wadden TA, et al. *Int J Obes.* 2013;37:1443-1451. [SCALE MAIN]; Enebo LB, et al. *Lancet*. 2021;397(10286):1736-1748. [Cag + Sema]; Wilding JPH, et al. *N Engl J Med.* 2021;384(11):989. [STEP 1]; Wadden TA, et al. *JAMA*. 2021;325(14):1403-1413. [STEP 3]; Rubino D, et al. *JAMA*. 2021;325(14):1414-1425. [STEP 4]; Ryan D. *Lancet Diabetes Endocrinol.* 2021;9(5):252-254. [STEP]; Sjöström L, et al. *N Engl J Med.* 2007;357:741-52; Jastreboff AM, et al. *N Engl J Med.* 2022;387(3):205-216.

For illustrative purpose only. AoM, anti-obesity medications. Bubble size represents mean % weight loss.

Choosing an AOM



Contraindications and cautions

Assess the clinical history of the patient and assess the risk/benefit of each AOM

Comorbidities

When appropriate, select an AOM that can treat obesity and improve other comorbidities

Cues

Consider patient-described appetite control symptoms, side effects, and preference on mode of delivery

Combinations

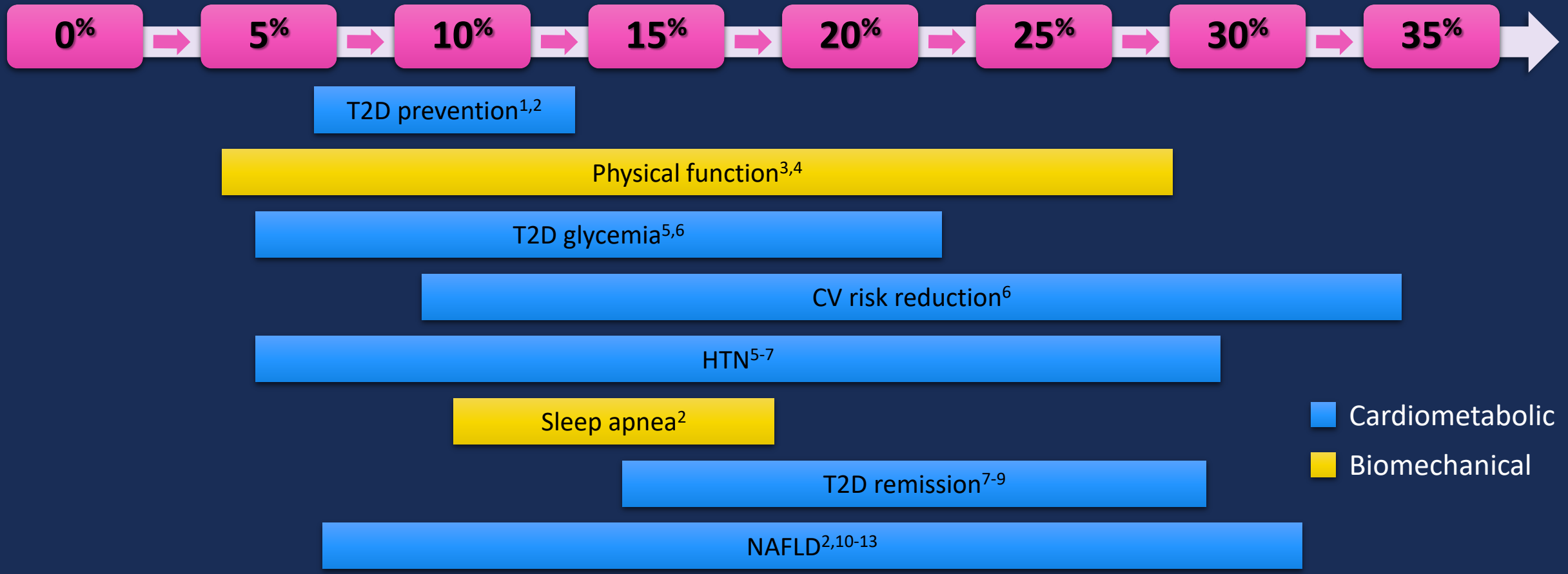
Consider combination therapy with lifestyle interventions, other AOMs, and surgical procedures

Cost/coverage

Consider the medication cost and the patient's insurance coverage

Horn DB, et al. *Postgrad Med*. 2022;134(4):359-375.

How Much Weight Loss Is Needed?



Slide courtesy of Tim Garvey, MD.

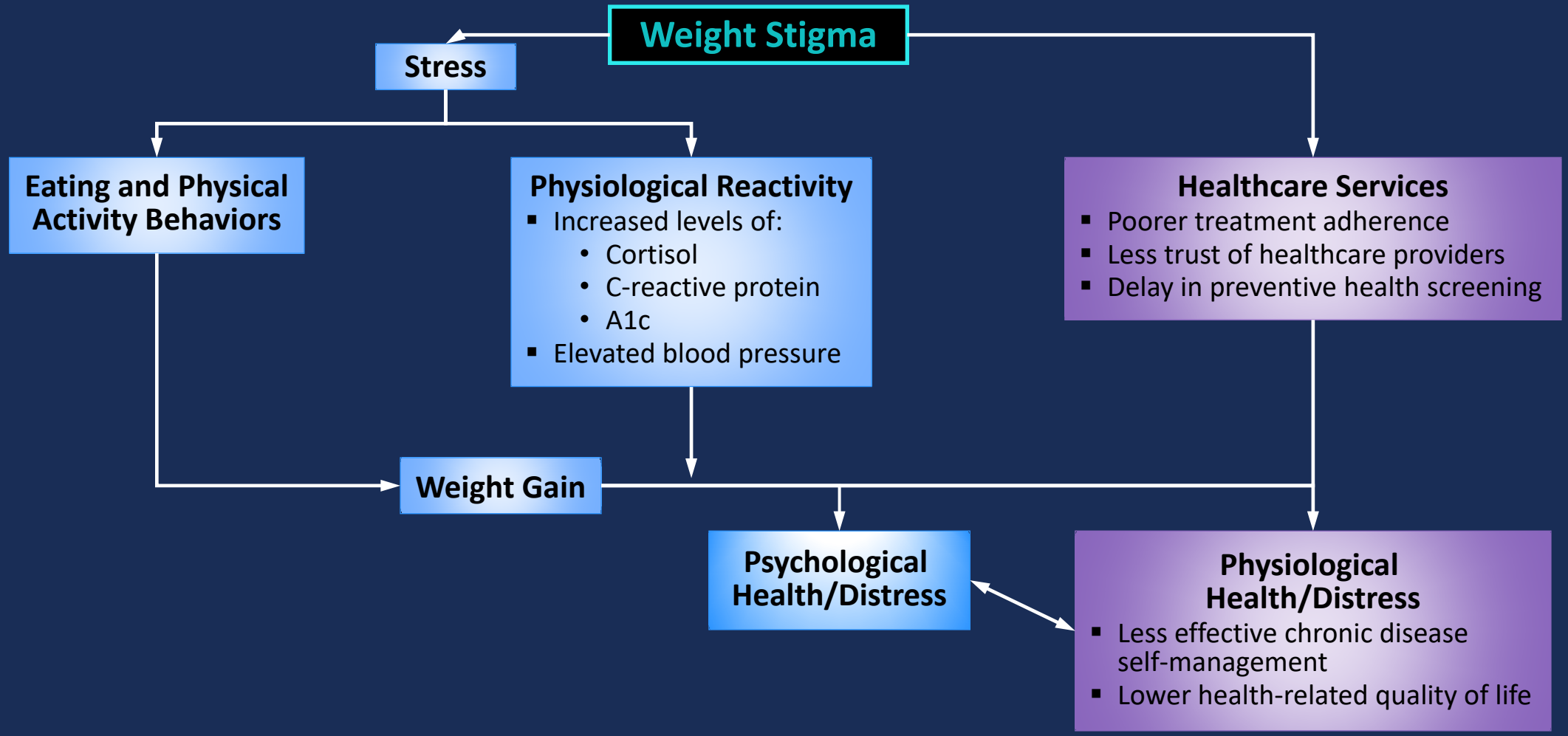
1. Knowler WC, et al. *N Engl J Med.* 2002;346:393-403. 2. Cefalu WT, et al. *Diabetes Care.* 2015;38:1567-1582. 3. Christensen R, et al. *Osteoarthritis Cartilage*. 2005;13:20-27. 4. Bliddal H, et al. *Obes Revs.* 2014;15:578-686. 5. Wing RR, et al. *Diabetes Care.* 2011;34:1481-1486. 6. Ooi GJ, et al. *Int J Obes.* 2017;41:902-908. 7. Courcoulas AP, et al. *JAMA Surg*. 2018;153:427-434. 8. Lean ME, et al. *Lancet.* 2018;391:541-551. 9. Dambha-Miller H, et al. *Diabet Med*. 2020;37:681-688. 10. Vilar Gomez E, et al. *Gastroenterology.* 2015;149:367-378. 11. Koutoukidis DA, et al. *Metabolism.* 2021;115:154455. 12. Promrat K, et al. *Hepatology.* 2010;51:121-129. 13. Liu X, et al. *Obesity Surgery.* 2007;17:486-492.

When Is Bariatric Surgery Appropriate?

- Patients with BMI ≥40 kg/m^2 who are unable to lose adequate weight via lifestyle interventions and who have 1 or more weight-related health comorbidities (eg, T2D; hypertension; hyperlipidemia; OSA)
- HCP/patient dialogue should include discussion of potential long-term side effects (eg, possible need for additional surgery; gallbladder disease; malabsorption)
- Patients should be referred to high-volume centers with experienced surgeons

Addressing Stigma in Obesity Care

Overcoming Weight Stigma in the Treatment of Obesity



Puhl RM, et al. *Clin Diabetes*. 2016;34(1):44-50.

American Medical Association People-First Language in Obesity

The American Medical Association (AMA):

1) encourages the use of person-first language (patients with obesity, patients affected by obesity) in all discussions, resolutions, and reports regarding obesity;

2) encourages the use of preferred terms in discussions, resolutions and reports regarding patients affected by obesity including weight and unhealthy weight, and discourages the use of stigmatizing terms including obese, morbidly obese, and fat; and

3) will educate healthcare providers on the importance of person-first language for treating patients with obesity; equipping their healthcare facilities with proper-sized furniture, medical equipment, and gowns for patients with obesity; and having patients weighed respectfully

AMA H-440.821, Resolution 402, A-17. Introduced by Dr. Ethan Lazarus on behalf of the Obesity Medicine Association.

Rudd Center of Food Policy and Obesity– Recommendations for Health Professionals

Consider	Consider patients' previous negative experiences
Recognize	Recognize that having obesity is a product of many factors
Explore	Explore all causes of presenting problems (not just weight)
Recognize	Recognize that many patients have tried to lose weight repeatedly
Emphasize	Emphasize importance of behavior change rather than weight
Acknowledge	Acknowledge the difficulty of making lifestyle changes
Recognize	Recognize that small weight losses can improve health

https://uconnruddcenter.org/

PART 2

Learning Lab: Overcoming Barriers to Optimal Obesity Care

Learning Lab Question 1

Do you follow expert guidance for obesity care? If so, which guidelines?

Learning Lab Question 2

How do you feel a diagnosis of obesity impacts patients?

Learning Lab Question 3

What modifications have you made or will you make to your practice to minimize patient perception of bias?

Learning Lab Question 4

What barriers do your patients face in accessing obesity treatment? How can these issues be addressed?

Learning Lab Question 5

How well do you collaborate with other members of the obesity care team? How have these approaches impacted patient outcomes?

Q&A

Claiming Credit

- At the conclusion of the activity, please scan the QR code to complete the post-activity test and evaluation. A paper copy is available if you prefer.

- You will receive your certificate within 2 to 4 weeks via email.

Staying in the Solution: How Do We Implement Evidence in Obesity Care?

Provided by
HME
Haymarket Medical Education

Supported by an educational grant from **Lilly**