

Weight No Longer: Addressing Overweight/Obesity as an Integral Part of Type 2 Diabetes Management

Davida F. Kruger, MSN, APN-BC, BC-ADM
Certified Nurse Practitioner
Henry Ford Health System
Division of Endocrinology, Diabetes, Bone and Mineral Disease
Detroit, MI

Disclosures

- **Davida F. Kruger, MSN, APN-BC, BC-ADM**, Receives consultant fee Abbott, CeQur, Embecta, Insulet, Lilly, Ascencia, Mannkind, Medtronic, Sanofi, and Proteomics. She is on the speaker bureau for Dexcom, CeQur, Lilly, Novo Nordisk, and Sanofi. She is contracted for Institutional Research with Abbott, Beta Bionics, Insulet, Novo Nordisk and Tandem. Stock options (NOT exercised): Pendulum.
- During this activity, Davida Kruger may mention the use of medications for both FDA-approved and nonapproved indications.

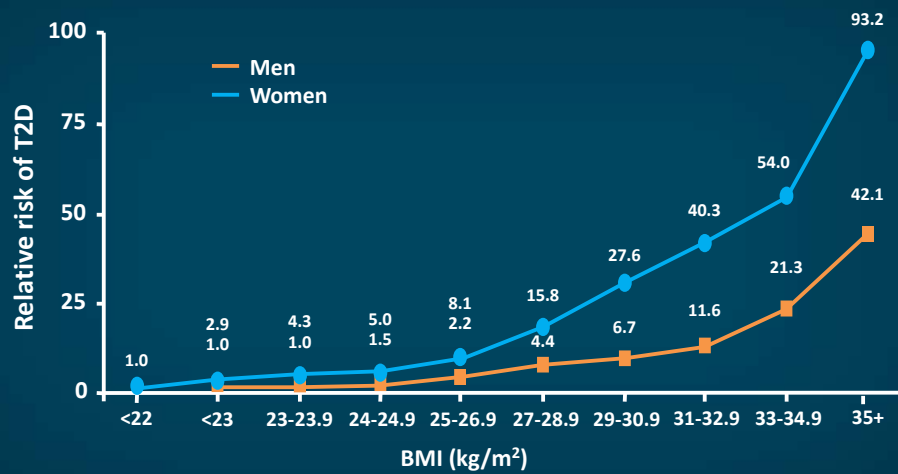
All relevant financial relationships have been mitigated.

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Learning Objectives

- Implement shared decision-making strategies to help patients with type 2 diabetes select and follow through with informed options for weight loss

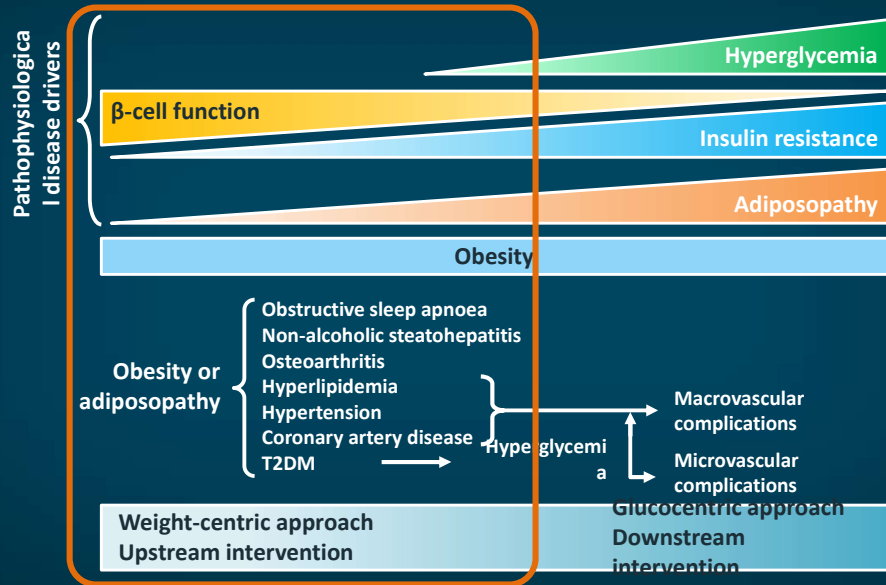
Relationship Between BMI and Risk of T2DM



BMI = body mass index (weight in kilograms divided by height in meters squared, kg/m²); T2DM = type 2 diabetes.

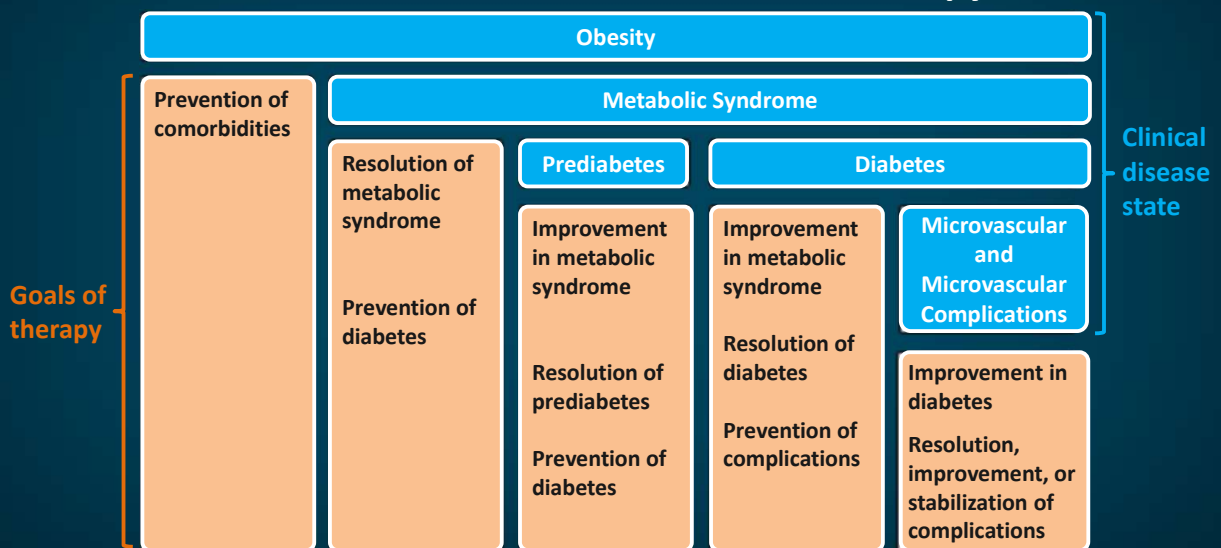
Chan JM, et al. *Diabetes Care*. 1994;17:961-969. Colditz GA, et al. *Ann Intern Med*. 1995;122:481-486.

Moving Toward Weight-Centric Focus to Treat and Prevent T2DM



Modified from Lingvay I, et al. *Lancet*. 2022;399:394-405.

The Disease Continuum for Weight-related Type 2 Diabetes: Clinical Disease States and Goals of Therapy



Modified from Lingvay I, et al. *Lancet*. 2022;399:394-405.

Assessment (ADA Standards of Care)

- 8.1** Use patient-centered, nonjudgmental language that fosters collaboration between patients and providers, including people-first language (eg, “person with obesity” rather than “obese person”). **E**
- 8.2** Measure height and weight and calculate BMI at annual visits or more frequently. Assess weight trajectory to inform treatment considerations. **E**
- 8.3** Based on clinical considerations, such as the presence of comorbid heart failure or significant unexplained weight gain or loss, weight may need to be monitored and evaluated more frequently. **B** If deterioration of medical status is associated with significant weight gain or loss, inpatient evaluation should be considered, especially focused on associations between medication use, food intake, and glycemic status. **E**

ADA evidence grading system: A = clear evidence from well-conducted, generalizable randomized, controlled trials that are adequately powered; B = supportive evidence from well-conducted cohort studies; C = supportive evidence from poorly controlled or uncontrolled studies; E = expert consensus or clinical experience.

ElSayed NA, et al. *Diabetes Care*. 2023;46(suppl 1):S128-S139. ElSayed NA, et al. *Diabetes Care*. 2023;46(suppl 1):S1-S4.

Assessment (ADA Standards of Care) (cont'd)

- 8.4** Accommodations should be made to provide privacy during weighing. **E**
- 8.5** Individuals with diabetes and overweight or obesity may benefit from modest or larger magnitudes of weight loss. Relatively small weight loss (approximately 3%-7% of baseline weight) improves glycemia and other intermediate cardiovascular risk factors. **A** Larger, sustained weight losses (>10%) usually confer greater benefits, including disease-modifying effects and possible remission of T2DM, and may improve long-term cardiovascular outcomes and mortality. **B**

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Pharmacotherapy (ADA Standards of Care)

- 8.14** When choosing glucose-lowering medications for patients with T2DM and overweight or obesity, consider a medication's effect on weight. **B**
- 8.15** Whenever possible, minimize medications for comorbid conditions that are associated with weight gain. **E**
- 8.16** Weight loss medications are effective as adjuncts to diet, physical activity, and behavioral counseling for selected people with T2DM and BMI ≥ 27 kg/m². Potential benefits and risks must be considered. **A**
- 8.17** If obesity pharmacotherapy is effective (typically defined as $\geq 5\%$ weight loss after 3 months of use), further weight loss is likely with continued use. When early response is insufficient (typically $< 5\%$ weight loss after 3 months of use) or if there are significant safety or tolerability issues, consider discontinuation of the medication and evaluate alternative medications or treatment approaches. **A**

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ElSayed NA, et al. *Diabetes Care*. 2023;46(suppl 1):S128-S139. ElSayed NA, et al. *Diabetes Care*. 2023;46(suppl 1):S1-S4.

Decision Cycle for Person-Centered Glycemic Management

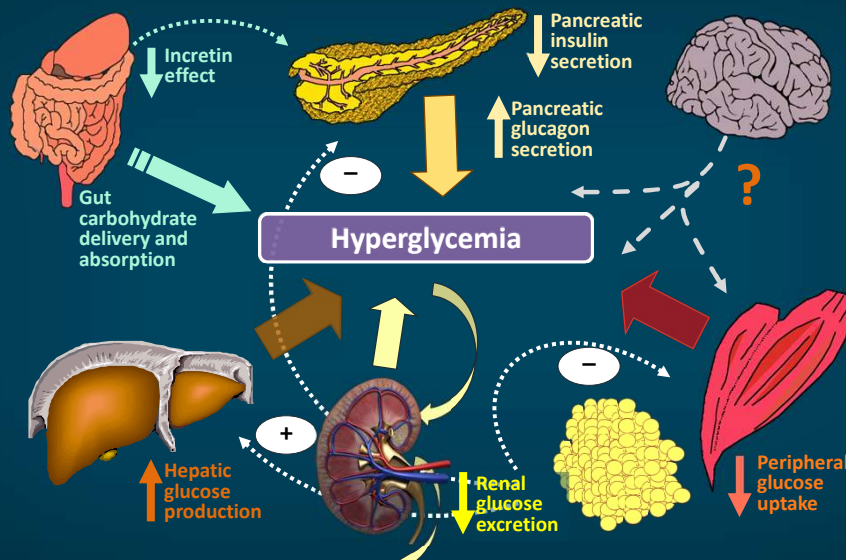


How Is Obesity Defined in Adults?

Weight status category	BMI (kg/m ²)
Underweight	<18.5
Normal weight	18.5-24.9
Overweight	25.0-29.9
Class 1 obesity	30.0-34.9
Class 2 obesity	35.0-39.9
Class 3 obesity	≥40

CDC. Defining adult overweight & obesity, 6/3/2022 (<https://www.cdc.gov/obesity/basics/adult-defining.html>). Accessed 12/19/2022.

Multiple, Complex Pathophysiological Abnormalities in T2DM



Modified from Inzucchi SE, Sherwin RS. Type 2 diabetes mellitus. In: Goldman L, Schafer AJ, eds. *Goldman's Cecil Medicine*, 24th ed. WB Saunders; 2011.

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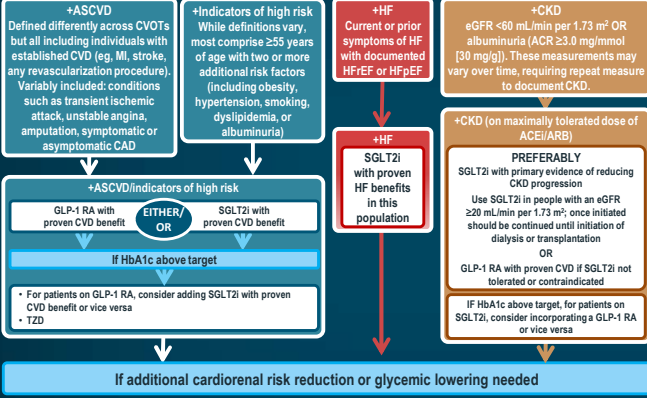
ElSayed NA, et al. *Diabetes Care*. 2023;46(suppl 1):S128-S139. ElSayed NA, et al. *Diabetes Care*. 2023;46(suppl 1):S1-S4.

Use of Glucose-Lowering Medications in Management of T2DM

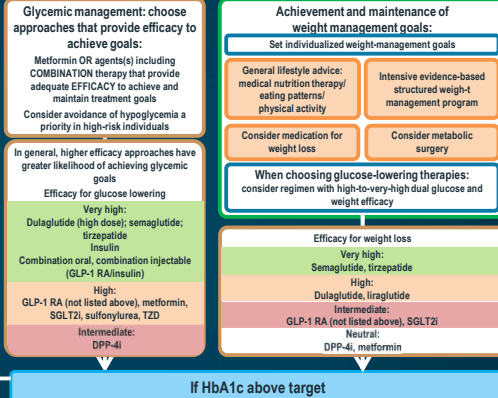
Healthy lifestyle behaviors; DSMES; social determinants of health (SDOH)



Goal: cardiorenal risk reduction in high-risk patients with T2DM (in addition to comprehensive CV risk management)



Goal: achievement and maintenance of glycemic and weight-management goals



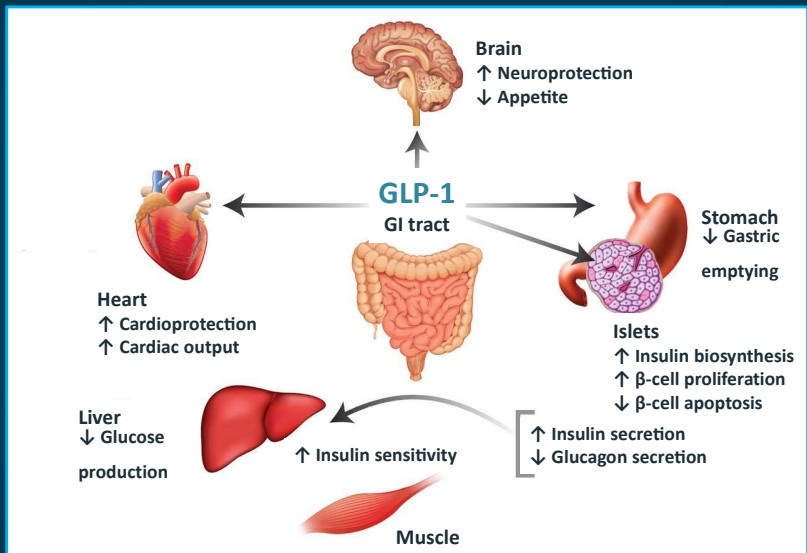
ACEi = angiotensin-converting enzyme inhibitor; ACR = albumin-to-creatinine ratio; ARB = angiotensin receptor blocker; ASCVD = atherosclerotic CVD; CAD = coronary artery disease; CGM = continuous glucose monitoring; CV = cardiovascular; CVOT = CV outcomes trial; DPP-4i = dipeptidyl peptidase 4 inhibitor; eGFR = estimated glomerular filtration rate; GLP-1 RA = GLP-1 receptor agonist; HF = heart failure; HFrEF = HF with preserved ejection fraction; HFpEF = HF with reduced ejection fraction; HHF = hospitalization for heart failure; MACE = major adverse CV events; MI = myocardial infarction; SGLT2i = sodium-glucose cotransporter 2 inhibitor; TZD = thiazolidinedione

ADA Professional Practice Committee. *Diabetes Care* 2023;46(suppl 1):S140-S157.

Identify barriers to goals:

- Consider DSMES referral to support self-efficacy in achievement of goals
- Consider technology (eg, diagnostic CGM) to identify therapeutic gaps and tailor therapy
- Identify and address SDOH that impact achievement of goals

GLP-1 RA Mechanism of Action



GI = gastrointestinal.

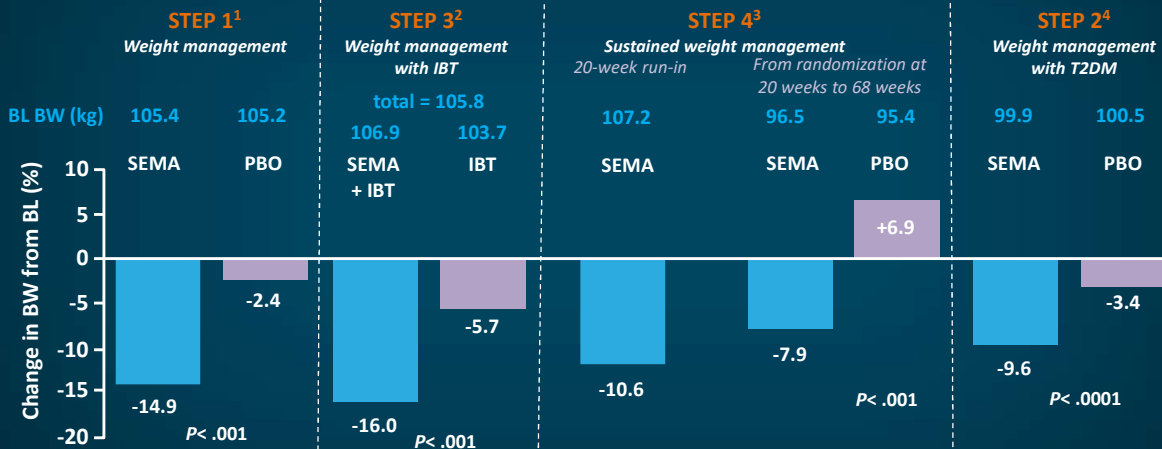
Hinnen D. *Diabetes Spectr*. 2017;30:202-210.

Weight Loss With Liraglutide

Trial	Participant characteristics	PBO-corrected weight loss	≥5% BW loss		≥10% BW loss	
			Liraglutide 3.0 mg	PBO	Liraglutide 3.0 mg	PBO
Astrup et al, 2009	76% women, stable body weight, BMI ≥30 kg/m ² and ≤40 kg/m ²	-4.4 kg	76.1%	29.6%	28.3%	2.0%
Astrup et al, 2012	76% women, stable body weight, BMI ≥30 kg/m ² and ≤40 kg/m ²	-5.8 kg	73%	28%	37%	10%
Wadden et al, 2013	81% women, stable body weight, BMI ≥30 kg/m ² or ≥27 kg/m ² with dyslipidemia or hypertension; lost ≥5% of initial body weight in low-calorie diet run-in period (4-12 weeks)	-5.9 kg	50.5%	21.8%	6.1%	6.3%
Pi-Sunyer et al, 2015	78% women, stable body weight, BMI ≥30 kg/m ² or ≥27 kg/m ² if with dyslipidemia or hypertension	-5.6 kg	63.2%	27.1%	33.1%	10.6%
Davies et al, 2015	50% women, stable body weight, BMI ≥27 kg/m ² ; T2D (HbA _{1c} = 7.0%-10.0%) treated with diet and exercise alone or in combination with 1-3 oral hypoglycemic agents	-4.2 kg	54.3%	21.4%	25.2%	6.7%
Blackman et al, 2015	28% women, stable body weight, BMI ≥30 kg/m ² , moderate-to-severe obstructive sleep apnea, unwilling or unable to use CPAP	-4.9 kg	46.4%	18.1%	22.4%	1.5%

CPAP = continuous positive airway pressure (machine); PBO = placebo.
Mehta A, et al. *Obes Sci Pract.* 2017;3:3-14. (Complete references for the studies cited can be found in Mehta et al.)

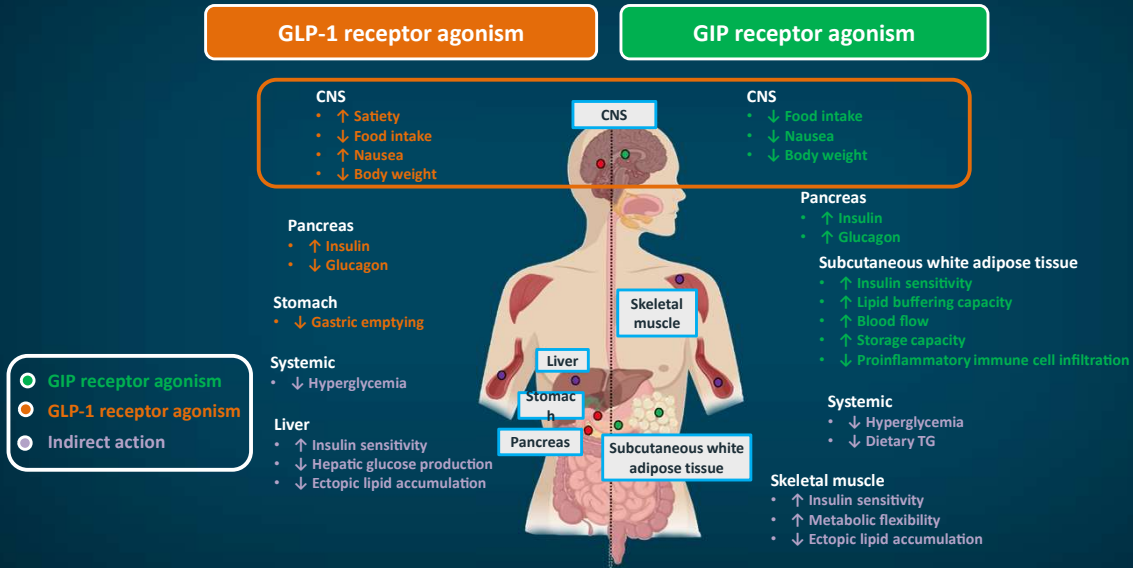
The STEP Trials: Higher-Dose Semaglutide in Obesity



IBT = intensive behavioral therapy; SEMA = semaglutide.

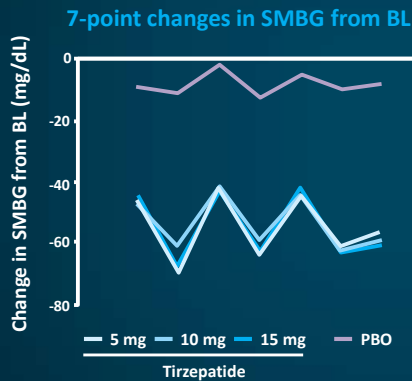
1. Wilding JPH, et al. *N Engl J Med.* 2021;384:989-1002. 2. Wadden TA, et al. *JAMA.* 2021;325:1403-1413. 3. Rubino D, et al. *JAMA.* 2021;325:1414-1425. 4. Davies M, et al. *Lancet.* 2021;397:971-984.

Mechanism of Benefit of Adding GIP to GLP-1

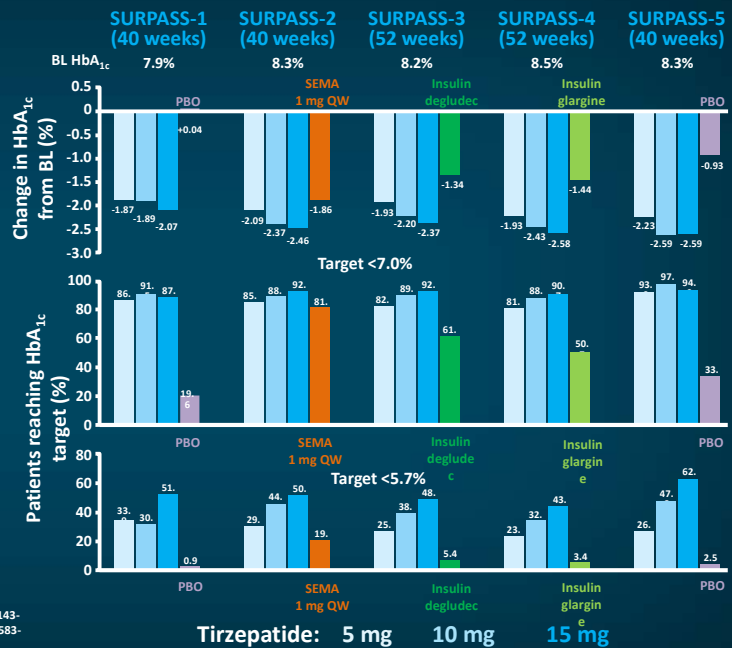


Samms RJ, et al. *Trends Endocrinol Metab.* 2020;31:410-421.

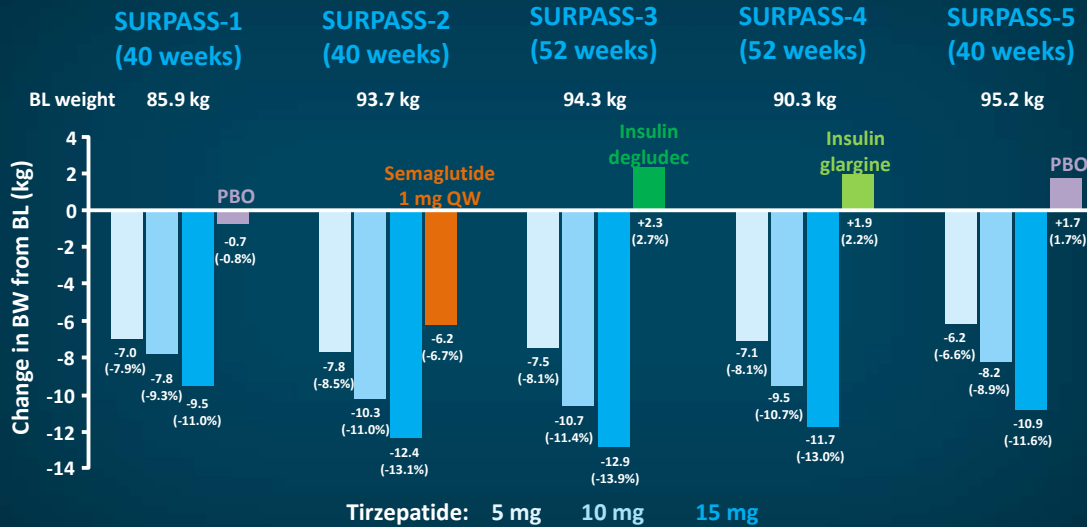
Tirzepatide: Results From SURPASS Clinical Trials



SMBG = self-monitored blood glucose.
 Kaneko S. *touchREV Endocrinol.* 2022;18:10-19. Rosenstock J, et al. *Lancet.* 2021;398:143-155. Frias JP, et al. *N Engl J Med.* 2021;385:503-515. Ludvik B, et al. *Lancet.* 2021;398:583-598.
 Del Prato S, et al. *Lancet.* 2021;398:1811-1824. Dahl D, et al. *JAMA.* 2022;327:534-545.



Tirzepatide: Change From Baseline in Body Weight in SURPASS

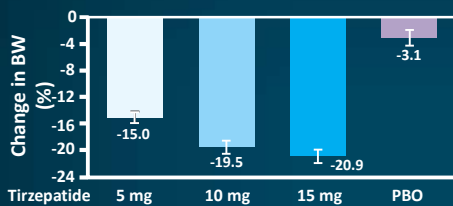


Kaneko S. *touchREV Endocrinol.* 2022;18:10-19. Rosenstock J, et al. *Lancet.* 2021;398:143-155. Frias JP, et al. *N Engl J Med.* 2021;385:503-515. Ludvik B, et al. *Lancet.* 2021;398:583-598. Del Prato S, et al. *Lancet.* 2021;398:1811-1824. Dahl D, et al. *JAMA.* 2022;327:534-545.

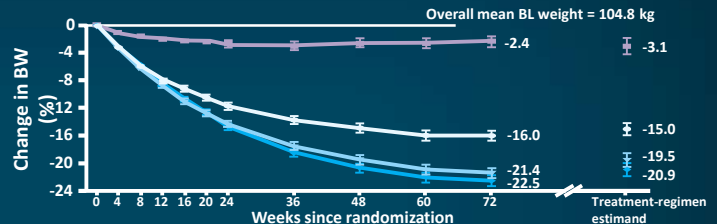
Effect of Once-Weekly Tirzepatide vs PBO on Body Weight

■ Tirzepatide 5 mg ■ Tirzepatide 10 mg ■ Tirzepatide 15 mg ■ PBO

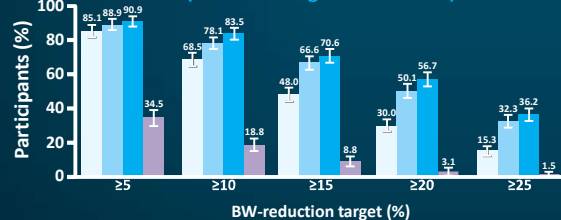
Change in BW from BL (treatment-regimen estimand)



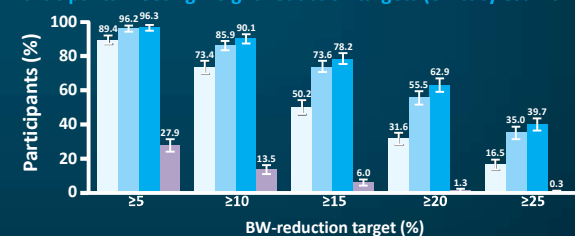
Change in BW by week (efficacy estimand)



Participants meeting weight-reduction targets (treatment-regimen estimand)



Participants meeting weight-reduction targets (efficacy estimand)



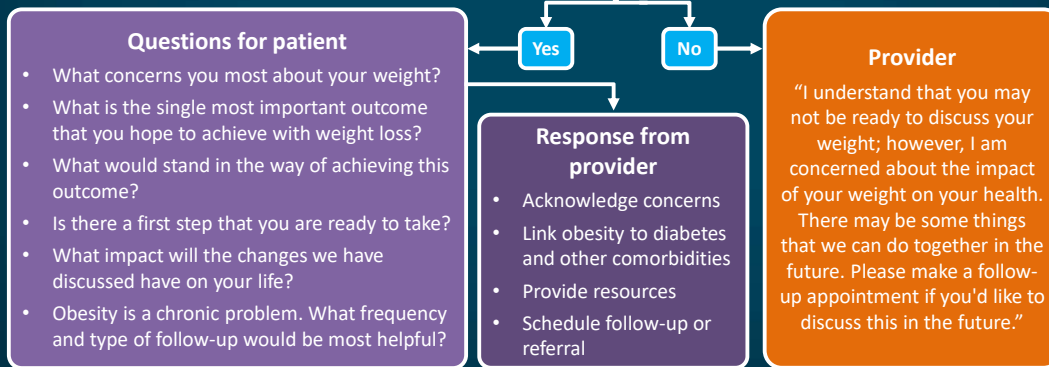
I bars indicate 95% CIs

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

Suggested Script for Initiating Discussion of Obesity

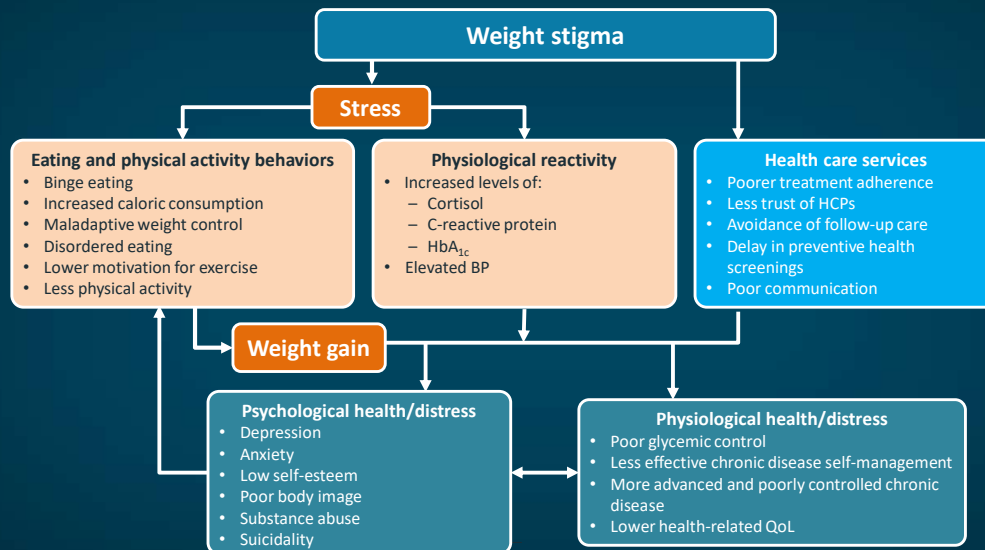
Pre-screen: BMI and weight trajectory; 24-hour dietary recall; personal weight history; medications; physical activity; existing comorbidities or risk factors (eg, stress, sleep, QoL, depression)

“Is now a good time for us to discuss how your weight and health may be affecting each other and how we can work together on it?”



Modified from Gallagher C, et al. *Obesity (Silver Spring)*. 2021;29:821-824.

Overcoming Weight Stigma in the Treatment of Obesity



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

Core Components of Shared Decision-Making

	Meaning	Objective
Justify	Recognize when best current evidence shows there is no clear best choice for a particular decision	Create a conversation and partnership
Share information (both ways)	Inform patient of available options and benefits and harms of each of them; listen to patient's concerns and opinions about options and evidence	2-way exchange of high-quality information
Elicit values and preferences (both ways)	Listen and elicit patient's preferences about outcomes, goals, concerns, and priorities for treatment	Understand what patient values most, given the circumstances
Shared decision talk	Reach a decision after integrating all information (including possibilities of no treatment or deferral of the decision)	Reach a decision that fits unique patient's values, preferences, and context

Modified from Rodriguez-Gutierrez R, et al. *Lancet Diabetes Endocrinol.* 2016;4:706-716.

Approach: The 5As

ASK	Ask the patient's permission "Would you be willing to discuss your weight and the treatment options?"
ASSESS	Usual PMH/PSH including weight history, family history of obesity, obesogenic medications; review food intake, current activity, sleep duration, and stressors
ADVISE	Advise on treatment options
AGREE	Utilize motivational interviewing and shared decision-making to develop a plan of treatment from the options discussed
ASSIST	During follow-up visits, assist the patient in staying on track and reassess for needed changes in treatment; provide referrals and resources

PMH = prior medical history; PSH = prior social history.

O'Shea D, et al. *Adv Ther.* 2021;38:4138-4150. Schlair S, et al. *JCOM.* 2012;19:221-229. Jay M, et al. *BMC Health Serv Res.* 2010;10:159.

Continuous Glucose Monitoring

Glucose Statistics and Targets

October 29, 2023 – November 11, 2023 Time CGM Active:	14 Days 58%
Ranges And Targets For	Type 1 or Type 2 Diabetes
Glucose Ranges	Targets % of Readings (Time/Day)
Target Range 70-180 mg/dL	Greater than 70% (16h 48min)
Below 70 mg/dL	Less than 4% (58min)
Below 54 mg/dL	Less than 1% (14min)
Above 180 mg/dL	Less than 25% (6h)
Above 250 mg/dL	Less than 5% (1h 12min)
<i>Each 5% increase in time in range (70-180 mg/dL) is clinically beneficial</i>	
Average Glucose	182 mg/dL
Glucose Management Indicator (GMI)	7.7%
Glucose Variability	37.1%
<i>Defined as percent coefficient of variation (% CV); target ≤36%</i>	

Time In Range

