CNR Seminar

Current Evidence & Guidelines for Obesity & Prediabetes Management and Type 2 Diabetes Prevention in Younger Adults: Healthy Lifestyle Interventions vs. Medical Management

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Learning Objectives

1. At the end of the activity, learners will be able to state the current evidence supporting healthy lifestyle interventions and medical management for obesity, prediabetes, and the prevention of type 2 diabetes in younger adults.

2. At the end of the activity, learners will report the risks and benefits of medical management for obesity, prediabetes, and the prevention of type 2 diabetes.

Outline

I. Overview of Prediabetes and Type 2 DM in Younger Adults
II. Current Evidence and Guidelines for Lifestyle Interventions for Prediabetes and Prevention of T2DM
III. Preliminary Results of DPP program “Healthy Women & Healthy Communities: A Tailored Diabetes Prevention Program Designed to Create Healthy Women, Healthy Communities, and Health Equity in Rural GA”
IV. Current Evidence and Guidelines for Medical Management for Prediabetes and Prevention of T2DM
V. Risks and Benefits of Medical Management

Overview of Prediabetes and Type 2 DM in Younger Adults

ADA Classification

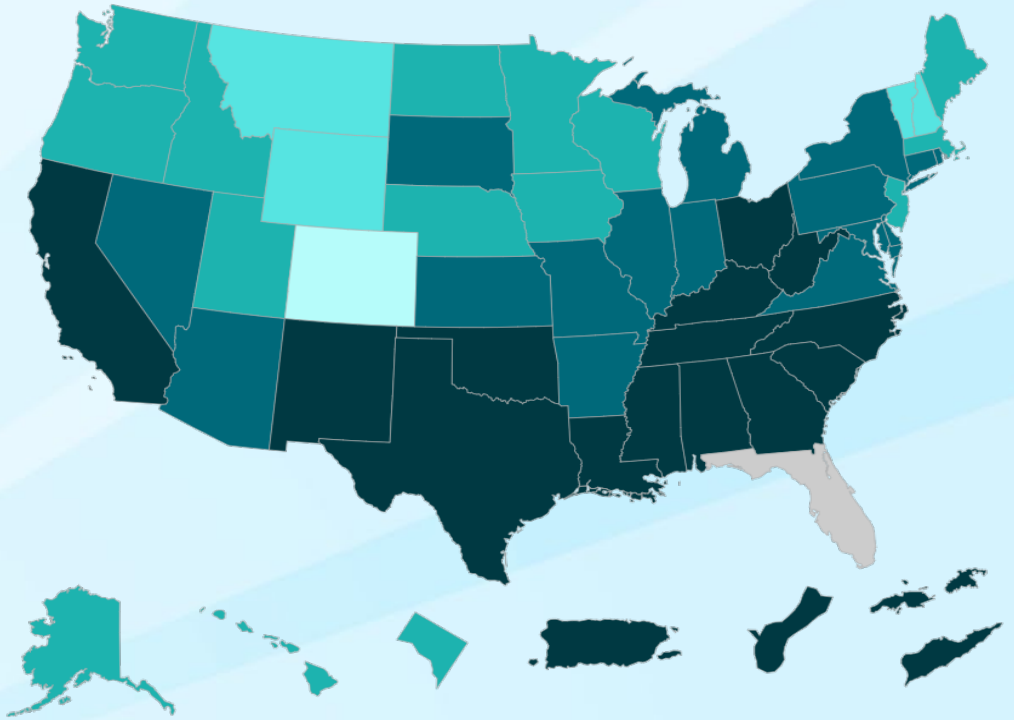
	Fasting BG	2-hour GTT	HgA1C
Normal	< 100	< 140	< 5.7%
Prediabetes	100 -125	140 -199	5.7-6.4%
Type 2 Diabetes	≥ 126	≥ 200	≥ 6.5%

Prevalence of Prediabetes and Type 2 Diabetes - Adults

	18-44 years Percentage	45 – 64 years Percentage	65 + years Percentage	Total (2017-2020) Percentage
Prediabetes	**27.8**	**44.8**	**48.8**	**36.5**
Type 2 DM	2.4	12.5	19.5	10.1
Undiagnosed	1.9	4.5	4.7	3.4
Gestational DM	4.5 – 11.7 per 100	15.3 per 100 (40 + years)	N/A	9.1 - 10.5 per 100 (NHIS) 6.5 - 7.8 per 100 (Vital Statistics) * 30% increase from 2016

Gregory, Elizabeth C.W. and Ely, Danielle M. (2022). Trends and Characteristics in Gestational Diabetes : United States, 2016–2020. 71(3).

Diagnosed Diabetes, Total, Adults Aged 18+ Years, Age-Adjusted Percentage, U.S. States, 2021



Percentage (Natural Breaks)

- 4.3 - 6.5
- 6.6 - 7.7
- 7.8 - 8.9
- 9 - 10.8
- 10.9 - 16.6
- No Data
- Suppressed

Source: USDSS

Disclaimer: This is a user-generated report. The findings and conclusions are those of the user and do not necessarily represent the views of the CDC.

Type 2 Diabetes in Youth

- Unique pathophysiologic features (rapid decline in beta cell function)
- TODAY study
- SEARCH longitudinal study on children and adolescents
  - Incidence has doubled since 2002
  - *9.0 to 17.9 per 100,000*
  - **Incidence of T2DM exceeded T1DM in 2017 - 2018**
  - *19.7 vs. 14.6 per 100,000 for 15 -19 years of age*

Wagenknecht LE, Lawrence JM, Isom S, Jensen ET, Dabelea D, Liese AD, Dolan LM, Shah AS, Bellatorre A, Sauder K, Marcovina S, Reynolds K, Pihoker C, Imperatore G, Divers J (2023). Trends in incidence of youth-onset type 1 and type 2 diabetes in the USA, 2002-18: results from the population-based SEARCH for Diabetes in Youth study. The Lancet Diabetes & Endocrinology 11:242-250

Type 2 Diabetes in Youth

SEARCH longitudinal study on children and adolescents

The number of youths with diabetes will increase from 213,000 in 2017 to 239,000 ***in 2060*** *if the incidence remains constant as observed in 2017. Corresponding relative increases were 3% for type 1 diabetes and 69% for type 2 diabetes. Assuming that increasing trends in incidence observed between 2002 and 2017 continue, the projected number of youths with diabetes will be 526,000.* ***Corresponding relative increases would be 65% for type 1 diabetes and 673% for type 2 diabetes****. In both scenarios, substantial widening of racial and ethnic disparities in type 2 diabetes prevalence are expected, with the highest prevalence among non-Hispanic Black youth*.

Thaddäus Tönnies, Ralph Brinks, Scott Isom, Dana Dabelea, Jasmin Divers, Elizabeth J. Mayer-Davis, Jean M. Lawrence, Catherine Pihoker, Lawrence Dolan, Angela D. Liese, Sharon H. Saydah, Ralph B. D'Agostino, Annika Hoyer, Giuseppina Imperatore; Projections of Type 1 and Type 2 Diabetes Burden in the U.S. Population Aged <20 Years Through 2060: The SEARCH for Diabetes in Youth Study. *Diabetes Care* 1 February 2023; 46 (2): 313–320. https://doi.org/10.2337/dc22-0945

Current Evidence and Guidelines for Lifestyle Interventions for Prediabetes and Prevention of T2DM

Lifestyle Interventions

- Nutrition
  - Mediterranean Diet – reduced risk of CVD and T2DM
    - ADA new recommendation (5.20) of Mediterranean diet for dietary fat to include monosaturated fat and polyunsaturated fat (fatty fish, nuts, seeds) to reduce risk of CVD and improve BG
    - Mixed results on reducing CV risk

    Karam G, Agarwal A, Sadeghirad B, et al. (2023). Comparison of seven popular structured dietary programmes and risk of mortality and major cardiovascular events in patients at increased cardiovascular risk: systematic review and network meta-analysis. *BMJ, 380*:e072003.

    - Strong evidence to support reduced risk of developing T2DM – 20 to 23% reduced risk

    Martín-Peláez, S., Fito, M., & Castaner, O. (2020). Mediterranean Diet Effects on Type 2 Diabetes Prevention, Disease Progression, and Related Mechanisms. A Review. *Nutrients, 12(*8), 2236. https://doi.org/10.3390/nu12082236
  - Plant-based/Vegetarian 5% lower mortality risk, 8-15% reduced risk of cancer, lower risk of T2DM - Relative Risk 0.77, improved lipids, A1C, and weight
    - Kim H, Caulfield LE, Rebholz CM. (2018). Healthy Plant-Based Diets Are Associated with Lower Risk of All-Cause Mortality in US Adults. J Nutr, 148:624.
    - Dinu M, Abbate R, Gensini GF, et al. (2017). Vegetarian, vegan diets and multiple health outcomes: A systematic review with meta-analysis of observational studies. Crit Rev Food Sci Nutr, 57:3640.
    - Qian, F., Liu, G., Hu, F. B., Bhupathiraju, S. N., & Sun, Q. (2019). Association Between Plant-Based Dietary Patterns and Risk of Type 2 Diabetes: A Systematic Review and Meta-analysis. *JAMA internal medicine*, *179*(10), 1335–1344. https://doi.org/10.1001/jamainternmed.2019.2195
  - Low-fat, Low-carbohydrate/KETO overall no benefit, esp. unhealthy macronutrients
    - Shan Z, Guo Y, Hu FB, et al. (2020). Association of Low-Carbohydrate and Low-Fat Diets With Mortality Among US Adults. JAMA Intern Med,180:513.

Lifestyle Interventions

- Non-pharmacological
  - FIBER 25 – 35 gm daily (barley, oats, rye are best)
  - Mimics GLP-1 response similar to new medications GLP1 agonists i.e. Wegovy, Mounjaro
  - Suppression of appetite/satiety/fullness, reduced postprandial glucose response, “second meal effect”

Costabile, G., Vetrani, C., Calabrese, I., Vitale, M., Cipriano, P., Salamone, D., Testa, R., Paparo, L., Russo, R., Rivellese, A. A., Giacco, R., & Riccardi, G. (2023). High Amylose Wheat Bread at Breakfast Increases Plasma Propionate Concentrations and Reduces the Postprandial Insulin Response to the Following Meal in Overweight Adults. The Journal of nutrition, 153(1), 131–137. https://doi.org/10.1016/j.tjnut.2022.10.007

- Lifestyle Change Programs - Diabetes Prevention Program
  - 5-7% weight loss goal and 150 minutes of physical activity per week
  - 35 - 50% reach goal
  - up to 43% reduced incidence of T2DM in programs for women with history of GDM

Lifestyle Interventions

- Diabetes Prevention Program – Knowler et al. 2002 Landmark Study
  - reduced incidence of **T2DM by 58% vs. Metformin by 31%**
  - Knowler, W. C., Barrett-Connor, E., Fowler, S. E., Hamman, R. F., Lachin, J. M., Walker, E. A., Nathan, D. M., & Diabetes Prevention Program Research Group (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *The New England Journal of medicine*, *346*(6), 393–403. https://doi.org/10.1056/NEJMoa012512
- Physical Activity
  - 2018 HHS Guidelines: 150 minutes per week (21- 23% lower mortality)
  - 300 – 600 minutes per week! (26-31% lower mortality)

  Lee, D. H., Rezende, L. F. M., Joh, H. K., Keum, N., Ferrari, G., Rey-Lopez, J. P., Rimm, E. B., Tabung, F. K., & Giovannucci, E. L. (2022). Long-Term Leisure-Time Physical Activity Intensity and All-Cause and Cause-Specific Mortality: A Prospective Cohort of US Adults. Circulation, 146(7), 523–534. https://doi.org/10.1161/CIRCULATIONAHA.121.058162

- Most RCT's included lifestyle intervention component with 500kcal reduction in diet and ≥150 minutes physical activity

"*Behavioral intervention consisted of counseling by a dietician or similarly qualified health professional every 4 weeks in person or via telephone and adherence to reduced calorie diet an increased physical activity and recorded daily. No further standardization of behavioral intervention was applied across study sites"* STEP – 5 Trial Garvey et al. 2022

Preliminary Results of DPP program *"Healthy Women & Healthy Communities: A Tailored Diabetes Prevention Program Designed to Create Healthy Women, Healthy Communities, and Health Equity in Rural GA"*

Augusta University Intramural Grant Program

June 2023-June 2025

Diabetes Prevention Program – Rural GA

Specific Aims:

1. Develop a tailored 3-month modification of the DPP, guided by a core ***socio-ecological needs assessment*** of younger women, 18-44, at high risk for developing Type 2 DM, living in rural counties of the Augusta Perinatal Region of GA
2. Examine the preliminary effectiveness of a ***tailored 3-month modification of the DPP*** to meet the specific needs of younger women, ages 18-44, at high risk for developing Type 2 DM, living in rural counties of the Augusta Perinatal Region of GA

Rationale:

1. Lack of DPP implementation/evidence in younger adult, rural population
2. Women with history of Gestational DM have 7-fold risk of DM and twice as likely to develop CVD
3. No integration of SDOH in DPP

Recruitment!

- Community Advisory Board
- AU Women's Clinic – Referrals
- Social Media Campaign

Baseline Demographics

	Urban (n=6)	Rural (n=6)
Mean Age	40	37.5
Race	Black/African American = 6	White = 2 Black/African American = 4
BMI	38.6	43.5
HgA1C	5.9%	5.2%
SDOH/Social Needs Survey	1 social isolation, 1 food insecurity and transportation, Financial strain –utilities, rent, medical costs, childcare	1 food insecurity, Financial strain –utilities, rent, medical costs

Other baseline surveys: Breastfeeding, Contraception Use, 24-hour food intake, Physical Activity, Preventive Health Screening, Diabetes Risk Perception, Diabetes Knowledge

Baseline Surveys - Diabetes Risk Perception

“I think that my personal efforts will help control my risks of getting diabetes”

“People who make a good effort to control the risks of getting diabetes are much less likely to get diabetes”

Agree = 12

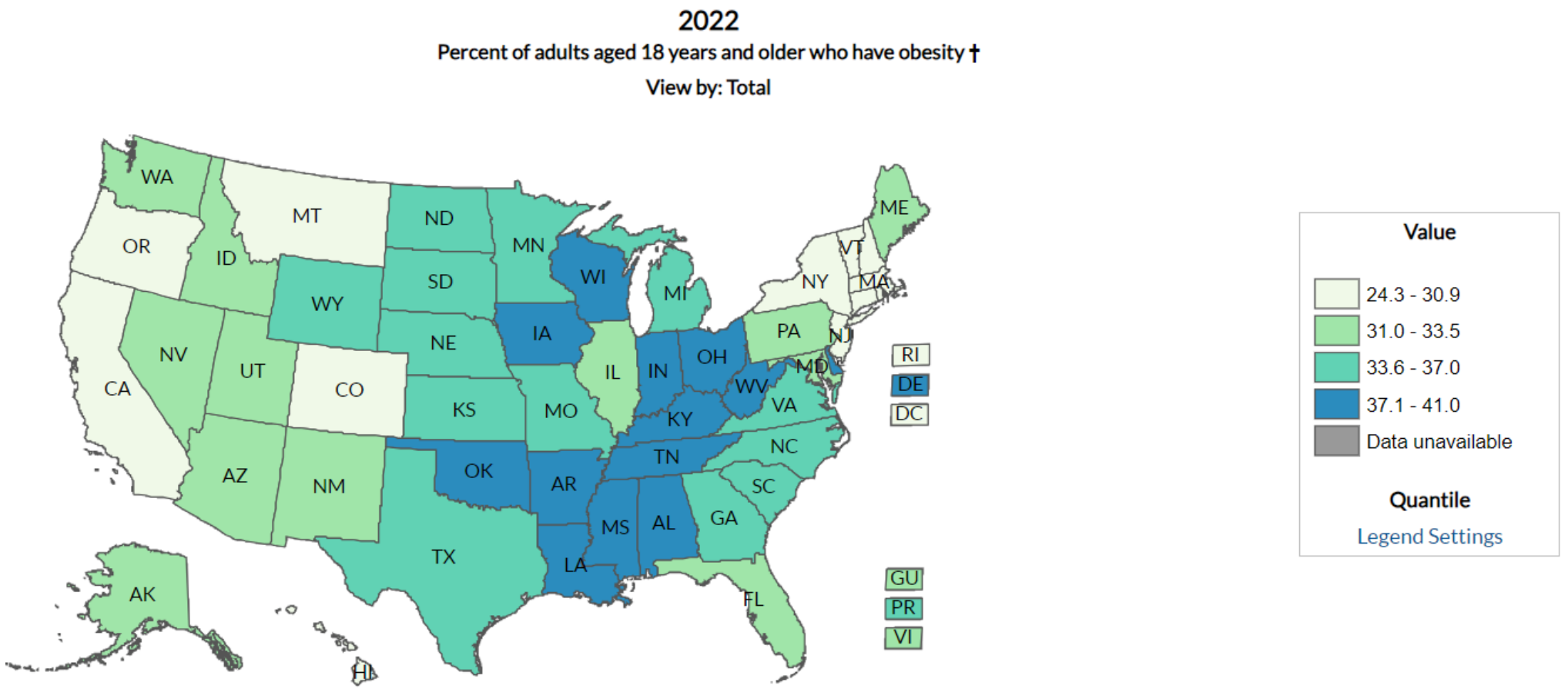
Disagree = ZERO

Behavior Change Theory:

Health Belief Model – Perceived Susceptibility, Perceived Severity, Personal Motivation, Perceived Benefits, Perceived Barriers → Action

Current Evidence and Guidelines for Medical Management for Prediabetes and Prevention of T2DM

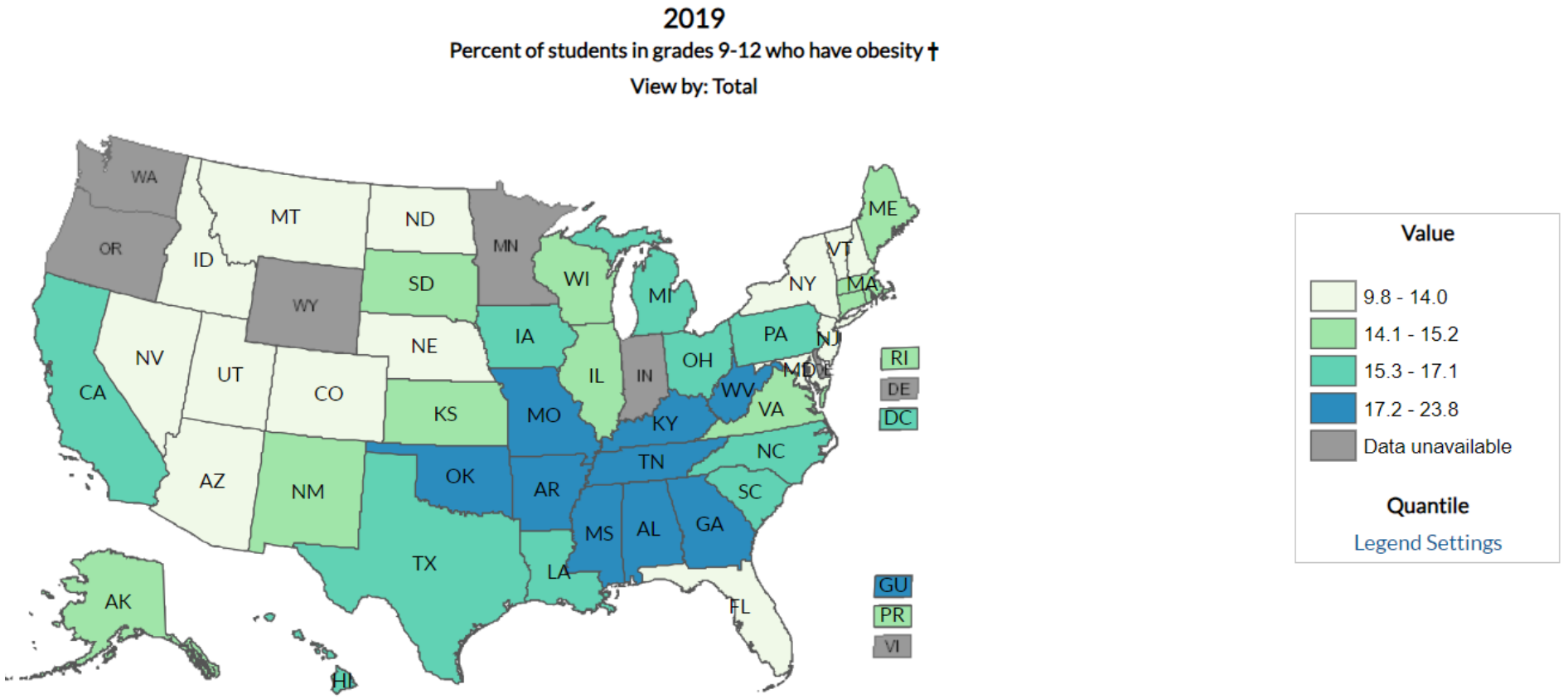
Adult Obesity in U.S.



National: 33%; W. Virginia: 41% (highest) **Georgia: 37%**

18-24: 20.5% 25-34: 32.2% 35-44: 37.4% **45-54: 39.9%** 55-64: 37.4% 65+: 30.6%

Adolescent Obesity in U.S.



National: 15.5% Mississippi: 23.4% (highest) **Georgia: 18.3%**

Current Guidelines for Obesity

- American Gastroenterological Association (AGA): Guideline on pharmacological interventions for adults with obesity 2022
  - Grunvald et al. (2022). AGA Clinical Practice Guideline on Pharmacological Interventions for Adults With Obesity. *Gastroenterology, 163(*5), 1198–1225. https://doi.org/10.1053/j.gastro.2022.08.045
- The Obesity Society (TOS): Position statement on obesity as a disease 2019
- American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE): Comprehensive clinical practice guidelines for medical care of patients with obesity 2016
- ACC/AHA/TOS: Guidelines for the management of overweight and obesity in adults 2013

Guidelines for Medical Management

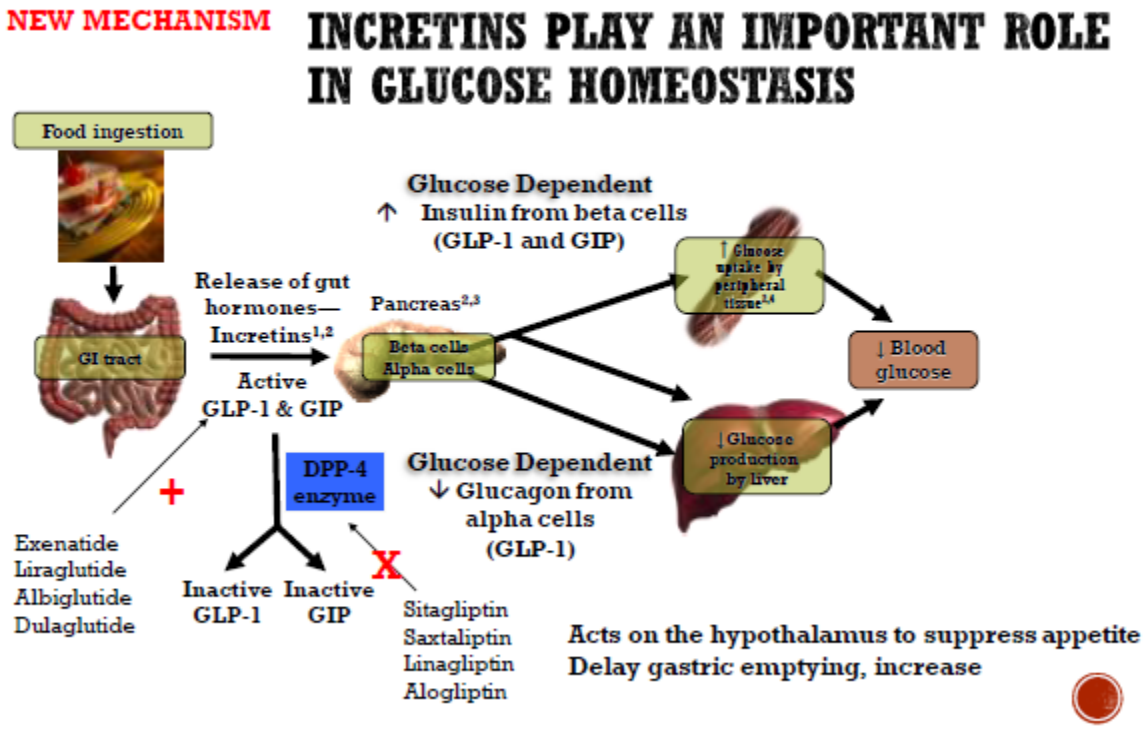
Pharmacological intervention recommended:

- Adults with overweight BMI ≥27 AND weight related complications
- Adults with obesity BMI ≥30 AND inadequate response to lifestyle interventions
- Youth ages 12 and older, BMI at or above 95th percentile for age and sex (Wegovy-Semaglutide only)
- SURPASS-PEDS study underway for Tirzepatide (Mounjauro)

ADA recommendations for Metformin therapy:

- High-risk for T2DM, i.e. hx of gestational DM
- BMI ≥35
- IFG ≥110 or A1C≥6.0%

GLP – 1 Agonist – Glucagon Like Peptide
GIP – Glucose Dependent Insulinotropic Polypeptide



Medical Management for Prediabetes & Prevention of T2DM

- Metformin 850mg bid
  - Knowler, W. C., Barrett-Connor, E., Fowler, S. E., Hamman, R. F., Lachin, J. M., Walker, E. A., Nathan, D. M., & Diabetes Prevention Program Research Group (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *The New England Journal of medicine*, *346*(6), 393–403. https://doi.org/10.1056/NEJMoa012512
- Orlistat (Xenical) 120mg tid with meals
- Phentermine 15 – 37.5mg daily – short term ≤ 12weeks
- Phentermine/Topiramate ER (Qysmia)15mg/92mg max dose daily
- Diethylproprion ER 75mg daily
- Naltrexone/Bupropion ER (Contrave) 16mg/180mg max dose twice daily
- Oral semaglutide (Rybelsus) 50mg daily (NOT FDA approved for tx of obesity)
  - OASIS 1 Knop et al. (2023) **Oral semaglutide 50 mg** taken once per day in adults with overweight or obesity (OASIS 1): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet, 402*(10403):705-719. doi:10.1016/S0140-6736(23)01185-6
- Glucagon-like peptide GLP-1 agonist (Liraglutide/Victoza/Saxenda, Semaglutide/Ozempic/Wegovy)
- GLP-1 and glucose-dependent insulinotropic polypeptide GIP agonist (Tirzapetide/Mounjaro/Zepbound)

Risks and Benefits of Medical Management

Benefits of Medical Management

- **> 5% Weight Loss**
  - Metformin (26-29%) - 3.5% or 2 kg
  - Orlistat (35-73%) – 2.8%
  - GLP 1 (43-63%) - 11%
  - **GLP-1/GIP – (79-91%) – 13 to 21%**
  - Phentermine/Topiramate ER (70%) – 8.5%
- Prevention of T2DM – 100% treatment group vs 97% placebo over 2 years (STEP 5 Trial)
- Cardiovascular Benefits
  - Improved lipid profile
  - Improvements in SBP
  - MACE (SELECT trial)
    - Lincoff, A. M., Brown-Frandsen, K., Colhoun, H. M., Deanfield, J., Emerson, S. S., Esbjerg, S., Hardt-Lindberg, S., Hovingh, G. K., Kahn, S. E., Kushner, R. F., Lingvay, I., Oral, T. K., Michelsen, M. M., Plutzky, J., Tornøe, C. W., Ryan, D. H., & SELECT Trial Investigators (2023). Semaglutide and cardiovascular outcomes in obesity without diabetes. *The New England Journal of Medicine*, *389*(24), 2221–2232. https://doi.org/10.1056/NEJMoa2307563

Anecdotal Benefits of GLP agonists

- Cardiovascular Risk Reduction by 20% (CV death, nonfatal MI or nonfatal stroke)
- HFpEF reduced heart failure–related symptoms, physical limitations
  - Butler et al. (2024) doi:10.1016/S0140-6736(24)00469-0
- Inhibit growth of ovarian, breast, prostate, and pancreatic cancer
  - Zhao et al. (2021). GLP-1 Receptor Agonists: Beyond Their Pancreatic Effects. *Frontiers in Endocrinology*, *12*, 721135. https://doi.org/10.3389/fendo.2021.721135
- Slows progression of Parkinson's Disease
  - Meissner et al. (2024). *The New England Journal of Medicine, 390* (13), 1176-1185. doi: 10.1056/NEJMoa2312323.
- Alcohol Use Disorder and Nicotine/Cannabis Abuse
  - Studies underway at UNC
  - Quddos *et al.* (2023) doi: 10.1038/s41598-023-48267-2
- Treatment of NAFLD/NASH
  - 82% reduction in liver fat

Potential Risks of GLP agonists

- **Contraindications:** medullary thyroid carcinoma (MTC), Multiple Endocrine Neoplasia syndrome type 2 (MEN 2), gastroparesis, pregnancy
- **Black Box Warning:** Thyroid C-cell tumors in rodents
- Acute Gallbladder Disease ~3%, Pancreatitis, Elevations in Lipase and Amylase
- GI side effects about 10-25% → dehydration and AKI
- Hypersensitivity reactions ~ 3%
- Increased heart rate
  - 10-20 bpm; increased by 10% Tirzepatide 15 mg
  - Contraindicated in persons with cardiac arrythmias, a. fibrillation?
- Unsustained weight loss after discontinuation

Clinical Trials

Indications for Obesity/Without T2DM – ALL INCLUDED LIFESTYLE INTERVENTION COMPONENT

STEP 1 – 68 weeks

Wilding JPH, Batterham RL, Davies M, et al. (2022). Weight regain and cardiometabolic effects after withdrawal of semaglutide: the STEP 1 trial extension. *Diabetes Obes Metab., 24(*8): 1553-1564. doi:10.1111/dom.14725

70% regained weight in 1 year after discontinuation

STEP 3 – 68 weeks

Wadden TA, Bailey TS, Billings LK, et al. (2021). 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, 325*(14): 1403-1413. doi:10.1001/jama.2021.1831

Mean age 46, 80% female, 18% Black

STEP 5 - 2 years

Garvey, W.T., Batterham, R.L., Bhatta, M. et al. Two-year effects of **semaglutide** in adults with overweight or obesity: the STEP 5 trial. Nat Med 28, 2083–2091 (2022). https://doi.org/10.1038/s41591-022-02026-4

Mean age 47, 80% female, 92% White, less than 5% Black

Zero - Type 2 DM

STEP 8 – 68 weeks

Rubino DM, Greenway FL, Khalid U, et al. (2022). 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, 327*(2): 138-150. doi:10.1001/jama.2021.23619

STEP TEENS – 68 weeks

Weghuber D, Barrett T, Barrientos-Pérez M, et al. (2022). Once-weekly Semaglutide in adolescents with obesity. *N Engl J Med, 387*(24): 2245-2257. doi:10.1056/NEJMoa2208601

Age 12-18 years, 62% female, 79% White, 73% weight loss of ≥5%,

SURMOUNT 1 – 72 weeks

Jastreboff AM, Aronne LJ, Ahmad NN, et al. (2022). **Tirzepatide** Once Weekly for the Treatment of Obesity. *N Engl J Med, 387(*3):205-216. doi:10.1056/NEJMoa2206038

Mean age 44.9, 67% female, 71% White, 8% Black

SURMOUNT 3 - after 3 months lifestyle modification

Wadden TA, Chao AM, Machineni S, et al. (2023).Tirzepatide after intensive lifestyle intervention in adults with overweight or obesity: the SURMOUNT-3 phase 3 trial. *Nat Med., 29*(11): 2909-2918. doi:10.1038/s41591-023-02597-w

SURMOUNT 4 weight loss maintenance

Aronne, L. J., Sattar, N., Horn, D. B., Bays, H. E., Wharton, S., Lin, W. Y., Ahmad, N. N., Zhang, S., Liao, R., Bunck, M. C., Jouravskaya, I., Murphy, M. A., & SURMOUNT-4 Investigators (2024). Continued Treatment With Tirzepatide for Maintenance of Weight Reduction in Adults With Obesity: The SURMOUNT-4 Randomized Clinical Trial. JAMA, 331(1), 38–48. https://doi.org/10.1001/jama.2023.24945

SURMOUNT 5 – ongoing

Semaglutide vs. Tirzepatide

Clinical Trials

Indications for Type 2 DM
Monotherapy - SURPASS 1
Rosenstock J, Wysham C, Frías JP, et al. Efficacy and safety of a novel dual GIP and GLP-1 receptor agonist **tirzepatide** in patients with type 2 diabetes (SURPASS-1): a double-blind, randomised, phase 3 trial [published correction appears in Lancet. 2021 Jul 17;398(10296):212]. Lancet. 2021;398(10295):143-155. doi:10.1016/S0140-6736(21)01324-6

Add on to Metformin - SURPASS 2
Frias, J. P., De Block, C., Brown, K., Wang, H., Thomas, M. K., Zeytinoglu, M., & Maldonado, J. M. (2024). Tirzepatide Improved Markers of Islet Cell Function and Insulin Sensitivity in People With T2D (SURPASS-2). The Journal of clinical endocrinology and metabolism, dgae038. Advance online publication. https://doi.org/10.1210/clinem/dgae038

Insulin + Metformin/and/or SGLT2-I – SURPASS 3
Ludvik B, Giorgino F, Jódar E, et al. **Once-weekly tirzepatide versus once-daily insulin degludec** as add-on to metformin with or without SGLT2 inhibitors in patients with type 2 diabetes (SURPASS-3): a randomised, open-label, parallel-group, phase 3 trial. Lancet. 2021;398(10300):583-598. doi:10.1016/S0140-6736(21)01443-4

Add on to Oral Agents and Insulin Glargine – SURPASS 4
Del Prato, S., Kahn, S. E., Pavo, I., Weerakkody, G. J., Yang, Z., Doupis, J., Aizenberg, D., Wynne, A. G., Riesmeyer, J. S., Heine, R. J., Wiese, R. J., & SURPASS-4 Investigators (2021). Tirzepatide versus insulin glargine in type 2 diabetes and increased cardiovascular risk (SURPASS-4): a randomised, open-label, parallel-group, multicentre, phase 3 trial. Lancet (London, England), 398(10313), 1811–1824. https://doi.org/10.1016/S0140-6736(21)02188-7

Add on to Basal Insulin and Metformin – SURPASS 5
CV outcomes – SURPASS-CVOT recruited 2020-2022
Nicholls, S. J., Bhatt, D. L., Buse, J. B., Stefano, D. P., Kahn, S. E., Lincoff, A. M., McGuire, D. K., Nauck, M. A., Nissen, S. E., Sattar, N., Zinman, B., Zoungas, S., Basile, J., Bartee, A., Miller, D., Nishiyama, H., Pavo, I., Weerakkody, G., Wiese, R. J., & D'Alessio, D. (2024). Comparison of tirzepatide and dulaglutide on major adverse cardiovascular events in participants with type 2 diabetes and atherosclerotic cardiovascular disease: SURPASS-CVOT design and baseline characteristics. The American Heart Journal, 267, 1-11. https://doi.org/10.1016/j.ahj.2023.09.007

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Balancing Risks vs. Benefits

Lifestyle vs. Medical Management

Thank You!

Questions? Comments?

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Healthy Moms, Strong Women: Preventing Diabetes Together

ADA 2024
Standards of Care

Section 8.

Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes

American Diabetes Association.
Connected for Life.

Assessment and Monitoring of the Individual with Overweight and Obesity

8.1 Use person-centered, nonjudgmental language that fosters collaboration between individuals and health care professionals, including person-first language (e.g., “person with obesity” rather than “obese person” and “person with diabetes” rather than “diabetic person”). **E**

8.2a To support the diagnosis of obesity, measure height and weight to calculate BMI and perform additional measurements of body fat distribution, like waist circumference, waist-to-hip ratio, and/or waist-to-height ratio. **E**

8.2b Monitor obesity-related anthropometric measurements at least annually to inform treatment considerations. **E**

8.3 Accommodations should be made to provide privacy during anthropometric measurements. **E**

Assessment and Monitoring of the Individual with Overweight and Obesity (continued)

8.4 In people with type 2 diabetes and overweight or obesity, weight management should represent a primary goal of treatment along with glycemic management. **A**

8.5 People with diabetes and overweight or obesity may benefit from any magnitude of weight loss. Weight loss of 3–7% of baseline weight improves glycemia and other intermediate cardiovascular risk factors. **A** Sustained loss of >10% of body weight usually confers greater benefits, including disease-modifying effects and possible remission of type 2 diabetes, and may improve long-term cardiovascular outcomes and mortality. **B**

8.6 Individualize initial treatment approaches for obesity (i.e., lifestyle and nutritional therapy, pharmacologic agents, or metabolic surgery) **A** based on the person's medical history, life circumstances, preferences, and motivation. **C** Consider combining treatment approaches if appropriate. **E**

Nutritional, Physical Activity, & Behavioral Therapy

8.7 Nutrition, physical activity, and behavioral therapy to achieve and maintain ≥5% weight loss are recommended for people with type 2 diabetes and overweight or obesity. **B**

8.8a Interventions including high frequency of counseling (≥16 sessions in 6 months) with focus on nutrition changes, physical activity, and behavioral strategies to achieve a 500–750 kcal/day energy deficit have been shown to be beneficial for weight loss and should be considered when available. **A**

8.8b Consider structured programs delivering behavioral counseling (face-to-face or remote) to address barriers to access. **E**

Nutritional, Physical Activity, & Behavioral Therapy (continued)

8.9 Nutrition recommendations should be individualized to the person's preferences and nutritional needs. Use nutritional plans that create an energy deficit, regardless of macronutrient composition, to achieve weight loss. **A**

8.10 When developing a plan of care, consider systemic, structural, and socioeconomic factors that may impact nutrition patterns and food choices, such as food insecurity and hunger, access to healthful food options, cultural circumstances, and other social determinants of health. **C**

Nutritional, Physical Activity, & Behavioral Therapy (continued)

8.11a For those who achieve weight loss goals, long-term (≥1 year) weight maintenance programs are recommended, when available. Effective programs provide monthly contact and support, recommend ongoing monitoring of body weight (weekly or more frequently) and other self-monitoring strategies, and encourage regular physical activity (200–300 min/week). **A**

8.11b For those who achieve weight loss goals, continue to monitor progress periodically, provide ongoing support, and recommend continuing adopted interventions to maintain goals long term. **E**

Nutritional, Physical Activity, & Behavioral Therapy (continued)

8.12 When short-term nutrition intervention using structured, very-low calorie meals (800–1,000 kcal/day) is considered, it should be prescribed to carefully selected individuals by trained practitioners in medical settings with close monitoring. Long-term, comprehensive weight maintenance strategies and counseling should be integrated to maintain weight loss. **B**

8.13 Nutritional supplements have not been shown to be effective for weight loss and are not recommended. **A**

Pharmacotherapy

8.14 Whenever possible, minimize medications for comorbid conditions that are associated with weight gain. **E**

8.15 When choosing glucose-lowering medications for people with type 2 diabetes and overweight or obesity, prioritize medications with beneficial effect on weight. **B**

8.16 Obesity pharmacotherapy should be considered for people with diabetes and overweight or obesity along with lifestyle changes. Potential benefits and risks must be considered. **A**

Pharmacotherapy (continued)

8.17 In people with diabetes and overweight or obesity, the preferred pharmacotherapy should be a glucagon-like peptide 1 receptor agonist or dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide 1 receptor agonist with greater weight loss efficacy (i.e., semaglutide or tirzepatide), especially considering their added weight-independent benefits (e.g., glycemic and cardiometabolic). **A**

8.18 To prevent therapeutic inertia, for those not reaching goals, reevaluate weight management therapies and intensify treatment with additional approaches (e.g., metabolic surgery, additional pharmacologic agents, and structured lifestyle management programs). **A**

Metabolic Surgery

8.19 Consider metabolic surgery as a weight and glycemic management approach in people with diabetes with BMI ≥30.0 kg/m^2 (or ≥ 27.5 kg/m^2 in Asian American individuals) who are otherwise good surgical candidates. **A**

8.20 Metabolic surgery should be performed in high-volume centers with interprofessional teams knowledgeable about and experienced in managing obesity, diabetes, and gastrointestinal surgery (facs.org/quality-programs/accreditationand-verification/metabolic-and-bariatricsurgery-accreditation-and-quality-improvement-program/). **E**

8.21 People being considered for metabolic surgery should be evaluated for comorbid psychological conditions and social and situational circumstances that have the potential to interfere with surgery outcomes. **B**

Metabolic Surgery (continued)

8.22 People who undergo metabolic surgery should receive long-term medical and behavioral support and routine micronutrient, nutritional, and metabolic status monitoring. **B**

8.23 If post-metabolic surgery hypoglycemia is suspected, clinical evaluation should exclude other potential disorders contributing to hypoglycemia, and management should include education, medical nutrition therapy with a registered dietitian/nutritionist experienced in post-metabolic surgery hypoglycemia, and medication treatment, as needed. **A** Continuous glucose monitoring should be considered as an important adjunct to improve safety by alerting individuals to hypoglycemia, especially for those with severe hypoglycemia or hypoglycemia unawareness. **E**

Metabolic Surgery (continued)

8.24 In people who undergo metabolic surgery, routinely screen for psychosocial and behavioral health changes and refer to a qualified behavioral health professional as needed. **C**

8.25 Monitor individuals who have undergone metabolic surgery for insufficient weight loss or weight recurrence at least every 6–12 months. **E** In those who have insufficient weight loss or experience weight recurrence, assess for potential predisposing factors and, if appropriate, consider additional weight loss interventions (e.g., obesity pharmacotherapy). **C**

Table 8.1—Obesity pharmacotherapy

Medication name and typical adult maintenance dose	Average wholesale price (median and range for 30-day supply) (142)	National Average Drug Acquisition Cost (30-day supply) (143)	Treatment arms	Weight loss (% loss from baseline)	Common side effects (144–149)	Possible safety concerns and considerations (144–149)
Short-term treatment (12 weeks)						
Sympathomimetic amine anorectic						
Phentermine (150)						
8–37.5 mg q.d.*	$43 ($5–$90), 37.5 mg/day	$2 (37.5 mg dose)	15 mg q.d. 7.5 mg q.d. Placebo	5.0 4.9 1.9	Dry mouth, insomnia, dizziness, irritability, increased blood pressure, elevated heart rate	• Contraindicated for use in combination with monoamine oxidase inhibitors
Long-term treatment (52 or 56 weeks)						
Lipase inhibitor						
Orlistat (4)						
60 mg t.i.d. (OTC)	$52 ($41–$82)	NA	120 mg t.i.d.†	9.6	Abdominal pain, flatulence, fecal urgency	• Potential malabsorption of fat-soluble vitamins (A, D, E, K) and of certain medications (e.g., cyclosporine, thyroid hormone, anticonvulsants) • Rare cases of severe liver injury reported • Cholelithiasis • Nephrolithiasis
120 mg t.i.d. (Rx)	$843 ($781–$904)	$722	Placebo	5.6		
Sympathomimetic amine anorectic/antiepileptic combination						
Phentermine/topiramate ER (47)						
7.5 mg/46 mg q.d.‡	$223 (7.5 mg/46 mg dose)	$179 (7.5 mg/46 mg dose)	15 mg/92 mg q.d.§ 7.5 mg/46 mg q.d.§ Placebo	9.8 7.8 1.2	Constipation, paresthesia, insomnia, nasopharyngitis, xerostomia, increased blood pressure	• Contraindicated for use in combination with monoamine oxidase inhibitors • Birth defects • Cognitive impairment • Acute angle-closure glaucoma
Opioid antagonist/antidepressant combination						
Naltrexone/bupropion ER (15)						
16 mg/180 mg b.i.d.	$750	$599	16 mg/180 mg b.i.d. Placebo	5.0 1.8	Constipation, nausea, headache, xerostomia, insomnia, elevated heart rate and blood pressure	• Contraindicated in people with unmanaged hypertension and/or seizure disorders • Contraindicated for use with chronic opioid therapy • Acute angle-closure glaucoma **Black box warning:** • Risk of suicidal behavior/ideation in people younger than 24 years old who have depression

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Table 8.1—Continued

Medication name and typical adult maintenance dose	Average wholesale price (median and range for 30-day supply) (142)	National Average Drug Acquisition Cost (30-day supply) (143)	Treatment arms	Weight loss (% loss from baseline)	Common side effects (144–149)	Possible safety concerns and considerations (144–149)
Glucagon-like peptide 1 receptor agonist						
Liraglutide (16,49)‖						
3 mg q.d.	$1,619	$1,294	3.0 mg q.d. 1.8 mg q.d. Placebo	6.0 4.7 2.0	Gastrointestinal side effects (nausea, vomiting, diarrhea, esophageal reflux), injection site reactions, elevated heart rate, hypoglycemia	• Pancreatitis has been reported in clinical trials, but causality has not been established. Discontinue if pancreatitis is suspected. • Use caution in people with kidney disease when initiating or increasing dose due to potential risk of acute kidney injury. • May cause cholelithiasis and gallstone-related complications. • Gastrointestinal disorders (severe constipation and small bowel obstruction/ileus progression) • Monitor for potential consequences of delayed absorption of oral medications. **Black box warning:** • Risk of thyroid C-cell tumors in rodents; human relevance not determined
Semaglutide (48,151)‖						
2.4 mg once weekly	$1,619	$1,295	2.4 mg weekly 1.0 mg weekly Placebo	9.6 7.0 3.4	Gastrointestinal side effects (nausea, vomiting, diarrhea, esophageal reflux), injection site reactions, elevated heart rate, hypoglycemia	• Pancreatitis has been reported in clinical trials, but causality has not been established. Discontinue if pancreatitis is suspected. • Use caution in people with kidney disease when initiating or increasing dose due to potential risk of acute kidney injury. • May cause cholelithiasis and gallstone-related complications. • Gastrointestinal disorders (severe constipation and small bowel obstruction/ileus progression) • Monitor for potential consequences of delayed absorption of oral medications. **Black box warning:** • Risk of thyroid C-cell tumors in rodents; human relevance not determined

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Table 8.1—Continued

Medication name and typical adult maintenance dose	Average wholesale price (median and range for 30-day supply) (142)	National Average Drug Acquisition Cost (30-day supply) (143)	Treatment arms	Weight loss (% loss from baseline)	Common side effects (144–149)	Possible safety concerns and considerations (144–149)
Dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide 1 receptor agonist						
Tirzepatide (83) 5 mg, 10 mg, or 15 mg once weekly	NA	NA	10 mg weekly 15 mg weekly Placebo	12.8 14.7 3.2	Gastrointestinal side effects (nausea, vomiting, diarrhea, esophageal reflux), injection site reactions, elevated heart rate, hypoglycemia	• Pancreatitis has been reported in clinical trials, but causality has not been established. Discontinue if pancreatitis is suspected. • Use caution in people with kidney disease when initiating or increasing dose due to potential risk of acute kidney injury. • May cause cholelithiasis and gallstone-related complications. • Gastrointestinal disorders (severe constipation and small bowel obstruction/ileus progression) • Monitor effects of oral medications with narrow therapeutic index (warfarin) or whose efficacy is dependent on threshold concentration. • Advise those using oral hormonal contraception to use or add a non-oral contraception method for 4 weeks after initiation and dose escalations. **Black box warning:** • Risk of thyroid C-cell tumors in rodents; human relevance not determined.

Select safety and side effect information is provided; for a comprehensive discussion of safety considerations, please refer to the prescribing information for each agent. b.i.d., twice daily; ER, extended release; OTC, over the counter; NA, data not available; Rx, prescription; t.i.d., three times daily, p.o., by mouth; SC, subcutaneous injection; AWP, average wholesale price; NADAC, National Average Drug Acquisition Cost. *Use lowest effective dose; maximum appropriate dose is 37.5 mg. Weight loss data were extracted from the 12-week time point, as phentermine is approved for use for up to 12 weeks. †Enrolled participants had normal (79%) or impaired (21%) glucose tolerance. ‡Maximum dose, depending on response, is 15 mg/92 mg q.d. §Approximately 68% of enrolled participants had type 2 diabetes or impaired glucose tolerance. ||Agent has indication for reduction of cardiovascular events (49,151). AWP and NADAC prices for 30-day supply of maximum or maintenance dose as of 6 September 2023.

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