

Presenter Disclosure

PRESENTER DISCLOSURE

Ariana M. Chao, PhD, CRNP, RN

Advisory Panel/Consultant: Boehringer Ingelheim; Eli Lilly and Company

Research Support: Eli Lilly and Company; National Institutes of Health

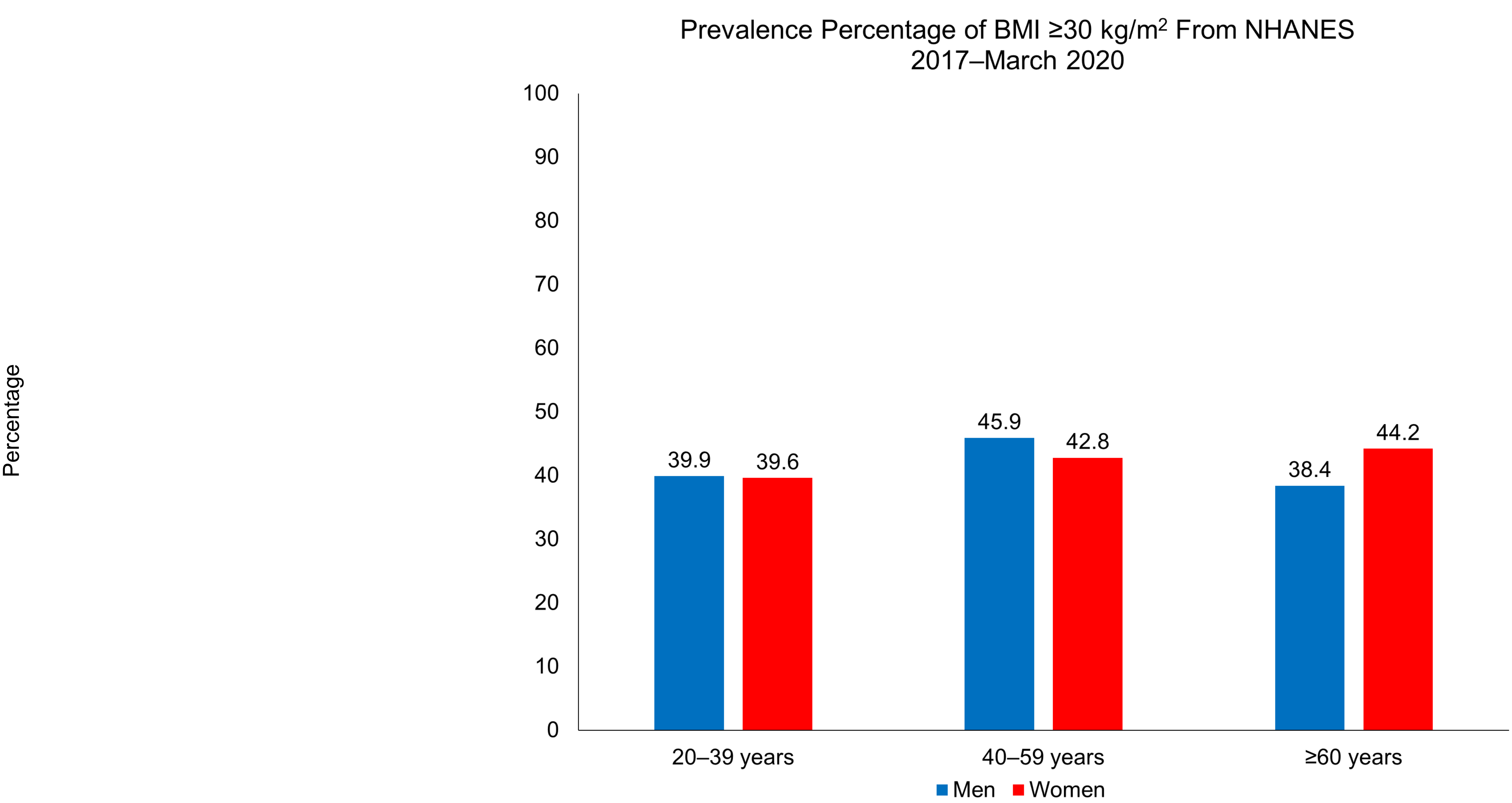
Body Weight Reduction Associated With Tirzepatide by Sex: A Subgroup Analysis of the SURMOUNT Clinical Trials

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Tammy Forrester², Farai Chigutsa²,
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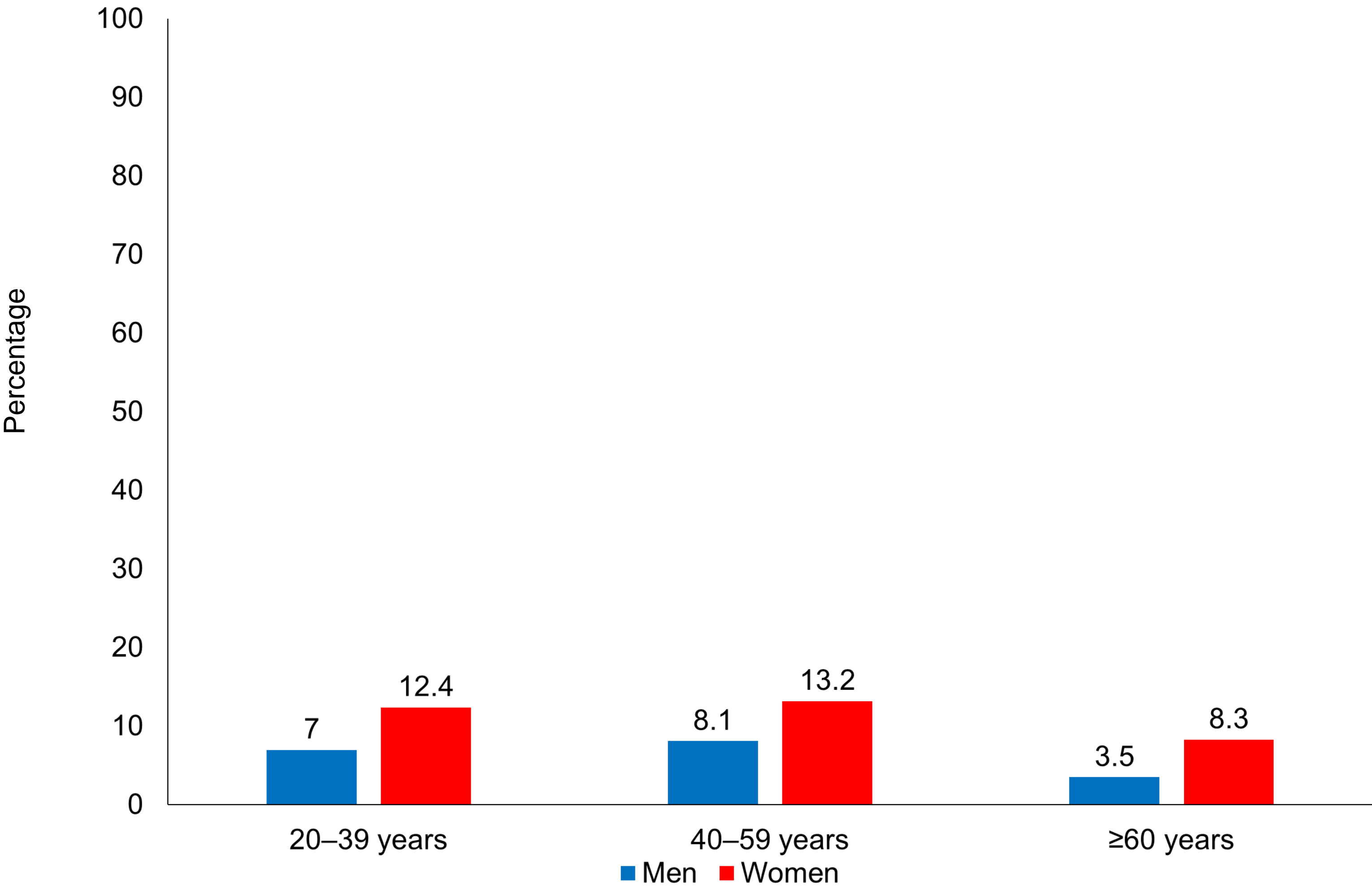
Sex Differences in Obesity and Treatment Outcomes



BMI, body mass index; NHANES, National Health and Nutrition Examination Survey.
Stierman B, et al. *Natl Health Stat Rep.* 2021;58:1–21; Williams RL, et al. *Obes Rev.* 2015;16(2):171–186.
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Sex Differences in Obesity and Treatment Outcomes

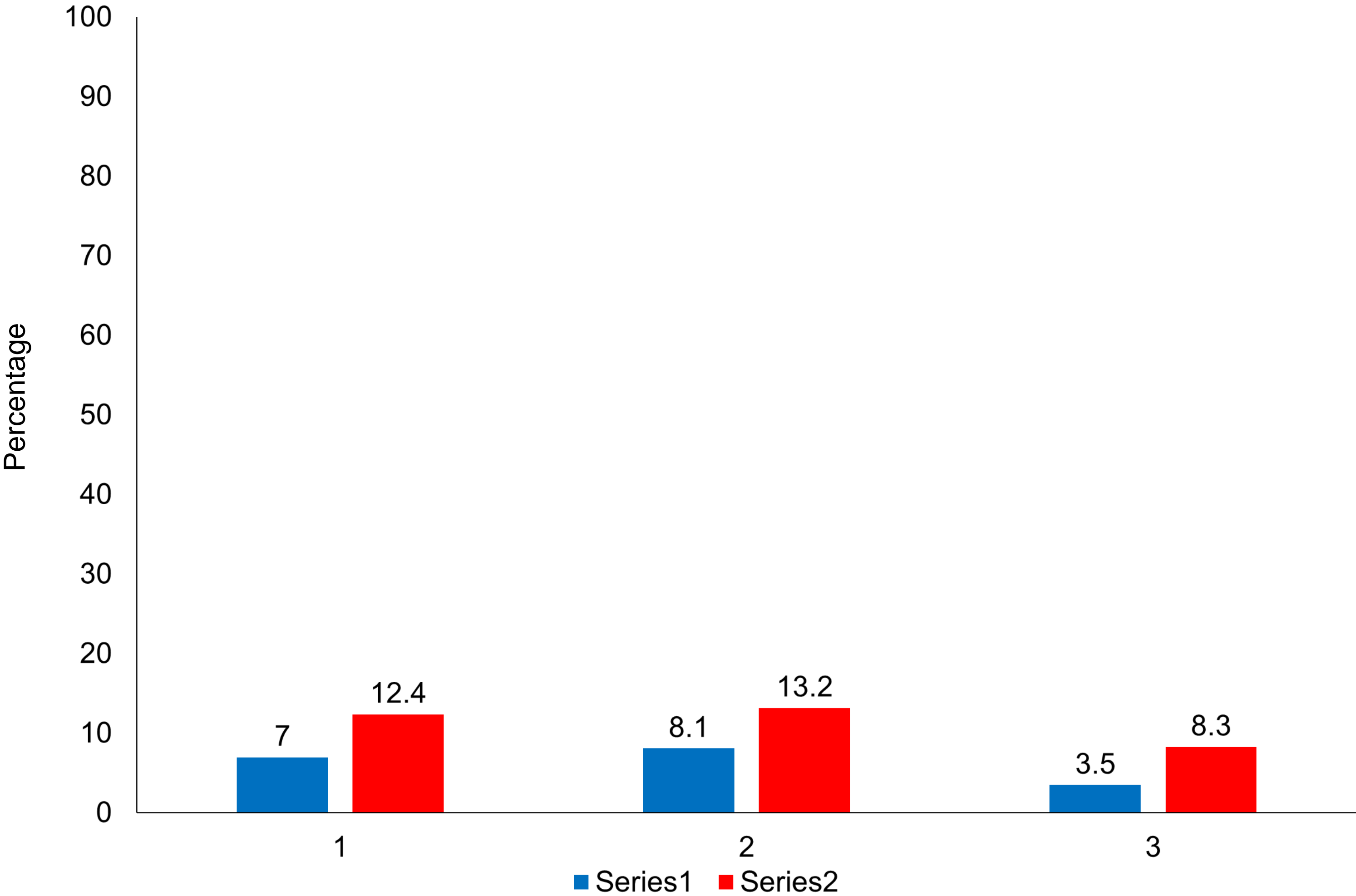
Prevalence Percentage of BMI ≥ 40 kg/m² From NHANES
2017–March 2020



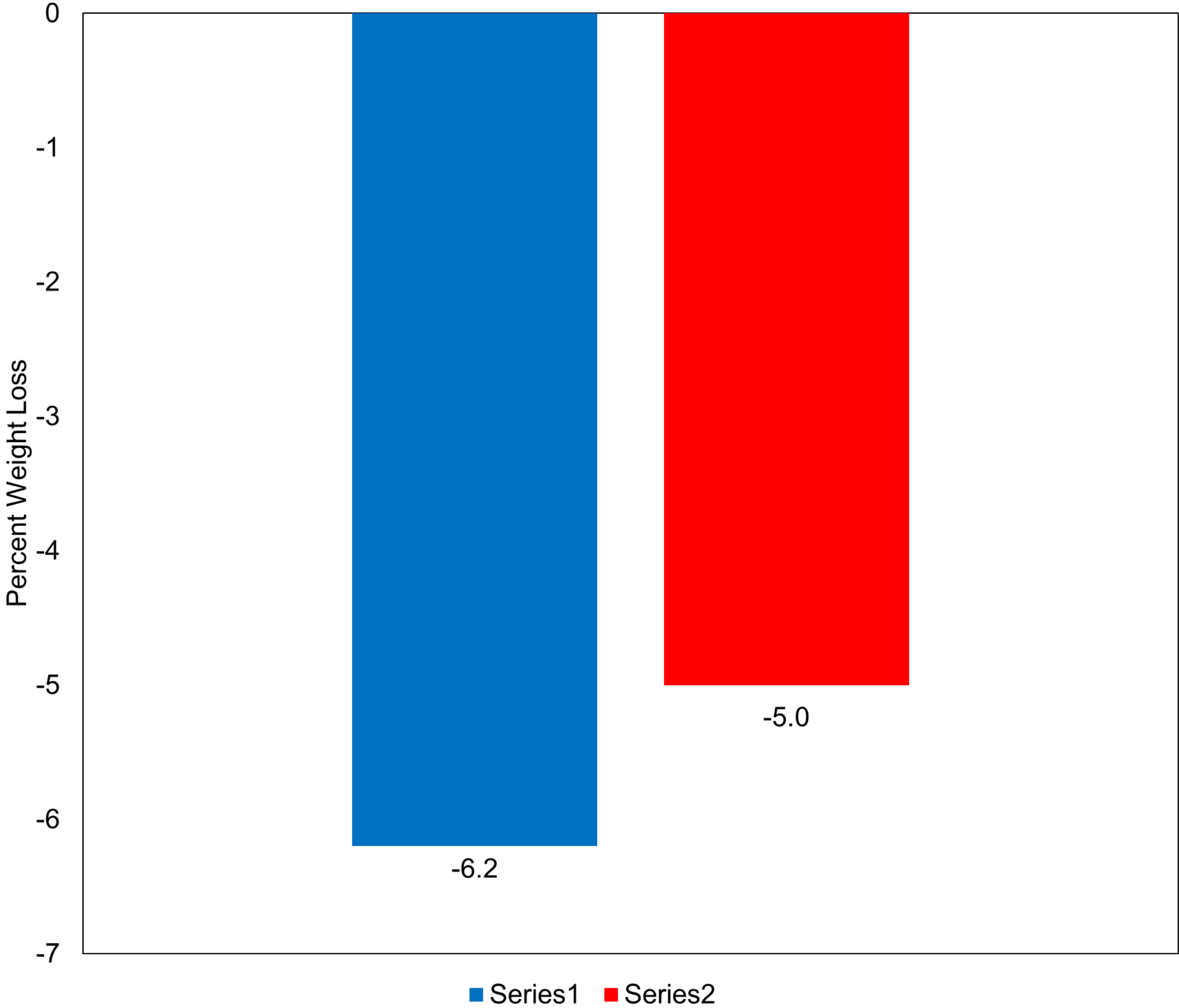
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Sex Differences in Obesity and Treatment Outcomes

Prevalence Percentage of BMI ≥ 40 kg/m² From NHANES 2017–March 2020



Mean Change in Percent Weight Loss From Meta-Analysis of Diet and/or Physical Activity Obesity Treatment Interventions

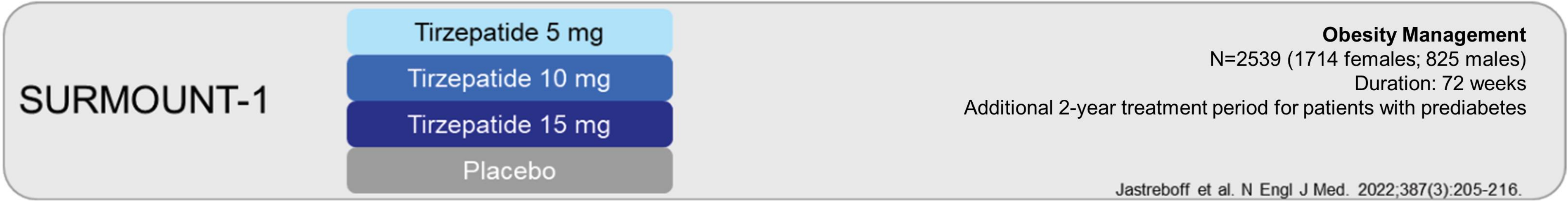


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Background

- Tirzepatide is a once-weekly glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptor agonist
- Treatment with tirzepatide in the SURMOUNT-1 to -4 trials demonstrated efficacy in weight reduction in adults with obesity and overweight, with or without type 2 diabetes
- A post hoc subgroup analysis was conducted to determine if the weight-lowering observations with tirzepatide varied by the sex of study participants

SURMOUNT Program Overview



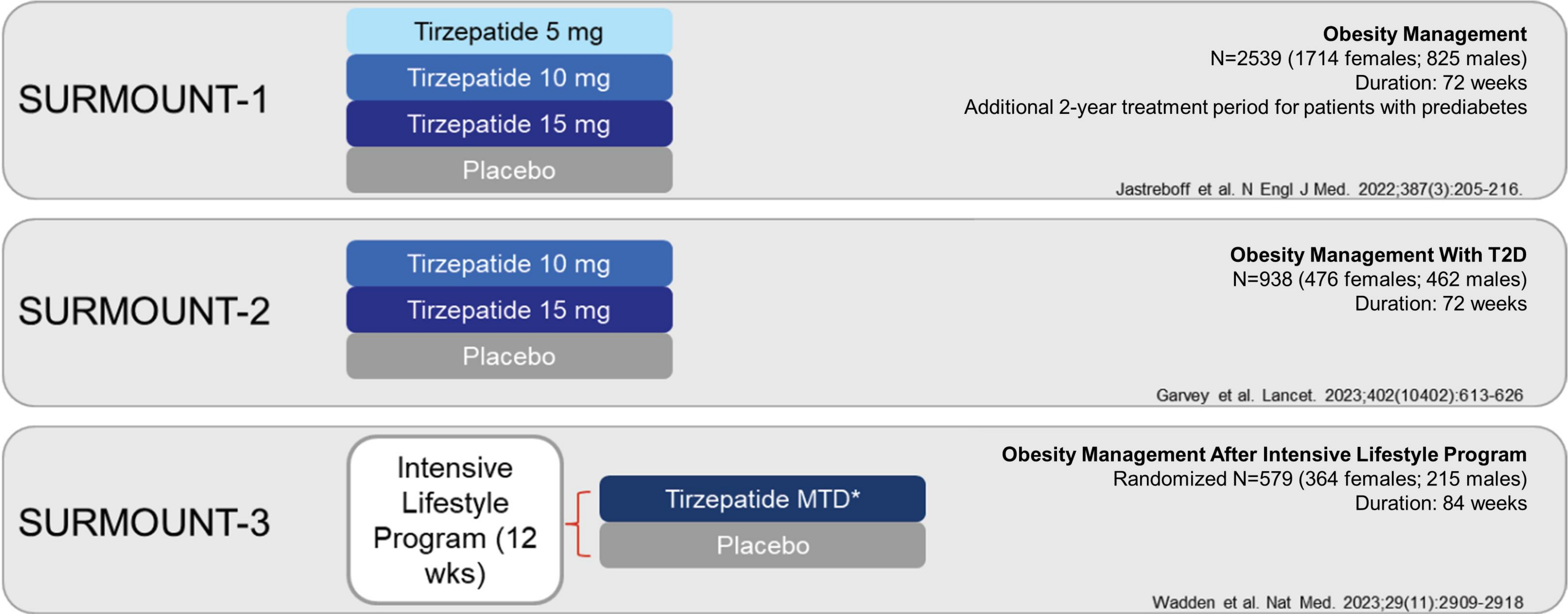
*MTD, maximal tolerated dose (10 mg or 15 mg).

SURMOUNT Program Overview

SURMOUNT-1	Tirzepatide 5 mg	Obesity Management N=2539 (1714 females; 825 males) Duration: 72 weeks Additional 2-year treatment period for patients with prediabetes Jastreboff et al. N Engl J Med. 2022;387(3):205-216.
	Tirzepatide 10 mg	
	Tirzepatide 15 mg	
	Placebo	
SURMOUNT-2	Tirzepatide 10 mg	Obesity Management With T2D N=938 (476 females; 462 males) Duration: 72 weeks Garvey et al. Lancet. 2023;402(10402):613-626
	Tirzepatide 15 mg	
	Placebo	

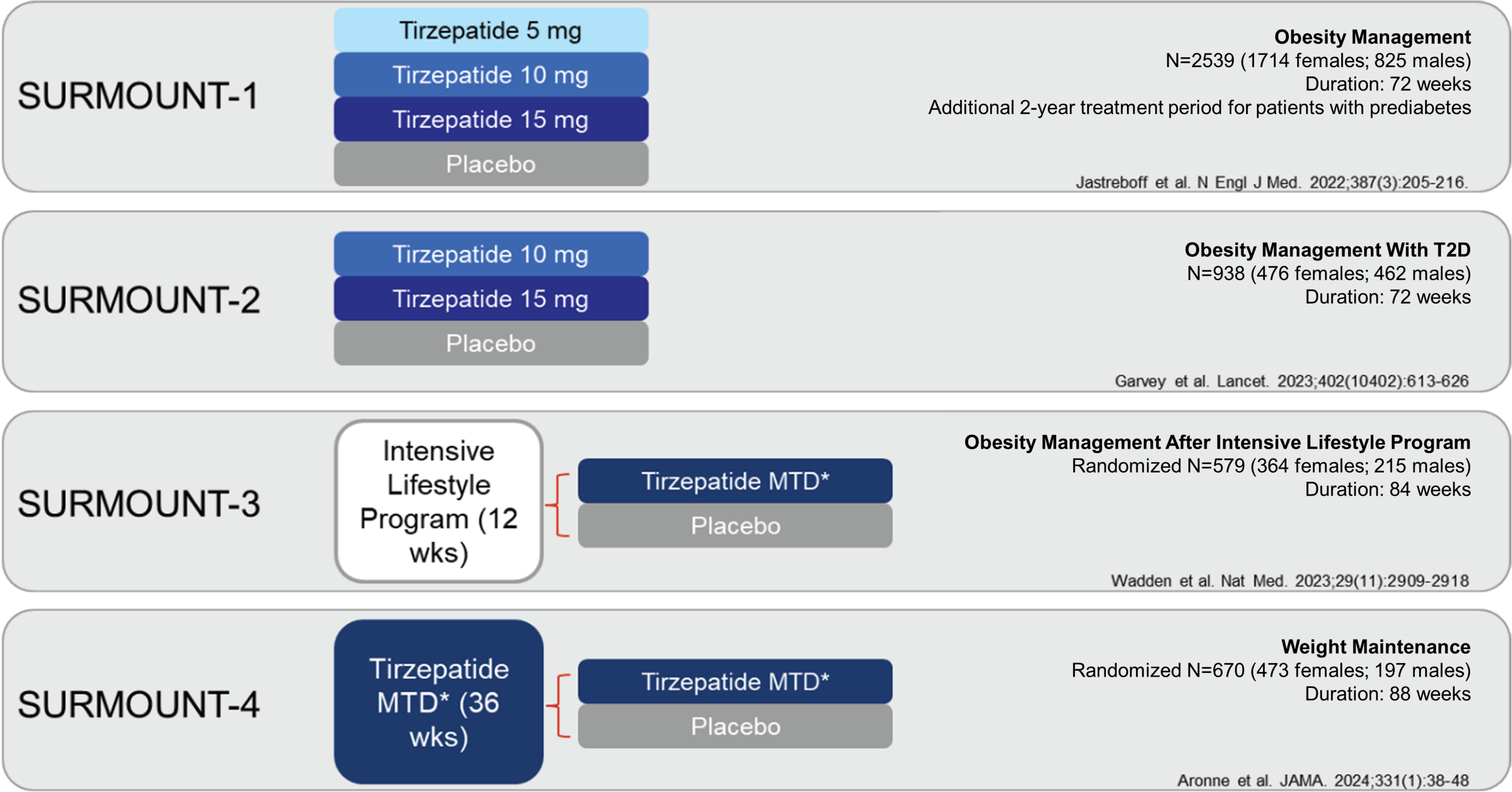
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SURMOUNT Program Overview



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SURMOUNT Program Overview



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Methods

- Participants in SURMOUNT-1 to -4 were categorized by sex
- This exploratory analysis examined percent change in body weight, using a mixed model for repeated measures (MMRM), and the proportion of participants achieving $\geq 5\%$, $\geq 10\%$, and $\geq 15\%$ reductions in body weight, using logistic regression, from randomization to:
 - Week 72 in SURMOUNT-1, -2, and -3, or
 - Week 88 (52 weeks after randomization) in SURMOUNT-4
- Safety data were examined by study, with the various doses used (tirzepatide 5 mg, 10 mg, 15 mg and the maximum tolerated dose [MTD]) combined into a single measure
- All analyses used the efficacy analysis data set (all randomized participants who received ≥ 1 dose of study treatment, excluding data after study drug discontinuation)

Baseline Characteristics

	SURMOUNT-1 (N=2539)		SURMOUNT-2 (N=938)		SURMOUNT-3 (N=579)		SURMOUNT-4 (N=670)	
	Females	Males	Females	Males	Females	Males	Females	Males
Sex, n (%)	1714 (67.5)	825 (32.5)	476 (50.7)	462 (49.3)	364 (62.9)	215 (37.1)	473 (70.6)	197 (29.4)
Age, mean, years	45.1	44.4	54.3	54.2	45.3	46.0	48.9	48.0

The proportion of males ranged from 29.4% to 49.3% across studies.

N, number of participants; n, number of participants in subgroup; BMI, body mass index.

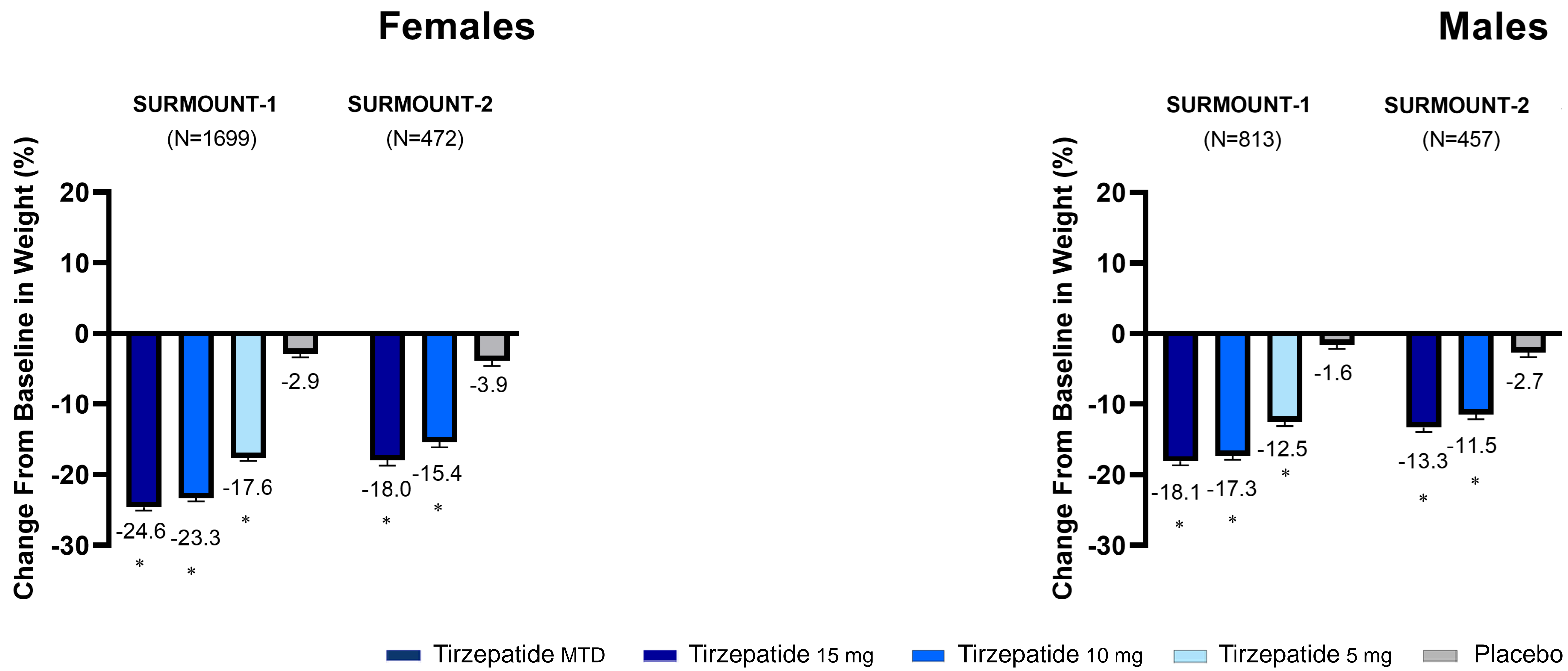
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Sex, n (%)	1714 (67.5)	825 (32.5)	476 (50.7)	462 (49.3)	364 (62.9)	215 (37.1)	473 (70.6)	197 (29.4)
Age, mean, years	45.1	44.4	54.3	54.2	45.3	46.0	48.9	48.0
White race, n (%)	1275 (74.4)	517 (62.7)	371 (77.9)	339 (73.4)	303 (83.2)	195 (90.7)	375 (79.3)	162 (82.2)
Body weight, mean, kg	99.8	115.2	94.8	106.8	95.4	112.9	79.6	98.6
Waist circumference, mean, cm	111.2	120.2	113.3	116.7	104.9	117.3	94.2	105.4
BMI, mean, kg/m²	38.2	37.6	36.7	35.4	36.1	35.8	30.1	31.4

N, number of participants; n, number of participants in subgroup; BMI, body mass index.

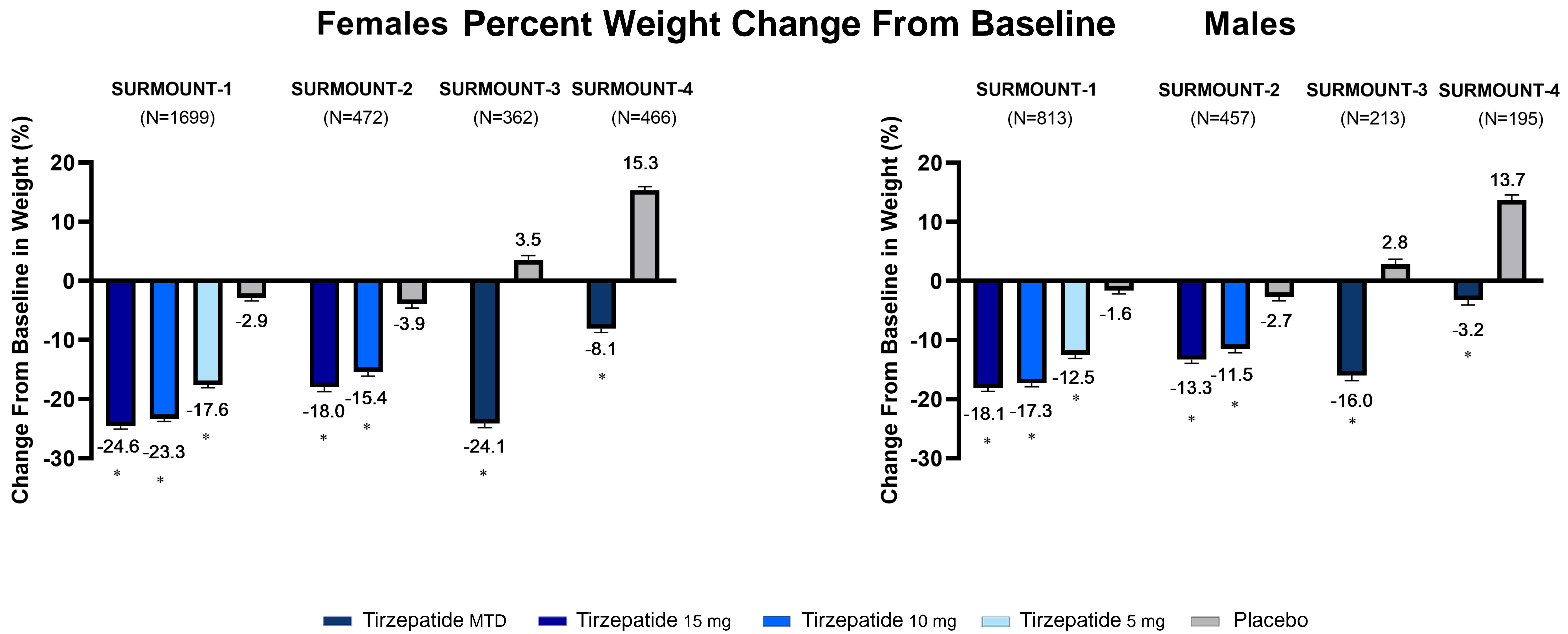
Tirzepatide Was Associated With Significant Weight Loss in Both Females and Males at All Doses

Percent Weight Change From Baseline



Data are shown as least-squares mean (standard error). * $P < 0.05$ for tirzepatide vs placebo. Analysis of the percent change in body weight from baseline was conducted using an MMRM. SURMOUNT-4 results are based on change from randomization (week 36 to week 88). N, number of participants.

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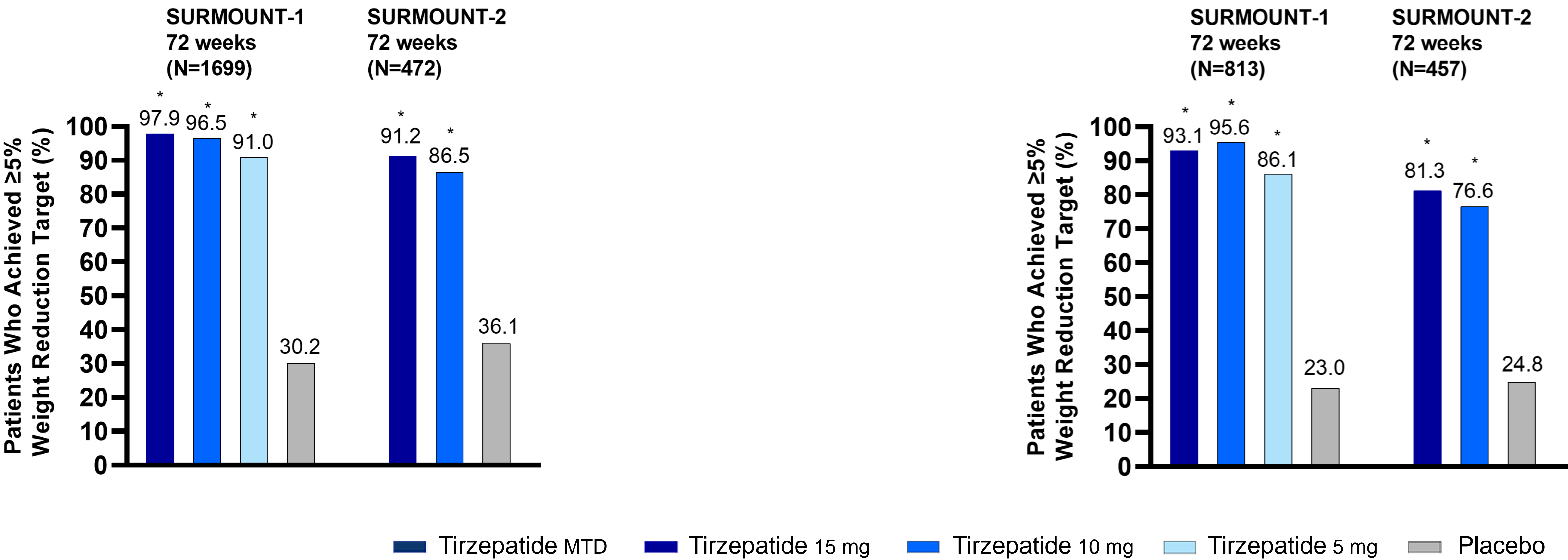
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Tirzepatide Was Associated With Achievement of Weight Reduction Thresholds in Both Females and Males

Proportion Achieving ≥5% Weight Reduction

Females

Males



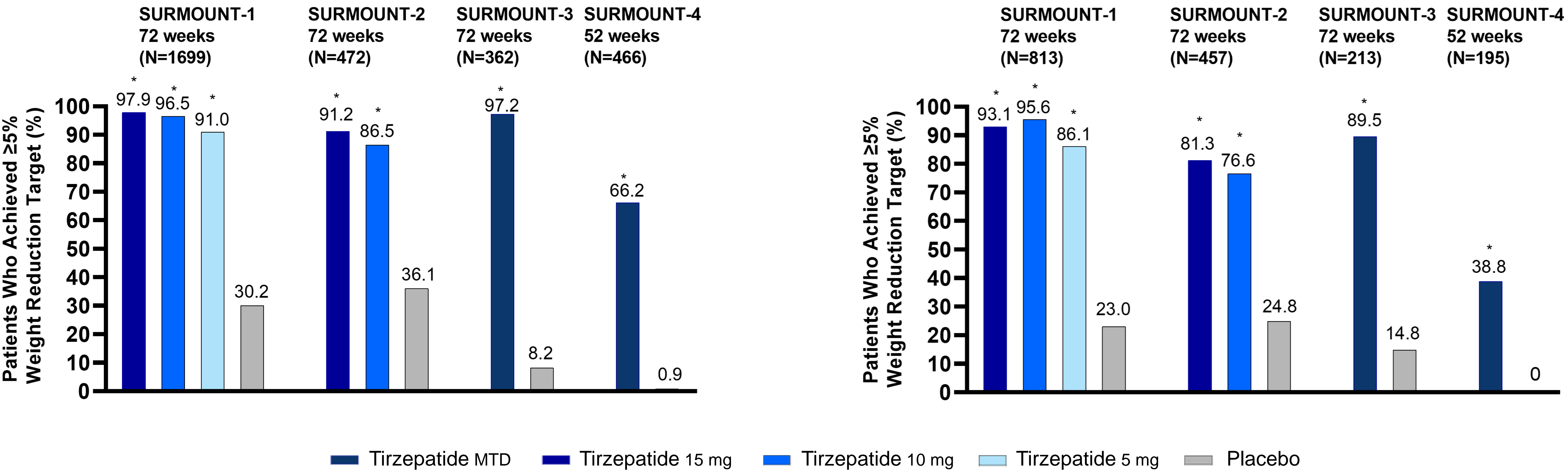
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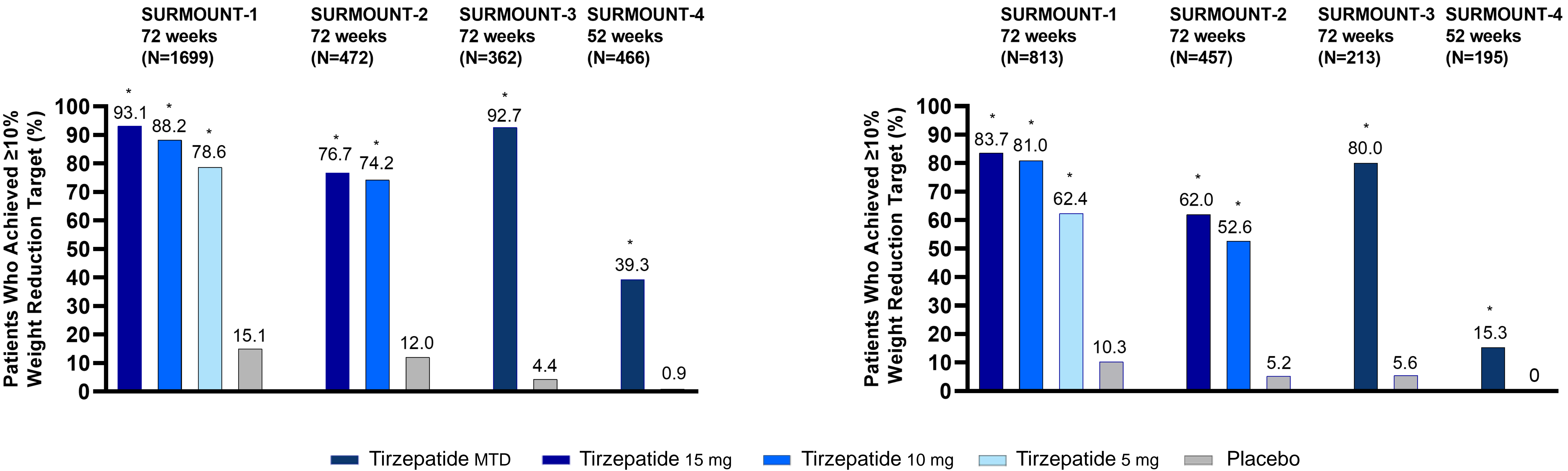
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Tirzepatide Was Associated With Achievement of Weight Reduction Thresholds in Both Females and Males

Proportion Achieving ≥10% Weight Reduction

Females

Males

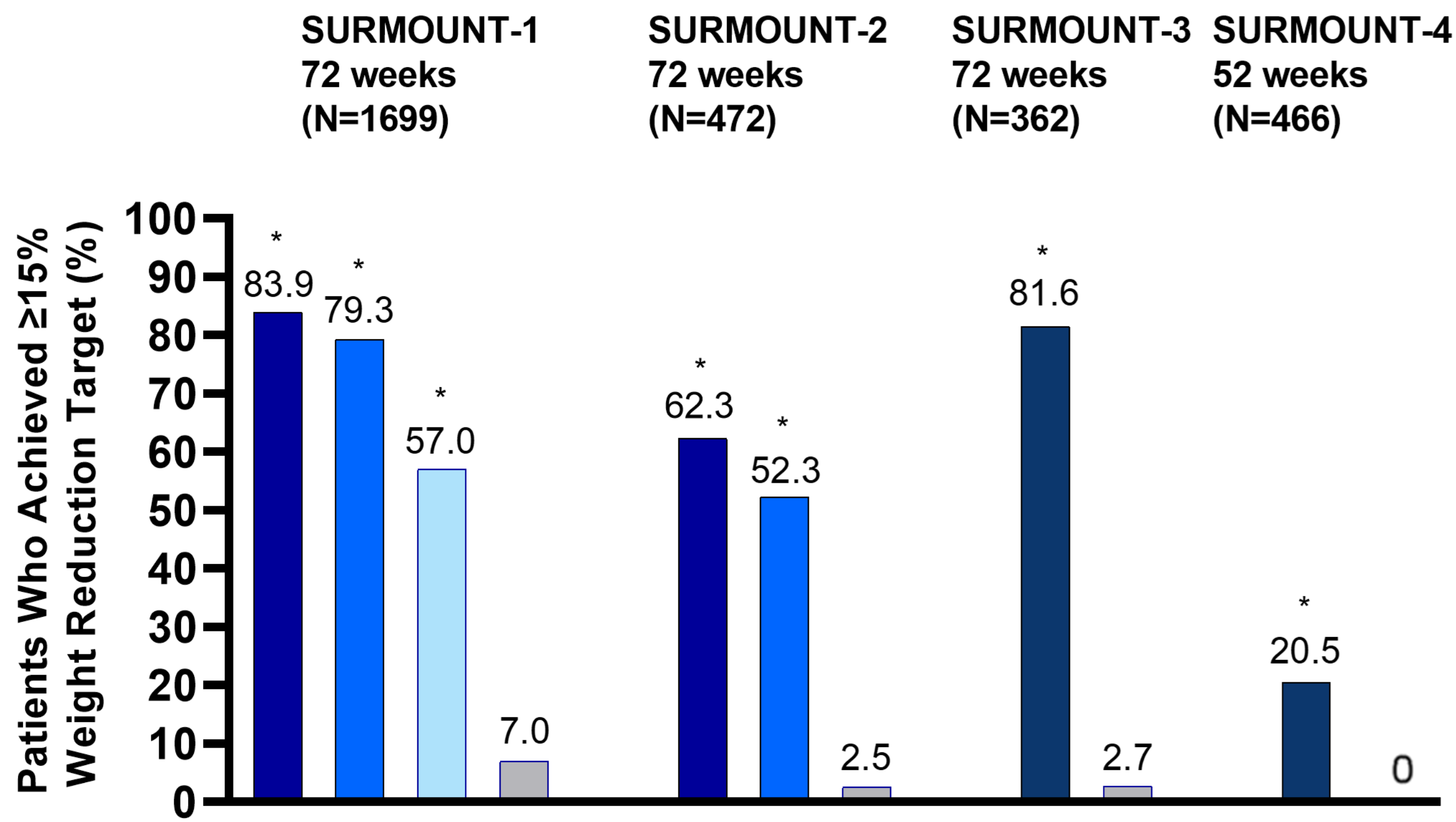


*P<0.05 for tirzepatide vs placebo. Analysis of the percent change in body weight from baseline was conducted using an MMRM. SURMOUNT-4 results are based on change from randomization (week 36 to week 88). N, number of participants.

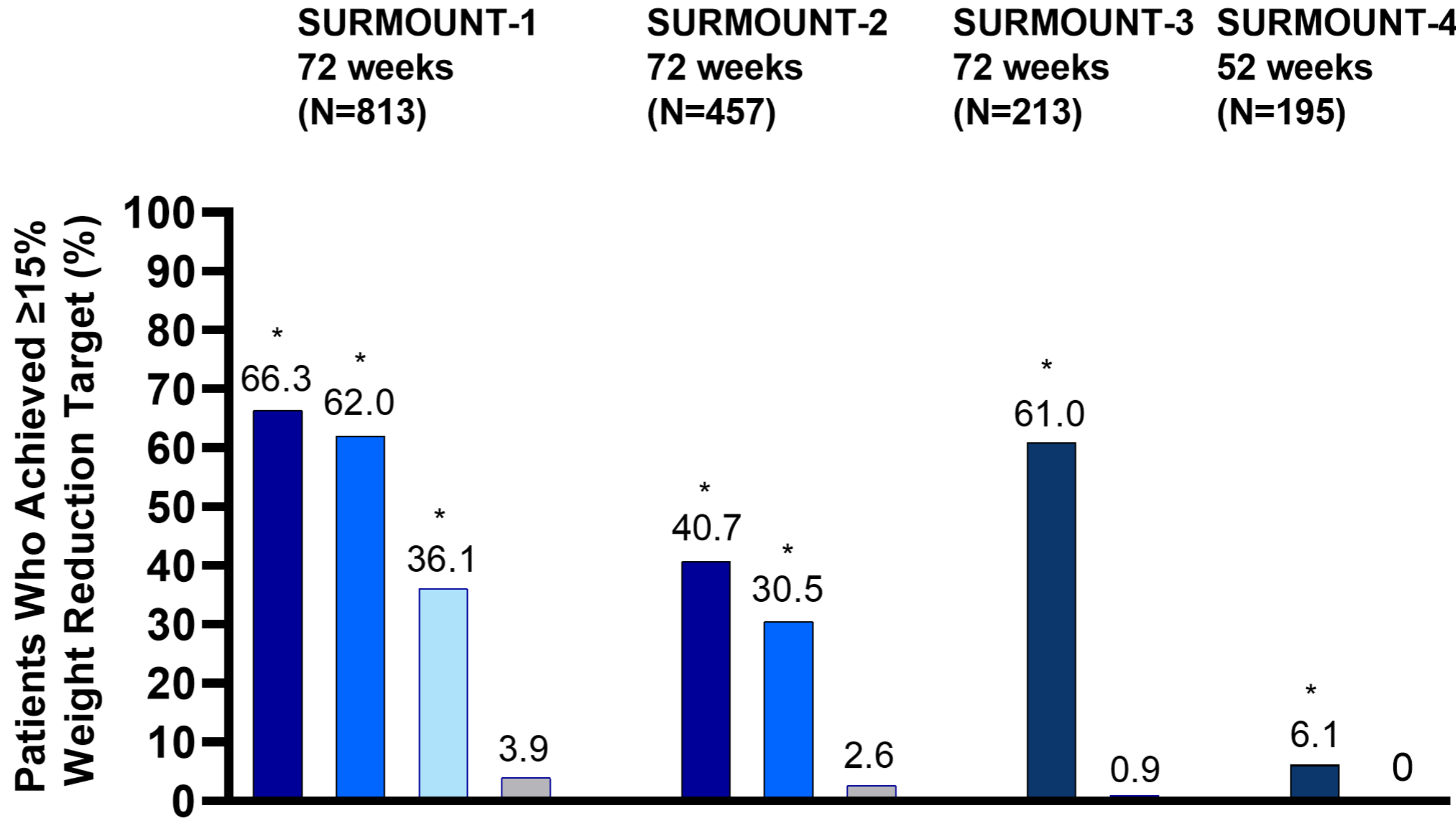
Tirzepatide Was Associated With Achievement of Weight Reduction Thresholds in Both Females and Males

Proportion Achieving ≥15% Weight Reduction

Females



Males



Tirzepatide MTD Tirzepatide 15 mg Tirzepatide 10 mg Tirzepatide 5 mg Placebo

*P<0.05 for tirzepatide vs placebo. Analysis of the percent change in body weight from baseline was conducted using an MMRM. SURMOUNT-4 results are based on change from randomization (week 36 to week 88). N, number of participants.

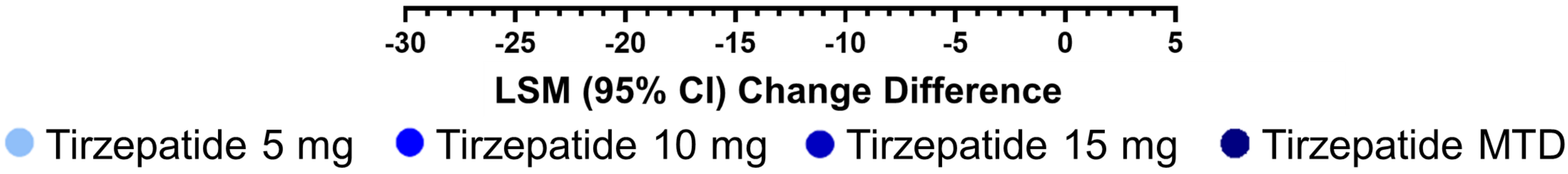
Females Receiving Tirzepatide Lost More Weight Than Males Receiving Tirzepatide

Differences in Percent Change in Body Weight for Tirzepatide Treatment Groups

Study	Sex	Treatment	n	Weight Loss	Test for Interaction
SURMOUNT-1	Female	Placebo	309		Treatment*Sex: P<0.001
		Tirzepatide 5 mg	364	-14.7 (-16.1, -13.4)	
		Tirzepatide 10 mg	361	-20.4 (-21.8, - 19.0)	
	Male	Tirzepatide 15 mg	360	-21.8 (-23.1, - 20.4)	
		Placebo	162		
		Tirzepatide 5 mg	175	-10.9 (-12.6, -9.3)	
SURMOUNT-2	Female	Tirzepatide 10 mg	142	-11.5 (-13.5, -9.6)	Treatment*Sex: P=0.03
		Tirzepatide 15 mg	133	-14.1 (-16.1, -12.2)	
		Placebo	131		
	Male	Tirzepatide 10 mg	140	-8.8 (-10.6, -7.0)	
		Tirzepatide 15 mg	132	-10.6 (-12.4, -8.8)	
		Placebo	127		
SURMOUNT-3	Female	Tirzepatide MTD	142	-27.6 (-29.7, -25.6)	Treatment*Sex: P<0.001
		Placebo	75		
	Male	Tirzepatide MTD	85	-18.9 (-21.3, -16.4)	
		Placebo	82		
SURMOUNT-4	Female	Tirzepatide MTD	211	-23.4 (-25.2, -21.7)	Treatment*Sex: P<0.001
		Placebo	82		
	Male	Tirzepatide MTD	88	-16.9 (-19.3, -14.5)	
		Placebo	88		

Data show the difference in weight loss with tirzepatide relative to placebo at week 72 for SURMOUNT-1 to -3 or from week 36 to 88 for SURMOUNT-4.

CI, confidence interval; LSM, least-squares mean; n, number of participants.

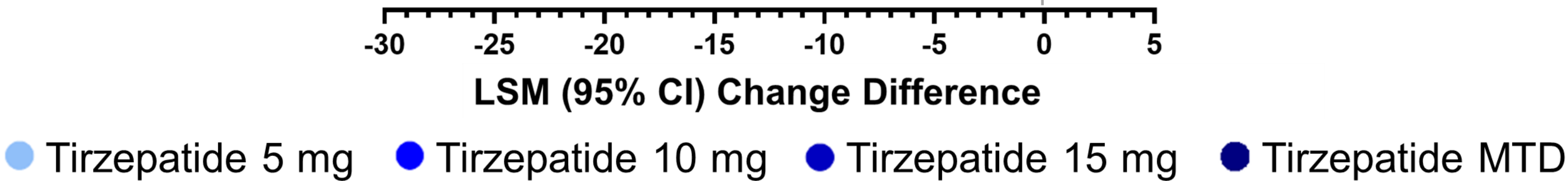


Females Receiving Tirzepatide Lost More Weight Than Males Receiving Tirzepatide

Differences in Percent Change in Body Weight for Tirzepatide Treatment Groups

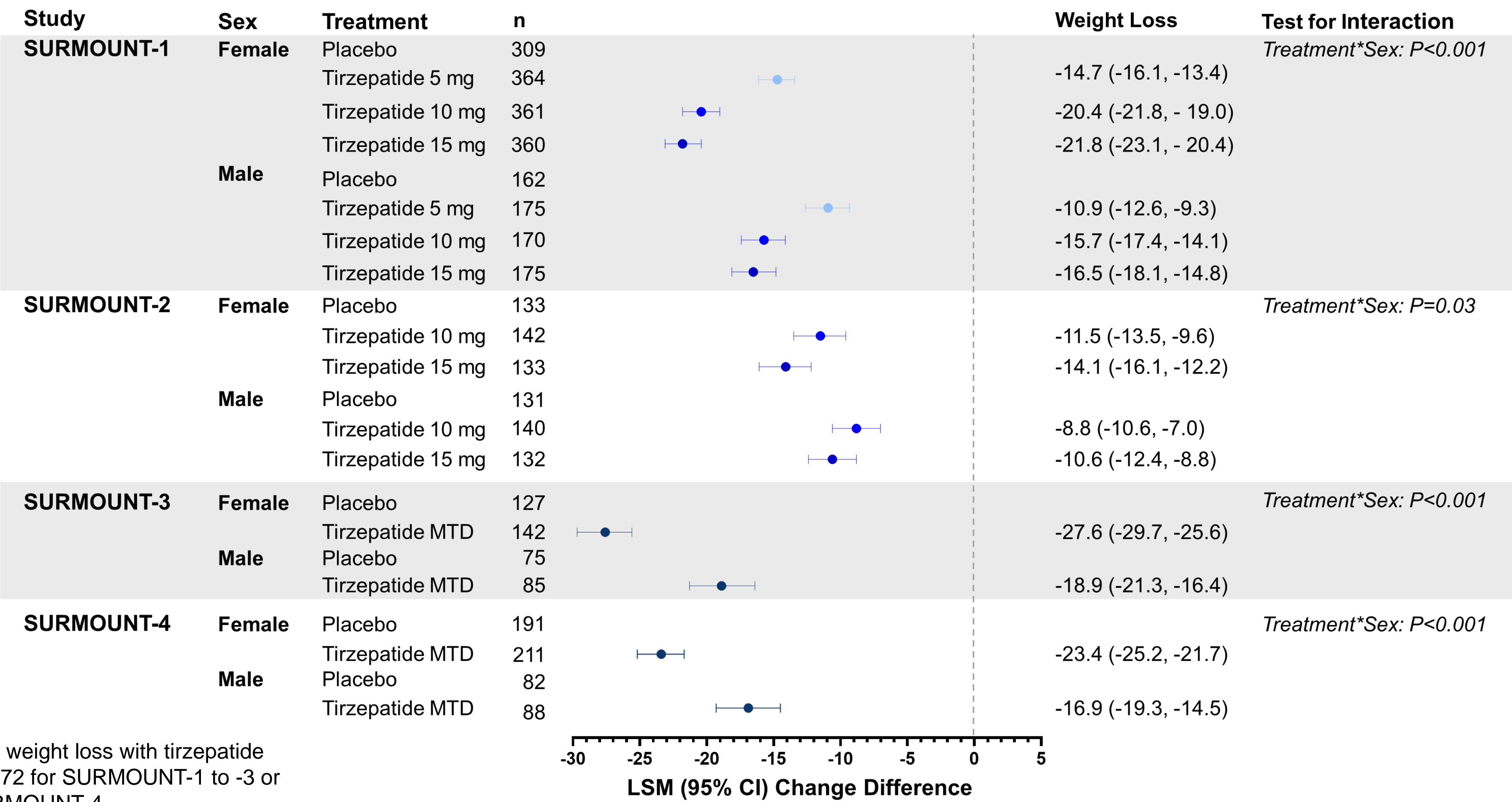
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	Male	Tirzepatide 15 mg	360	-21.8 (-23.1, - 20.4)	
		Placebo	162		
		Tirzepatide 5 mg	175	-10.9 (-12.6, -9.3)	
		Tirzepatide 10 mg	170	-15.7 (-17.4, -14.1)	
		Tirzepatide 15 mg	175	-16.5 (-18.1, -14.8)	
SURMOUNT-2	Female	Placebo	133		Treatment*Sex: P=0.03
		Tirzepatide 10 mg	142	-11.5 (-13.5, -9.6)	
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	Male	Placebo	131		
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		Tirzepatide MTD	85	-18.9 (-21.3, -16.4)	
SURMOUNT-4	Female	Placebo	191		Treatment*Sex: P<0.001
		Tirzepatide MTD	211	-23.4 (-25.2, -21.7)	
	Male	Placebo	82		
		Tirzepatide MTD	88	-16.9 (-19.3, -14.5)	

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CI, confidence interval; LSM, least-squares mean; n, number of participants.



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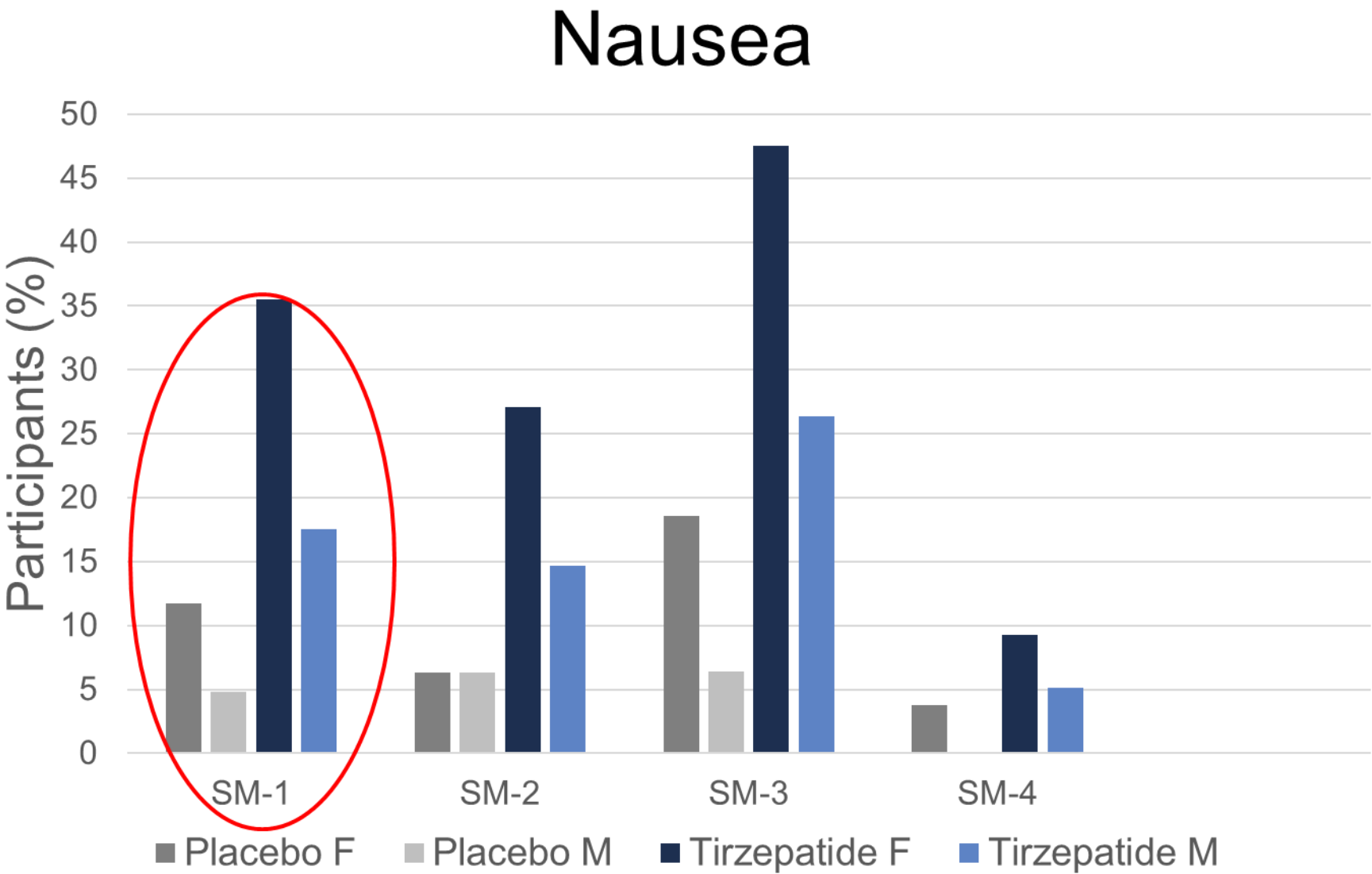


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Nausea and Vomiting Were Consistently Reported More Frequently in Females than Males

Adverse Reactions

FEMALES	Placebo, % of Participants				Tirzepatide (Pooled), % of Participants			
Preferred Term	SM-1 (n=436)	SM-2 (n=159)	SM-3 (n=183)	SM-4 (n=237)	SM-1 (n=1278)	SM-2 (n=317)	SM-3 (n=181)	SM-4* (n=236)
Nausea	11.7	6.3	18.6	3.8	35.5	27.1	47.5	9.3



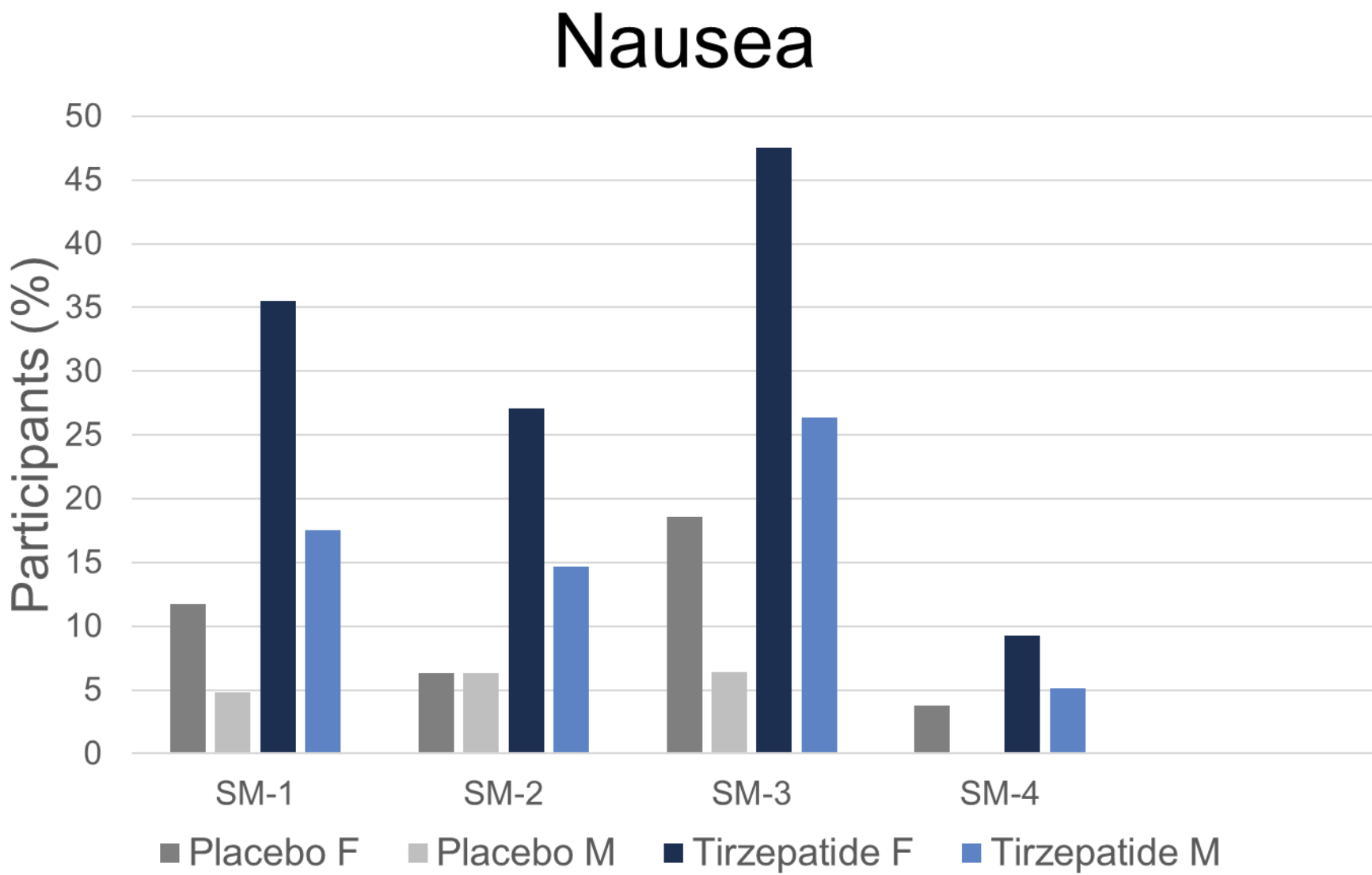
MALES	Placebo, % of Participants				Tirzepatide (Pooled), % of Participants			
Preferred Term	SM-1 (n=207)	SM-2 (n=156)	SM-3 (n=109)	SM-4 (n=98)	SM-1 (n=618)	SM-2 (n=306)	SM-3 (n=106)	SM-4* (n=99)
Nausea	4.8	6.4	6.4	0	17.5	14.7	26.4	5.1

*SURMOUNT-4 included a 36-week open label period of TZP treatment. Participants entering the double-blind period were already established on maximum tolerated dose of TZP. Gastrointestinal events occurred more frequently during the dose-escalation phase of the open-label period and hence were not captured as frequently after week 36.

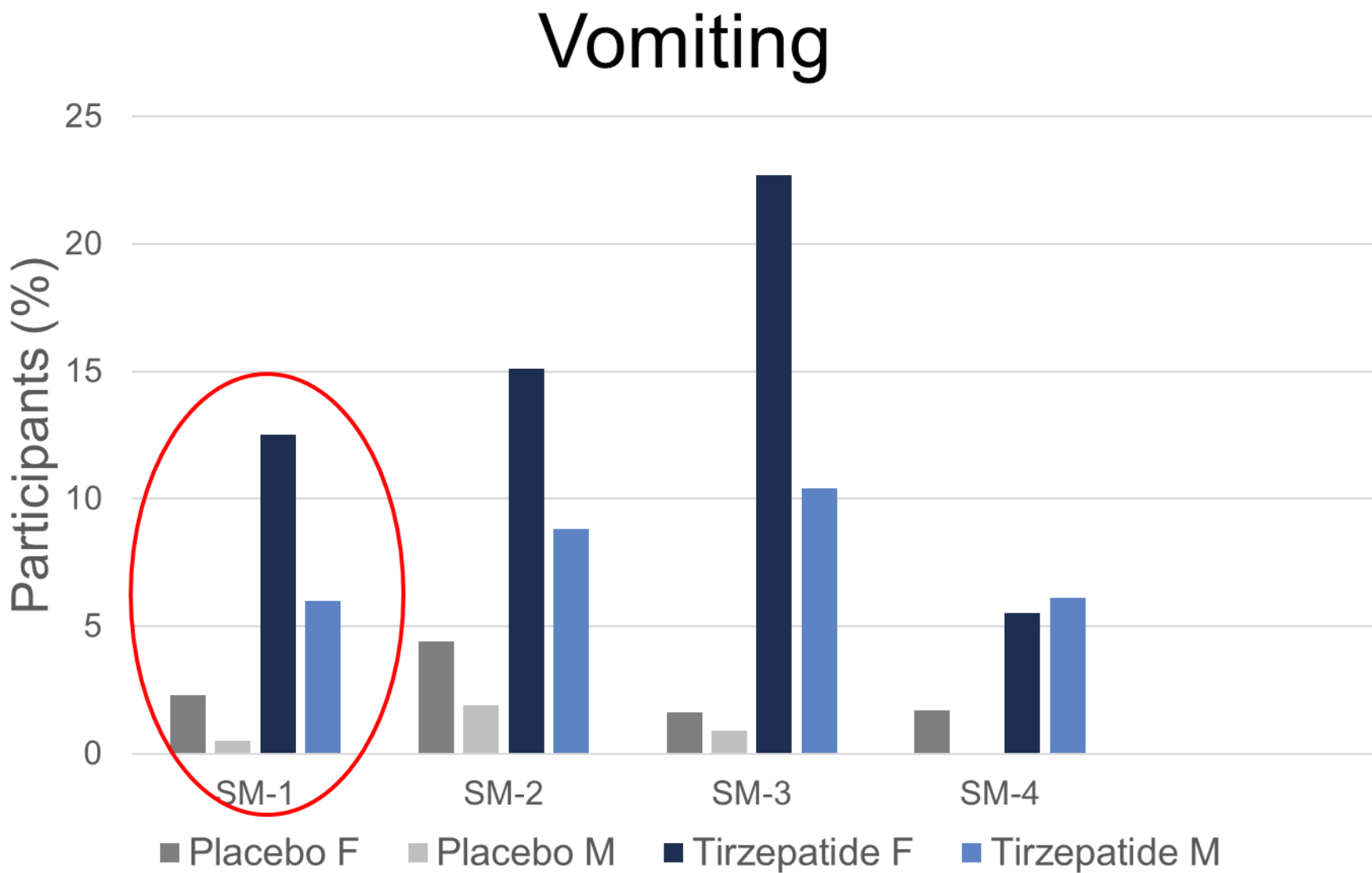
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Nausea	11.7	6.3	18.6	3.8	35.5	27.1	47.5	9.3
Diarrhea	8.3	9.4	13.1	4.6	21.9	19.6	30.4	11.0
Constipation	6.9	3.8	9.8	2.5	16.8	8.8	24.9	3.8
Vomiting	2.3	4.4	1.6	1.7	12.5	15.1	22.7	5.5
Dyspepsia	5.3	4.4	4.4	0	10.9	8.2	9.9	0.4
Decreased appetite	3.4	3.1	4.9	0.4	10.7	8.5	10.5	2.1



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Preferred Term	SM-1 (n=207)	SM-2 (n=156)	SM-3 (n=109)	SM-4 (n=98)	SM-1 (n=618)	SM-2 (n=306)	SM-3 (n=106)	SM-4* (n=99)
Nausea	4.8	6.4	6.4	0	17.5	14.7	26.4	5.1
Diarrhea	5.3	8.3	2.8	5.1	19.1	21.9	32.1	10.1
Constipation	3.4	4.5	1.8	2.0	12.0	8.2	19.8	3.0
Vomiting	0.5	1.9	0.9	0	6.0	8.8	10.4	6.1
Dyspepsia	1.9	1.9	0.9	1.0	8.1	6.2	8.5	0
Decreased appetite	2.9	1.3	2.8	3.1	7.9	11.1	7.5	2.0



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Conclusion

- In this exploratory analysis, all tirzepatide doses were associated with a significant reduction in body weight in both males and females in comparison to placebo
- A higher proportion of females and males achieved weight reduction thresholds with tirzepatide versus placebo
- Body weight reduction was associated with sex, and tirzepatide was associated with greater weight reduction in females than in males

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