Time Well Spent:
Treating Obesity and Diabetes

This activity is supported by an educational grant from Lilly.

Faculty

Robert F. Kushner, MD
Professor, Departments of Medicine and Medical Education
Northwestern University Feinberg School of Medicine
Chicago, IL

Carlos Campos, MD, MPH, CDCES
Clinical Adjunct Professor
Dept. of Family Medicine
UT Health San Antonio
New Braunfels, TX

Keisha Harvey-Mansfield, MD
Diplomate ABFM, Diplomate ABOM, Diplomate ACLM
Medical Director and Founder
Dr. Ks Family Medicine
Bogalusa, LA

Eden Miller, DO, Dip ABOM
Co-Founder
Diabetes and Obesity Care LLC
Bend, OR

Kevin Miller, DO
Physician
Diabetes and Obesity Care LLC
Bend, OR

Activity Overview

Target Audience

This activity is intended for physicians, physician associates, nurse practitioners, and nurses, involved in the care of patients with both T2D and obesity.

Educational Objectives

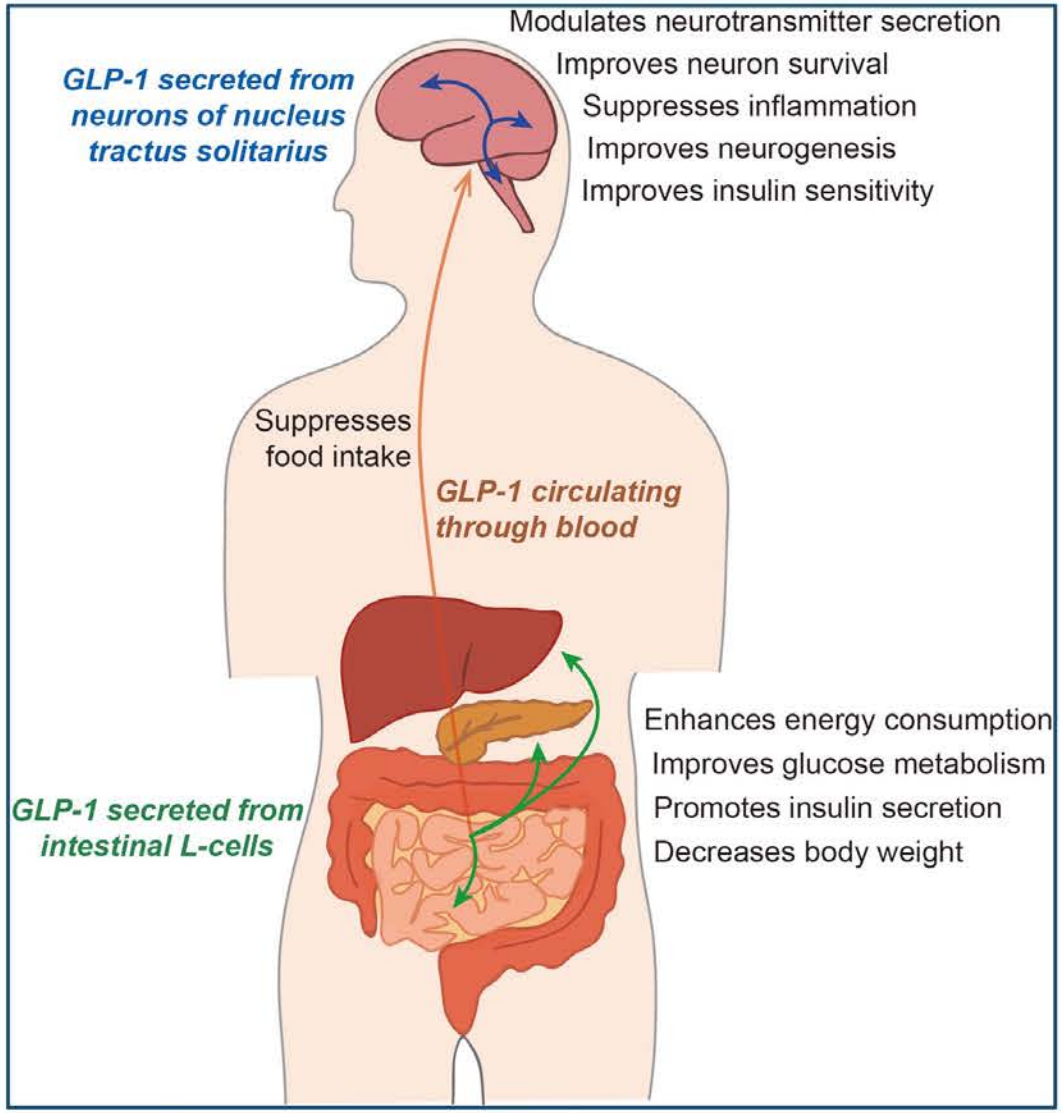
After completing this activity, the participant should be better able to:

- Utilize three evidence-based screening metrics beyond HbA1C (OGTT, GV, TIR) to assess whether to initiate or intensify T2D therapy, with consideration of obesity as a comorbidity.
- Determine the chronicity of obesity as a comorbidity and the importance of its timely management to mitigate risk of longterm complications in T2D.
- Select the most appropriate therapy for an individual patient with T2D and obesity with consideration of the latest safety and efficacy data of GLP-1 RAs and dual GLP-1/GIP RAs and ADA/EASD Consensus Statements.
- Identify patient- and disease- appropriate goals for the long-term management of weight loss and T2D related complications utilizing shared decision-making approaches and patient-reported outcomes

Expanding the Role of GLP-1 Receptor Agonists and GIP/GLP-1 Dual Agonists in the Management of T2D and Obesity:

Practical Applications for PCPs

Biological Actions of GLP-1 and GIP



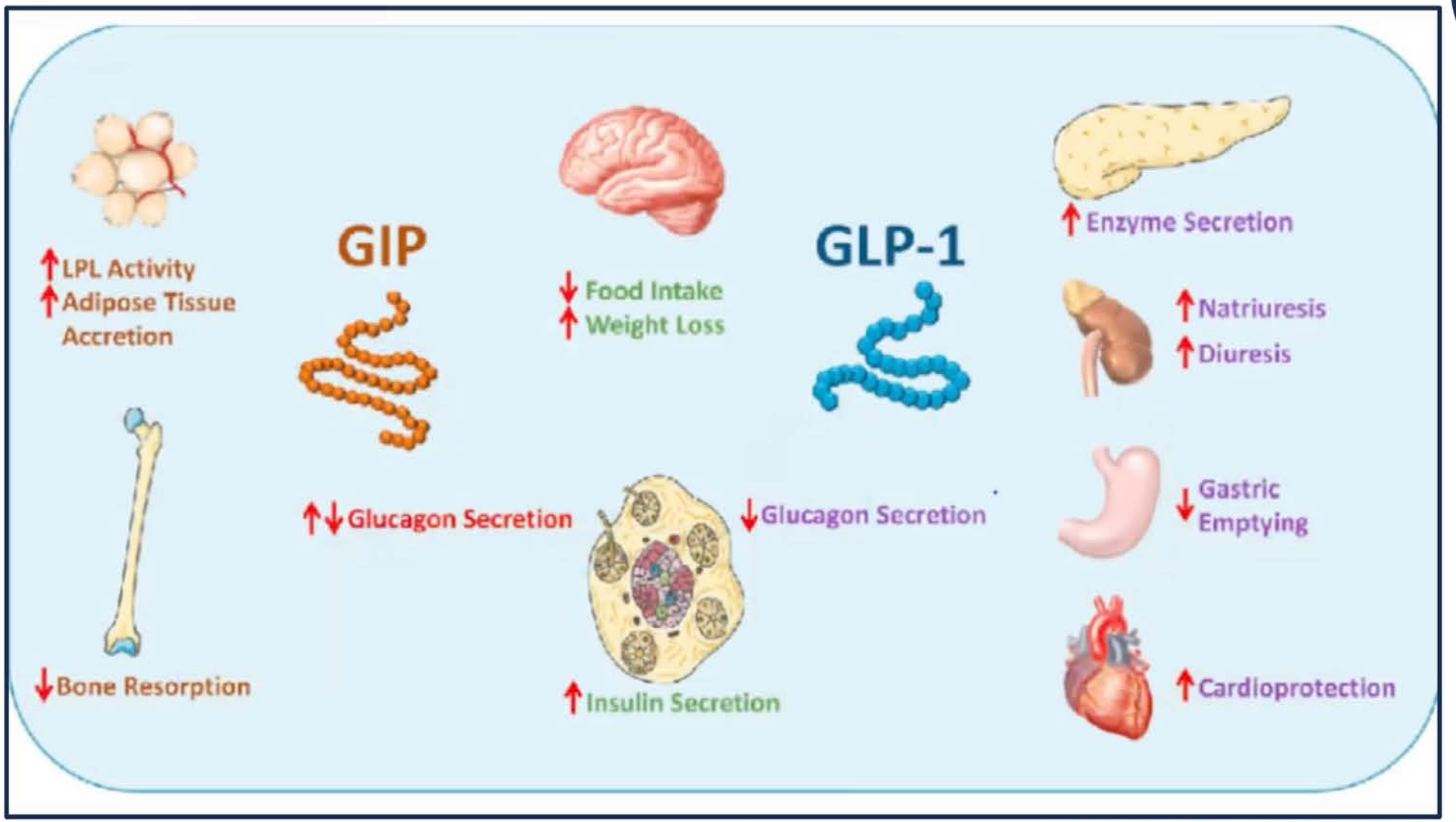
GLP-1 receptors can be used in either 1st or 2nd line regardless of baseline HgA1c

Established atherosclerotic cardiovascular disease

High risk of atherosclerotic cardiovascular disease, chronic kidney disease or heart failure

1. Kim YK, et al. *Front Pharmacol*. 2020. 2. Nachawi N et al. *Cleveland Clin J Med* 2022;89(8):457-464.

Biological Actions of GLP-1 and GIP



GLP-1 RA and GIP/GLP-1 RA Medications for Lowering Glucose

Improvement of HbA1c by:

- Augment glucose dependent
- Insulin secretion and glucagon suppression
- Decelerate gastric emptying
- Curb post-meal glycemic increments
- Reduce appetite, energy intake, and body weight

AND

Approved for:

- Reducing risk of MACE in adults with T2D with established CVD* or multiple cardiovascular risk factors†
- Chronic weight management‡

Davies MJ et al. *Diabetes Care*. 2022;45(11):2753-2786.
*dulaglutide, liraglutide, and subcutaneous semaglutide; †dulaglutide; ‡subcutaneous liraglutide titrated to 3.0 mg once daily; subcutaneous semaglutide titrated to 2.4 mg once weekly
GIP, glucose-dependent insulinotropic polypeptide; GLP-1 RA, glucagon-like peptide 1 receptor agonist

Pharmacologic Management of T2D

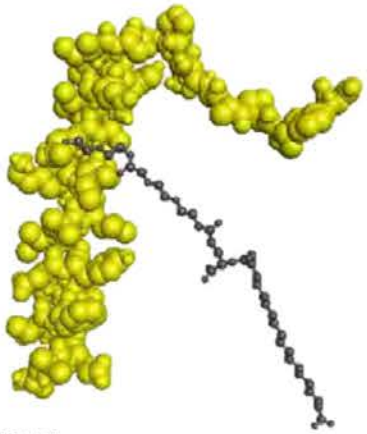
GLP-1 RA and GIP/GLP-1 RA T2D Medications with Obesity Benefit

Generic (Brand)	FDA Approval Date	MOA	Indication of Use	How taken	Weight loss
Liraglutide (Victoza)	2010	GLP-1 receptor agonist	Chronic T2D Mitigate CV risk	SQ, QD	~5-7%
Dulaglutide (Trulicity)	2014	GLP-1 receptor agonist	Chronic T2D Mitigate CV risk	SQ, QWK	~2-6%
Semaglutide (Wegovy)	2017	GLP-1 receptor agonist	Chronic obesity	SQ, QWK	~10-16%
Semaglutide (Ozempic)	2017	GLP-1 receptor agonist	Chronic T2D Mitigate CV risk	SQ, QWK	~15%
Tirzepatide (Mounjaro)	2022	Dual GIP/GLP-1 receptor agonist	Chronic T2D	SQ, QWK	~16-23%
Tirzepatide (Zepbound)	2023	Dual GIP/GLP-1 receptor agonist	Chronic obesity	SQ, QWK	~18%

As of November 8th, 2023, the U.S. Food and Drug Administration approved tirzepatide injection for chronic weight management in adults with obesity (BMI greater or equal to 30 kg/m2) or overweight (BMI greater or equal to 27 kg/m2) with at least one weight-related condition, in addition to a reduced calorie diet and increased physical activity.

GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide-1; PO, oral; QD, once daily; QWK, once a week; SQ, subcutaneous injection.
FDA Prescribing Information.

Tirzepatide: A Novel GIP and GLP-1 Receptor Agonist



Molecular Attributes:

- Multi-functional peptide engineered and modified to
- bind to both GIP and GLP-1 receptors

Pharmacokinetics and Pharmacodynamics:

- Mean half-life of ~5 days (116.7 hours), enabling once-weekly dosing
- Enhances 1st and 2nd phase insulin secretion and reduces glucagon levels, both in a glucose-dependent manner
- Concentrations in people with renal and hepatic impairment do not differ versus healthy people

Clinical Efficacy:

- Very high glycemic efficacy, low inherent risk of hypoglycemia, high activity for weight loss, cardiorenal effects unknown (trials in progress)

Coskun T, et al. *Mol Metab*. 2018; Heise T, et al. *Lancet*. 2022; Urva S, et al. *Diabetes*. 2020; Urva S, et al. *Clin Pharmacokinet*. 2021; Davis MJ et al. *Diabetes Care*. 2022. Wadden T, et al. *Nat Med*. 2023.

Case Study: Mr. Nixon

52-old-male presents in clinic for a check-up

He complains has been taking daily blood pressure readings and has noticed they have been higher than normal the last week

Medical History

Obesity	Hypertension	Obstructive sleep apnea	Non-alcoholic fatty liver disease
Type 2 Diabetes	Dyslipidemia	Coronary artery disease	

Current Medications

Metformin 500 mg BID	Glimepiride 4 mg	Metoprolol 5 mg
Amlodipine 10 mg	Rosuvastatin 10 mg	
Empagliflozin 25 mg	Losartan-HCTZ 100-25	

CAD, coronary artery disease.

Case Study: Mr. Nixon

52-old-male presents in clinic for a check-up

He complains has been taking daily blood pressure readings and has noticed they have been higher than normal the last week

Medical History	Current Medications	Related Labs and Physical Exam Findings
Type 2 Diabetes	Metformin 500 mg BID; Empagliflozin 25 mg; Glimepiride 4 mg	**Glucose:** 175 mg/dL; **A1C:** 7.9%
Hypertension	Losartan-HCT 100 mg-25 mg; Amlodipine 10 mg	**BP:** 155/90 mmHg
Dyslipidemia	Rosuvastatin 10 mg	**LDL-C:** 190 mg/dL; **HDL-C:** 30 mg/dL; **TG:** 360 mg/dL
Obesity		**Weight:** 275 lbs; **Height:** 72”; **WC:** 46”; **BMI:** 36
Non-alcoholic fatty liver disease		**ALT:** 80 u/L; **AST:** 72 u/L; **Plt:** 202/µL; **FIB-4:** 2.23
Non-obstructive CAD		**CAC:** 199
Other: obstructive sleep apnea		

A1C, glycated hemoglobin; ALT, alanine transaminase; AST, aspartate transaminase; BID, twice daily; BMI, body mass index; BP, blood pressure; CAC, coronary artery calcium; CAD, coronary artery disease; Fib-4, Fibrosis-4 index score; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Plt, platelet; TG, triglycerides; WC, waist circumference.

Choosing Between Medication Options

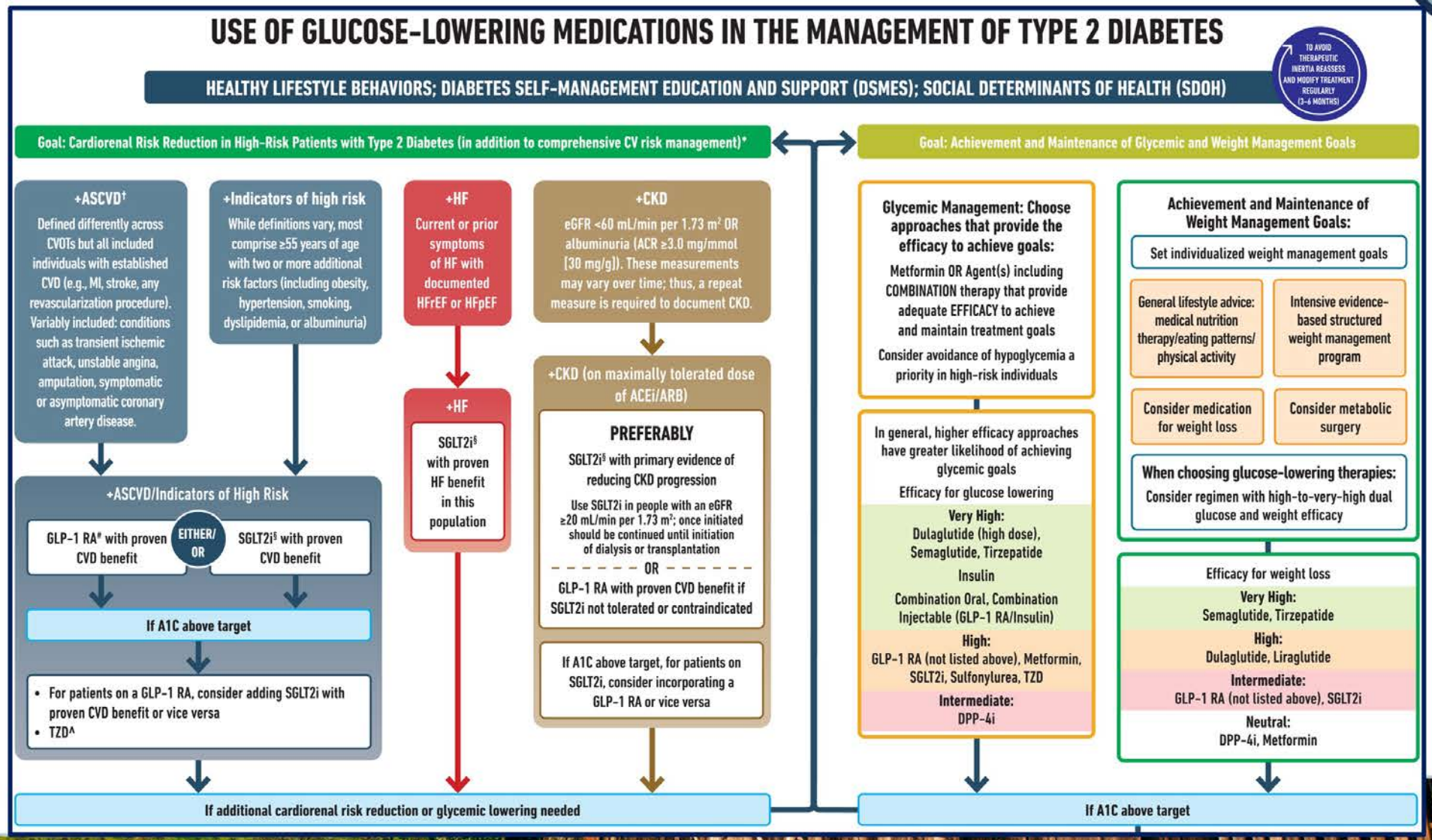
SDOH considerations

Health inequity considerations

Drug-related factors	Provider-related factors	Patient-related factors
• Efficacy and safety data • Population benefits based on clinical trials	• Education and comfort • Availability • Cost • Misperceptions	• Personal values, beliefs, cultural norms, preferences • Adherence

Pharmacologic Approaches to Glycemic Treatment

Standards of Care in Diabetes – 2023



ElSayed NA, et al. *Diabetes Care*. 2023.

Pharmacologic Approaches to Glycemic Treatment

Standards of Care in Diabetes – 2023

Achievement and Maintenance of Weight Management Goals:

- Set individualized weight management goals
- General lifestyle advice: medical nutrition therapy/eating patterns/ physical activity
- Intensive evidence-based structured weight management program
- Consider medication for weight loss
- Consider metabolic surgery
- **When choosing glucose-lowering therapies:** Consider regimen with high-to-very-high dual glucose and weight efficacy

→

Efficacy for weight loss
Very High: Semaglutide, Tirzepatide
High: Dulaglutide, Liraglutide
Intermediate: GLP-1 RA (not listed above), SGLT2i
Neutral: DPP-4i, Metformin

ElSayed NA, et al. *Diabetes Care*. 2023.

Incretins for Diabetes Prevention and Associated Weight Loss

Liraglutide

- Medication as monotherapy, as an add-on to other treatments
  - LEAD trials for patients living with T2D

Dulaglutide

- Medication as monotherapy, as an add-on to other treatments
  - AWARD trials for patients living with T2D

Semaglutide

- Medication as monotherapy, as an add-on to other treatments, and against established glucose-lowering drugs
  - SUSTAIN trials for patients living with T2D
  - PIONEER trials for patients living with T2D
  - STEP trials for patients living with obesity

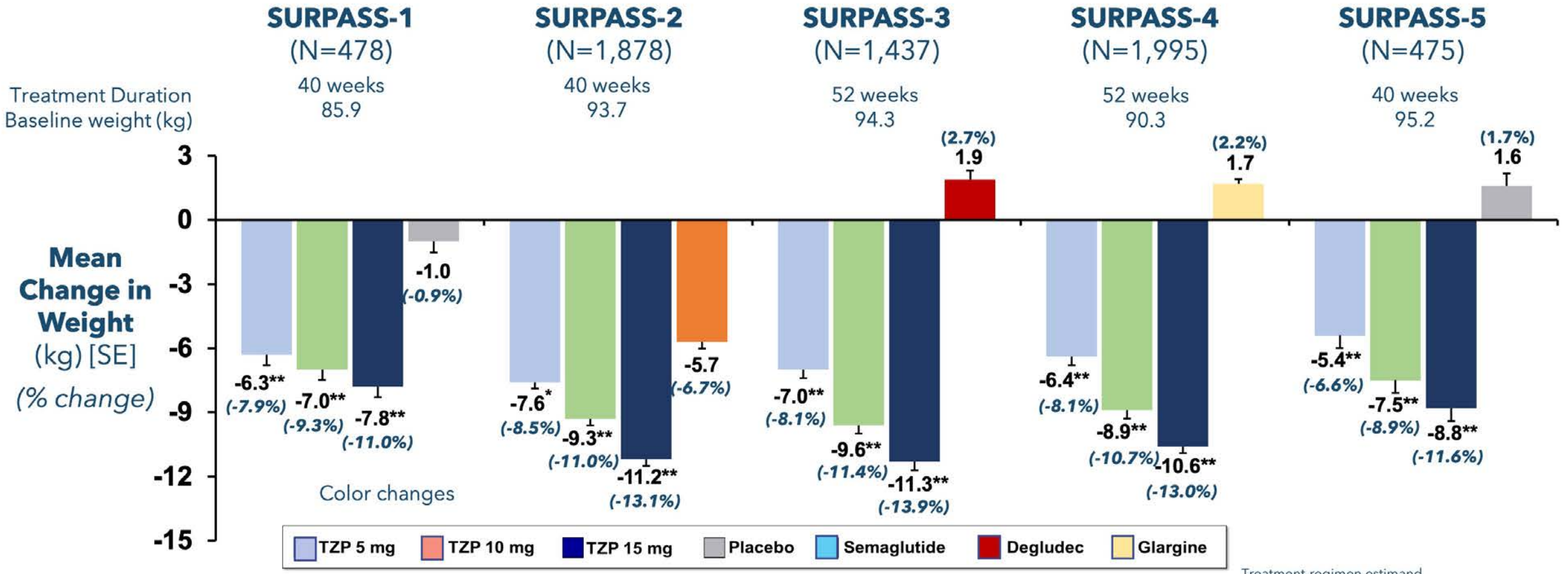
Tirzepatide

- Medication as monotherapy, as an add-on to other treatments, and against established glucose-lowering drugs
  - SURPASS trials for patients living with T2D
  - SURMOUNT trials as a weight-loss agent for patients with obesity with or without T2D

T2D, type 2 diabetes.
FDA Prescribing Information.

Weight Loss with Tirzepatide vs. Comparators in SURPASS Trials

Patients with Type 2 Diabetes

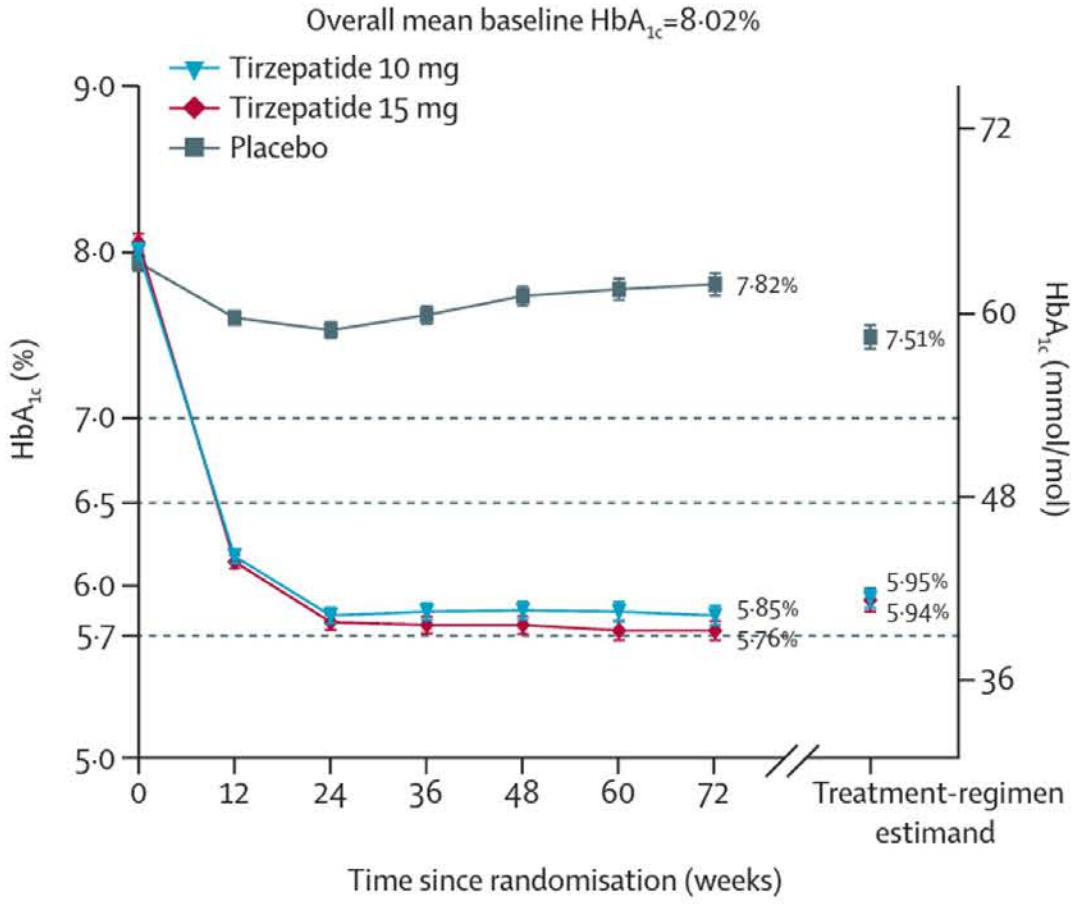


Treatment-regimen estimand
Superiority vs placebo or active comparator: *P<0.05; **P<0.001

Rosenstock J, et al. *Lancet*. 2021; Frías JP, et al. *N Engl J Med*. 2021; Ludvik B, et al. *Lancet*. 2021; Del Prato S, et al. *Lancet*. 2021; Dahl D, et al. *JAMA*. 2022.

SURMOUNT-2 Trial: Phase 3 Trial Investigating Tirzepatide in Adults with T2D and Overweight/Obesity

Patients with BMI ≥27 with HbA1C 7-10% (N=938)

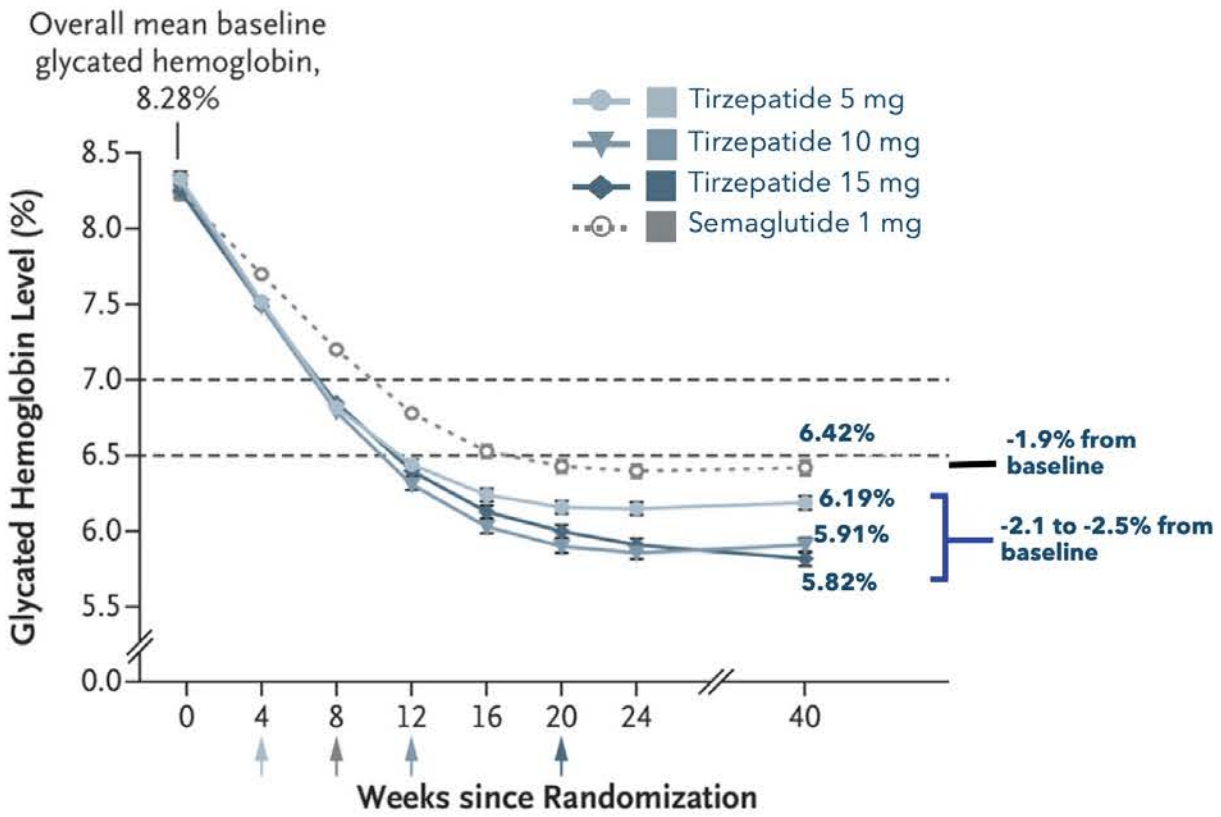


Overall safety profile of tirzepatide was similar to previously reported SURMOUNT and SURPASS trials and to incretin-based therapies approved for the treatment of obesity and overweight

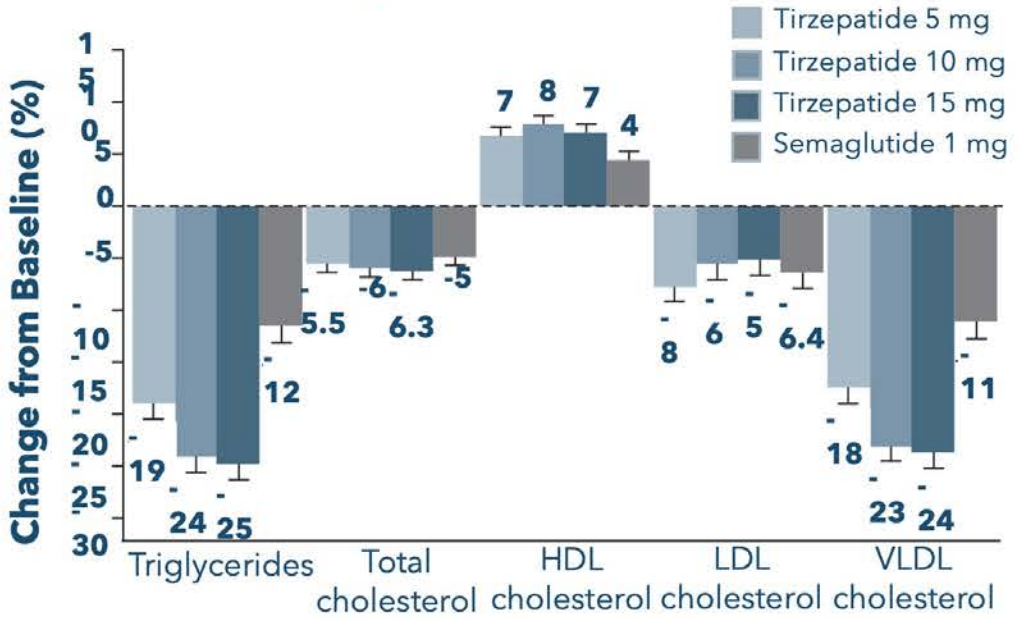
Garvey WT, et al. *Lancet*. 2023.

Benefits Beyond Weight Loss with Tirzepatide and Semaglutide

Glycemic Control in T2D



Lipid Levels in T2D



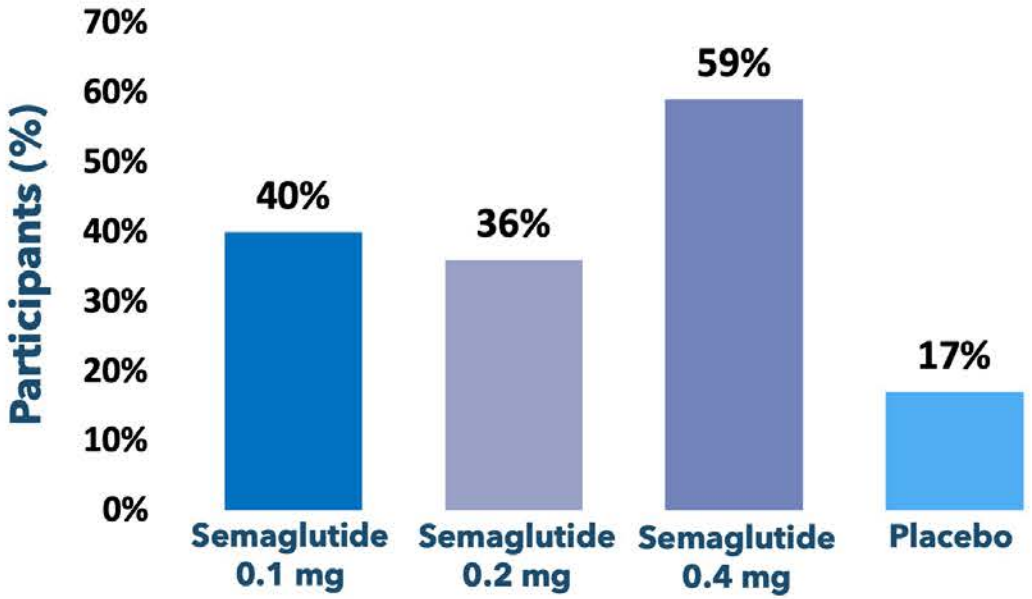
Lipid Levels in Obesity *% baseline change*	Semaglutide	Tirzepatide
TC	-3.3 to 7.1	-4.9 to -7.4
LDL-C	-6.5 to 1	-5.3 to -8.6
TG	-6 to -22.5	-24 to -31
HDL-C	-0.3 to 18	7 to 8.6

Frías JP, et al. *N Engl J Med*. 2021; Bergmann NC, et al. *Diabetes Obes Metab*. 2023; Jastreboff AM, et al. *N Engl J Med*. 2022.

Hepatic Outcomes with Tirzepatide and Semaglutide

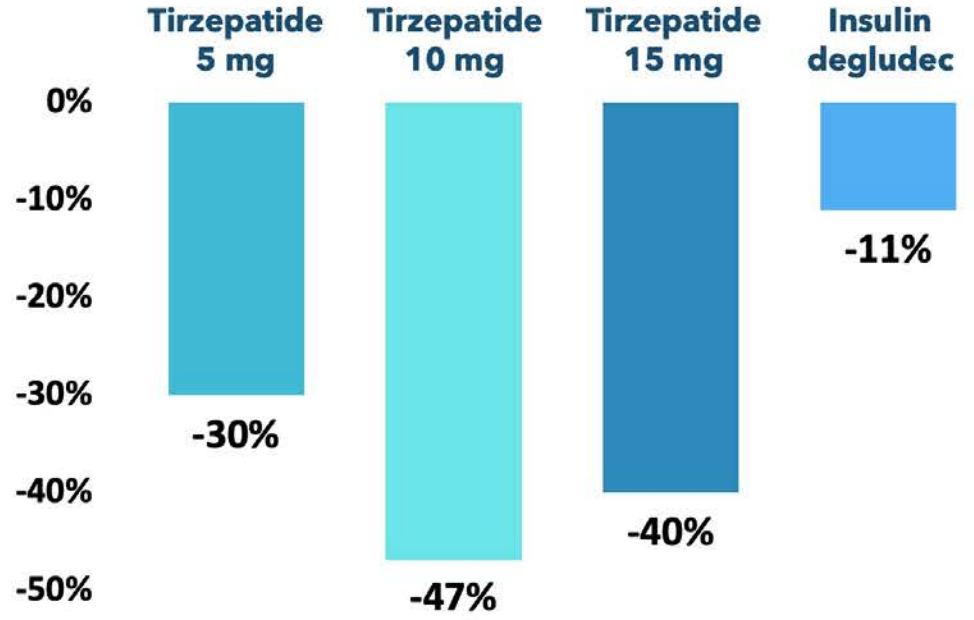
Semaglutide Phase 2 Trial for Biopsy-Confirmed NASH

Resolution of NASH with no worsening of liver fibrosis



SURPASS-3 MRI: Sub study with Tirzepatide

Relative Change (%) of Liver Fat Content (LFC)



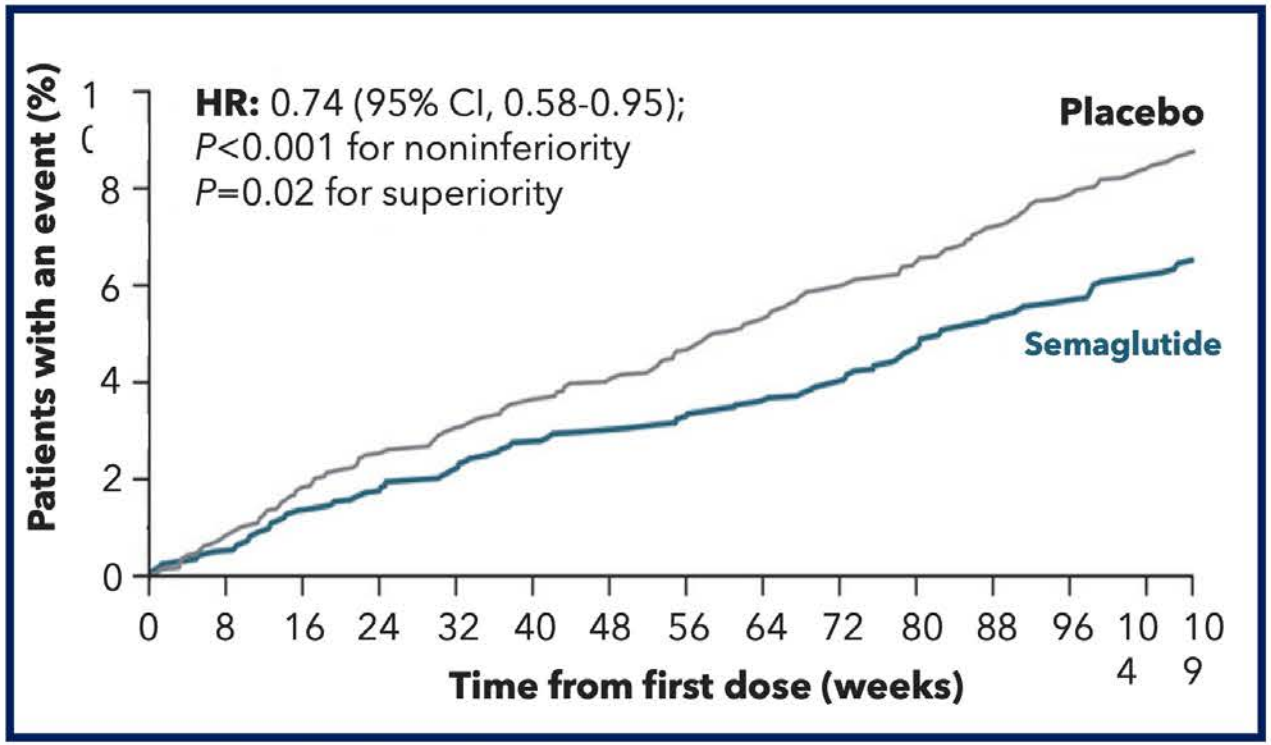
Newsome PN, et al. *N Engl J Med*. 2021; Gastaldelli A, et al. *Lancet Diabetes Endocrinol*. 2022.

Cardiovascular Outcomes with Tirzepatide and Semaglutide

SUSTAIN 6 – T2D with CVD Risk

Patients with Primary Outcome Event

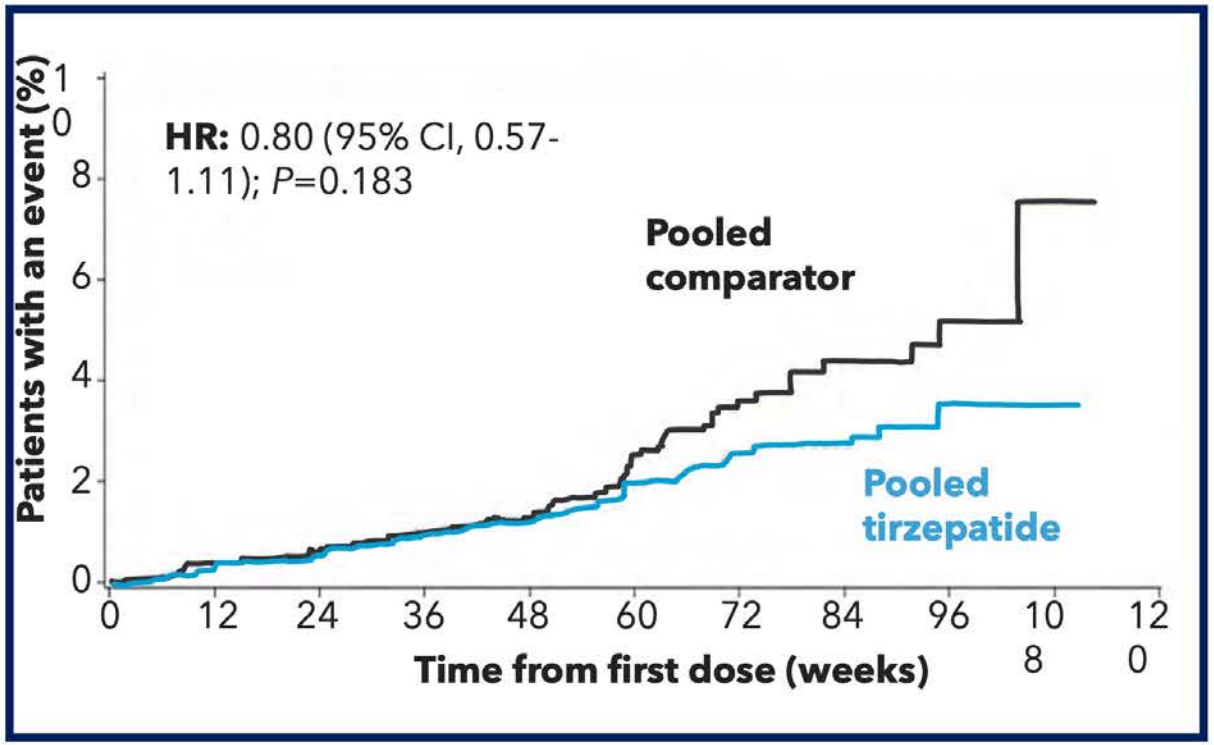
(a composite of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke)



SURPASS T2D Trials Meta-Analysis

Patients with Primary Outcome Event

(MACE-4; cardiovascular death, myocardial infarction, stroke and hospitalized unstable angina)



Marso SP, et al. *N Engl J Med*. 2016; Sattar N, et al. *Nat Med*. 2022.

Important to note the differences in primary outcomes being measured here vs. with semaglutide as well as the fact that this is including comparators, not placebo (as is done with semaglutide)

AE and DDIs of GLP-1 RA and GIP/GLP-1 RA Medications

Drug	Adverse Events	DDIs
Liraglutide (Victoza)	• Common: nausea, diarrhea, vomiting, decreased appetite, dyspepsia, constipation • Serious: thyroid c-cell tumors, pancreatitis, hypoglycemia, AKI, hypersensitivity reaction, acute gallbladder disease • Contraindications: personal/family history of MTC or MEN2, drug hypersensitivity or any of its excipients	Delays gastric emptying and has the potential to reduce the rate of absorption of concomitantly administered oral medications
Dulaglutide (Trulicity)	• Common: nausea, diarrhea, vomiting, abdominal pain, decreased appetite • Serious: thyroid c-cell tumors, pancreatitis, hypoglycemia, hypersensitivity reactions, AKI, severe GI disease, DR complications, acute gallbladder disease • Contraindications: personal/family history of MTC or MEN2, drug hypersensitivity or any of its excipients	
Semaglutide (Wegovy)	• Common: nausea, diarrhea, vomiting, constipation, abdominal pain, headache, fatigue, dyspepsia, dizziness, abdominal distension, eructation, hypoglycemia in patients with T2D, flatulence, gastroenteritis, gastroesophageal reflux disease, nasopharyngitis • Serious: thyroid c-cell tumors, acute pancreatitis, acute gallbladder disease, hypoglycemia, AKI, hypersensitivity reactions, DR complications, heart rate increase, suicidal behavior/ideation • Contraindications: personal/family history of MTC in patients with MEN2, drug hypersensitivity or any of its excipients	
Semaglutide (Ozempic)	• Common: nausea, abdominal pain, diarrhea, vomiting, constipation • Serious: thyroid c-cell tumors, pancreatitis, DR, hypoglycemia, AKI, hypersensitivity reactions, acute gallbladder disease • Contraindications: personal/family history of MTC or MEN2, drug hypersensitivity or any of its excipients	
Tirzepatide (Mounjaro)	• Common: nausea, diarrhea, decreased appetite, vomiting, constipation, dyspepsia, abdominal pain • Serious: thyroid c-cell tumors, pancreatitis, hypoglycemia with concomitant use of secretagogues/insulin, hypersensitivity reactions, AKI, severe GI disease, DR complications, acute gallbladder disease • Contraindications: Personal/family history of MTC or patients with MEN2, drug hypersensitivity or any of its excipients	
Tirzepatide (Zepbound)	• Common: nausea, diarrhea, vomiting, constipation, dyspepsia, abdominal pain, injection site reactions, fatigue, hypersensitivity reactions, eructation, hair loss, gastroesophageal reflux disease • Serious: thyroid c-cell tumors, severe GI disease, AKI, acute pancreatitis, hypersensitivity reactions, hypoglycemia, DR complications, acute gallbladder disease, suicidal behavior and ideation • Contraindications: Personal/family history of MTC or patients with MEN2, drug hypersensitivity or any of its excipients	

AKI, acute kidney injury; AE, adverse events; DDI, drug-drug interaction; DR, diabetic retinopathy; GI, gastrointestinal; HR, heart rate; HTN, hypertension; MEN, Multiple Endocrine Neoplasia syndrome type 2; MTC, medullary thyroid cancer; URTI, upper respiratory tract infection.

FDA Prescribing Information.

Counseling Patients for AE Risk

The use of GLP-1 receptor agonists is associated with an increased risk of thyroid cancer

GLP-1 receptor agonists and the risk of thyroid cancer

Bezin J., Gouverneur A., Pénichon M., Mathieu C., Garrel R., Hillaire-Buys D., Pariente A., Faillie J-L.

Nationwide population-based study on French SNDS database

3,746,672 individuals with type 2 diabetes treated with second-line antidiabetes drugs between 2006-2018

2,562 cases of thyroid cancers

45,184 matched control subjects

	Case subjects *n* = 2,572	Control subjects *n* = 45,184	Adjusted hazard ratio (95%CI)*
GLP-1 receptor agonists			
No use	2,255 (88.0)	40,836 (90.4)	Reference
Cumulative use ≤1 year	117 (4.6)	1,767 (3.9)	1.22 (0.99 to 1.50)
Cumulative use 1-3 years	112 (4.4)	1,419 (3.1)	1.58 (1.27 to 1.95)
Cumulative use >3 years	78 (3.0)	1,162 (2.6)	1.36 (1.05 to 1.74)
DPP-4 inhibitors			
No use	1,522 (59.4)	27,406 (60.7)	Reference
Cumulative use ≤1 year	333 (13.0)	5,209 (11.5)	1.12 (0.99 to 1.28)
Cumulative use 1-3 years	310 (12.1)	5,918 (13.1)	0.96 (0.84 to 1.10)
Cumulative use >3 years	397 (15.5)	6,651 (14.7)	1.19 (1.04 to 1.35)

*Adjusted for social deprivation index, goiter, hypo- and hyperthyroidism in the last year, and use of other antidiabetes drugs in the last 6 years considered in therapeutic class.

- GLP-1 receptor agonists are currently contraindicated in patients with medullary thyroid cancer and multiple endocrine neoplasia 2 (MEN-2)
- Counsel patients with familial thyroid cancer or genetic predisposition to papillary or follicular thyroid cancer when using GLP-1 receptor agonists

Bezin J et al. GLP-1. *Diabetes Care*. 2023;46(2):384-390.

Most Common Side Effects of Semaglutide and Tirzepatide

Abdominal pain	Constipation	Dyspepsia	Vomiting	Diarrhea	Nausea
3-5%	5-7%	6-9%	6-10%	12-16%	17-22%
					

It is important to communicate with your patient strategies to manage side effects to encourage adherence to therapy

FDA Prescribing Information.

Most Common Side Effects of Semaglutide and Tirzepatide

Abdominal pain

Constipation

Dyspepsia

Vomiting

Diarrhea

Nausea

Headache

Fatigue

Abdominal bloating

Belching

Hypoglycemia in patients with T2D

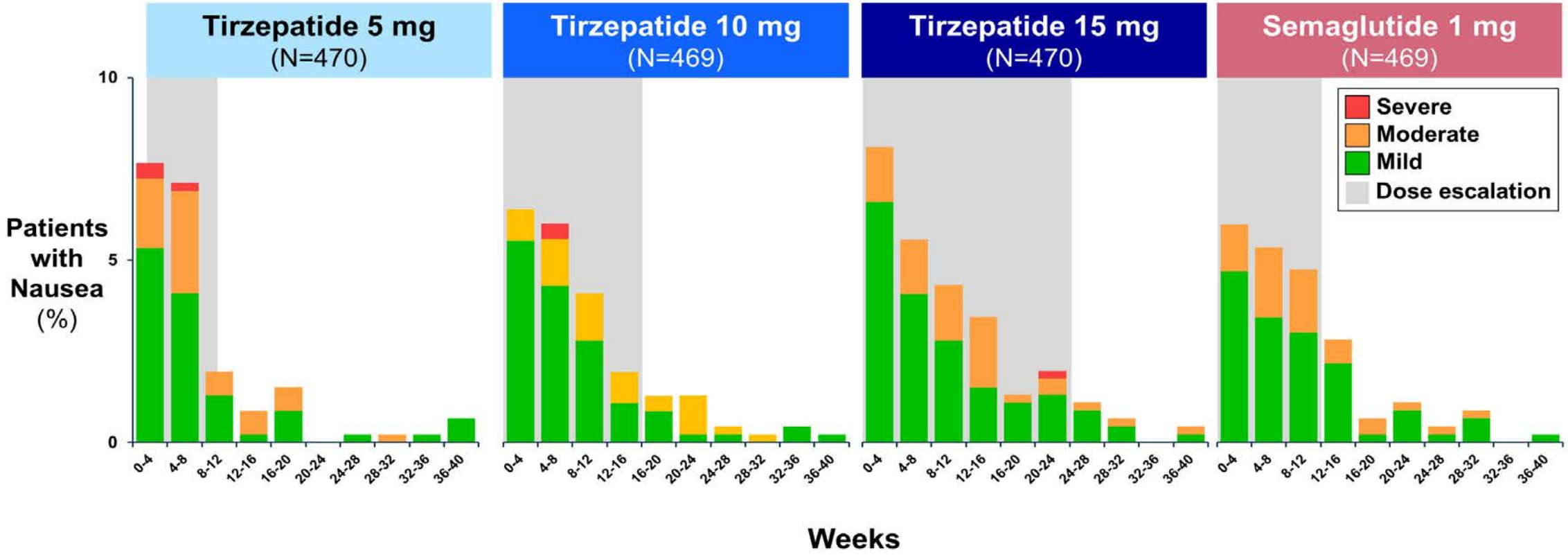
Gas and flatulence

Gastroenteritis

GERD

1. FDA Prescribing Information. 2. Jastreboff AM, et al. *N Engl J Med*. 2022.

Incidence of Nausea Over Time Through 40-Weeks of the SURPASS-2 Trial

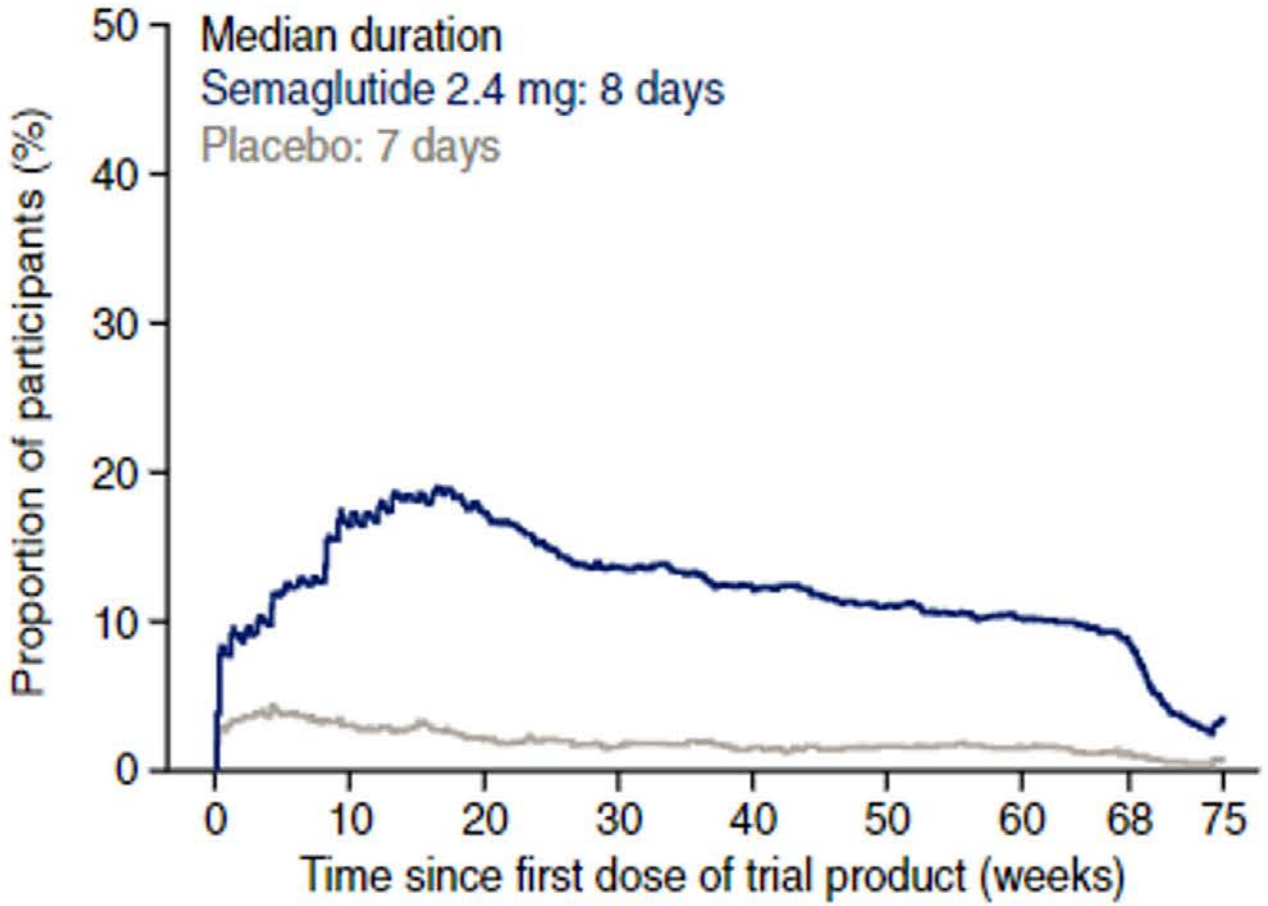


Most cases of nausea were mild to moderate, transient, and occurred during the dose-escalation period in all groups

Frías JP, et al. *N Engl J Med*. 2021.

Tolerability of High Dose Semaglutide

Incidence of Nausea Over Time in the (A-D) STEP 1-3 Trials



The prevalence of nausea, diarrhea and vomiting in the semaglutide 2.4 mg arm peaked at about week 20 and decreased thereafter

Individual nausea, diarrhea, and vomiting events were relatively short-lived

Warton S, et al. *Diabetes Obes Metab*. 2022.

Patient Consultation and Counseling

GI side effects are typically mild-moderate and temporary in nature
HCPs should titrate doses up to help mitigate adverse events

Tips to Reduce Side Effects from GLP-1 RA and GIP/GLP-1 RA

- ✓ Eat slowly
- ✓ Smaller portions
- ✓ Do not skip meals
- ✓ Eat when hungry
- ✓ Increase meal frequency
- ✓ Limit overactivity after meal
- ✓ Incorporate a low-fat diet
- ✓ Refrain from lying down after a meal

FDA Prescribing Information; Wharton S, et al. *Postgrad Med.* 2022; Gorgojo-Martinez JJ, et al. *J Clin Med.* 2023.

Choosing Between Medication Options

SDOH considerations

Health inequity considerations

Drug-related factors	Provider-related factors	Patient-related factors
• Efficacy and safety data • Population benefits based on clinical trials	• Education and comfort • Availability • Cost • Misperceptions	• Personal values, beliefs, cultural norms, preferences • Adherence

Why Does Therapeutic Inertia Exist for GLP-1 RA and GIP/GLP-1 RA Medications?

Clinicians are busy managing multiple chronic diseases with designated time for each patient visit

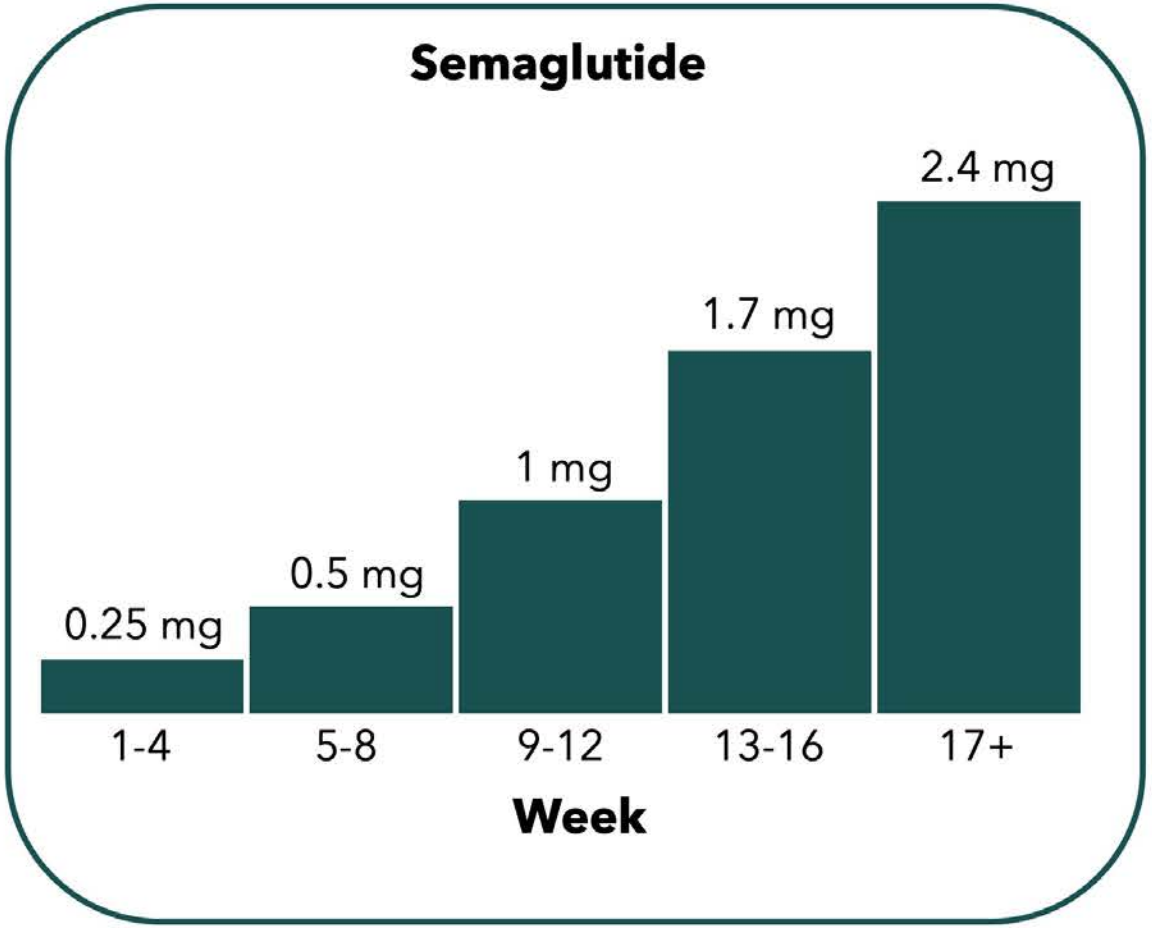
Clinicians lack comfort prescribing new medications with which they do not have experience

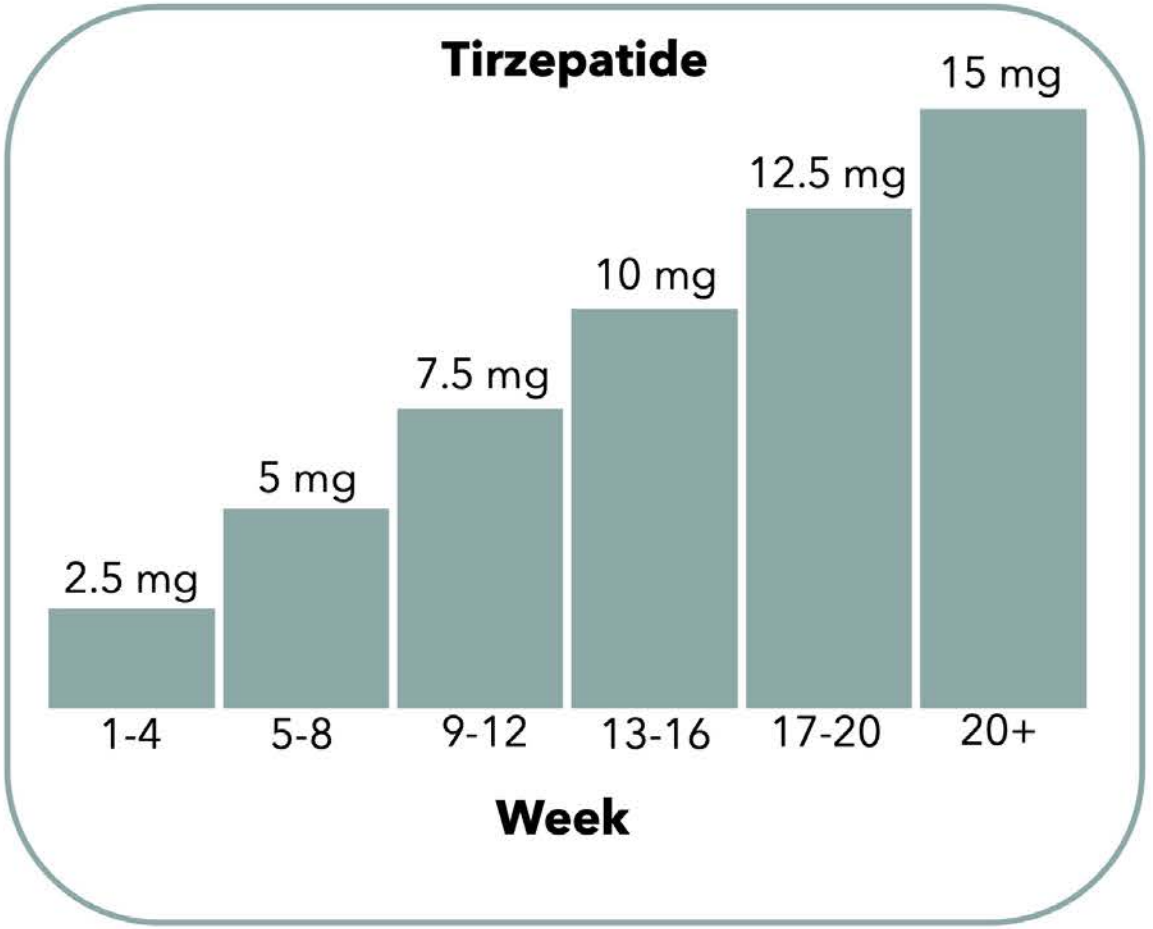
Misconceptions around pharmacologic treatment

- Medication is less effective than lifestyle modification
- New medications that target T2D and weight loss are not safe
- Medication is only a short-term solution

Busetto L, et al. *Eat Weight Discord*. 2022; Lau DC, et al. *Diabetes*. 2022.

Dose Escalation of Semaglutide and Tirzepatide for AE Management





FDA Prescribing Information; Jastreboff AM, et al. *N Engl J Med*. 2022.

Optimizing and Treating GI Adverse Events

Dose-escalation

If GI AEs occur, **slow down** the planned dose increments to reach success

For this purpose, choose one/several among these:

- Extend current phase for 2-4 more weeks before moving forward to next dose
- Suspend treatment temporarily
- If GI AEs appear just after escalation, go back to prior dose for a few days, then increase dose gradually
- If problem persists, consider setting up as maintenance therapy a dose lower than the maximum one

Dose-escalation or maintenance phase

If GI AEs persist beyond normal in time/severity, **implement additional** measures

Consider one/several of these:

- Start a differential diagnosis procedure to rule out underlying conditions that may be responsible
- Check patient understands/complies with diet/lifestyle guidelines
- Start measures specifically focused on the troublesome symptoms, with pharmacological support (short-term)

Nausea and Vomiting

- Anti-emetics
- Prokinetics (domperidone)
- Standard care for severe cases of vomiting (eg, IV rehydration)

Diarrhea

- Probiotics
- Antidiarrheals (loperamide)
- Consider metformin dose reduction when needed

Constipation

- Stool softeners
- Consider reducing dose

Gorgojo-Martinez JJ, et al. *J Clin Med*. 2023.

GLP-1 RA and GIP/GLP-1 RA Deprescribing Considerations

Situational factors leading to deprescribing

- HgA1c falls below target due to lifestyle changes that lead to weight reduction or increased effectiveness of treatment regimen
- New onset of clinical conditions that lead to contraindications
- New/worsened onset of chronic kidney disease
- Hypoglycemia
- Treatment failure
- Need for less intensive regimen due to adherence or tolerability issues or medication burden
- Frailty and lack of social support
- Low cognitive function
- Short life expectancy

Dose Reduction Recommendations

- If patient is on a high dose, reduce to a maintenance dose
- Can stop completely but advise patient of potential risk of weight gain
- Monitor for signs of hyperglycemia and check HgA1c in 3 months

Ali S. *Diabetes & Primary Care. 2023;*25(3):1-2.

Interdisciplinary Teams and the Management of Patient-Related Factors

SDOH considerations

Health inequity considerations

Evaluation T2D and Obesity Burden

Patient Quality of Life

Quality of life factors for patients with T2D

- Dosing frequency
- Timing flexibility
- Ease of use of injection devices
- Unpleasant side effects
- Long-term management

1. Schneider D & Taddei-Allen P. *Am J Manag Care*. 2020:S356-S367. 2. Valentine et al. *Patient Related Outcomes Measures*. 2022(2022)13:97–111.

Evaluation T2D and Obesity Burden

Patient-Reported Outcomes (PROs)

Any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else.

- **Health-related QOL**
- **Symptom indices**
- **Adherence to medications**
- **Social health**
- **Self-efficacy**
- **Willingness to change**
- **Satisfaction of care**
- **Value of treatment**

QOL, quality of life.

1. FDA. 2021. https://www.regdesk.co/fda-patient-reported-outcome-measures/#:~:text=According%20to%20the%20present%20FDA%20guidance%2C%20the%20patient-reported,patient%60s%20response%20by%20a%20clinician%20or%20anyone%20else.
2. Francis DO et al. *Syst Rev*. 2016;5(1):129.

Impact of Weight on Self-Perception (IW-SP)

3-item PRO measure of self-perception among patients with T2D and overweight/obese

The following questions ask about ways in which your weight may affect your self-perceptions.

For each question, please mark the one option that best describes you.

	Never	Rarely	Sometimes	Frequently	Always
1. How often do you feel unhappy with your appearance due to your weight?	5	4	3	2	1
2. When going out in public, how often do you feel self-conscious due to your weight?	5	4	3	2	1
3. When comparing yourself to others, how often do you feel unhappy, due to your weight?	5	4	3	2	1

Demonstrated:

- ✓ Reliable
- ✓ Valid
- ✓ Responsive

PRO, patient-reported outcomes

Hayes RP & DeLozier AM. *Diabetes Technol Ther*. 2015 Mar;17(3):210-214.

Ability to Perform Physical Activities of Daily Living Questionnaire (APPADL)

7-item PRO measure of ability of patients with T2D and obesity to perform daily physical activities based on a 5-point scale from "unable to do from not at all difficult"

Demonstrated:

- ✓ Reliable
- ✓ Valid

Item number	*How difficult is it for you to:*
1	... get up from the floor or ground?
2	... get down—for example, to sit, squat, or kneel on the floor or ground?
3	... stand for 2–3 h?
4	... walk up two flights of stairs?
5	... do household chores or yard work that require you to bend over or squat down, such as cleaning the bathtub or weeding?
6	... engage in moderate physical activity for 30 min, such as walking quickly, playing softball, playing volleyball, or ice skating?
7	... engage in strenuous physical activity for 30 min such as running, playing basketball, biking skiing, or swimming laps?

Previously was referred to as the Impact of Weight on Activities of Daily Living Questionnaire (IWADL).
Hayes RP & DeLozier AM. Diabetes Technol Ther. 2012 Dec;14(12):1118-1125. .

Assessment of Health Inequities by Accounting for Patient QOL

Shift in focus on quality of care should yield:

Achieved patient goals and clinical effectiveness

Perceived enhancement in care received

Improved physical, mental, and emotional well-being

- Better understanding of patient experience and health outcomes
- Make informed, appropriate treatment decisions

QOL, quality of life.

Schneider D & Taddei-Allen P. *Am J Manag Care.*2020;26:S356-S367.

Case Study: Mr. Nixon

A1C started at 7.9% and reduced to 5.5, T2D stable at 12 months

28.7% weight loss, weight stable at 12 months

Mr. Jay was able to stop glimepiride and HCTZ

Labs and PE	Baseline	6-mo follow-up	12-mo follow-up
Glucose	175 mg/dL*	106 mg/dL*	92 mg/dL
A1C	7.9%*	6.4%*	5.5%*
BP	155/90 mmHg*	134/80 mmHg*	120/75 mmHg
LDL-C	190 mg/dL*	180 mg/dL	110 mg/dL
HDL-C	30 mg/dL	37 mg/dL	41 mg/dL
TG	360 mg/dL*	-	160 mg/dL
Weight	275 lbs	242 lbs	196 lbs
WC	46"*	40"*	34"
BMI	36*	32*	26*
ALT/AST	80 u/L*; 72 u/L*	-	50 u/L; 32 u/L
FIB-4	2.23*	-	0.91
	Obesity Class II; Very High Risk	→ Obesity Class I; Very High Risk	→ Overweight; Increased Risk

A1C, glycated hemoglobin; ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; BP, blood pressure; Fib-4, Fibrosis-4 index score; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; WC, waist circumference.