

COMMUNITY COLLECTIVE™



HARNESSING THE POWER OF THE COMMUNITY TO BATTLE OBESITY

Activity 1

IMPORTANCE OF CONVERSATIONS ABOUT AN OBESITY DIAGNOSIS

Activity 2

PRACTICAL APPLICATION OF NEW AND EMERGING DATA

This activity is supported by an educational grant from Lilly





Case Study: Mr. Jay

Mr. Jay presents in clinic for a check-up.
He complains of being more lethargic than usual.

Medical History



Obesity	Hypertension	Obstructive sleep apnea	Gout	Non-obstructive CAD
Type 2 Diabetes	Dyslipidemia	Non-alcoholic fatty liver disease	Osteoarthritis	Acanthosis nigricans

Current Medications



Metformin 500 mg BID	Glimepiride 4 mg	Losartan-HCT 100-25	Empagliflozin 25 mg
Amlodipine 10 mg	Rosuvastatin 10 mg	Allopurinol 100 mg	



Case Study: Mr. Jay

Mr. Jay presents in clinic for a check-up. He complains of being more lethargic than usual.



Medical History and Current Medications	Related Labs and Physical Exam Findings
Type 2 Diabetes <ul style="list-style-type: none"> Metformin 500 mg BID Empagliflozin 25 mg Glimepiride 4 mg 	Glucose: 190 mg/dL; A1C: 8.1%
Hypertension <ul style="list-style-type: none"> Losartan-HCT 100 mg-25 mg Amlodipine 10 mg 	BP: 150/90 mmHg
Dyslipidemia <ul style="list-style-type: none"> Rosuvastatin 10 mg 	LDL-C: 122 mg/dL; HDL-C: 38 mg/dL; TG: 360 mg/dL
Gout <ul style="list-style-type: none"> Allopurinol 100 mg 	N/A
Obesity	Weight: 258 lbs; Height: 69"; WC: 48"; BMI: 38
Non-alcoholic fatty liver disease	ALT: 80 u/L; AST: 72 u/L; Plt: 202/ μ L; FIB-4: 2.23
Non-obstructive CAD	CAC: 199
Other: obstructive sleep apnea, osteoarthritis, acanthosis nigricans	

Classification of Overweight and Obesity by BMI

Waist Circumference and Associated Disease Risks



Disease Risk Relative to Normal Weight and Waist Circumference

	BMI (kg/m ²)	Obesity Class	Men (≤102 cm) ≤40 in Women (≤88 cm) ≤35 in	Men (>102 cm) >40 in Women (>88 cm) >35 in
Underweight	<18.5			
Normal	18.5-24.9			
Overweight	25.0-29.9		Increased	High
Obesity	30.0-34.9	I	High	Very High
	35.0-39.9	II	Very High	Very High
Extreme obesity	≥40	III	Extremely High	Extremely High

On Exam (Mr. Jay)

Weight: 258 lbs
Height: 69"
WC: 48"
BMI: 38

Mr. Jay has a BMI of 38 and waist circumference of 121.9 cm (48 inches)

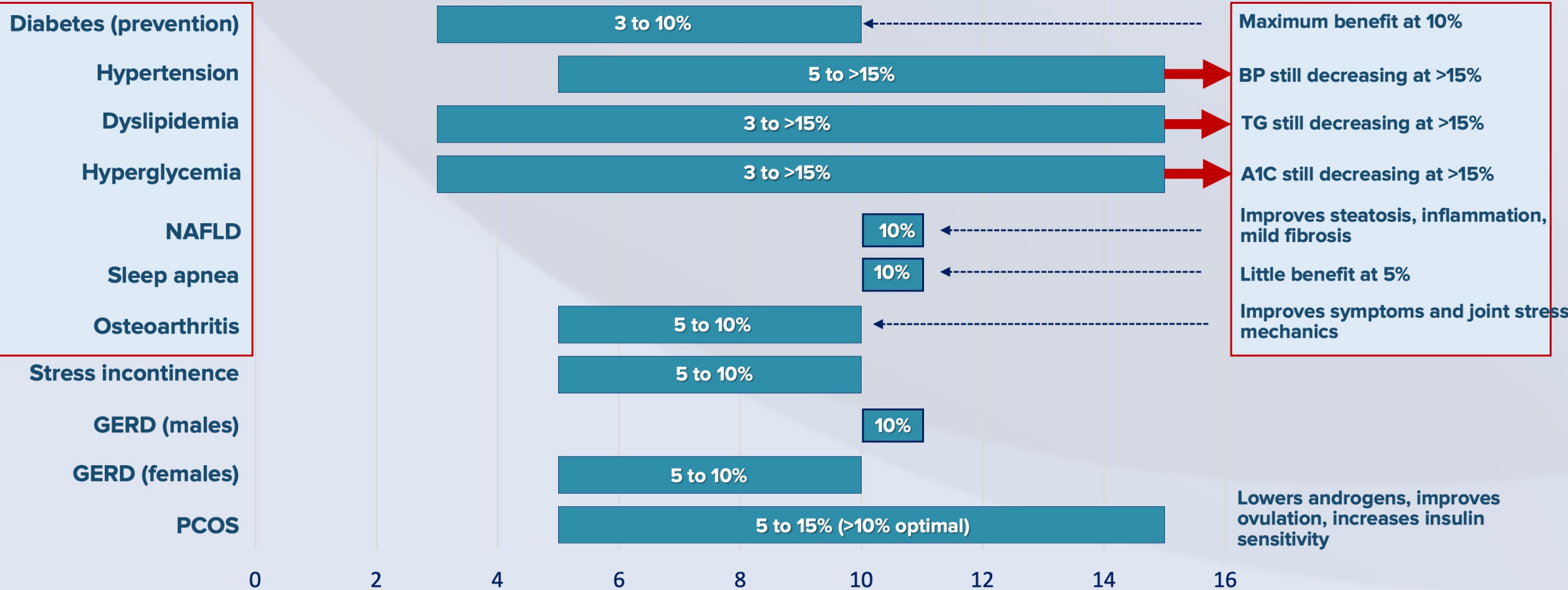


Treating the Obesity

Therapeutic Weight Loss Reduces Complications



Weight loss required for therapeutic benefit (%)



GERD, gastroesophageal reflux disease; NAFLD, nonalcoholic fatty liver disease; PCOS, polycystic ovary syndrome, m, male; f, female; OA, osteoarthritis. Cefalu WT, et al. *Diabetes Care*. 2015.

Choosing Between Medication Options



Drug factors

- Efficacy and safety data
- Dual benefits
- Studied populations
- Contraindications

Provider factors

Patient factors

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

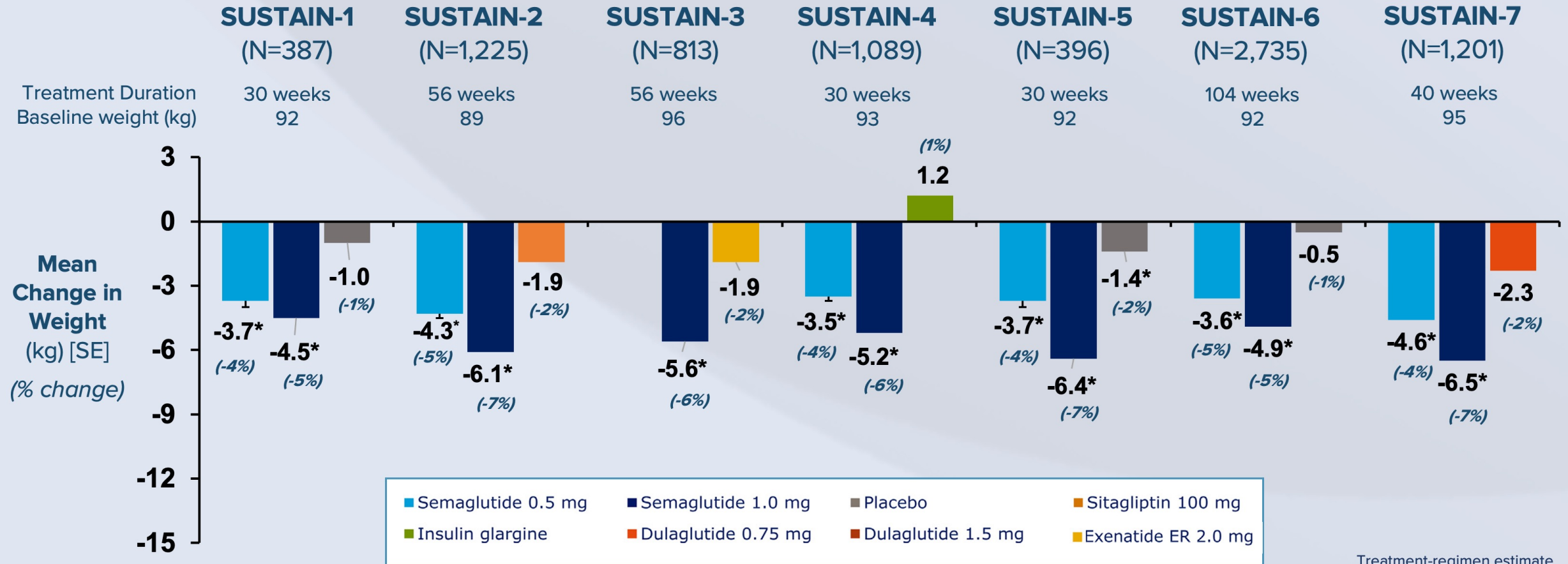


Efficacy for weight loss

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

Weight Loss with Semaglutide vs. Comparators in SUSTAIN Trials

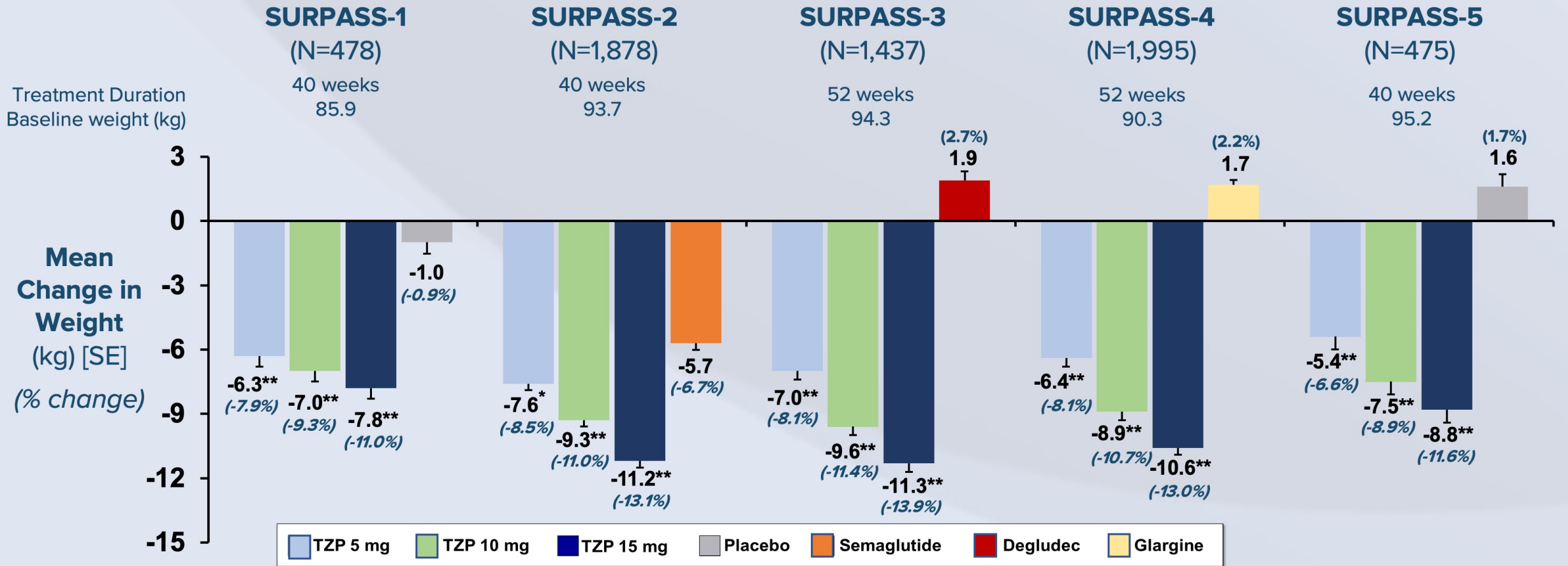
Patients with Type 2 Diabetes



Treatment-regimen estimate
 Superiority vs placebo or active comparator: *P<0.01.

Weight Loss with Tirzepatide vs. Comparators in SURPASS Trials

Patients with Type 2 Diabetes



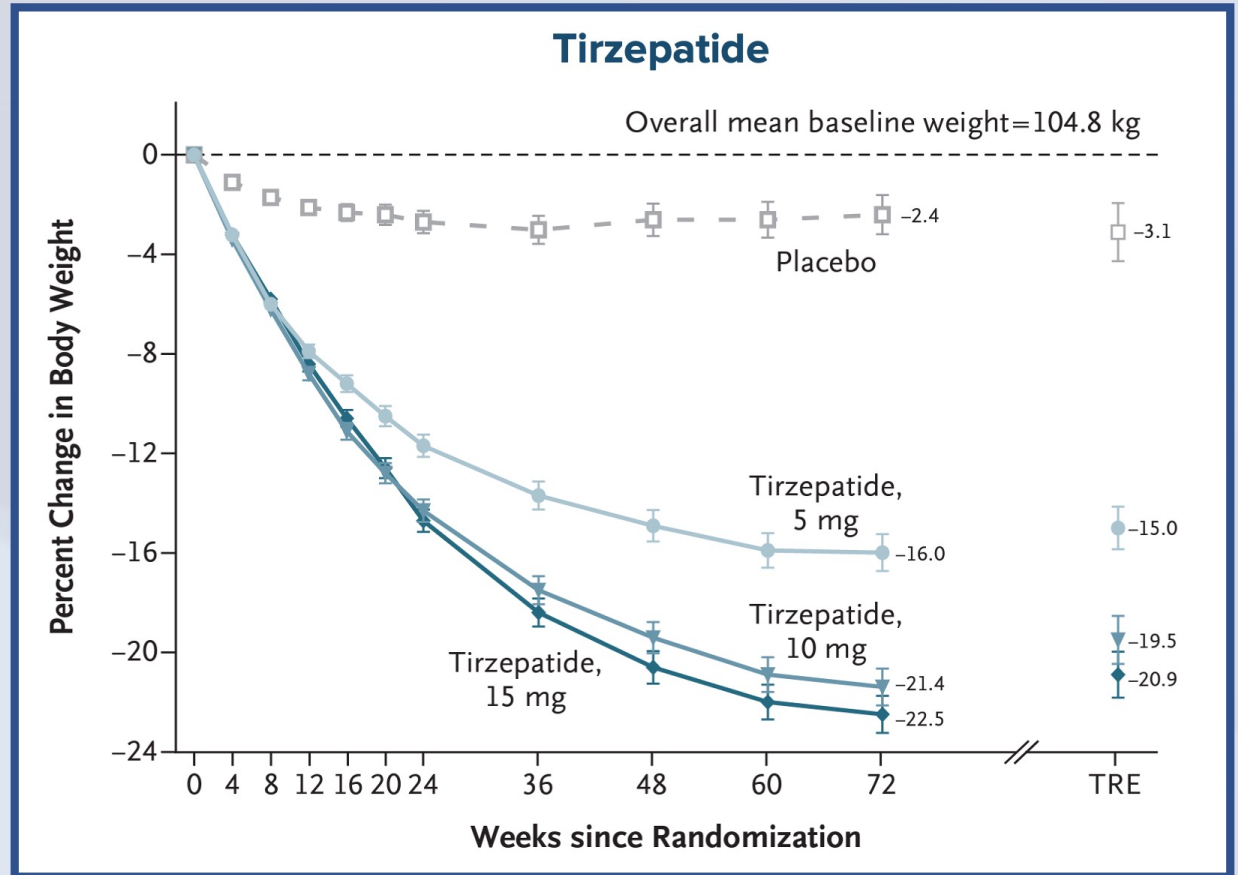
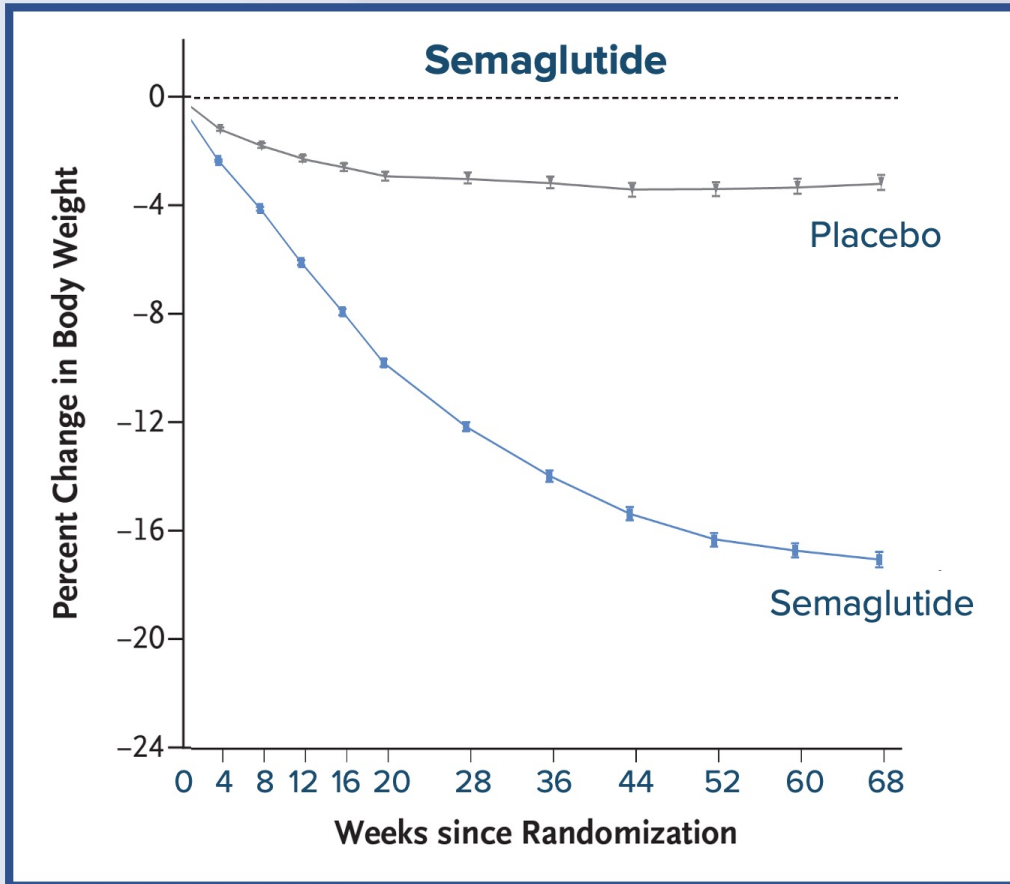
Treatment-regimen estimand
 Superiority vs placebo or active comparator: *P<0.05; **P<0.001

Treatment of Obesity: Weight Loss with Semaglutide and Tirzepatide vs Placebo



**STEP-1, Phase 3 Trial in BMI ≥ 30
(excluding diabetes)**

**SURMOUNT-1, Phase 3 Trial in BMI ≥ 30 or ≥ 27 with
comorbidity (excluding diabetes)**

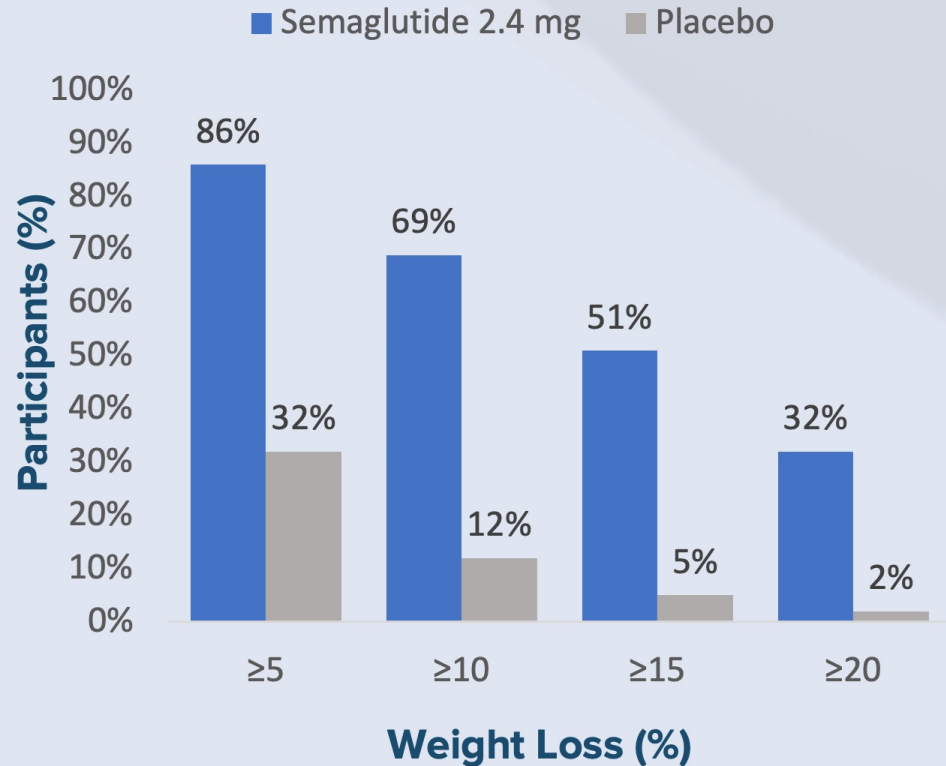


***Please note:** these are not head-to-head trials.

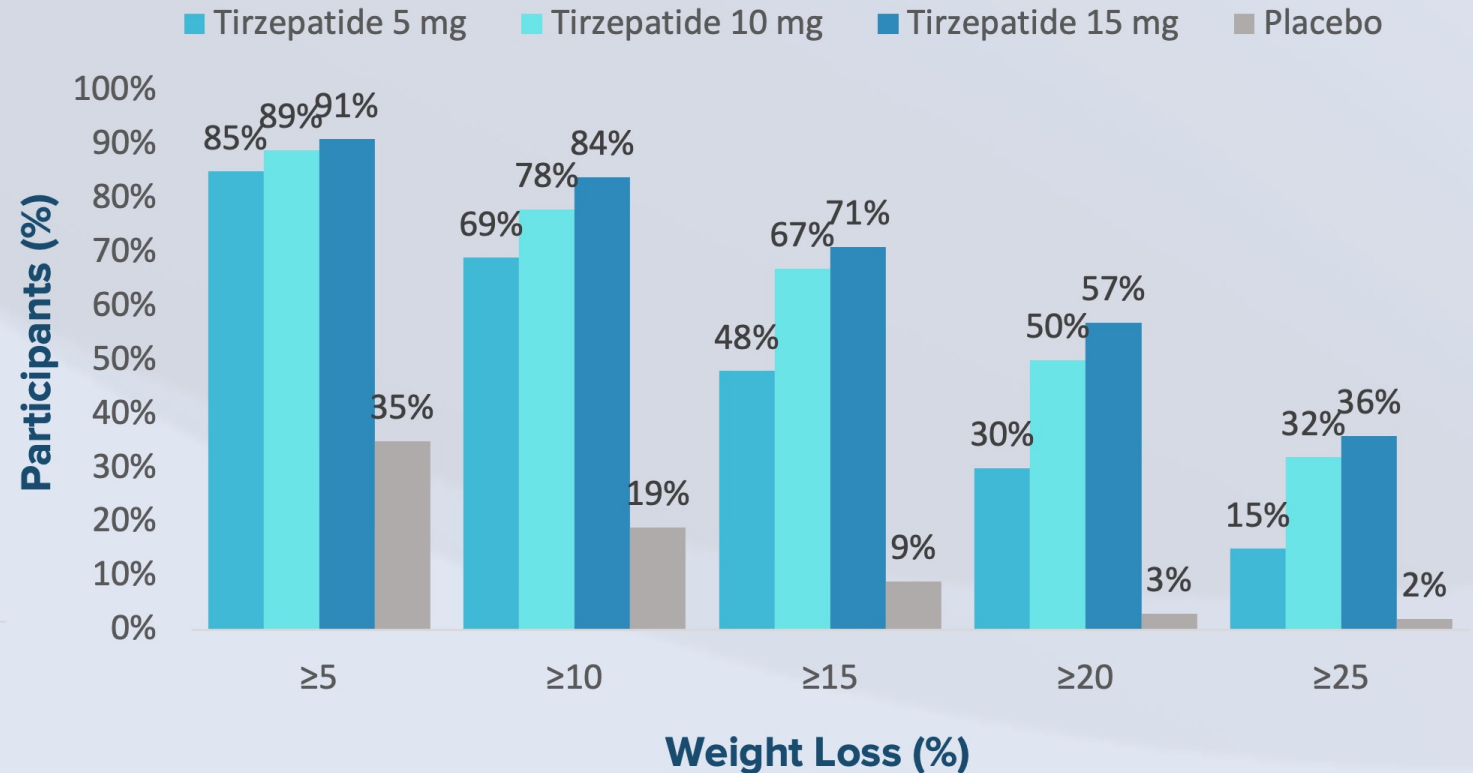
Weight Loss Categories with Semaglutide and Tirzepatide



STEP-1, Phase 3 Trial in BMI ≥ 30 excluding diabetes



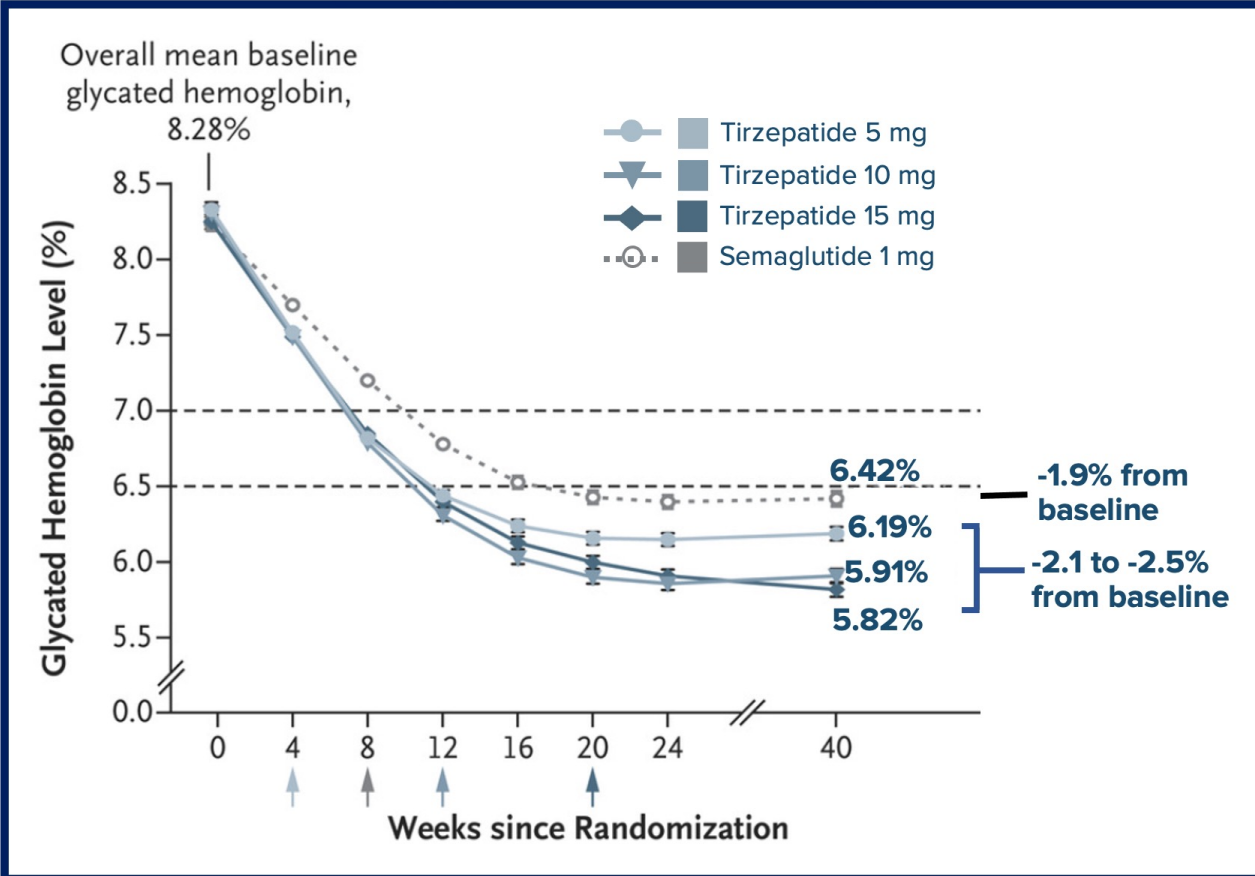
SURMOUNT-1, Phase 3 Trial in BMI ≥ 30 or ≥ 27 with comorbidity (excluding diabetes)



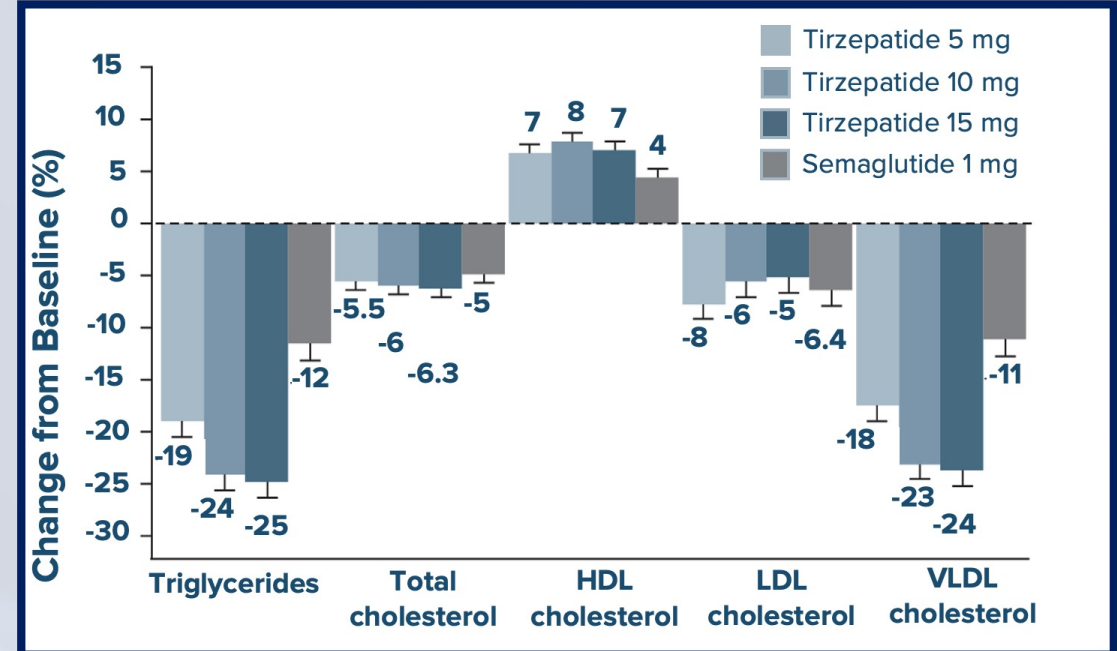
Benefits Beyond Weight Loss with Tirzepatide and Semaglutide



Glycemic Control in T2D



Lipid Levels in T2D



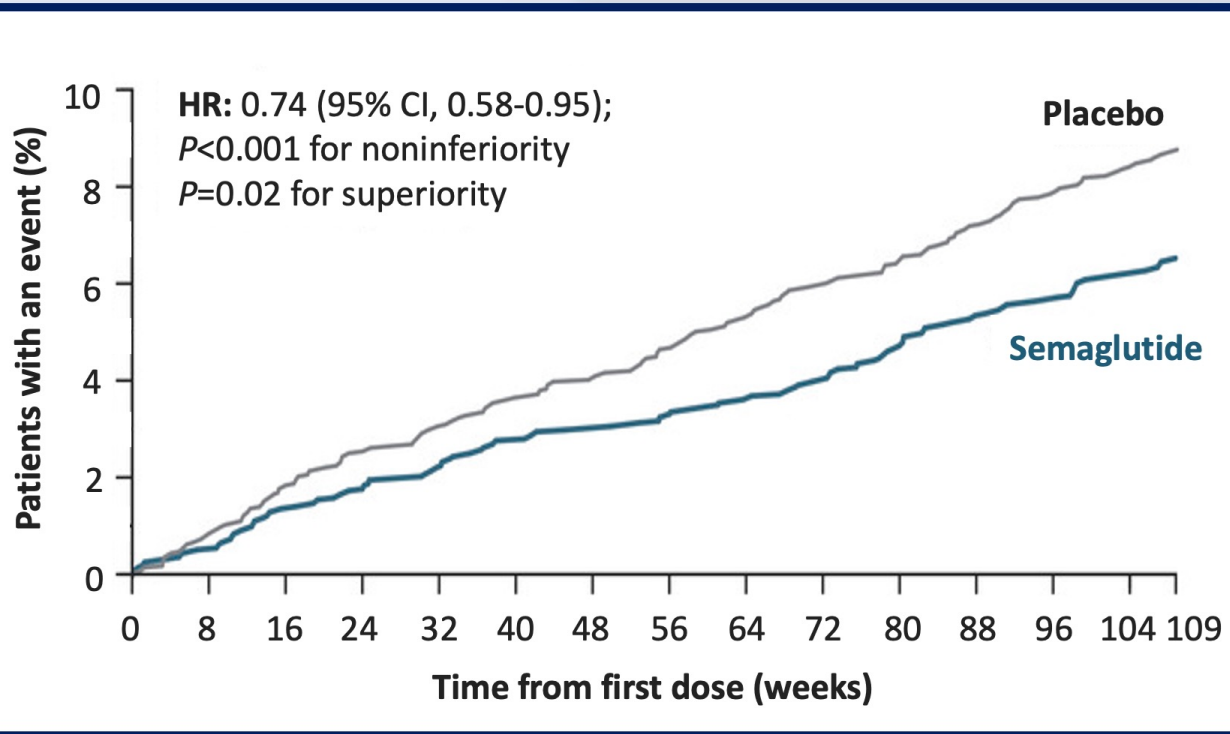
Lipid Levels in Obesity % baseline change	Semaglutide	Tirzepatide
TC	-3.3 to 7.1	-4.9 to -7.4
LDL-C	-6.5 to 1	-5.3 to -8.6
TG	-6 to -22.5	-24 to -31
HDL-C	-0.3 to 18	7 to 8.6

Cardiovascular Outcomes with Semaglutide and Tirzepatide



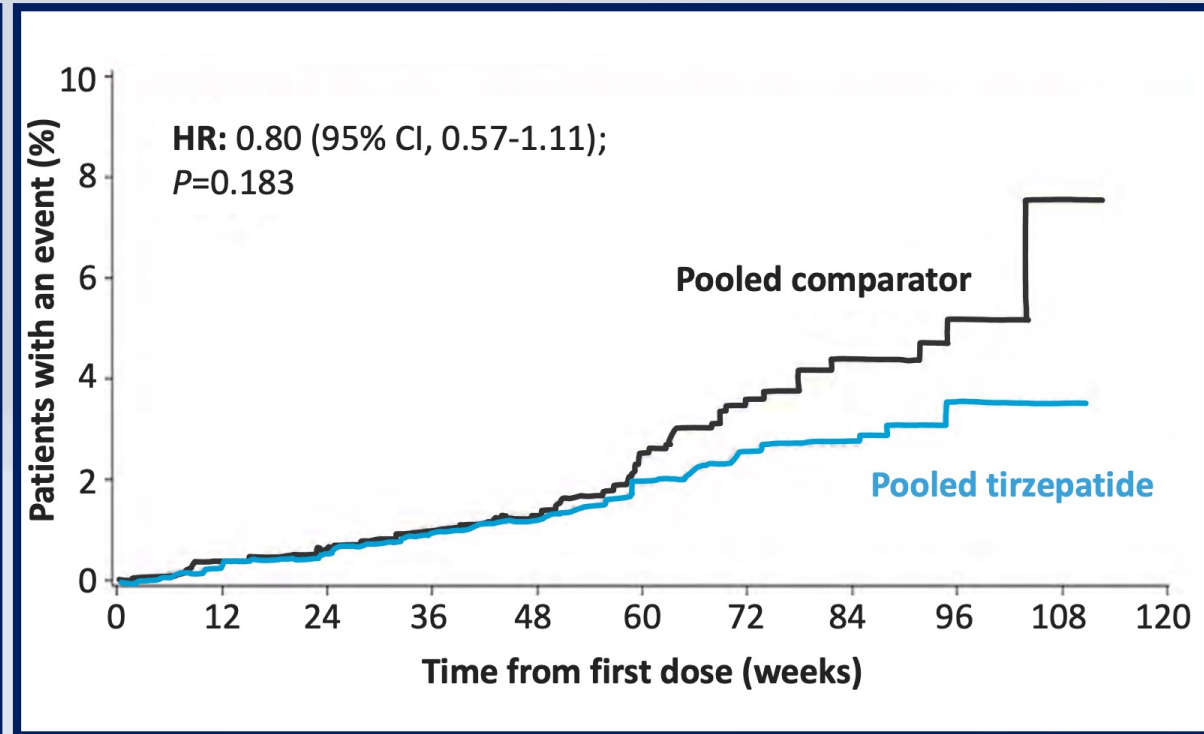
SUSTAIN 6 – T2D with CVD Risk

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)

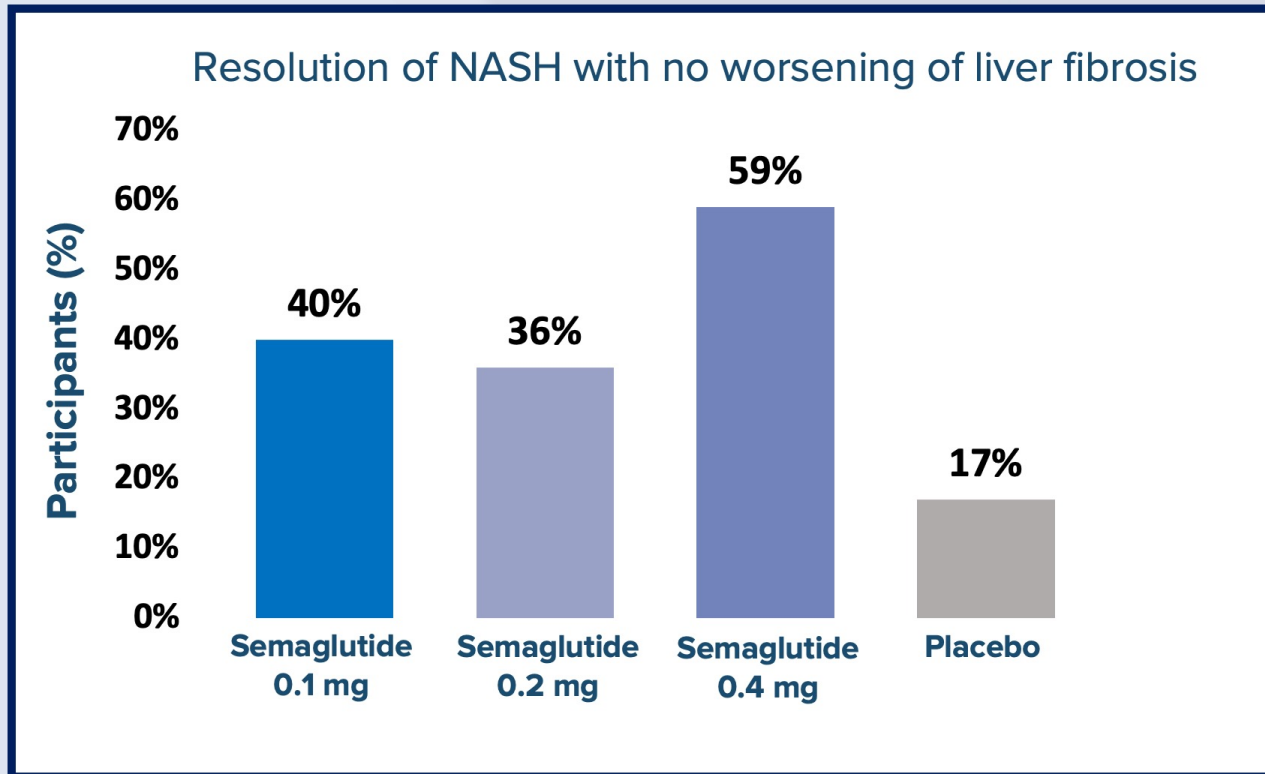


Important to note the differences in primary outcomes being measured here vs. with semaglutide as well as the fact that this is including comparators, not placebo (as is done with semaglutide)

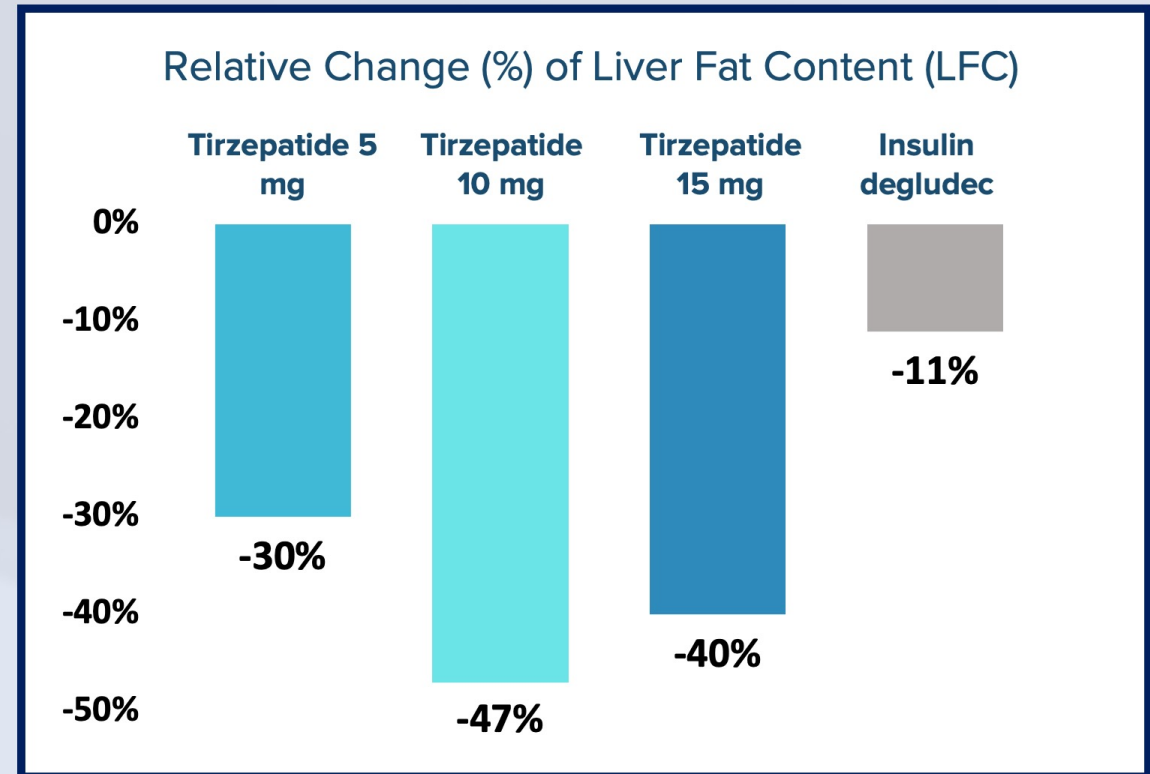
Hepatic Outcomes with Semaglutide and Tirzepatide



Semaglutide Phase 2 Trial for Biopsy-Confirmed NASH¹

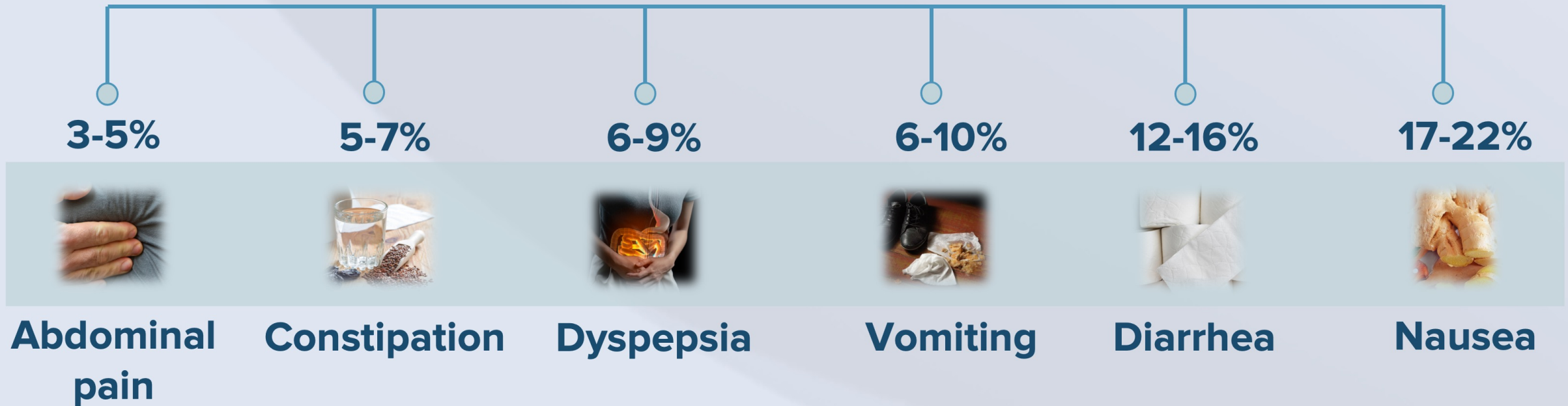


SURPASS-3 MRI: Sub study with Tirzepatide²



¹Newsome PN, et al. *N Engl J Med.* 2021; ²Gastaldelli A, et al. *Lancet Diabetes Endocrinol.* 2022.

Most Common Side Effects of Semaglutide and Tirzepatide



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

Contraindications and Limitations of Use

Semaglutide and Tirzepatide



Contraindications

- Personal or family history of medullary thyroid cancer or patients with Multiple endocrine neoplasia syndrome type 2
- Known serious hypersensitivity to tirzepatide/semaglutide or any of the excipients

Limitations of Use

- Has not been studied in patients with a history of pancreatitis
- Is not indicated for use in patients with type 1 diabetes

Warnings and Precautions

Semaglutide and Tirzepatide



- 1 Pancreatitis
- 2 Hypoglycemia with concomitant use of insulin secretagogues or insulin
- 3 Hypersensitivity reactions
- 4 Acute kidney injury
- 5 Severe gastrointestinal disease
- 6 Diabetic retinopathy complications in patient with a history of diabetic retinopathy
- 7 Acute gallbladder disease

Choosing Between Medication Options



Drug factors

Provider factors

- Provider knowledge/comfort
- Therapeutic inertia

Patient factors



Choosing Between Medication Options

Drug factors

Provider factors

Patient factors

- Prior experiences
- Access
- Patient preferences/adherence

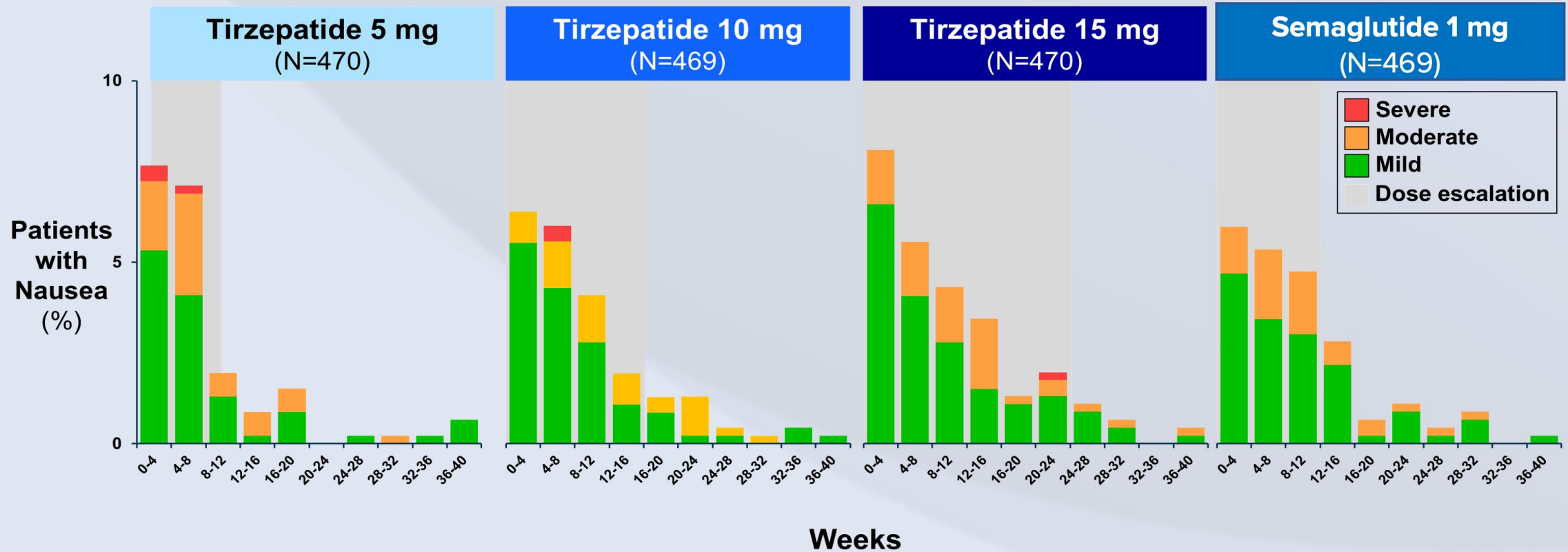
Most Common Side Effects of Semaglutide and Tirzepatide



- **Abdominal pain**
- **Constipation**
- **Dyspepsia**
- **Vomiting**
- **Diarrhea**
- **Nausea**
- **GERD**
- **Headache**
- **Fatigue**
- **Abdominal bloating**
- **Belching**
- **Hypoglycemia (in patients with T2D)**
- **Gas and flatulence**
- **Gastroenteritis**

Incidence of Nausea Over Time Through 40 Weeks

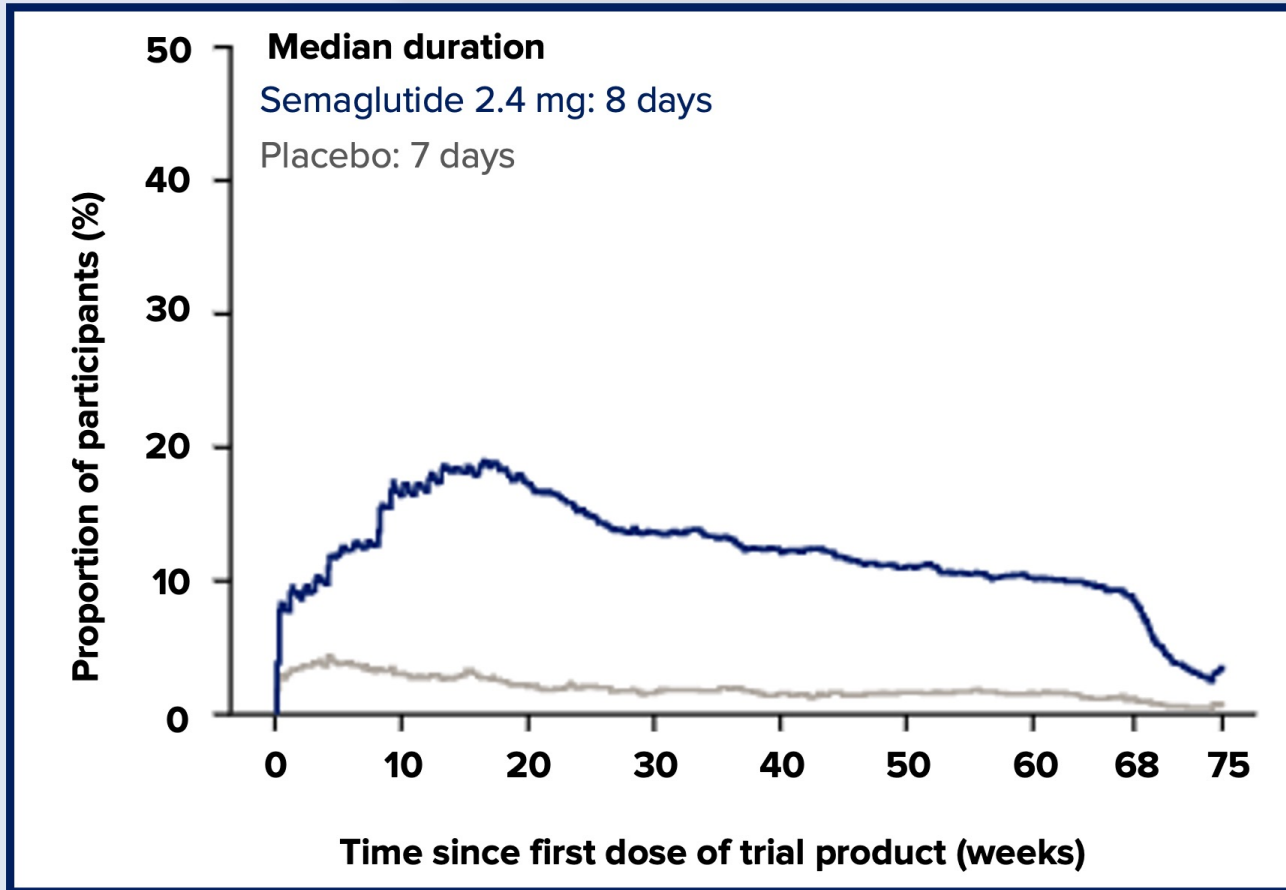
SURPASS-2



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

Tolerability of High Dose Semaglutide

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

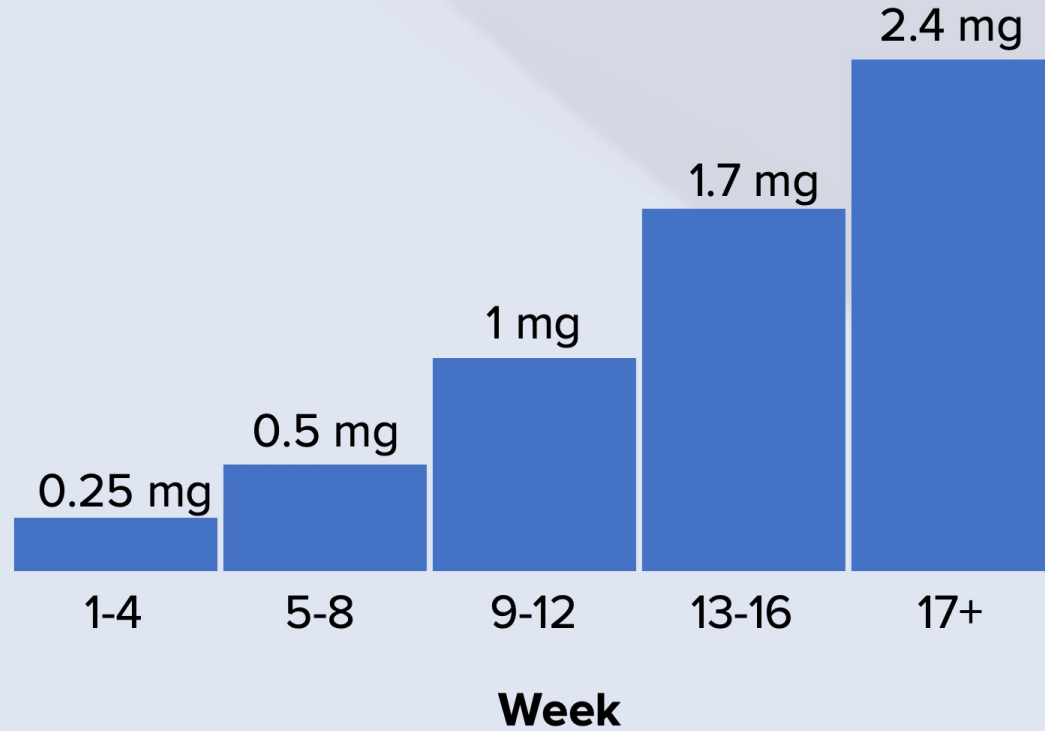


The prevalence of nausea, diarrhea and vomiting in the semaglutide 2.4 mg arm peaked at about week 20 and decreased thereafter. Individual nausea, diarrhea, and vomiting events were relatively short-lived.

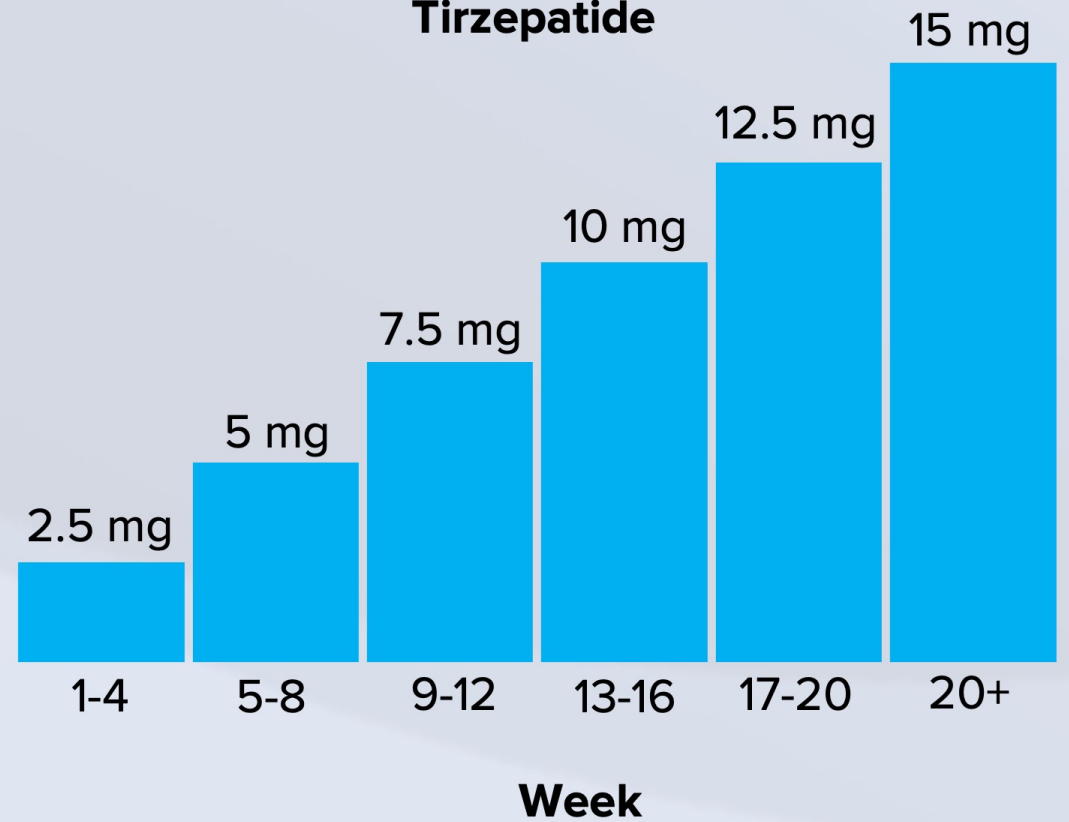
Dose Escalation



Semaglutide



Tirzepatide



Case Study: Mr. Jay



Labs and PE	Baseline	6-mo follow-up	12-mo follow-up
Glucose	190 mg/dL*	110 mg/dL*	99 mg/dL
A1C	8.1%*	6.5%*	5.8%*
BP	150/90 mmHg*	130/80 mmHg*	120/80 mmHg
LDL-C	122 mg/dL*	-	120 mg/dL
HDL-C	38 mg/dL	-	48 mg/dL
TG	360 mg/dL*	-	140 mg/dL
Weight	258 lbs	230 lbs	196 lbs
WC	48"*	42"*	36"
BMI	38*	34*	29*
ALT/AST	80 u/L*; 72 u/L*	-	50 u/L; 32 u/L
FIB-4	2.23*	-	0.91

24% weight loss, weight stable at 12 mo

Mr. Jay was able to stop glimepiride and HCTZ



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.