Obesity Medicine Updates

2025

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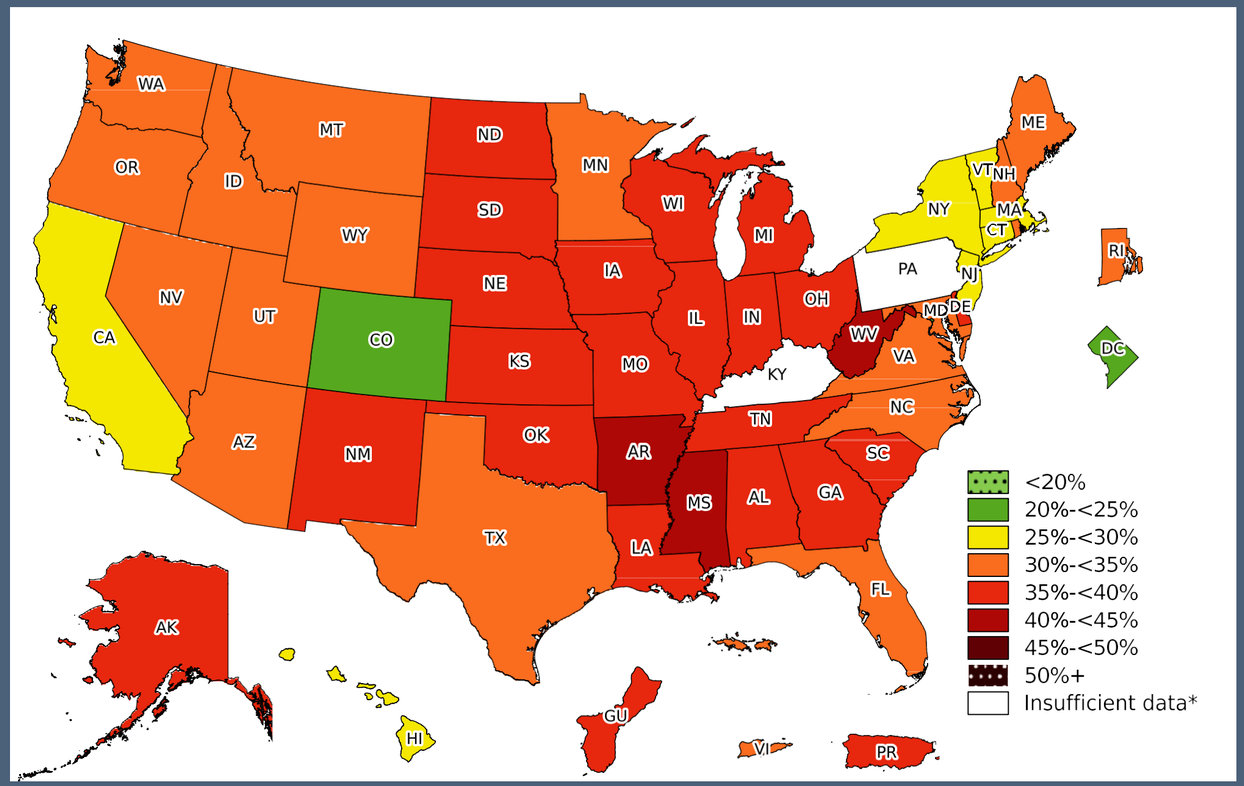
Learning Objectives

- Review latest updates in Obesity Medicine, including new definitions
- Understand recent changes in clinical guidelines for obesity pharmacotherapy, including 2025 perioperative management of GLP-1 receptor agonists (GLP-1 RAs)
- Review latest safety data related to GLP-1 RA's, including Pancreatitis, Gastroparesis, Ophthlamic Events, and Depression/Suicidal Ideation
- Review latest FDA-approved indications for Wegovy (Semaglutide) and Zepbound (Tirzepatide), including cardiovascular disease, obstructive sleep apnea, and MASH

Current Landscape

- As of 2024
  - 43% of adults have Obesity
  - 75% of adults are considered to have either Overweight or Obesity



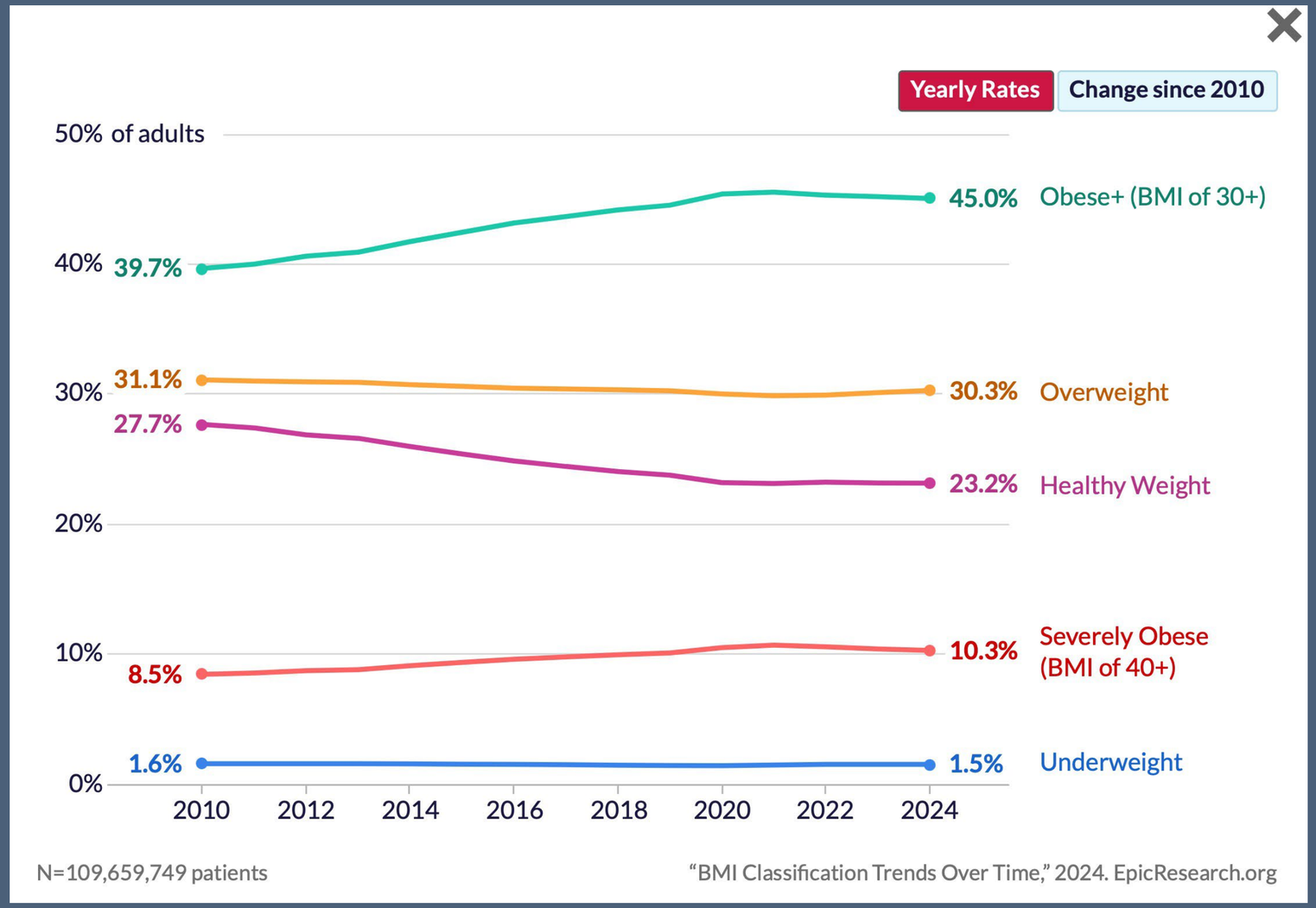
*CDC Adult Obesity Prevalence Map 2023

Current Landscape

- Obesity-related Comorbidities
  - 1 in 3 adults (34-38%) have prediabetes
  - 1 in 3 adults (~37%) have have MASLD / Metabolic dysfunction-associated steatotic liver disease

Peaked?

- Based on Epic data; rates may be plateauing or decreasing?



New Definitions (moving beyond BMI)

- 2025 AACE Consensus & Algorithm for Obesity Care (Sept, 2025)
  - Shift from BMI-centric approach to complication-centric model
  - BMI and Waist Circumference as a screening tool
  - Diagnosis also requires Waist-to-Heigh Ratio and comorbidities
    - Waist-to-Height Ratio ≥ 0.5 (signifies increased metabolic risk)
    - Waist Circumference should be measured in all adults with BMI ≥ 25
      - Not recommended in pts with BMI ≥ 35 (as BMI already implies high risk)
  - Ethnic and regional cutoffs should be applied
    - Asia-Pacific region (Obesity at BMI ≥ 25)

New Definitions (moving beyond BMI)

- 2025 AACE Consensus & Algorithm for Obesity Care (Sept, 2025)
  - Populations Most Affected by Redefinition
    - Individuals with BMI 25-29.9 who demonstrated elevated WC and/or have obesity-related complication
    - Normal BMI with central adiposity

New Definitions (moving beyond BMI)

- Obesity-related complication / disease

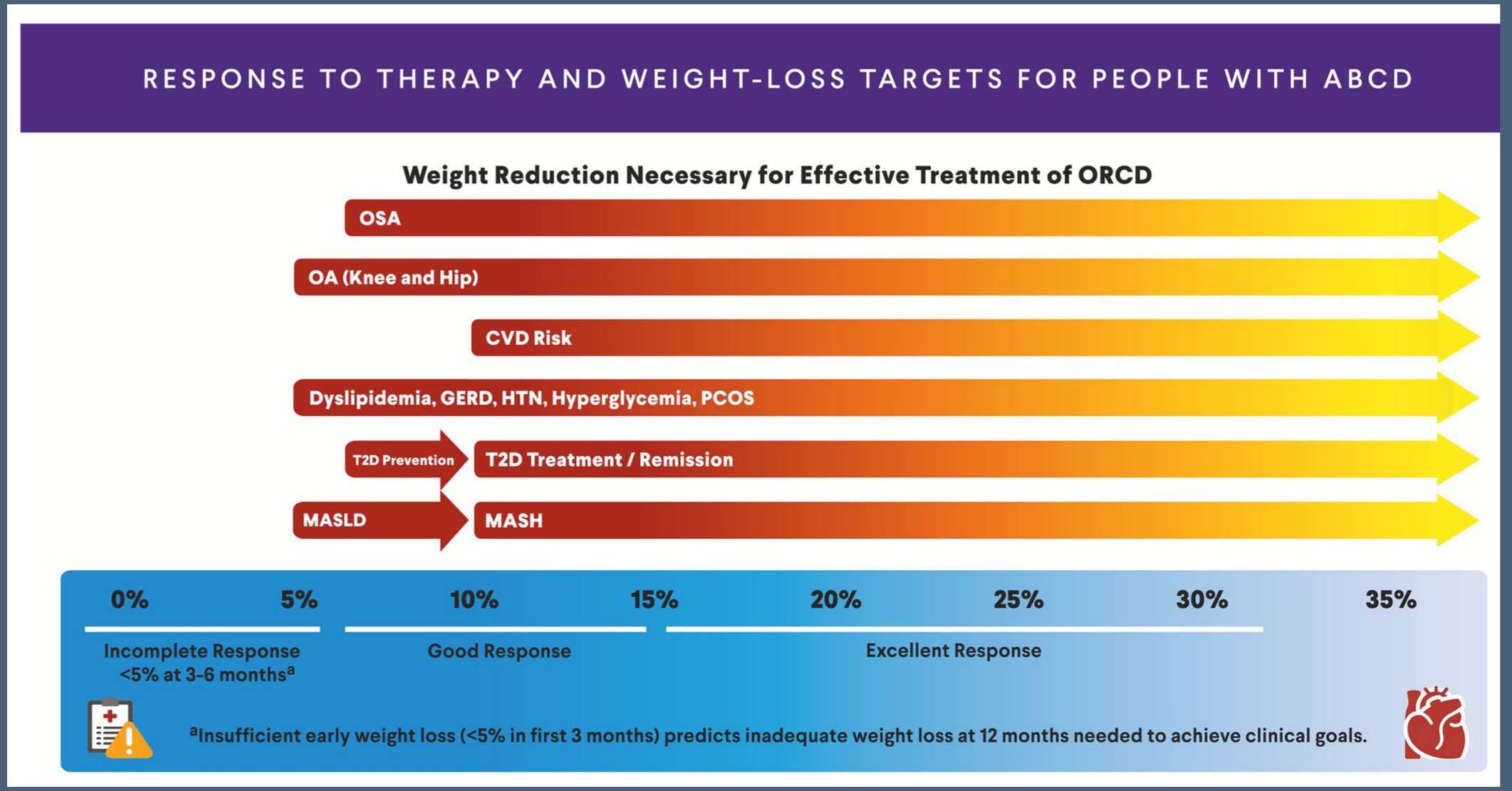
ABCD Stage 1	ABCD Stage 2 or 3	
No ORCD identified following intake evaluation	**Obesity Complications***	**Obesity-Related Diseases***
	• OA (knee, hip) • OSA • Obesity hypoventilation syndrome • Lymphedema • Stress urinary incontinence • GERD • Prediabetes and metabolic syndrome • MASLD • Obesity glomerulopathy, CKD • HFpEF • ASCVD • Thromboembolism • Idiopathic intracranial hypertension • Disability limiting activities of daily living	• T2D • MASH • HFrEF • Atrial fibrillation • Certain cancers • Cholelithiasis, cholecystitis • Asthma • Depression, anxiety • Internalized weight bias • Stigmatization • Disordered eating • Cognitive decline, dementia • Inflammatory skin diseases • Intertrigo

*There can be overlap between complications and related diseases depending on the pathophysical role of obesity in individual patients. See Box A for definitions.

New Definitions (moving beyond BMI)

- Obesity Diagnosis Requirements (two-component approach)
  - Anthropometric component
    - BMI ≥ 30 + at least 1 elevated anthropometric measure (WC, waist-to-hip ratio, waist-to-height ratio), or BMI ≥ 40
    - At least 2 elevated anthropometric measures, even if BMI < 30
    - Direct evidence of excess body fat (e.g. via DEXA scan)
  - Clinical component
    - Diagnosis requires assessment of obesity-related complications
      - Metabolic (DM2, HTN, Dyslipidemia, GERD, MAFLD, Prediabetes, Metabolic Syndrome)
      - Mechanical (Sleep Apnea, OA)
      - Psychological

Response to therapy targets



• Algorithm Figure 6 - Response to Therapy and Weight-Loss Targets (AACE 2025)

GLP-1 Medications Landscape

- 1 in 8 US adults say they've used GLP-1 drug for weight loss or health reasons (Rand Report)
- Among adults with diabetes, 26.5% report current GLP-1 injectable use

Perioperative Management of GLP-1 RA's

- Still significant variation among major societies regarding whether to hold, when to hold, or continue these agents before surgery
- American Society of Anesthesiologists:
  - Hold daily GLP-1 RA's on the day of surgery (Liraglutide, oral Semaglutide)
  - Hold weekly GLP-1 RA's at least 7 days prior to elective procedures
  - Risk assessment should be personalized
- American Gastroenterological Association
  - "Generally, in patients on GLP-1 RAs who have followed standard perioperative procedures (typically 8 hour solid food fast and 2-hour liquid fast) and who do not have symptoms of nausea, vomiting, dyspepsia, or abdominal distention, we advise proceeding with upper and/or lower endoscopy

Update on Safety and Adverse Events

- PANCREATITIS
  - Post marketing cases exist, but large RCTs and Cohort studies reassuring
  - NO significant increase in acute pancreatitis risk
    - Retrospective cohort study between 2010-2020, in DM2 (Am J Gastroenterology, Sept 2025)
    - Another retrospective cohort study 2015-2023, in DM2 (Am J Gastroenterology, May 2025)
    - Systematic Review Meta-analysis of 99k patients (J Am Coll Cardiology, Aug 2025)

Update on Safety and Adverse Events

- GASTROPARESIS
  - Associated with HIGHER risk of gastroparesis (HR 1.6 - 2.3) based on cohort studies and meta-analyses
  - Absolute risk increase of about 2-4%
  - Most cases are mild and reversible upon discontinuation
  - Seen mostly in pts with DM2
  - More pronounced in patients with obesity

Update on Safety and Adverse Events

- BILIARY DISEASE (Cholelithiasis and Cholecystitis)
  - Both Semaglutide and Tirzepatide are linked to increased risk of cholelithiasis and composite biliary disease
  - Absolute risk increase of ~27 per 10,000 per year
  - Likely due to rapid weight loss and possible effect on gallbladder motility

Update on Safety and Adverse Events

- Ophthalmic Events
  - Diabetic Retinopathy
    - Semaglutide may worsen pre-existing diabetic retinopathy, especially with rapid HbA1c reduction.
    - Tirzepatide shows similar, but less pronounced risk
  - NAION (Non-arteritic anterior ischemic optic neuropathy)
    - Possible association between Semaglutide and NAION (HR 2.2 - 7.7)
      - Am J Opthalmol, June 2025
    - Meta-analyses of RCTs have not confirmed this link; absolute risk is low (< 0.1%)

Update on Safety and Adverse Events

- Medullary Thyroid Cancer
  - Black Box Warning
  - Based on data in rodents
  - Current large-scale human studies do NOT demonstrate a significant increase
  - Contra-indicated if personal or family history of MTC or MEN2

Update on Safety and Adverse Events

- Suicidal Ideation
  - Possible signal on pharmacovigilance analyses based on FDA, WHO databases
  - Meta-analyses of RCTs and cohort studies found no statistically significant difference in rates so far
    - JAMA Psychiatry, March 2025

New FDA-Approved indications

- WEGOVY (Semaglutide)
  - Now FDA-approved for 3 main indications
    - Chronic weight management (12 yo and older)
    - Reducing risk of major adverse cardiovascular events (MACE)
      - In adults with established cardiovascular disease
      - SELECT Trial - 20% reductoin in MACE, including CV Death, Non-fatal MI, and Non-fatal stroke
    - Noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH, formerly NASH)
      - Approved under accelerated approval
      - For moderate to advanced liver fibrosis (F2 or F3)

New FDA-Approved indications

- ZEPBOUND (Tirzepatide)
  - Now FDA-approved for 2 main indications
    - Chronic weight management (adults)
    - Obstructive Sleep Apnea
      - 55-60% reduction in apnea-hypopnea index (AHI)

GLP-1 Clinical Pearls

- Start low, and titrate slow; don’t increase dose if doing well
- Discuss potential GI symptoms up front - nausea, diarrhea, constipation; dietary changes
- Reinforce:
  - Hydration
  - Smaller, but more frequent meals (high protein, lower saturated fat); increase fiber as tolerated
  - Resistance training and movement
- Discuss potential interruptions and restarting strategies
- Reproductive counseling
- Perioperative coordination

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