# Session 2 General Cardiology/Prevention
# Updates in Medical Management of Obesity to Reduce CV Risk
# 8:45-9:45
# April 22,2023
# Ohio ACC Spring Summit
# Embassy Suites Hilton Cleveland Rockside


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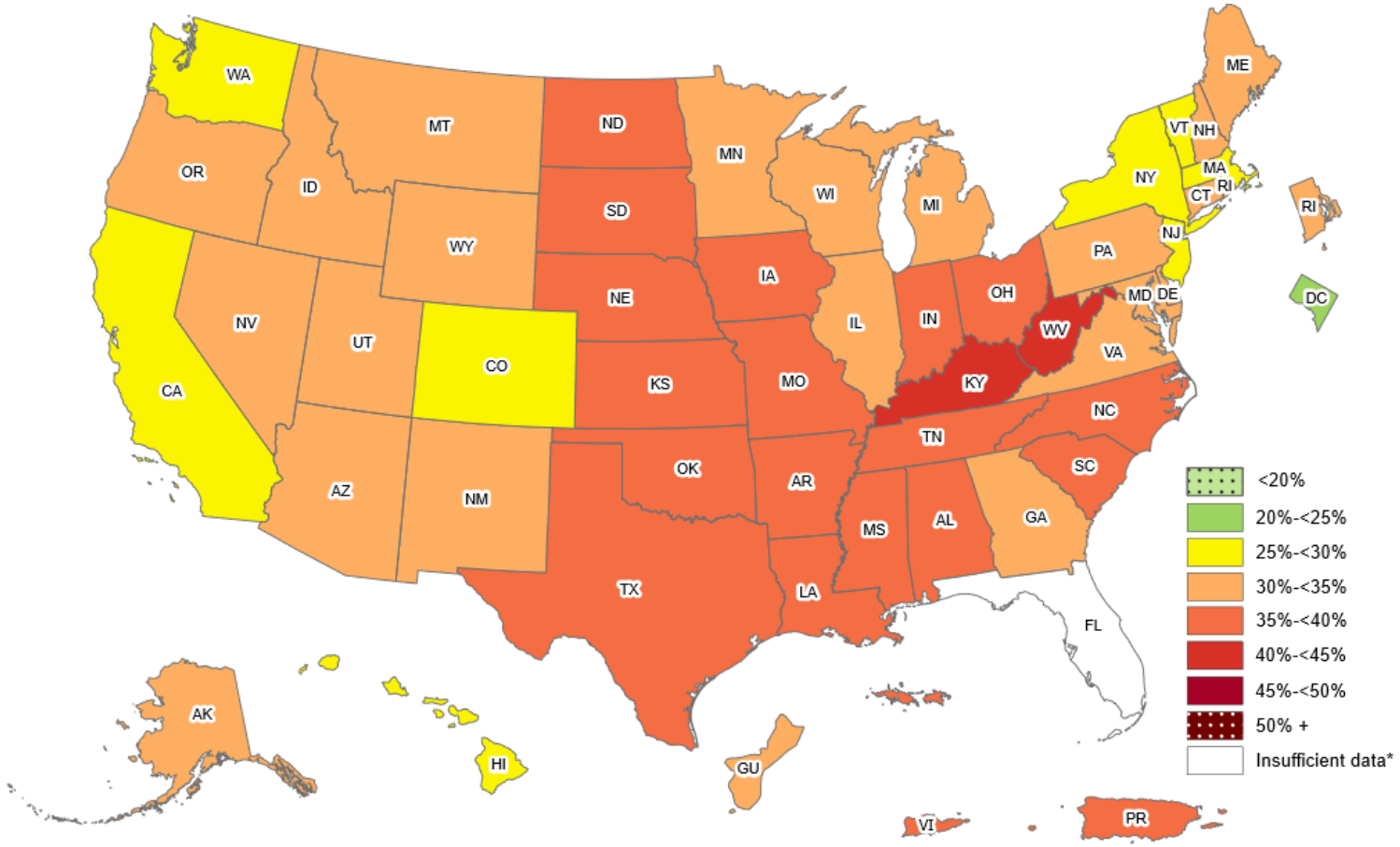
# Objectives

## Learners will:

- View updated prevalence trends for obesities as assessed by BMI, visceral adipose tissues and severe obesity and implications for treatment
- Consider current evidence for the role of diet, activity, and obesity in CVD prevention and major adverse cardiovascular events (MACE) prevention
- Become familiar with obesity treatment goals to sustain weight loss of 15% or more for chronic disease remission or substantial treatment and use of percent weight loss as guide
- Review the currently available medications for obesity treatment and typical results
- Consider the role of medications and lifestyle in combination to optimize outcomes

# Prevalence¶ of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2021

**¶ Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.**



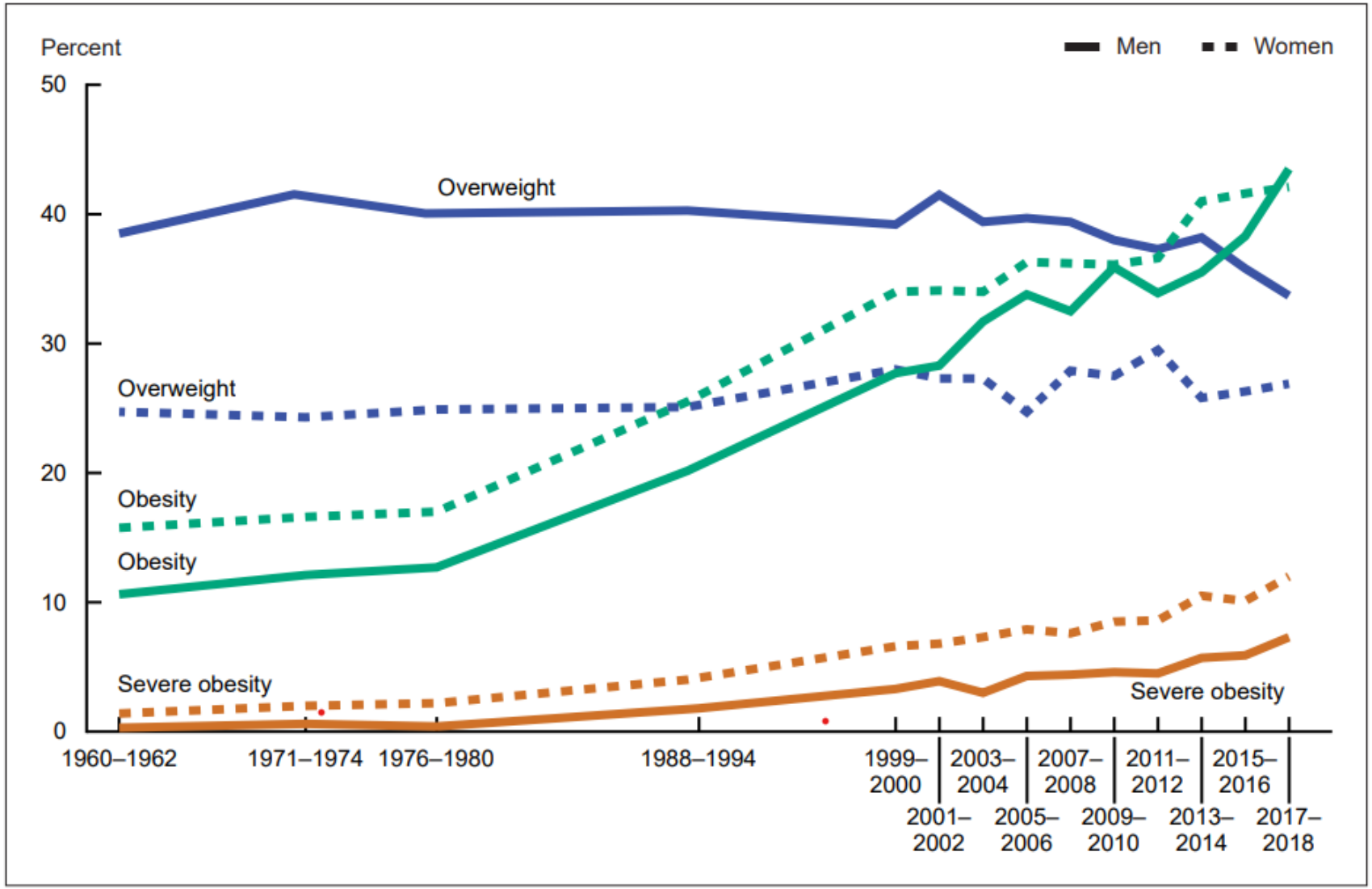

***Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥30%, or no data in a specific year.**

## Definitions

- Obesity: Body Mass Index (BMI) of 30 kg/m$^2$ or higher.
- Body Mass Index (BMI): Calculated by using the adult's weight in kilograms divided by the square of their height in meters.

# Adult Obesity Prevalence in U.S.

**Figure. Age-adjusted trends in overweight, obesity, and severe obesity among men and women aged 20–74: United States, 1960–1962 through 2017–2018**




NOTES: Data are age adjusted by the direct method to U.S. Census 2000 estimates using age groups 20–39, 40–59, and 60–74. Overweight is body mass index (BMI) of 25.0–29.9 kg/m$^2$. Obesity is BMI at or above 30.0 kg/m$^2$. Severe obesity is BMI at or above 40.0 kg/m$^2$. Pregnant women are excluded from the analysis.
SOURCES: National Center for Health Statistics, National Health Examination Survey and National Health and Nutrition Examination Surveys.

Fryar CD, Carroll MD, Afful J. Prevalence of overweight, obesity, and severe obesity among adults aged 20 and over: United States, 1960–1962 through 2017–2018. NCHS Health E-Stats. 2020.

# The Scope of Obesity in the U.S.

2017–2018 National Health and Nutrition Examination Survey (NHANES), using measured heights and weights, indicate that:

- An estimated 42.5% of U.S. adults aged 20 and over have obesity, including 9.0% with severe obesity, and another 31.1% are overweight[1]
- An estimated 19.3% of U.S. children and adolescents aged 2–19 years have obesity, including 6.1% with severe obesity, and another 16.1% are overweight[2]
- Between 2011 to 2012 and 2017 to 2020, obesity increased for children aged 2 to 5 years, adolescents aged 12 to 19 years, and children aged 2 to 19 years of all races and ethnicities.[3]

Because of the significant increase in obesity, there is an urgent need for identification of antecedents and correlates of adiposity and cardiometabolic risk for early obesity prevention

1. Fryar CD, Carroll MD, Afful J. Prevalence of overweight, obesity, and severe obesity among adults aged 20 and over: United States, 1960–1962 through 2017–2018. NCHS Health E-Stats. 2020.

2. Fryar CD, Carroll MD, Afful J. Prevalence of overweight, obesity, and severe obesity among children and adolescents aged 2–19 years: United States, 1963–1965 through 2017–2018. NCHS Health E-Stats. 2020.

3. Hu, Kathy, and Amanda E. Staiano. "Trends in obesity prevalence among children and adolescents aged 2 to 19 years in the US from 2011 to 2020." *JAMA pediatrics* 176.10 (2022): 1037-1039..

# Scope of Obesity in the U.S.

- Overweight + obesity prevalence is 77-80% for non-Hispanic blacks, Hispanics, and Mexican-Americans

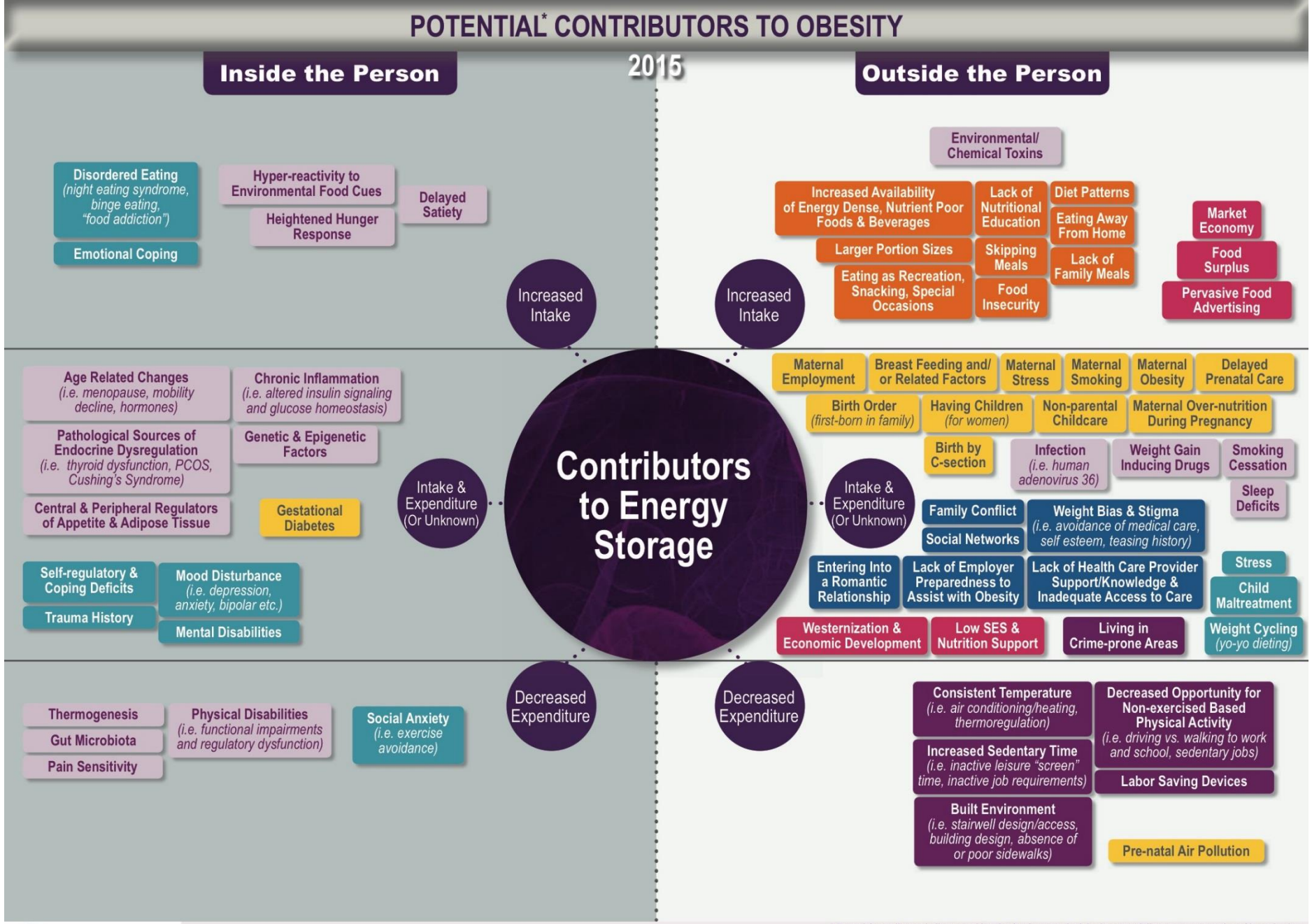
- Obesity rates highest in lowest socioeconomic levels and in women who self-identify a part of an ethnic minority -rates of obesity 50% in some groups


1.Flegal KM, Kruszon-Moran D, Carroll MD, Fryar CD, Ogden CL. Trends in Obesity Among Adults in the United States, 2005 to 2014. *Jama.* Jun 7 2016;315(21):2284-2291.

2.Ogden CL, Carroll MD, Fryar CD, Flegal KM. Prevalence of Obesity Among Adults and Youth: United States, 2011-2014. *NCHS data brief.* Nov 2015(219):1-8.

3. Fryar CD, Carroll MD, Afful J. Prevalence of overweight, obesity, and severe obesity among children and adolescents aged 2–19 years: United States, 1963–1965 through 2017–2018. NCHS Health E-Stats. 2020.

4. Flegal KM, Kit BK, Orpana H, Graubard BI. Association of all-cause mortality with overweight and obesity using standard body mass index categories: A systematic review and meta-analysis. *Jama.* 2013;309(1):71-82.

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# Obesity Related Medical Co-Morbid Conditions (1 of 2)

- **Cardiovascular System:** Hypertension, Coronary Artery Disease (CAD) ,Heart Failure, Atrial Fibrillation (AF), Stroke, Venous Thromboembolism, lymphedema, venous stasis disease
- **Respiratory System**: Obstructive Sleep Apnea (OSA), Obesity Hypoventilation Syndrome (OHS)
- **Endocrinology:** Type 2 Diabetes Mellitus (T2DM), Dyslipidemia, Metabolic Syndrome, Vitamin D Deficiency
- **Neurology:** Idiopathic Intracranial Hypertension (IIH)
- **Musculoskeletal System:** Osteoarthritis: weight bearing joints, Higher risk of falls and fractures
- **Gastrointestinal Tract:** Non-alcoholic Fatty Liver Disease (NAFLD), Gallstones, Gastroesophageal reflux disease (GERD), Barrett's esophagus, esophageal adenocarcinoma.
- **Urinary Tract:** Urinary incontinence, particularly stress incontinence

Lim Y, Boster J. Obesity and Comorbid Conditions. [Feb 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK574535/Updated 2023

# Obesity Related Medical Co-Morbid Conditions (2 of 2)

- **Reproductive System:** Ovulatory dysfunction and infertility, increased risk of miscarriage and pregnancy complications, Endometrial hyperplasia and malignancy, Polycystic ovary syndrome, Obesity is also associated with sexual dysfunction in women and erectile dysfunction in men.

- **Psychiatric Disorders:** higher incidence of depression

- **Integumentary System:** risk of infection, poor wound healing, and the development of pressure sores in obese patients. Lastly, increased androgens and insulin resistance contributes to the development of hirsutism and acanthosis nigricans, respectively.

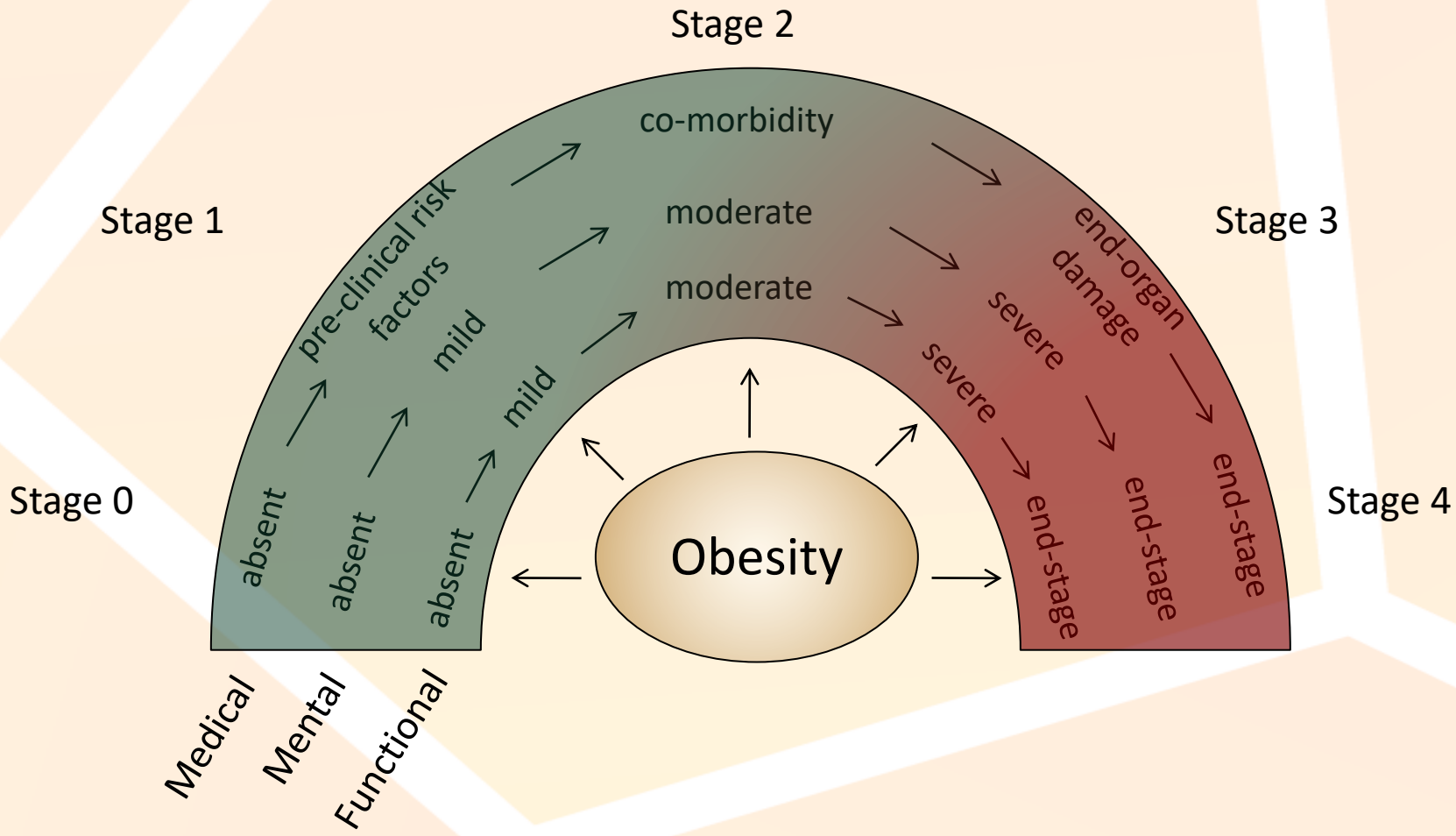
- **Infection:** post-surgical infections, and increased mortality from flu and COVID-19**.**

- **Neoplasm:** Cancers well-associated with obesity: Esophageal adenocarcinoma, Gastric cancer, particularly of the cardia, Colorectal cancer, Hepatocellular carcinoma, Cholangiocarcinoma, Pancreatic cancer, Endometrial carcinoma, Ovarian cancer, Breast cancer, Renal cell carcinoma, Multiple myeloma

Lim Y, Boster J. Obesity and Comorbid Conditions. [Updated 2023 Feb 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK574535/

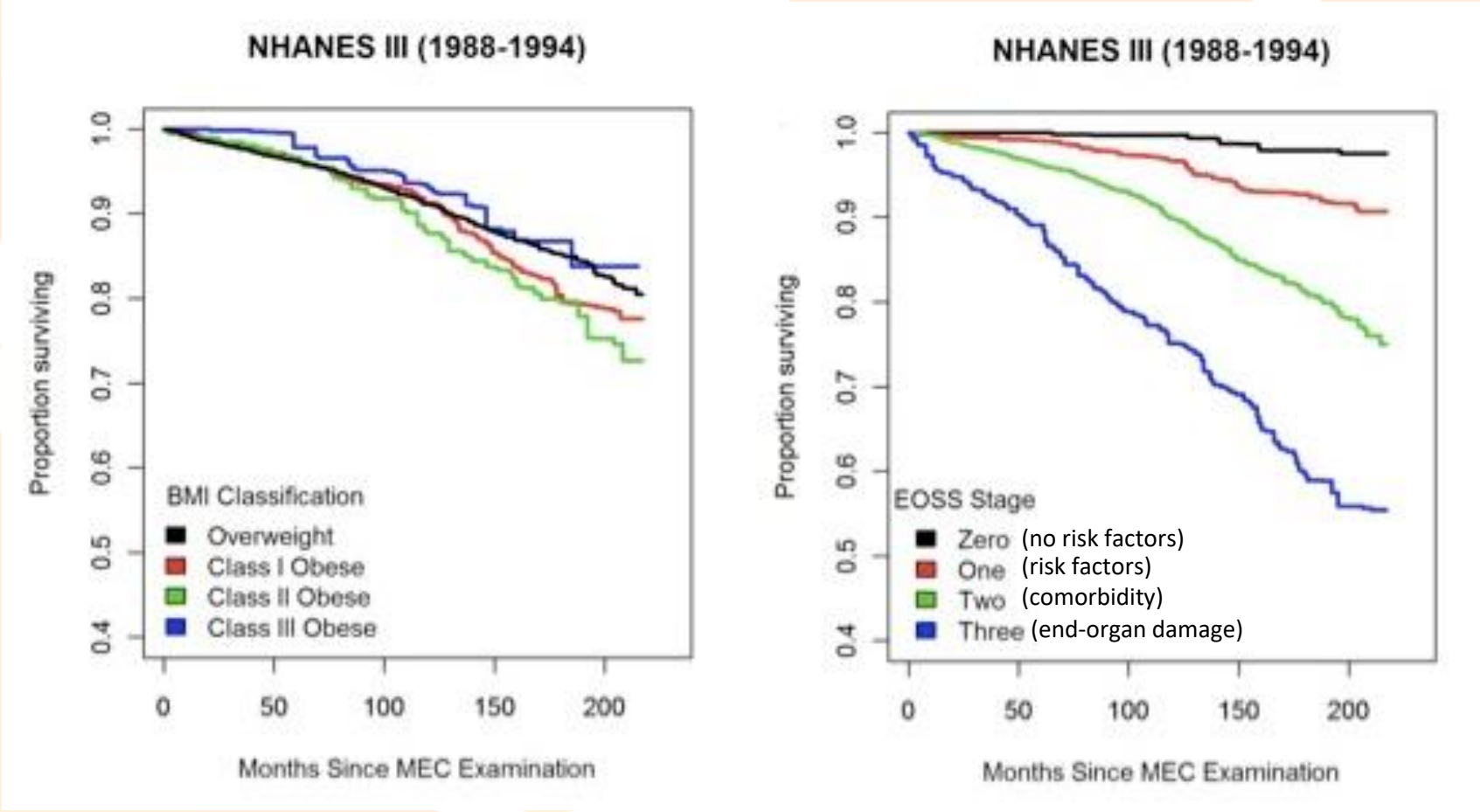
# ASSESS

## Edmonton Obesity Staging System (EOSS)



# ASSESS

## EOSS Predicts Mortality in NHANES III




Padwal RS, Pajewski NM, Allison DB, Sharma AM. Using the Edmonton obesity staging system to predict mortality in a population-representative cohort of people with overweight and obesity. **CMAJ**. 2011;183:E1059-66

# Treating Obesities – Emerging Concepts and Terminology

- ABCD – Adiposity based chronic disease
- Obesity severity worsening and has most complications
- BMI is a screening tool for risk, not percent fat. Waist circumference is more predictive, imaging most accurate
- Metabolic health obesity transient
- Ectopic fat the key issue – also called visceral adipose tissue (VAT) which can be in muscle, liver, pancreas, heart, kidneys and is strongly associated with insulin resistance, liver disease, and major adverse cardiovascular events (MACE)
- Weight loss to mitigate risk for higher BMI or VAT may be 15% or more

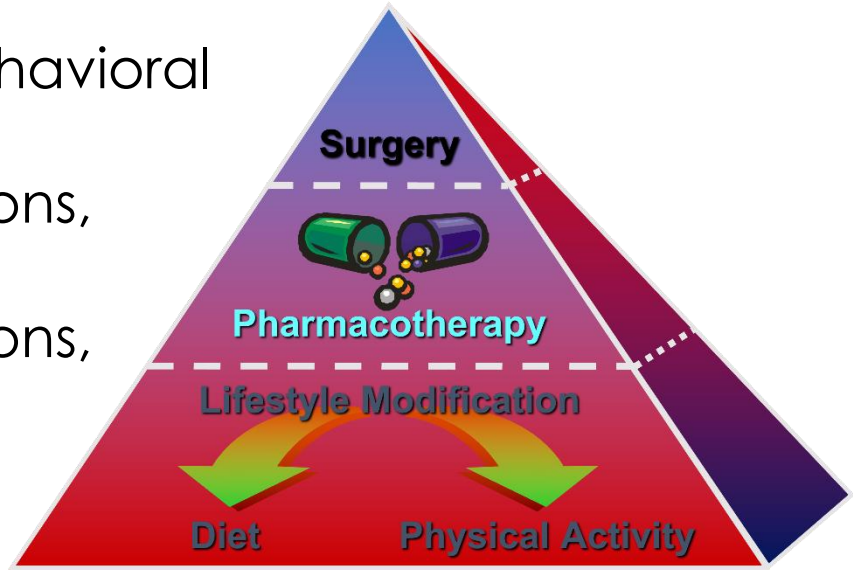
Garvey WT. Is Obesity or Adiposity-Based Chronic Disease Curable: The Set Point Theory, the Environment, and Second-Generation Medications. Endocr Pract. 2022 Feb;28(2):214-222. doi: 10.1016/j.eprac.2021.11.082. Epub 2021 Nov 22. PMID: 34823000.

Piché, M. E., Tchernof, A., & Després, J. P. (2020). Obesity Phenotypes, Diabetes, and Cardiovascular Diseases. *Circulation research*, *126*(11), 1477–1500. https://doi.org/10.1161/CIRCRESAHA.120.316101

# Obesity Treatment guidelines

## USPSTF and Management of Obesity - Reference at end of handout

- Screen by body mass index (BMI) for obesity
- Screen for and treat comorbid conditions and make sure cancer screening is up to date
- Assess patient's readiness for managing
- If ready offer Intensive behavioral treatment - more than monthly visit, at least 4 months, long-term f/u
- Behavioral treatment includes diet, activity, behavioral skills and systems skills
- If BMI >30 or >25 with medically related conditions, consider medication
- If BMI >40 or >35 with medically related conditions, >30 with uncontrolled type 2 diabetes consider metabolic/bariatric surgery




**Obesity Treatment Pyramid**

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# Obesity Treatment Individual Response

- Not everyone responds to any one treatment (loses)
- Not everyone can participate
- Less intensive therapy, less intensive impact (i.e. small steps) unclear
- Most responders regain some weight lost

# Weight loss, Diet, and Physical activity to prevent ACVD

- When people with obesity adopt physical activity recommendations, visceral fat often improves and outcomes improve with little or no weight loss. Those with metabolic syndrome considerably benefit from increasing their level of cardiorespiratory fitness, which has been shown to be a powerful protective factor against CVD in individuals who are either obese or nonobese,
- Improving diet to follow Mediterranean or Healthy Eating index patterns improves risk factors over time and outcomes
- Current study in process for weight loss in adults without DM and prevention of MACE

# Intensive Lifestyle Behavioral Therapy ALONE does not reduce Major Adverse Cardiovascular Events

- Look AHEAD RCT randomly assigned **5145 adults with DM2 to intensive lifestyle(IL) modification aimed at 7% weight loss or usual care**. At 4-year follow-up, participants in the IL group lost a mean of 4·7% of bodyweight vs. 0·8% in the control group. Few (ie, 7% in the intervention group vs 2% in the control group) people had HbA1c <6%. Suggests more weight loss required for a meaningful effect on DM2 disease course.
- At about 10 years of follow-up; mean weight loss of 6% in the intervention group vs 3·5% in the control group) the **primary endpoint of cardiovascular events was not significantly different between groups**
- Post-hoc analysis showed 21% (1013 of 4899) of **participants who lost at least 10% of their bodyweight in the first year had a 21% lower risk of cardiovascular events over 10 years than did people with stable weight or weight gain**. Supports benefits of losing >10% bodyweight on type 2 diabetes, diabetes-related endpoints, and complications, including cardiovascular events. Mean weight loss long term with lifestyle interventions often fall short

van Trier, T.J., Mohammadnia, N., Snaterse, M. *et al.* Lifestyle management to prevent atherosclerotic cardiovascular disease: evidence and challenges. *Neth Heart J* **30**, 3–14 (2022). https://doi.org/10.1007/s12471-021-01642-y

# Why medications for weight loss maintenance?

Weight loss medications to treat obesity are given **in addition to diet and activity changes** to:

- Increase the amount of weight lost
- Increase the sustainment of weight loss long-term
- Improve medical and functional outcomes

# Evidence Based Anti-Obesity Medications

- Topiramate*
- Phentermine
- Phentermine/Topiramate ER (Qsymia)
- Bupropion/naltrexone (Contrave)
- Bupropion/zonisamide*
- Orlistat (Alli, Xenical)
- Gelesis100/Cellulose-Citric Acid Hydrogel (Plenity)
- Pramlintide (Symlin)*
- SGLT-2 inhibitors*
- DPP-4 inhibitors*
- Metformin*
- Dulaglutide* (Trulicity*)
- Liraglutide (Victoza*, Saxenda)
- Semaglutide (Ozempic*, Wegovy)
- Tirzepatide* (Mounjaro*)

* Denotes that FDA approval indication is evidence based but used off label for weight loss

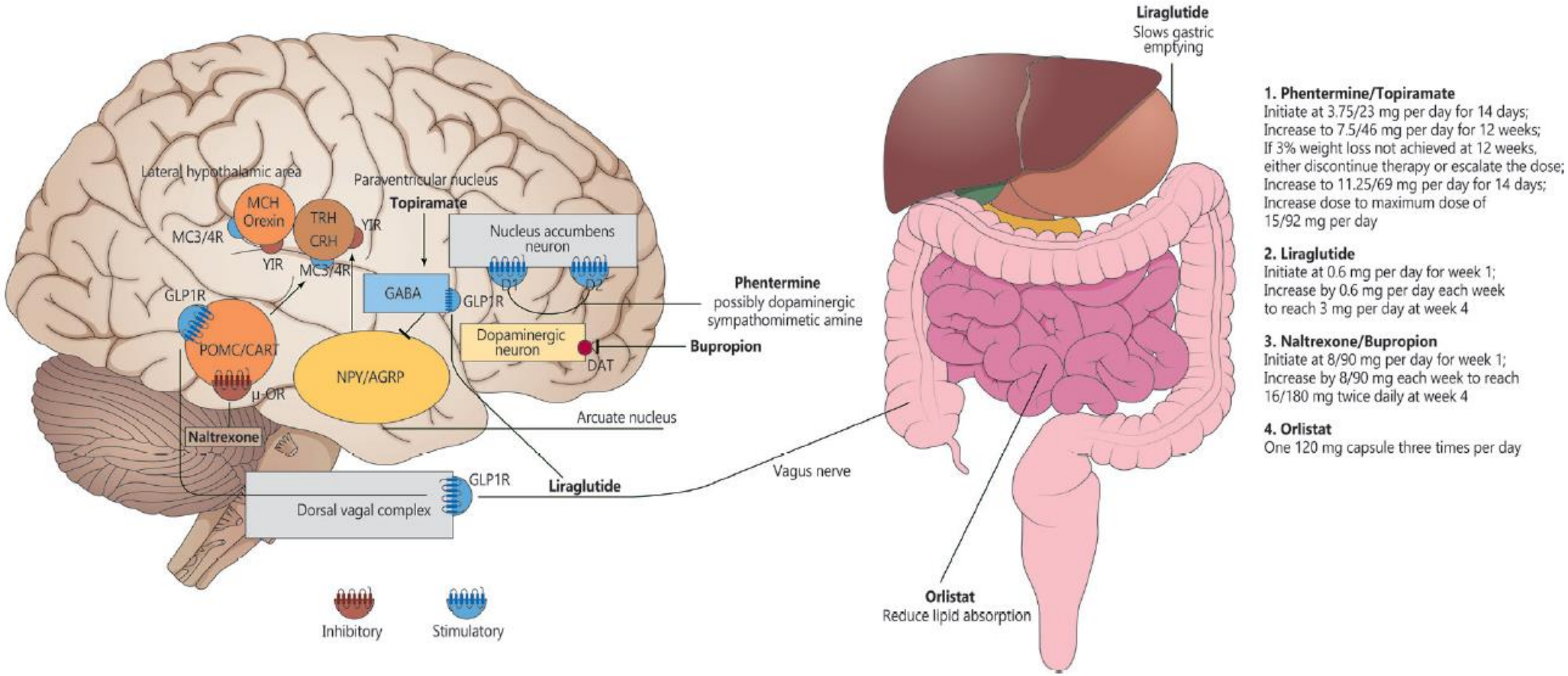


**Fig. 1.** Mechanism of action and dosing schedule of anti-obesity drugs. Some images were downloaded from the Smart Servier website. MCH, melanin-concentrating hormone; TRH, thyrotropin-releasing hormone; CRH, corticotropin-releasing hormone; MC3/4R, melanocortin receptor type 3/4 receptor; Y1R, Y1 receptor; GABA, gamma-aminobutyric acid; GLP1R, glucagon-like peptide 1 receptor; D1, dopamine 1 receptor; D2, dopamine 2 receptor; POMC/CART, pro-opiomelanocortin/cocaine amphetamine-related transcript (anorexigenic); μ-OR, μ-opioid receptor; NPY/AGRP, neuropeptide Y/agouti-related peptide (orexigenic); DAT, dopamine active transporter.

Son JW, Kim S. Comprehensive Review of Current and Upcoming Anti-Obesity Drugs. Diabetes Metab J. 2020 Dec;44(6):802-818. doi: 10.4093/dmj.2020.0258. Epub 2020 Dec 23. PMID: 33389955; PMCID: PMC7801751.

# Phentermine-topiramate (Qsymia) - *controlled*

- Approval: 2012 for: chronic weight management, as an adjunct to a reduced-calorie diet and exercise, for BMI ≥ 30 or ≥ 27, in the presence of other risk factors such as hypertension, diabetes or hyperlipidemia
- Efficacy: **10.7 kg mean weight loss beyond that achieved by placebo** (12.6 kg vs. 1.9 kg) at one year (Phase 3 RCT; *Obesity* (2012); 20 2, 330–342)
- Adverse effects: tachycardia, insomnia, paresthesias, dizziness, distorted taste sensation, constipation, dry mouth, anxiety, suicidality (rare), acute angle closure glaucoma (rare), metabolic acidosis (rare), increased serum creatinine (rare)
- Contraindications: pregnancy, glaucoma, hyperthyroidism, MAOIs, history of suicide attempt

Fujioka, K. (2015). Current and emerging medications for overweight or obesity in people with comorbidities. *Diabetes, Obesity & Metabolism*, *17*(11), 1021–1032. http://doi.org/10.1111/dom.12502

# Phentermine-topiramate (Qsymia) - *controlled*

- In an RCT of topiramate (64–384mg daily) for weight loss in obesity, adverse events of the central or peripheral nervous system observed, included paresthesia, somnolence and difficulty with memory, concentration and attention. Most events dose-related, and topiramate monotherapy has not been pursued further for weight management.
- Four doses available for phentermine/ topiramate ER combination therapy, but only two are recommended for long-term treatment (7.5mg phentermine/ 46 mg topiramate ER once daily and 15 mg/92mg once daily). The remaining two doses of 3.75mg/23mg and 11.25mg/69mg once daily are titration doses
- When prescribing this drug, a 2-week course of 3.75mg/23mg is recommended before the recipient is placed on a 'mid-range' maintenance dose of 7.5mg/46mg. It is recommended that the drug is either discontinued or escalated where people have not lost 3% of their body weight after 3 months on 7.5mg/46mg.
- At the mid-dose of 7.5mg/46mg, the medication can simply be stopped without titration. At the maximum dose of15mg/92mg, taper for drug discontinuation

Fujioka, K. (2015). Current and emerging medications for overweight or obesity in people with comorbidities. *Diabetes, Obesity & Metabolism*, *17*(11), 1021–1032. http://doi.org/10.1111/dom.12502

# Bupropion/Naltrexone (Contrave)

**Type: Opiate blocker and dopamine reuptake inhibitor**

**Mechanism of action:** Sustained-release combination of naltrexone, an opioid receptor antagonist and bupropion, a catecholamine reuptake inhibitor, Naltrexone and bupropion synergistically stimulate central melanocortin pathways and antagonize inhibitory feedback loops that limit weight reduction, leading to improved energy expenditure and reduced appetite Naltrexone and bupropion synergistically stimulate central melanocortin pathways and antagonize inhibitory feedback loops that limit weight reduction, leading to improved energy expenditure and reduced appetite

**Year of approval:** September, 2014 for weight loss in people with overweight or obesity (brand name Contrave®)

**Dosing:** .Maximum recommended treatment dose of naltrexone/bupropion is two 8 mg naltrexone/90mg bupropion tablets taken twice daily, to give a total daily dose of 32mg naltrexone/360mg bupropion

Fujioka, K. (2015), Current and emerging medications for overweight or obesity in people with comorbidities. Diabetes Obes Metab, 17: 1021–1032. doi:10.1111/dom.12502

# Bupropion/Naltrexone (Contrave)

**Efficacy:**

**Mean weight loss at week 56** of 5.4% (COR-I) and 8.1% (COR-BMOD) from baseline. Compared with placebo, significant reductions in weight **(COR-I:5.4% vs 1.3%; COR-BMOD: 8.1% vs 4.9%; p<0.001 in each case)**

**Increase in the proportion of individuals ≥5% weight loss (COR-I: 42% vs 17%; COR-BMOD: 57% vs 43%; p<0.001 in each case)** were observed (Table 1). Similar findings were made in a phase III trial in people with **T2D (COR-Diabetes), with a significant reduction in weight (3.7% vs 1.7%; p<0.001)** and a significant increase in the proportion of participants achieving ≥5% weight loss

Fujioka, K. (2015), Current and emerging medications for overweight or obesity in people with comorbidities. Diabetes Obes Metab, 17: 1021–1032. doi:10.1111/dom.12502

# Bupropion/Naltrexone (Contrave)

**Adverse effects:** nausea (32.5% vs 6.7% with placebo), constipation (19.2% vs 7.2%), headache (17.6% vs 10.4%), vomiting (10.7% vs 2.9%) and dizziness (9.9% vs 3.4%); nausea, headache and vomiting were the most common. included in the medication label)

***Contraindications***: pregnancy (category X) and interferes with opiate based medication treatment. Avoid giving in high risk for or history of seizure disorder and active bulimia nervosa also

**Cost**: about $75/month

The drug should be discontinued if individuals have not lost at least 5% of their baseline body weight

Fujioka, K. (2015), Current and emerging medications for overweight or obesity in people with comorbidities. Diabetes Obes Metab, 17: 1021–1032. doi:10.1111/dom.12502

# Glucagon-like Protein-1

- Site of Synthesis: secreted of the L- cells distal small intestine, Also made in the NTS, hypothalamus and amygdala
- Site(s) of action: Inhibits NPY neurons and stimulates the POMC system, PYY decreases ghrelin levels, activates neurons in the area postrema of the PVN
- Factors affecting production: secreted in response to rapid passage of food to hindgut with contact with chyme
- Major known effects: increases insulin secretion and increases insulin sensitivity. It leads to decreased food ingestion and weight.

# GLP-1 – Liraglutide (Saxenda)

**Type:** Glucagon Like peptide analogue at 3.0 mg

**Mechanism of action:** activates 5-$HT_{2C}$ receptors in the hypothalamus, resulting in increased proopiomelanocortin (POMC) production, which promotes satiety

- **Year of approval:** 2015 – **Liraglutide 3.0mg is first GLP-1 analogue to be approved for long-term weight management in individuals with overweight or obesity.**
- **Efficacy: 3.6 kg mean weight loss beyond that achieved by placebo (5.8 kg vs. 2.2 kg) at one year** (Phase 3 RCT; *N Engl J Med* 2010; 363:245-256) (usually 3-5% without lifestyle) In phase III trials of liraglutide 1.2 and 1.8mg, reductions in body weight that accompanied robust improvements in HbA1c and led to development of liraglutide at the higher dose of 3.0mg for weight management in people with overweight or obesity, with or without diabetes. **Liraglutide 3.0mg (brand name Saxenda®)was approved for chronic weight management in the USA in December 2014**

Fujioka, K. (2015), Current and emerging medications for overweight or obesity in people with comorbidities. Diabetes Obes Metab, 17: 1021–1032. doi:10.1111/dom.12502

# GLP-1 – Liraglutide (Saxenda)

- **Adverse effects:** *headache, nasopharyngitis*
- ***Contraindications***: pregnancy, MAOIs, SSRIs (caution)
- **Cost**: >$250/month
- The FDA recommends liraglutide 3.0mg be discontinued after 16weeks if ecipient has not lost 5% of initial weight

Fujioka, K. (2015), Current and emerging medications for overweight or obesity in people with comorbidities. Diabetes Obes Metab, 17: 1021–1032. doi:10.1111/dom.12502

# Intensive Behavioral Therapy (IBT) + Liraglutide 3.0mg

52 Week results from 150 participants

- IBT only: - 6.1% ± 1.3
- IBT + liraglutide: -11.5% ± 1.3%,
- IBT + liraglutide + 12 week meal: replacement + veggies: -11.8% ± 1.3%

Wadden, T. A., Walsh, O. A., Berkowitz, R. I., Chao, A. M., Alamuddin, N. , Gruber, K. , Leonard, S. , Mugler, K. , Bakizada, Z. and Tronieri, J. S. (2019), Intensive Behavioral Therapy for Obesity Combined with Liraglutide 3.0 mg: A Randomized Controlled Trial. Obesity, 27: 75-86. doi:10.1002/oby.22359

# Liraglutide 3mg/day (Saxenda) in DM2

- **Even with insulin at *1 year if IBT and liraglutide > 6% loss and Hba1c improves and less CV risk***
- Nearly equal to better than those without DM for loss and discontinuation rate
- No increase in pancreatitis

Garvey WT, Birkenfeld AL, Dicker D, Mingrone G, Pedersen SD, Satylganova A, Skovgaard D, Sugimoto D, Jensen C, Mosenzon O. Efficacy and Safety of Liraglutide 3.0 mg in Individuals With Overweight or Obesity and Type 2 Diabetes Treated With Basal Insulin: The SCALE Insulin Randomized Controlled Trial. Diabetes Care. 2020 May;43(5):1085-1093. doi: 10.2337/dc19-1745. Epub 2020 Mar 5. PMID: 32139381; PMCID: PMC7171937.

# Semaglutide 2.4/week (Wegovy) Step 3

Step 3: Compare weekly **semaglutide 2.4 vs placebo + ILI in low calorie diet**

- Method: **68 week phase 3a trial** at 41 sites 8/2018 to April 2020; Adults without DM and BMI >27 with comorbidity or BMI>30. Intervention group semaglutide (n= 407) or placebo (n=204) Both with 8 week ILI run in then 30 visits
- Primary outcome measures and Results: Mean age 46, BMI 38; 81% female; 93% retention and 83% taking treatment.

- **Weight loss:**
  - **5%: 86.6 vs 47.6%**
  - **10%: 75% vs 27%**
  - **15%: 55.8% vs 13%**
- GI side effects: 82% vs 63% and dropout/discontinue: 3.4% vs 0%

Wadden TA, Bailey TS, Billings LK, Davies M, Frias JP, Koroleva A, Lingvay I, O'Neil PM, Rubino DM, Skovgaard D, Wallenstein SOR, Garvey WT; STEP 3 Investigators. Effect of Subcutaneous Semaglutide vs Placebo as an Adjunct to Intensive Behavioral Therapy on Body Weight in Adults With Overweight or Obesity: The STEP 3 Randomized Clinical Trial. JAMA. 2021 Apr 13;325(14):1403-1413. doi: 10.1001/jama.2021.1831. PMID: 33625476; PMCID: PMC7905697.

# Semaglutide 2.4/week (Wegovy) Step 4

Step 4 – Continue vs withdraw 2.4 semaglutide

- Method: – Phase study 3A – 73 sites/10 countries from June2018 to March 2020 in adults with Adults without DM and BMI >27 with comorbidity or BMI>30. Intervention group 902 with weekly semaglutide run-in of 20 weeks (16 of escalation and 4 weeks maintenance). 803 participants (89%) randomized 2:1 to continue (n= 535) or placebo (n=268). Participants were 803 who lost 10% in run-in randomized to trial. Primary outcome measure: Change in weight Wt, waist circumference, blood pressure and  functioning
- Results: Mean age 46, 79% women; Mean weight107 kg. 98% completed; Mean weight change : 17.8%  with treatment vs 4.9% placebo

Rubino D, Abrahamsson N, Davies M, Hesse D, Greenway FL, Jensen C, Lingvay I, Mosenzon O, Rosenstock J, Rubio MA, Rudofsky G, Tadayon S, Wadden TA, Dicker D; STEP 4 Investigators. Effect of Continued Weekly Subcutaneous Semaglutide vs Placebo on Weight Loss Maintenance in Adults With Overweight or Obesity: The STEP 4 Randomized Clinical Trial. JAMA. 2021 Apr 13;325(14):1414-1425. doi: 10.1001/jama.2021.3224. PMID: 33755728; PMCID: PMC7988425.

**Table 1.** Efficacy of obesity medications in randomized clinical trials

| Drug | % Weight loss | | % with ≥ 10% | | % with ≥ 15% | | % with ≥ 20% | |
|---|---|---|---|---|---|---|---|---|
| | Drug | Placebo | Drug | Placebo | Drug | Placebo | Drug | Placebo |
| Orlistat (ref 25) | | | | | | | | |
| XENDOS 1 year | 10.6 | 6.2 | 41 | 20.8 | | | | |
| XENDOS 4 year | 5.8 | 3.0 | 26.2 | 15.6 | | | | |
| Phentermine/topiramate ER[a] (26-28) | | | | | | | | |
| EQUIP | 10.9 | 1.6 | 47.2 | 7.4 | 32.3 | 3.4 | | |
| CONQUER | 9.8 | 1.2 | 37.0 | 7.0 | | | | |
| SEQUEL 2 yr | 9.3 | 1.8 | 50.3 | 11.5 | 24.2 | 6.6 | 9.2 | 2.2 |
| Naltrexone ER/bupropion ER (29-31) | | | | | | | | |
| COR-I | 6.1 | 1.3 | 25.0 | 7.0 | 12 | 2 | | |
| COR-II | 6.4 | 1.2 | 28.3 | 5.7 | 13.5 | 2.4 | | |
| COR-BMOD | 9.3 | 5.1 | 41.5 | 20.2 | 29.1 | 10.9 | | |
| Liraglutide 3 mg (32-34) | | | | | | | | |
| SCALE Maintenance | 6.7 | 0.1 | 26.1 | 6.3 | 11.0 | 3.1 | | |
| SCALE Ob & PreDM 1 year | 9.2 | 3.5 | 33.1 | 10.6 | 14.4 | 3.5 | | |
| SCALE Ob & PreDM 3 year | 7.1 | 2.7 | 24.8 | 9.9 | 11.0 | 3.1 | | |
| Semaglutide 2.4 mg (22-24,35,36) | | | | | | | | |
| STEP 1 | 14.8 | 2.4 | 69.1 | 12.0 | 50.5 | 4.9 | 32.0 | 1.7 |
| STEP 3 | 16.0 | 5.7 | 75.3 | 27.0 | 55.8 | 13.2 | 35.7 | 3.7 |
| STEP 4 | 17.4 | 5.0 | 79.0 | 20.4 | 63.7 | 9.2 | 39.6 | 4.8 |
| STEP 5 2 year | 15.2 | 2.6 | 61.6 | 13.3 | 52.1 | 7.0 | 36.1 | 2.8 |
| STEP 8 | 15.8 | 1.9 | 70.9 | 15.4 | 55.6 | 6.4 | 38.5 | 2.6 |

All data represents primary analyses for each study [eg, intention to treat (ITT), ITT/last observation carried forward (LOCF), LOCF with imputation, treatment policy estimand].

Abbreviations: % with ≥, % = % of subjects achieving ≥ 10%, ≥ 15%, and ≥ 20% weight loss from baseline; Ob, obesity; PreDM, prediabetes.

[a]Dose is phentermine 7.5 mg/topiramate 46 mg except 15 mg/92 mg in EQUIP.

## Participants (%) beyond placebo with ≥10% weight loss

- Phentermine/topiramate – 39%
- naltrexone/bupropion – 20%
- Liraglutide 3mg – 10%
- Semaglutide 2.4 – 55%

## Participants (%) beyond placebo with ≥15% weight loss

- Phentermine/topiramate – 17%
- naltrexone/bupropion – 8%
- Liraglutide 3mg – 8%
- Semaglutide 2.4 – 49%

Garvey W. T. (2022). New Horizons. A New Paradigm for Treating to Target with Second-Generation Obesity Medications. *The Journal of clinical endocrinology and metabolism*, *107*(4), e1339–e1347. https://doi.org/10.1210/clinem/dgab848

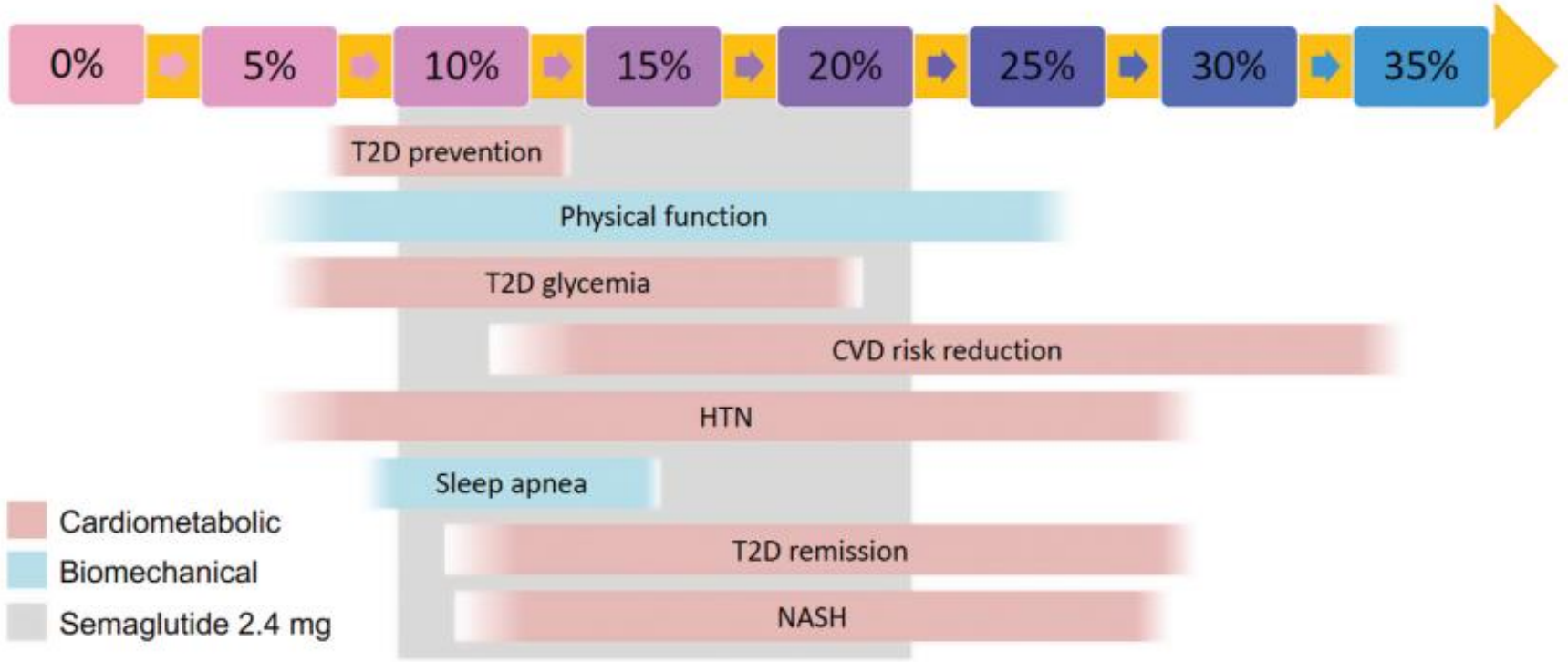


**Figure 2.** Treating ABCD/obesity to target for prevention and treatment of complications. Abbreviations: ABCD: adiposity-based chronic disease; CVD: cardiovascular disease; HTN: hypertension; NASH, nonalcoholic steatohepatitis; T2D, type 2 diabetes.

Garvey W. T. (2022). New Horizons. A New Paradigm for Treating to Target with Second-Generation Obesity Medications. *The Journal of clinical endocrinology and metabolism*, *107*(4), e1339–e1347. https://doi.org/10.1210/clinem/dgab848

# First GLP-1 and GIP agonist for Obesity: Tirzepatide

**Table 3** Key information of the SURMOUNT-1 trial [30]

| | Tirzepatide, 5 mg | Tirzepatide, 10 mg | Tirzepatide, 15 mg | Placebo |
|---|---|---|---|---|
| | least-squares mean (95% CI) | | | |
| **Co-primary endpoints**[a] | | | | |
| Change in body weight (in %) | − 15.0 | − 19.5 | − 20.9 | − 3.1 |
| Difference from placebo in percentage change in body weight (in %) | − 11.9 | − 16.4 | − 17.8 | – |
| Weight reduction of 5% or more at week 72 (% of participants) | 85.1 | 88.9 | 90.9 | 34.5 |
| **Key secondary endpoints**[a] | | | | |
| Weight reduction of 10% or more at week 72 (% of participants) | 68.5 | 78.1 | 83.5 | 18.8 |
| Weight reduction of 15% or more at week 72 (% of participants) | 48.0 | 66.6 | 70.6 | 8.8 |
| Weight reduction of 20% or more at week 72 (% of participants) | 30.0 | 50.1 | 56.7 | 3.1 |
| Change in waist circumference (in cm) | − 14.0 | − 17.7 | − 18.5 | − 4.0 |
| Difference from placebo in change in waist circumference (in cm) | − 10.1 | − 13.8 | − 14.5 | – |
| **Gastrointestinal (GI)-related adverse events (occurring in at least 5% of the participants)** | | | | |
| Nausea (Event rate in %) | 24.6 | 33.3 | 31.0 | 9.5 |
| Diarrhea (Event rate in %) | 18.7 | 21.2 | 23.0 | 7.3 |
| Constipation (Event rate in %) | 16.8 | 17.1 | 11.7 | 5.8 |
| Dyspepsia (Event rate in %) | 8.9 | 9.7 | 11.3 | 4.2 |
| Vomiting (Event rate in %) | 8.3 | 10.7 | 12.2 | 1.7 |

Data shown as Treatment-Regimen-Estimands

[a] The primary and key secondary end points were tested under a type 1 error–control procedure, and all comparisons with placebo were significant at $p < 0.001$

**Figure and Study Citations**: Schnell, O., Battelino, T., Bergenstal, R. *et al.* CVOT Summit 2022 Report: new cardiovascular, kidney, and glycemic outcomes. *Cardiovasc Diabetol* **22**, 59 (2023). https://doi.org/10.1186/s12933-023-01788-6Jastreboff, A. M.,

Aronne, L. J., Ahmad, N. N., Wharton, S., Connery, L., Alves, B., Kiyosue, A., Zhang, S., Liu, B., Bunck, M. C., Stefanski, A., & SURMOUNT-1 Investigators (2022). Tirzepatide Once Weekly for the Treatment of Obesity. *The New England journal of medicine*, *387*(3), 205–216. https://doi.org/10.1056/NEJMoa2206038

# Systematic Review and Meta-analysis of the effect of SGLT inhibitors on weight and lipid metabolism at 24weeks of treatment in patients with diabetes mellitus

36 studies selected and included in this study and they found that:

- All SGLT inhibitors were effective at reducing weight; canagliflozin was the most effective.
- SGLT inhibitors and placebo not associated with significantly different serum cholesterol levels.
- SGLT inhibitors lowered serum triglyceride levels and increased serum high-density and low-density lipoprotein cholesterol levels.
- SGLT inhibitors reduced the level of alanine aminotransferase.
- SGLT inhibitors are hepatoprotective and appear to be safe for patients with mild to moderate liver dysfunction.

Chen MB, Wang H, Cui WY, Xu HL, Zheng QH. Effect of SGLT inhibitors on weight and lipid metabolism at 24 weeks of treatment in patients with diabetes mellitus: A systematic review and network meta-analysis. Medicine (Baltimore). 2021 Feb 12;100(6):e24593. doi: 10.1097/MD.0000000000024593. PMID: 33578559; PMCID: PMC7886459.

Table 2. Change in Efficacy Outcomes From Baseline to Week 68 (Treatment Policy Estimand; Full Analysis Set)[a,b]

| | Estimated mean change (95% CI) [No.] | | Difference for semaglutide, 2.4 mg, vs liraglutide, 3.0 mg (95% CI)[c] | *P* value |
|---|---|---|---|---|
| | Semaglutide, 2.4 mg (n = 126) | Liraglutide, 3.0 mg (n = 127) | | |
| **Primary end point** | | | | |
| Body weight, % change | -15.8 (-17.6 to -13.9) [117] | -6.4 (-8.2 to -4.6) [117] | -9.4 (-12.0 to -6.8) | <.001 |
| **Confirmatory secondary end points** | | | | |
| Weight loss at week 68, No. (%)[d] | | | | |
| Participants with ≥10% | 83/117 (70.9) | 30/117 (25.6) | Odds ratio: 6.3 (3.5 to 11.2) | <.001 |
| Participants with ≥15% | 65/117 (55.6) | 14/117 (12.0) | Odds ratio: 7.9 (4.1 to 15.4) | <.001 |
| Participants with ≥20% | 45/117 (38.5) | 7/117 (6.0) | Odds ratio: 8.2 (3.5 to 19.1) | <.001 |
| **Supportive secondary end points** | | | | |
| Body weight, kg | -15.3 (-17.3 to -13.4) [117] | -6.8 (-8.8 to -4.9) [117] | -8.5 (-11.2 to -5.7) | |
| Waist circumference, cm | -13.2 (-15.0 to -11.5) [114] | -6.6 (-8.3 to -4.9) [113] | -6.6 (-9.1 to -4.2) | |
| Blood pressure, mm Hg | | | | |
| Systolic | -5.7 (-8.1 to -3.3) [114] | -2.9 (-5.3 to -0.5) [112] | -2.8 (-6.1 to 0.6) | |
| Diastolic | -5.0 (-7.0 to -3.1) [114] | -0.5 (-2.3 to 1.3) [112] | -4.5 (-7.1 to -1.9) | |
| Fasting lipid profile, % change[e] | | | | |
| Cholesterol | | | | |
| Total | -7.1 (-10.7 to -3.3) [113] | -0.1 (-3.3 to 3.2) [107] | -7.0 (-11.7 to -2.1) | |
| HDL | -0.3 (-3.6 to 3.0) [112] | 1.9 (-1.0 to 5.0) [107] | -2.2 (-6.5 to 2.2) | |
| LDL | -6.5 (-12.4 to -0.1) [112] | 0.9 (-4.4 to 6.5) [107] | -7.3 (-14.9 to 1.0) | |
| VLDL | -20.7 (-25.1 to -16.0) [112] | -10.9 (-16.7 to -4.8) [107] | -11.0 (-18.5 to -2.7) | |
| Free fatty acids | -12.6 (-22.1 to -2.0) [108] | -8.8 (-19.0 to 2.7) [110] | -4.2 (-18.8 to 13.1) | |
| Triglycerides | -20.7 (-25.6 to -15.6) [112] | -11.0 (-16.9 to -4.7) [107] | -11.0 (-18.9 to -2.2) | |
| CRP, % change[e] | -52.6 (-61.3 to -42.0) [113] | -24.5 (-36.1 to -10.9) [110] | -37.2 (-51.7 to -18.5) | |
| $HbA_{1c}$, % | -0.2 (-0.3 to -0.2) [113] | -0.1 (-0.1 to 0.0) [107] | -0.2 (-0.2 to -0.1) | |
| Fasting plasma glucose, mg/dL | -8.3 (-10.4 to -6.1) [112] | -4.3 (-6.7 to -1.9) [106] | -3.9 (-7.2 to -0.7) | |
| Fasting serum insulin, % change[e] | -27.8 (-36.5 to -17.9) [108] | -15.4 (-23.1 to -7.0) [110] | -14.6 (-27.3 to 0.3) | |
| **Exploratory end point** | | | | |
| Participants with ≥5% weight loss at week 68, No./total (%)[d] | 102/117 (87.2) | 68/117 (58.1) | NA | |
| **Prespecified sensitivity analysis (J2R)** | | | | |
| Body weight, % change[f] | -15.3 (-17.0 to -13.6) [117] | -6.0 (-7.7 to -4.3) [117] | -9.2 (-11.6 to -6.8) | |
| **Post hoc sensitivity analysis** | | | | |
| Body weight, % change[g] | -15.8 (-17.7 to -13.8) [117] | -6.4 (-8.2 to -4.5) [117] | -9.4 (-12.0 to -6.7) | |

# Step 8: Semaglutide 2.4 vs. Liraglutide 3.0

**Weight loss**:
≥10%: 70.9%/26.6%
≥15%: 55.6%/12%
≥20%: 38.5%/6%
**Waist Circ:** -13cm/-6cm
**BP Syst:** -5.70/-0.05
**BP Diast-** 5.0/-1.3
**HDL:** -0.3/+1.9
**LDL**: -6.0/0.9
**Trig:** -20.7/-11.0
**CRP:** -52/-24
**HbA1c:** 0.2/0.1

Rubino DM, Greenway FL, Khalid U, et al. Effect of Weekly Subcutaneous Semaglutide vs Daily Liraglutide on Body Weight in Adults With Overweight or Obesity Without Diabetes: The STEP 8 Randomized Clinical Trial. *JAMA.* 2022;327(2):138–150. doi:10.1001/jama.2021.23619

# Meta-Analysis of long-term effects of weight reducing meds on people with Pre-DM

**Included studies:**

- Liraglutide: 3 trials 4557 participants
- Qsymia: 2 trials 3015 participants
- Contrave: 4 trials 3952 participants
- Lorcaserin: 3 trial 6893 participants
- Orlistat: 17 trials 10, 702 participants
- Liraglutide vs orlistat: 1 trial 188 patients

**Summary of Included study participants**

- Mean age 46(41-60)
- 77% women
- Median BMI: 36 (32.7-42)
- Medial glucose: 104 mg/dl (94-161)
- Median LDL Cholesterol: 122.7mg/dl
- Median HDL: 46.4
- Median systolic blood pressure 127mm/Hg
- Median diastolic blood pressure 79 mm/Hg
- Hypertension diagnosis: 23%
- Waist Circumference 110 cm

Khera R, Pandey A, Chandar AK, et al. Effects of Weight-Loss Medications on Cardiometabolic Risk Profiles: A Systematic Review and Network Meta-analysis. *Gastroenterology*. 2018;154(5):1309–1319.e7. doi:10.1053/j.gastro.2017.12.024

# Meta-Analysis of long-term effects of weight reducing meds on people with Pre-DM

**Outcomes:**

- Systolic BP: Overall reduction of -1.8mmHg
  - Qsymia: -3.7;  liraglutide: -2.8; orlistat: -1.7
- Diastolic BP: Overall reduction of -2.0- mm/Hg
  - Qsymia most
- Fasting Glucose:  Overall modest reduction 4mg/dl
  - liraglutide 15.6, orlistat 8
- HbA1c:  overall minimal change
  - Liraglutide: -0.5;  orlistat: 0.4, no change on others
- LDL cholesterol: Overall minimal reduction
  - Orlistat: -8.7; and Qsymia: -4.2
- HDL cholesterol: minimal increase
  - Qsymia and Contrave + 2.5; worse with orlistat
- Waist Circumference: 3.3 cm decrease Qsymia, 4cm liraglutide, 3.5 Contrave, 2.3 orlistat

Khera R, Pandey A, Chandar AK, et al. Effects of Weight-Loss Medications on Cardiometabolic Risk Profiles: A Systematic Review and Network Meta-analysis. *Gastroenterology*. 2018;154(5):1309–1319.e7. doi:10.1053/j.gastro.2017.12.024

# Incidence of MACE and relationship to GLP-1 agonists in DM

- GLP-1 Agonists (liraglutide, sc semaglutide, and dulaglutide, respectively) were superior to placebo, showing lower incidence of the composite MACE endpoint.

Trials of the GLP-1 Receptor agonists liraglutide, semaglutide and dulaglutide show:

- Different percent weight loss and tolerance the different medications
- No increased risk for thyroid cancer with use of these medications
- lower incidence of composite major adverse cardiovascular events for in participants with diabetes

# Weight reducing drugs in people with hypertension

Meta-analysis in Hypertension 2016

Summary results from trials – none had blood pressure reduction as a primary outcome. As a secondary outcome:

- Orlistat: (-2.46/-1.92) lowered BP consistent with level of weight loss
- Blood pressure was not changed with Contrave treatment and weight loss (single study)
- Lorcaserin, Liraglutide, Qsymia – indeterminate effect

Siebenhofer A, Jeitler K, Horvath K, Berghold A, Posch N, Meschik J, Semlitsch T. Long-term effects of weight-reducing drugs in people with hypertension. Cochrane Database of Systematic Reviews 2016, Issue 3. Art. No.: CD007654. DOI: 10.1002/14651858.CD007654.pub4.

# Improvement in liver fat content with medications to treat obesity

- Only liraglutide and orlistat shown to reduce liver fat content

- No trials measuring other approved medications

Polyzos S.A., Kountouras J., Mantzoros C.S. Obesity and nonalcoholic fatty liver disease: From pathophysiology to therapeutics.(2019) *Metabolism: Clinical and Experimental*, 92 , pp. 82-9

# Reducing ASCVD event or lowering risk MACE

- Based cardiovascular outcome trials (CVOTs) of new diabetes medications, the American Diabetes Association (ADA) Standards of Medical Care in Diabetes – 2021 now **recommends to consider adding either glucagon-like peptide-1 receptor agonists (GLP-1RAs) or sodium-glucose co-transporter 2 inhibitors (SGLT-2is) in individuals with diabetes who have either established atherosclerotic cardiovascular disease (ASCVD) or increased cardiovascular (CV) risk**.
- A review suggests that in women with increased CV risk or established ASCVD, GLP-1RA resulted in a significantly lower incidence of MACE and may be favored. While **SGLT-2 did not achieve statistically significant reductions in MACE in women, studies** were limited, and their use may still be considered given their improvement in glycemic control and potential for overall cardio-renal benefit.

Schnell, O., Battelino, T., Bergenstal, R. *et al.* CVOT Summit 2022 Report: new cardiovascular, kidney, and glycemic outcomes. *Cardiovasc Diabetol* **22**, 59 (2023). https://doi.org/10.1186/s12933-023-01788-6

ElSayed NA, Aleppo G, Aroda VR, et al., American Diabetes Association. Summary of revisions: Standards of Care in Diabetes—2023. Diabetes Care 2023;46(Suppl. 1):S5–S9

# Tirzepatide cardiovascular event risk assessment:

Tirzepatide is a novel, once weekly, dual GIP/GLP-1 receptor agonist and is under development for the treatment of type 2 diabetes (T2D) and obesity. Its association with **cardiovascular outcomes requires evaluation**. This pre-specified cardiovascular **meta-analysis included all seven randomized controlled trials with a duration of at least 26 weeks from the tirzepatide T2D clinical development program, SURPASS.**

The pre-specified primary objective of this meta-analysis was the **comparison of the time to first occurrence of confirmed four-component major adverse cardiovascular events (MACE-4; cardiovascular death, myocardial infarction, stroke and hospitalized unstable angina) between pooled tirzepatide groups and control groups.** A stratified Cox proportional hazards model, with treatment as a fixed effect and trial-level cardiovascular risk as the stratification factor, was used for the estimation of hazard ratios (HRs) and confidence intervals (CIs) comparing tirzepatide to control.

Results: Data from 4,887 participants treated with tirzepatide and 2,328 control participants were analyzed. Overall, **142 participants, 109 from the trial with high cardiovascular risk and 33 from the six trials with lower cardiovascular risk, had at least one MACE-4 event**. The **HRs comparing tirzepatide versus controls were 0.80 (95% CI, 0.57–1.11) for MACE-4; 0.90 (95% CI, 0.50–1.61) for cardiovascular death; and 0.80 (95% CI, 0.51–1.25) for all-cause death.** No evidence of effect modifications was observed for any subgroups, although the evidence was stronger for participants with high cardiovascular risk. **Tirzepatide did not increase the risk of major cardiovascular events in participants with T2D versus controls.**

Sattar N, McGuire DK, Pavo I, Weerakkody GJ, Nishiyama H, Wiese RJ, Zoungas S. Tirzepatide cardiovascular event risk assessment: a pre-specified meta-analysis. Nat Med. 2022 Mar;28(3):591-598. doi: 10.1038/s41591-022-01707-4. Epub 2022 Feb 24. PMID: 35210595; PMCID: PMC8938269.

# Preventing ABCD complications, the dose-response for weight loss to achieve clinical benefit varies by various complications

**Prediabetes/metabolic syndrome:** 10% weight loss most effective to prevent progression to diabetes

**Type 2 Diabetes Meillitus:** More weight loss better and where weight loss of >5% to 15% or more provides progressive improvements in HbA1c, blood pressure, and lipids

**obstructive sleep apnea:** ≥10% weight loss for predictable improvements in the apnea/ hypopnea index

**Nonalcoholic fatty liver disease:** 5% to 10% weight loss will reduce steatosis but >10% weight loss is required in nonalcoholic steatohepatitis to improve inflammation and fibrosis

**Prevention of CVD events and mortality:** may require >10% weight loss based on case-control studies and meta-analyses of the bariatric surgery literature and on results from the Look AHEAD study in patients with T2D that assessed outcomes as a function of degree of weight loss

In considering the degree of weight loss required to ameliorate these common complications in ABCD, **interventions are needed that reliably produce 10% to 20% weight loss**.

Garvey W. T. (2022). New Horizons. A New Paradigm for Treating to Target with Second-Generation Obesity Medications. *The Journal of clinical endocrinology and metabolism*, *107*(4), e1339–e1347. https://doi.org/10.1210/clinem/dgab848

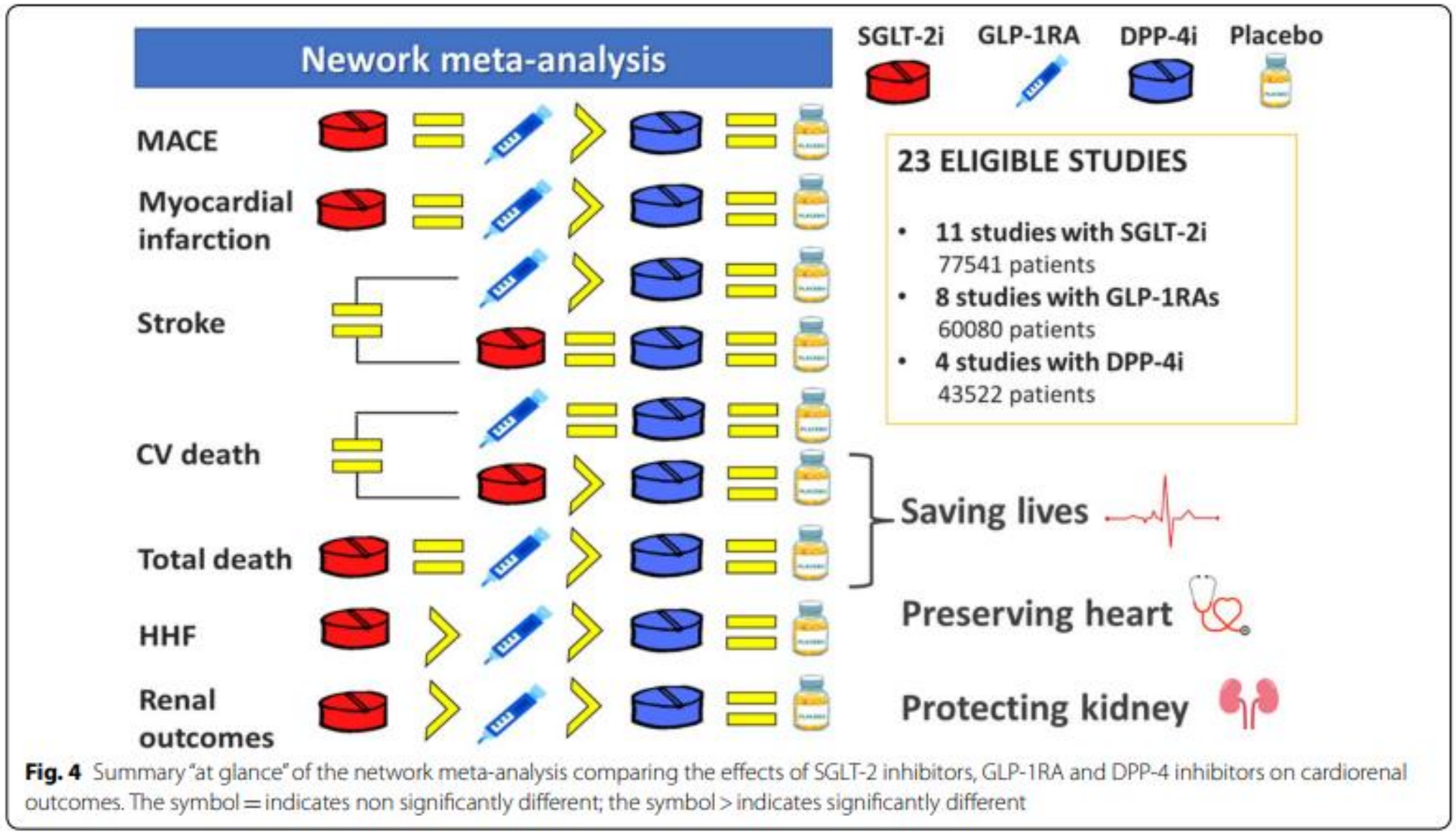


**Fig. 4** Summary "at glance" of the network meta-analysis comparing the effects of SGLT-2 inhibitors, GLP-1RA and DPP-4 inhibitors on cardiorenal outcomes. The symbol = indicates non significantly different; the symbol > indicates significantly different

Giugliano, D., Longo, M., Signoriello, S., Maiorino, M. I., Solerte, B., Chiodini, P., & Esposito, K. (2022). The effect of DPP-4 inhibitors, GLP-1 receptor agonists and SGLT-2 inhibitors on cardiorenal outcomes: a network meta-analysis of 23 CVOTs. *Cardiovascular diabetology*, *21*(1), 42. https://doi.org/10.1186/s12933-022-01474-z

# Statistical power for MACE and individual secondary endpoints in cardiovascular outcomes trials for type 2 diabetes: a systematic review.

- Our analysis has shown that **cardiovascular outcomes studies performed as part of the development of novel glucose-lowering drugs are typically adequately powered for the main (primary) endpoint MACE**, but that they have variable power, depending on sample size and the number of cardiovascular events accrued, to provide significance for the effect size of differences that are typically observed with SGLT-2 Is and GLP-1 RAs. As a result, indirect comparisons between placebo-controlled cardiovascular outcomes trials with different glucose-lowering drugs do not appear uniformly suitable to detect differences in their ability to elicit a unique pattern of effects on various cardiovascular endpoints.

Birker, S., Meier, J.J. & Nauck, M.A. Statistical power for MACE and individual secondary endpoints in cardiovascular outcomes trials for type 2 diabetes: a systematic review. *Sci Rep* **12**, 21069 (2022). https://doi.org/10.1038/s41598-022-25296

# Anti-obesity medication impact on ACVD in obesity w/o DM

- **SELECT** is the first cardiovascular outcomes trial to evaluate superiority in major adverse cardiovascular eventsreduction for an antiobesity medication in such a population. As such, SELECT has the potential for advancing new approachesto CVD risk reduction while targeting obesity. (Am Heart J 2020;229:61-9.

- **Results Pending**

Ryan DH, Lingvay I, Colhoun HM, Deanfield J, Emerson SS, Kahn SE, Kushner RF, Marso S, Plutzky J, Brown-Frandsen K, Gronning MOL, Hovingh GK, Holst AG, Ravn H, Lincoff AM. Semaglutide Effects on Cardiovascular Outcomes in People With Overweight or Obesity (SELECT) rationale and design. Am Heart J. 2020 Nov;229:61-69. doi: 10.1016/j.ahj.2020.07.008. Epub 2020 Jul 17. PMID: 32916609.

# Putting it together

- Obesity weight loss goals for best medical outcomes, especially in adults with increased cardiovascular risk should often be ≥15% for best medical outcome.
- Medication (long-term) or bariatric surgery, in addition to lifestyle interventions, have best evidence for achieving and improving outcomes.
- For weight loss over 20%, severe obesity, or moderate obesity with comorbid conditions, management for comorbid conditions, and risk factor reduction should include offering obesity treatment according to guidelines.
- Partner with your patient provide a behavioral framework they are ready for and work to find out what options for obesity treatment are affordable and preferred.
- Medications are to be thought of long-term and in conjunction with active lifestyle and comorbid condition management

# Supports and Partners

- Obesity Medicine Physicians
- Dieticians with obesity treatment experience
- Behaviorists with obesity and eating disorder training
- Bariatric Surgeons
- Medication support resources:
- Coaching and tools
- Evidence-based programs
- Organizations
- Community resources and groups

# Consensus Statement on Obesity and the treatment of people with Obesity

- *Obesity is a highly prevalent chronic disease characterized by excessive fat accumulation or distribution that presents a risk to health and requires life-long care. Virtually every system in the body is affected by obesity. Major chronic diseases associated with obesity include diabetes, heart disease and cancer.*
- *The body mass index (weight in kilograms/height in meters 2) (BMI) is used to screen for obesity but it does not displace clinical judgment. BMI is not a measure of body fat. Social determinants, race, ethnicity and age may modify the risk associated with a given BMI.*
- *Bias and stigmatization directed at people with obesity contributes to poor health and impairs treatment.*
- *Every person with obesity should have access to evidence-based treatment.*

Organizations joining The Obesity Society in this effort include the Academy of Nutrition and Dietetics (the Academy), American Society of Metabolic and Bariatric Surgery (ASMBS), Obesity Action Coalition (OAC), Obesity Medicine Association (OMA), and the Strategies to Overcome and Prevent (STOP) Obesity Alliance. Country's Leading Obesity Care Organizations Develop Consensus Statement on Obesity (prnewswire.com)

# Additional Selected Resources for Communication, Treatment and Prioritization

1. Strategies to Overcome and Prevent (STOP) Obesity Alliance ©2014 www.stopobesityalliance.org

2. 2013 AHA/ACC Guideline for the Management of Overweight and Obesity in Adults. E-Published on November 12, 2013, at: http://circ.ahajournals.org/lookup/doi/10.1161/01.cir.0000437739.71477.ee

Full-text guidelines on Web sites:ACC (www.cardiosource.org) and AHA (my.americanheart.org)www.nwcr.ws/default.htm

3. The Obesity Society (TOS) (www.obesity.org)

4. The American Board of Obesity Medicine (ABOM)

5. Obesity Action Coalition (OAC) https://www.obesityaction.org/

# Obesity-Related Resources
# Professional Associations

| | |
|---|---|
| The Obesity Society (TOS) | www.obesity.org |
| American Board of Obesity Medicine | www.abom.org |
| American Academy of Family Physicians (AAFP) | www.aafp.org |
| American College of Sports Medicine (ACSM) | www.acsm.org |
| American Diabetes Association (ADA) | www.diabetes.org |
| American Dietetic Association (ADA) | www.eatright.org |
| American Gastroenterological Association (AGA) | www.gastro.org |
| American Heart Association (AHA) | www.americanheart.org |
| Obesity Medicine Association (OMA) | www.obesitymedicine.org |
| American Society for Metabolic and Bariatric Surgery (ASMBS) | www.asmbs.org |

# Obesity-Related Resources
# Government Organizations

| | |
|---|---|
| Centers for Disease Control (CDC): *Obesity and Overweight* | www.cdc.gov/nccdphp/dnpa/obesity/index.htm |
| Centers for Disease Control (CDC): *Prevalence data and growth charts* | www.cdc.gov/nchs/nhanes.htm |
| National Institutes of Health (NIH) | www.nih.gov |
| National Institutes of Diabetes & Digestive & Kidney Diseases (NIDDK) *Weight-Control Information Network (WIN)* | www.niddk.nih.gov/health/nutrit/win.htm |
| National Institutes of Diabetes & Digestive & Kidney Diseases (NIDDK) *Weight Loss and Control* | www.niddk.nih.gov/health/nutrit/nutrit. htm |
| National Library of Medicine, MEDLINE Plus | www.nlm.nih.gov/medlineplus/obesity.html |