

# Why are treatment targets important if obesity is not one disease?

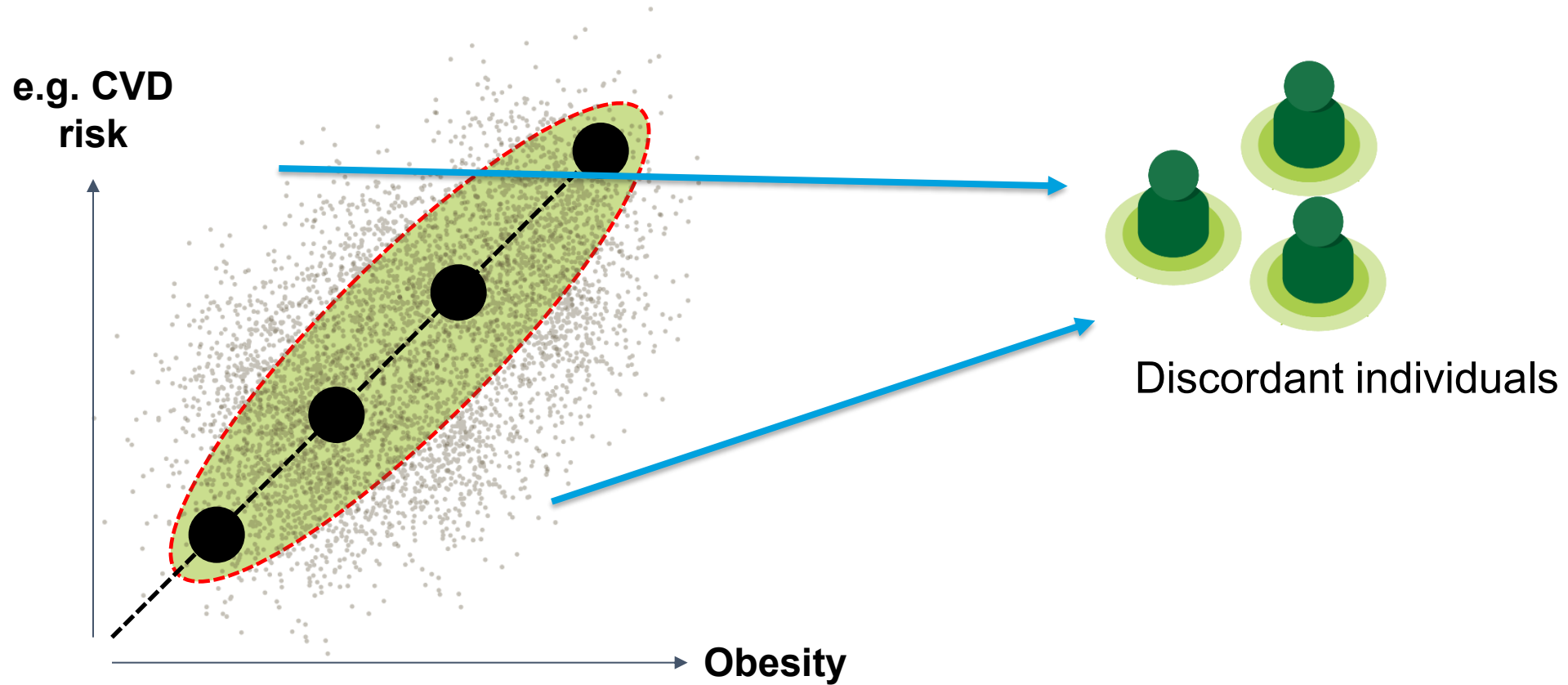
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Dublin  
Ulster University



Scene of the Plague in Florence in 1348 Described by Boccaccio by Baldassarre Calamai

# Obesity is likely more than one disease



**Weight**  
 120 ✓  
 kg

**Height**  
 170 ✓  
 cm

**Age**  
 65 ✓  
 years

Non-smoker  Smoker

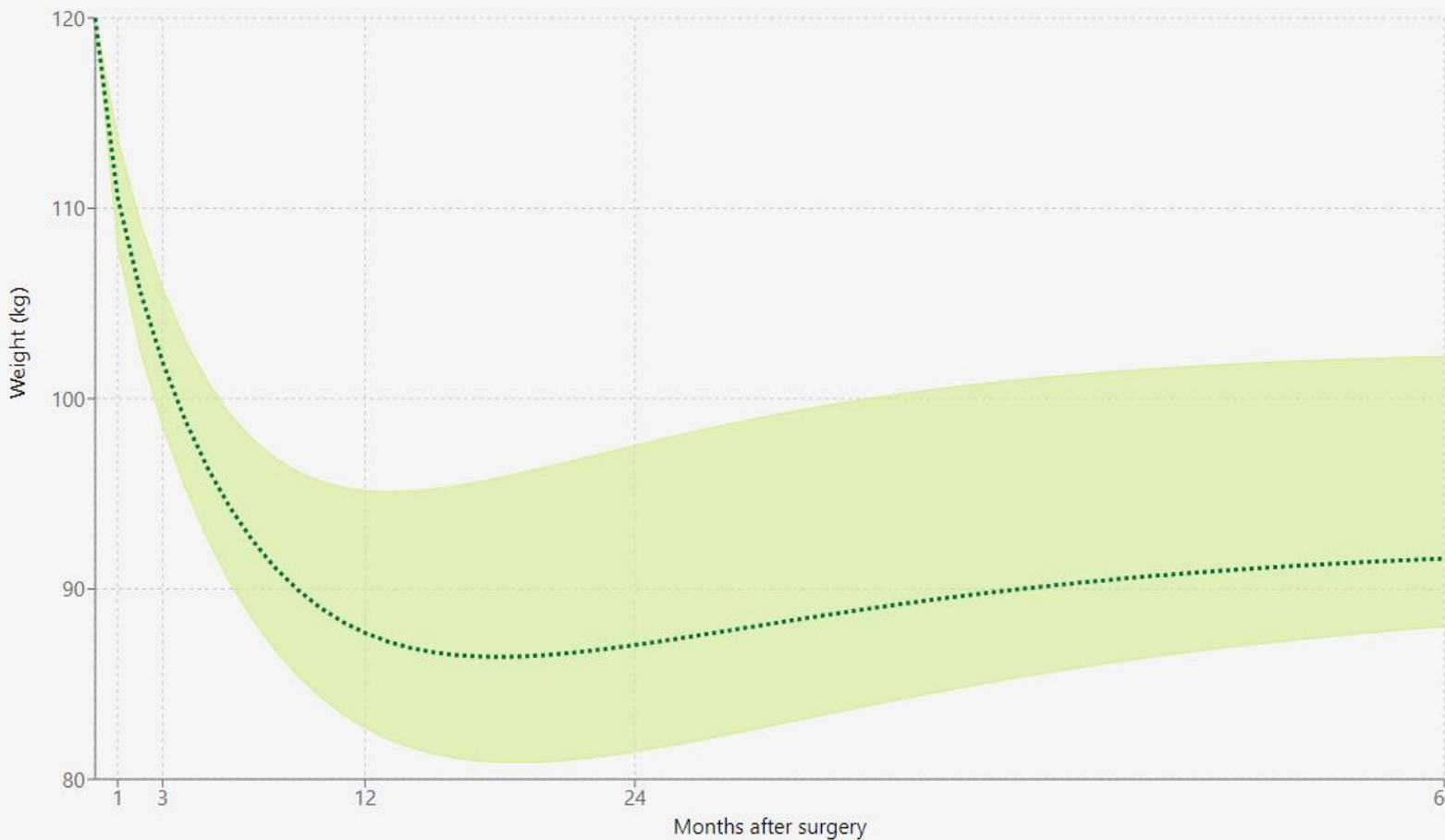
**Type 2 diabetes**  
 Diabetes ✓ ▾

**Diabetes duration**  
 10 ✓  
 years

**Type of intervention**  
 Gastric Bypass ✓ ▾

	Weight (kg)	Height (cm)	Age (years)	Smoker	Type 2 diabetes	Diabetes duration (years)	Type of intervention
<b>Current prediction</b>	120	170	65	Yes	Diabetes	10	Gastric Bypass

Weight ▾



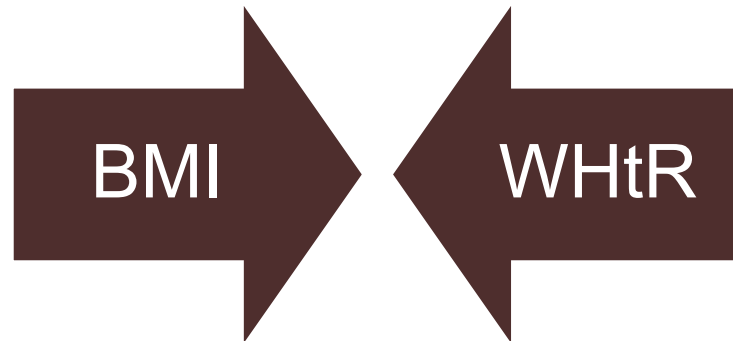
Prediction of weight trajectory after surgery

**Predict trajectory**

# Proposed Obesity Treat to Target thresholds

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- Busetto, L et al. ECO 2024
- Investigated changes in BMI and WHtR with 10-year ORC risk
- >45K UK adults, 41% Overweight, 59% Obesity



- Results: **WHtR <0.53** and/or **BMI <27 kg/m<sup>2</sup>** after weight loss
  - Predictors of low risk for incident T2D, HTN, hip/knee OA, ASCVD

ASCVD = Atherosclerotic cardiovascular disease; BMI = body mass index; HTN = hypertension; OA = osteoarthritis; ORC = obesity-related complication; T2D = type 2 diabetes; WHtR = waist to height ratio.

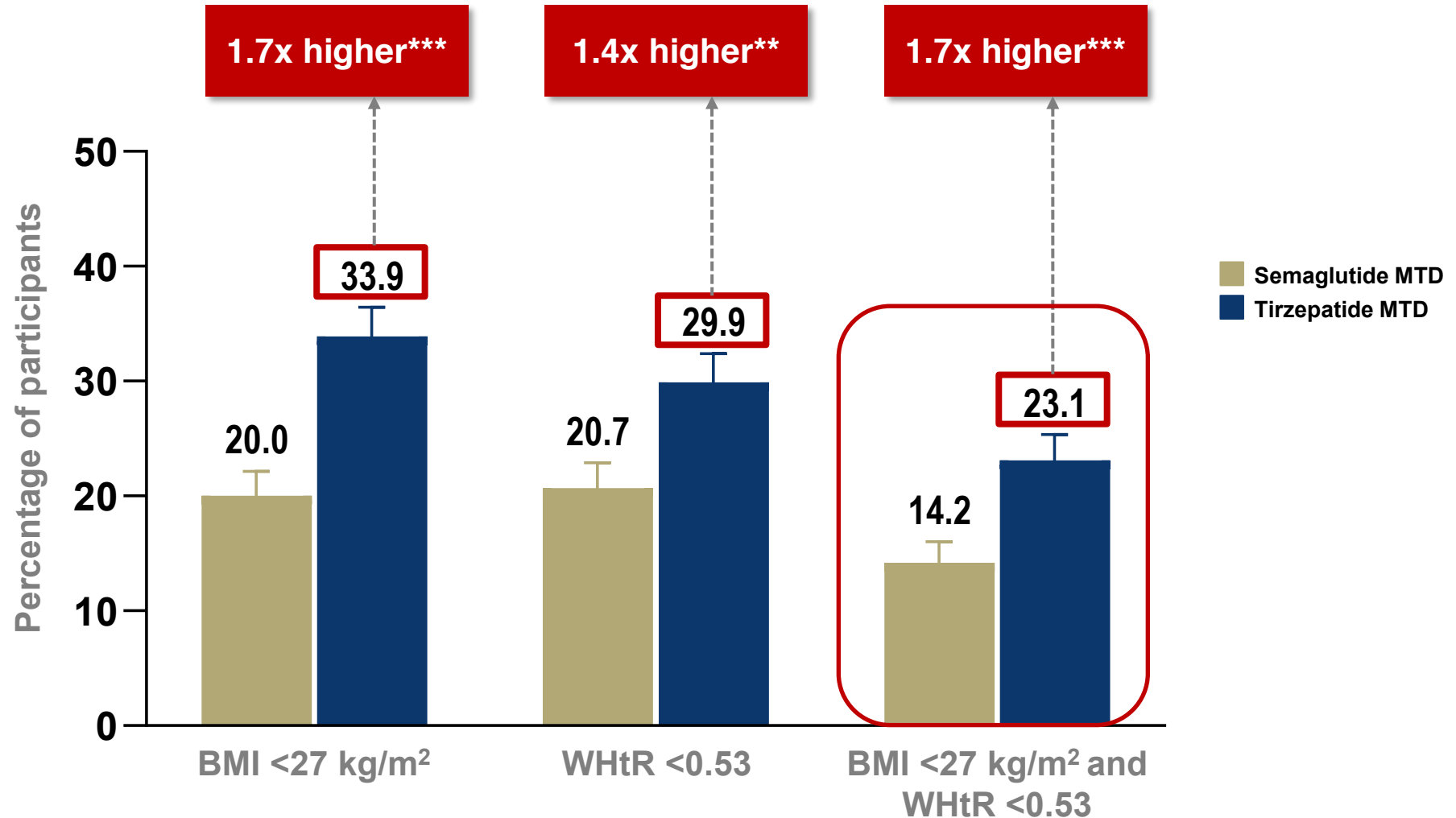
<sup>1</sup>Busetto L, et al. AS07.02. Obes Facts 2024; 17 (supp 1):56.

# Objective

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- In a post hoc analysis of the SURMOUNT-5 trial, compare the proportion of participants treated with tirzepatide vs semaglutide who achieve the TtT thresholds of WHtR <0.53 and/or BMI <27 kg/m<sup>2</sup>
- Describe in the participants who achieve the TtT thresholds the proportion who maintain or achieve normalization of cardiometabolic parameters
  - Normoglycemia (HbA1c <5.7% and FSG <100 mg/dL)
  - Blood pressure <130/80 mmHg
  - Triglycerides <150 mg/dL
  - HDL (female ≥50 mg/dL, male ≥40 mg/dL)

# Percent of Participants Reaching Treat to Target Thresholds at Week 72

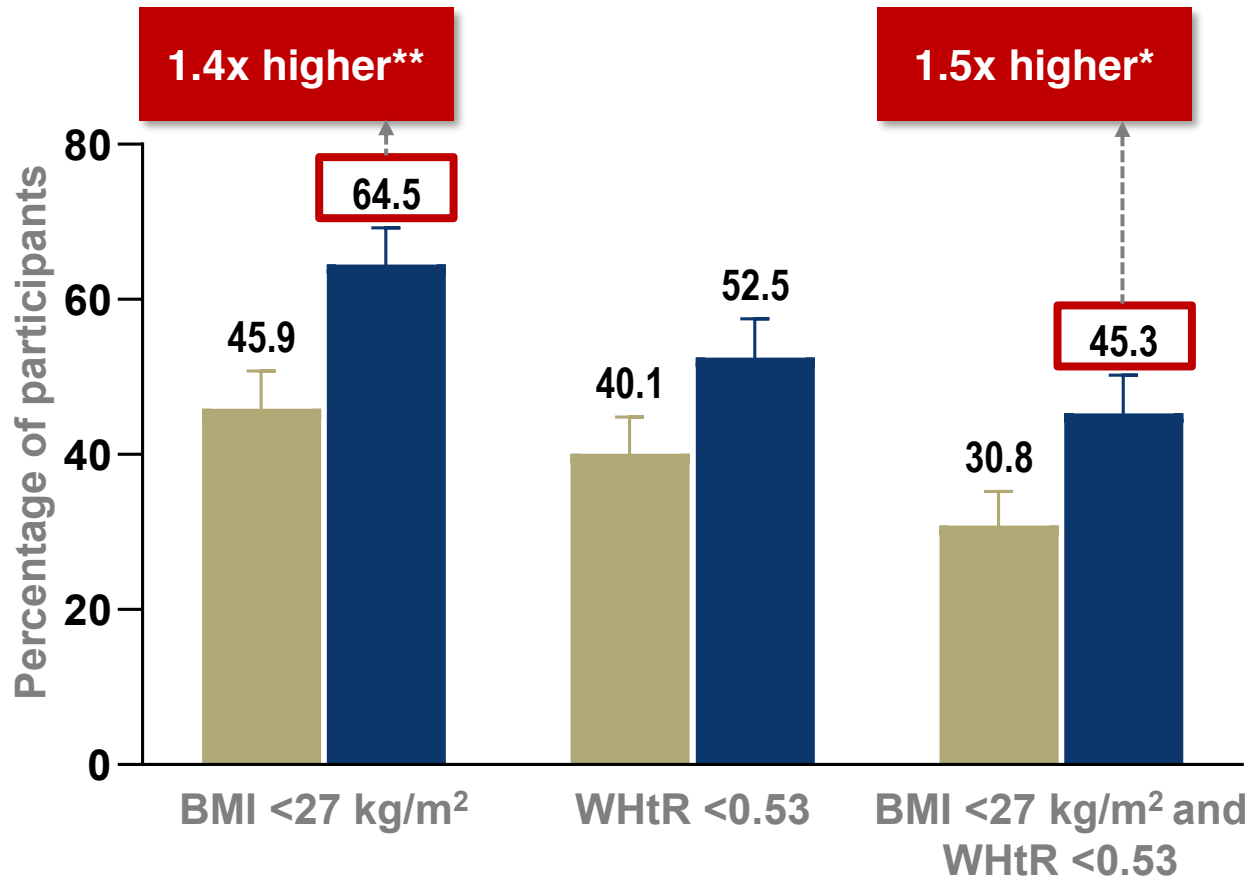


\*\*p<0.01 vs semaglutide. \*\*\*p<0.001 vs. semaglutide.

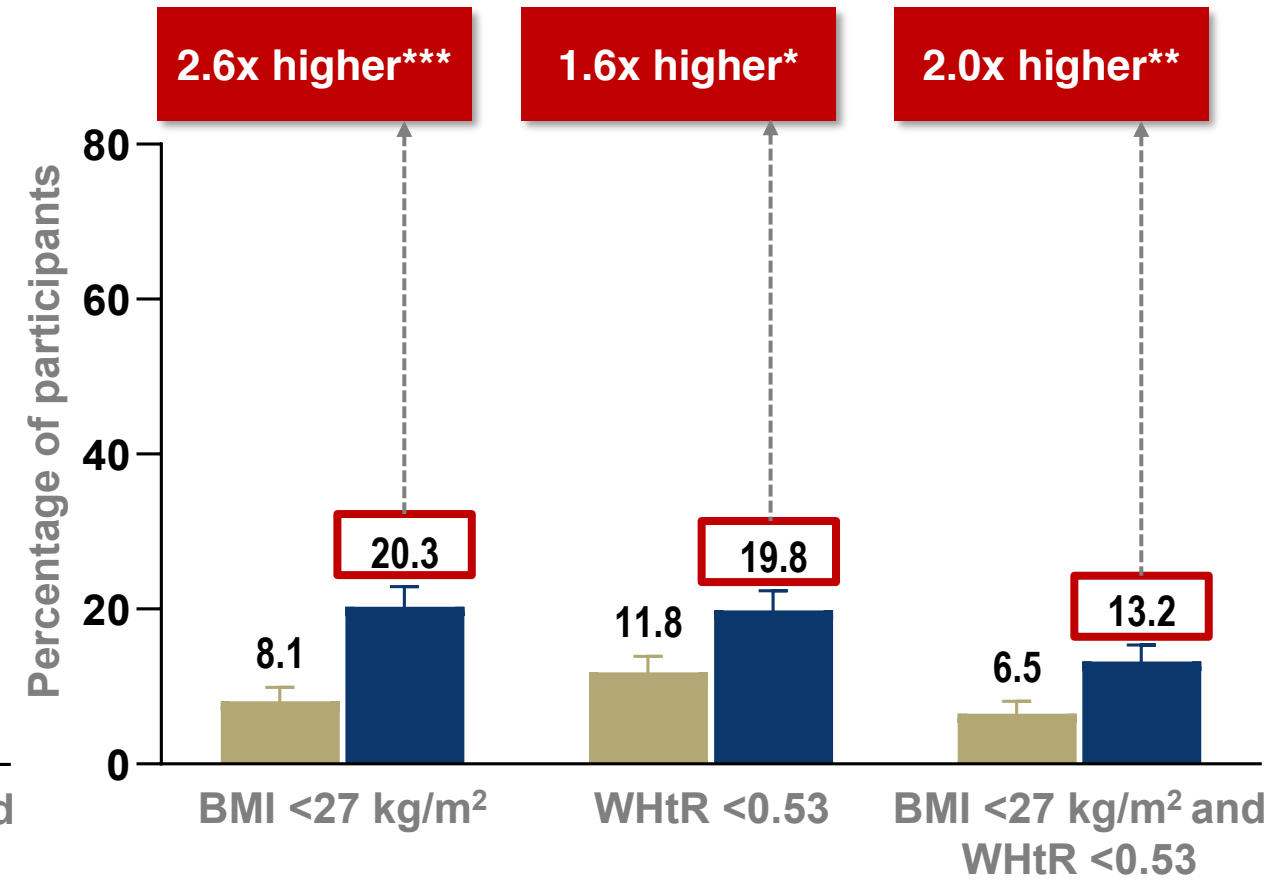
Note: Week 72 data in participants who discontinued study drug early was imputed by multiple imputation based on missing at random (MAR) assumption using on-treatment data. Treatment comparisons were made via logistic regression with the aid of Rubin's rule.

# Percent of Participants by Baseline BMI Reaching Treat to Target Thresholds at Week 72

## BMI <35 kg/m<sup>2</sup> at baseline



## BMI ≥35 kg/m<sup>2</sup> at baseline



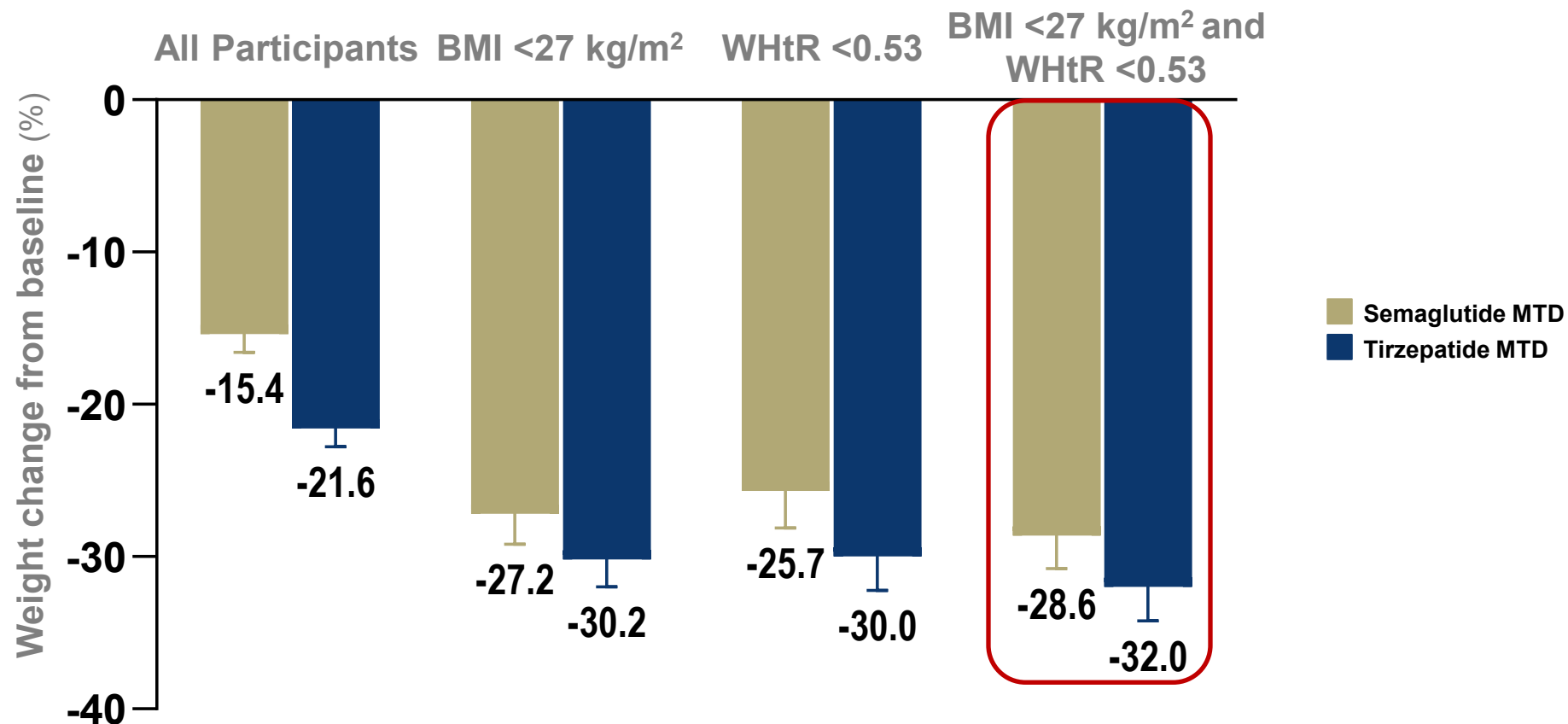
■ Semaglutide MTD  
■ Tirzepatide MTD

\*p<0.05. \*\*p<0.01 vs semaglutide.\*\*\*p<0.001 vs. semaglutide.

Note: Week 72 data in participants who discontinued study drug early was imputed by multiple imputation based on missing at random (MAR) assumption using on on-treatment data. Treatment comparisons were made via logistic regression with the aid of Rubin's rule.

# Weight Reduction from Baseline to Week 72

Participants achieving treat to target thresholds had greater than average weight reduction in both study treatments

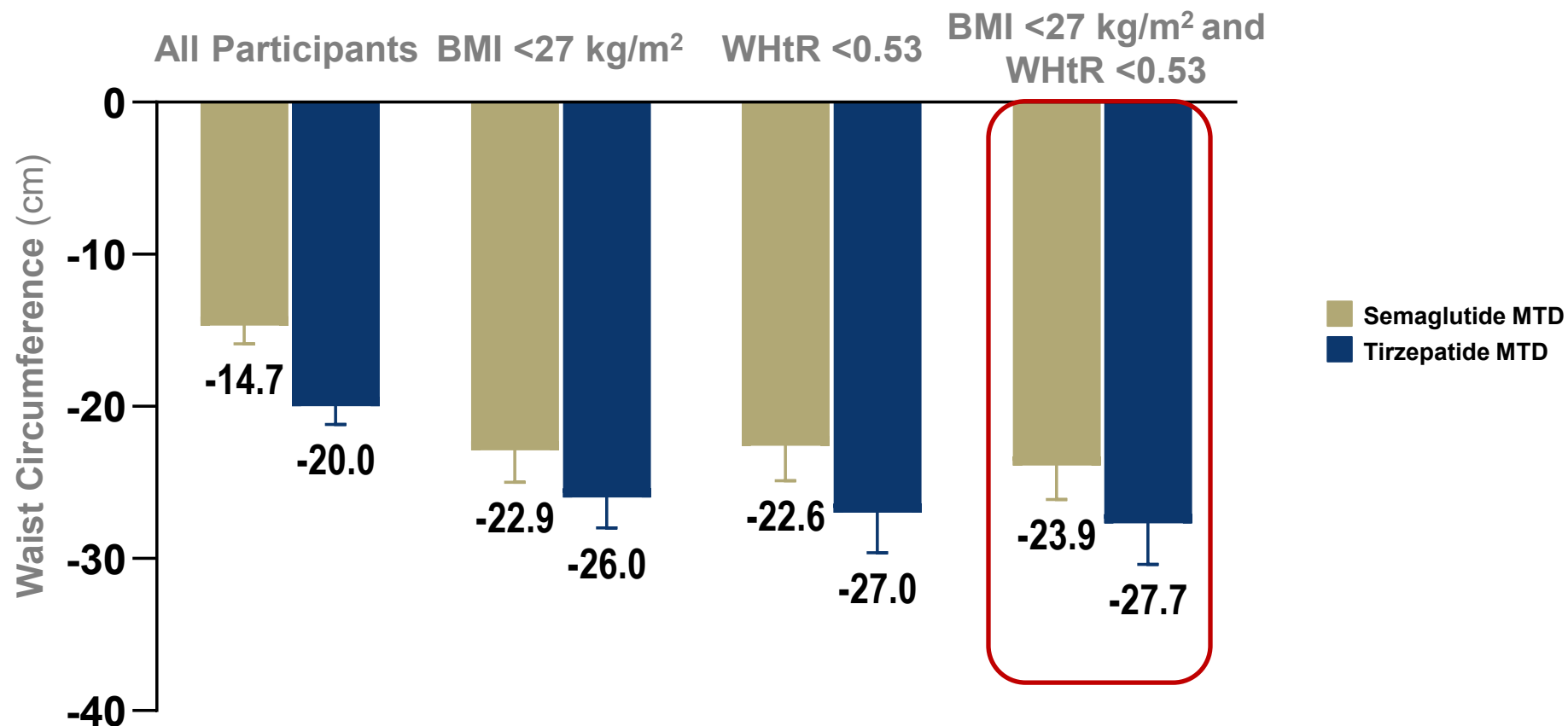


Data for All Participants are LSMeans from MMRM model.

Data for participants meeting BMI and WHtR targets are means based on observed data at Week 72 for participants who completed treatment.

# Waist Circumference Reduction from Baseline to Week 72

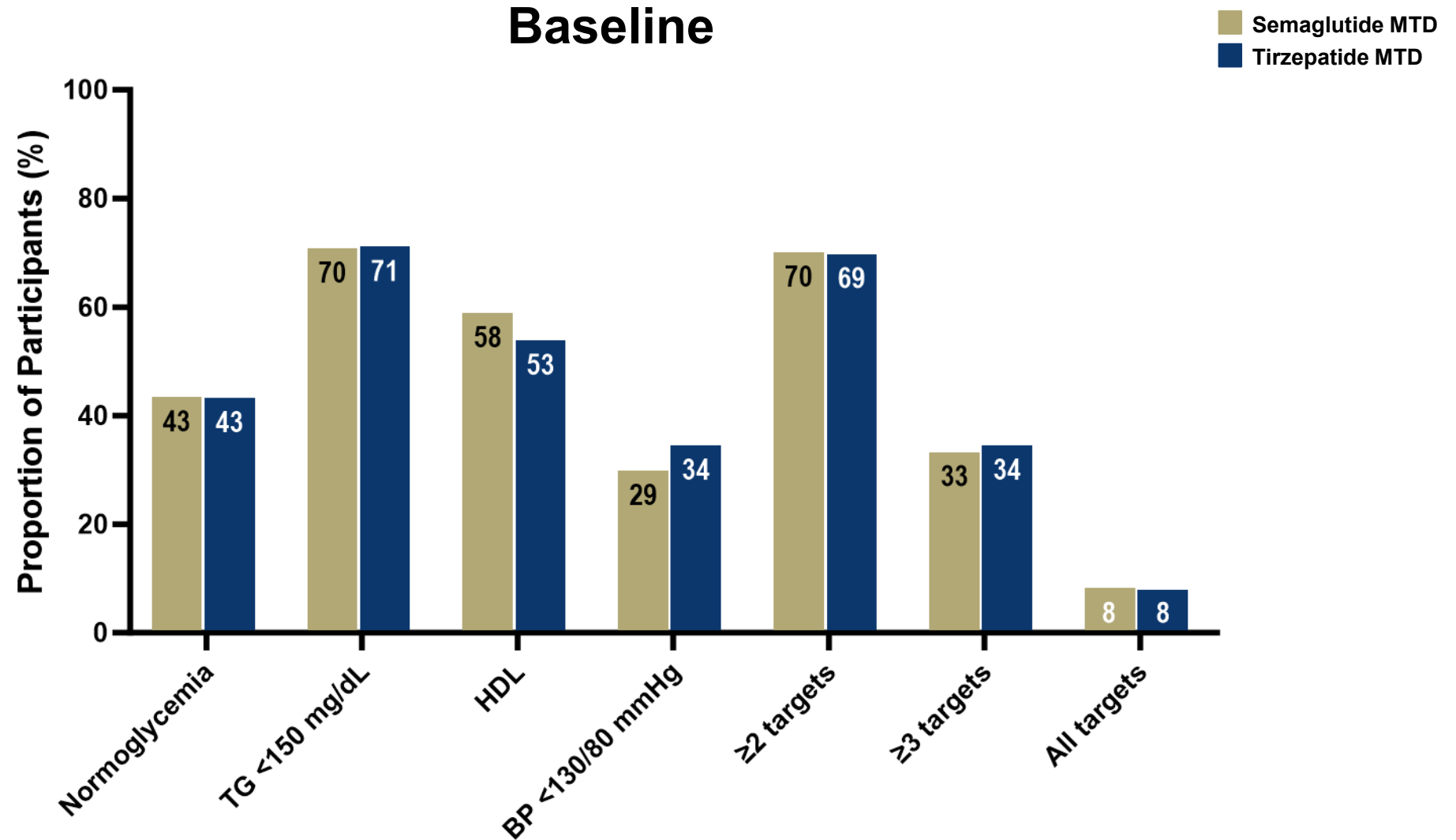
Participants achieving treat to target thresholds had greater than average waist circumference reduction in both study treatments



Data for All Participants are LSMeans from MMRM model.

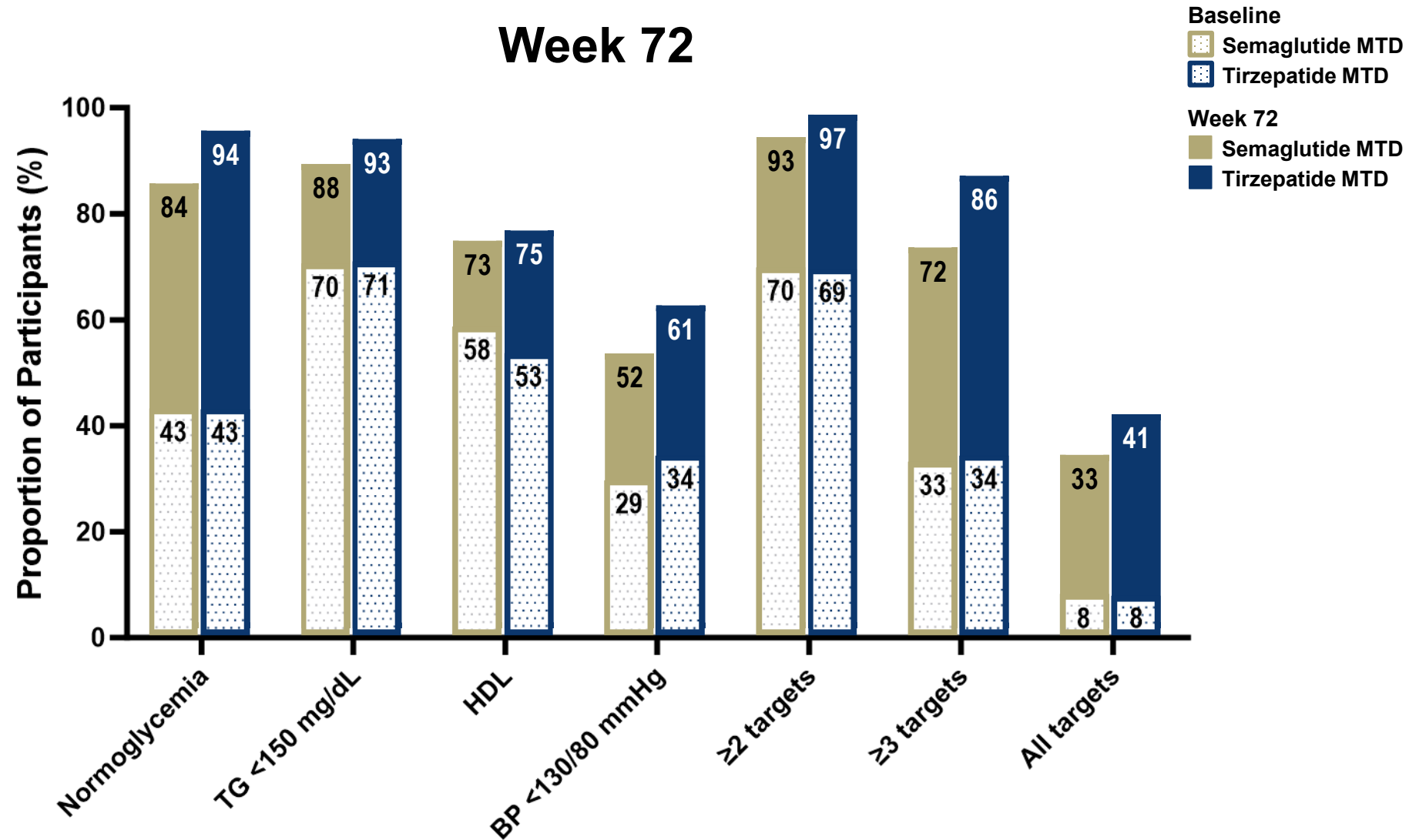
Data for participants meeting BMI and WHtR targets are means based on observed data at Week 72 for participants who completed treatment.

# Percent of Participants with Normalization of Cardiometabolic Parameters



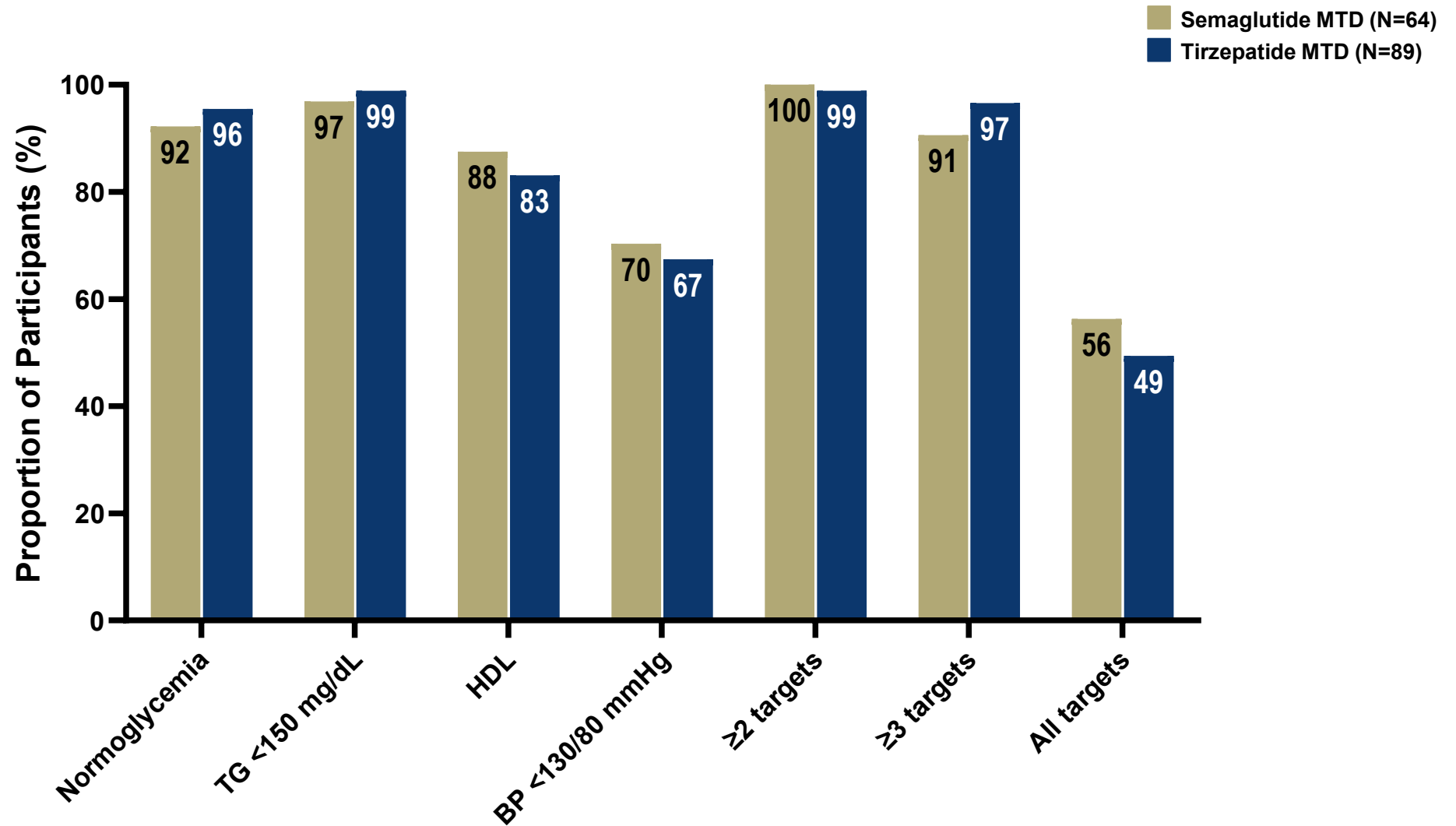
Normoglycemia (HbA1c <5.7% and FSG <100 mg/dL). HDL sex-specific goals (female ≥50 mg/dL, male ≥40 mg/dL). Data are means based on observed data at baseline for participants who completed treatment.

# Percent of Participants with Normalization of Cardiometabolic Parameters



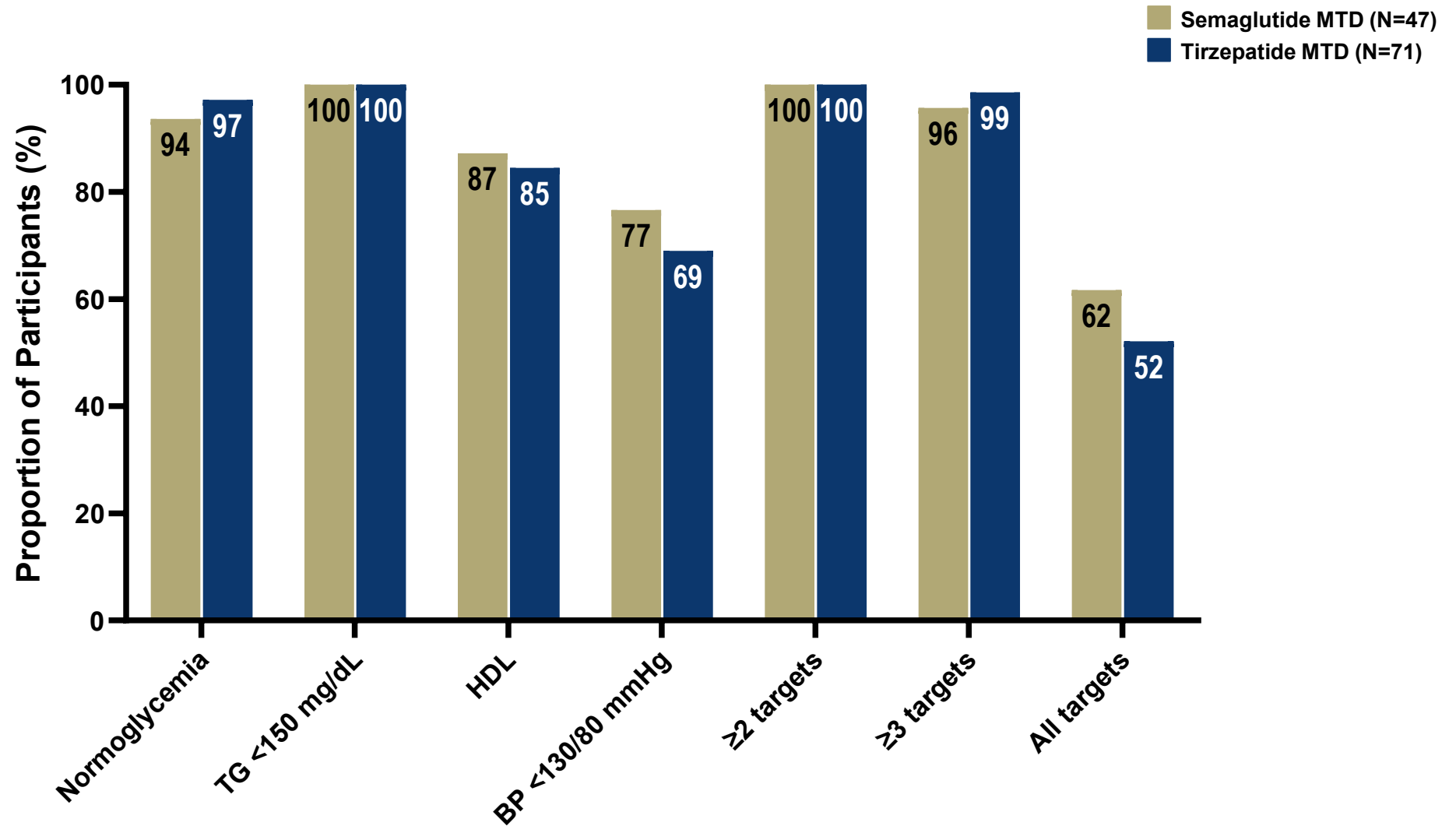
Normoglycemia (HbA1c <5.7% and FSG <100 mg/dL). HDL sex-specific goals (female ≥50 mg/dL, male ≥40 mg/dL). Data are means based on observed data at Week 72 or LOCF for participants who completed treatment.

# Normalization of Cardiometabolic Parameters in Participants Reaching WHtR <0.53 at Week 72



Normoglycemia (HbA1c <5.7% and FSG <100 mg/dL). HDL sex-specific goals (female ≥50 mg/dL, male ≥40 mg/dL). N = number of participants meeting WHtR <0.53 at Week 72. Data are means based on observed data at Week 72 or LOCF for participants who completed treatment.

# Normalization of Cardiometabolic Parameters in Participants Reaching WHtR <0.53 & BMI <27 at Week 72



Normoglycemia (HbA1c <5.7% and FSG <100 mg/dL). HDL sex-specific goals (female ≥50 mg/dL, male ≥40 mg/dL). N = number of participants meeting WHtR <0.53 and BMI <27 kg/m<sup>2</sup> at Week 72. Data are means based on observed data at Week 72 or LOCF for participants who completed treatment.

# Limitations

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- In the Busetto et al TtT thresholds analysis
  - Method of intentional weight reduction was primarily unknown (suspected lifestyle)
    - Modality specific analysis may be more informative
  - Median BMI was 31 kg/m<sup>2</sup>, versus 38 kg/m<sup>2</sup> in SURMOUNT-5
- Likely some participants were still in the weight loss phase
  - Previous research: 10-30% tirzepatide treated participants not at weight plateau by week 72<sup>2</sup>
- The TtT thresholds proposed herein are preliminary and require further study before applied in clinical practice

# Conclusion

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- Greater proportion of participants treated with tirzepatide achieved the proposed TtT thresholds compared to those treated with semaglutide
- In the SURMOUNT 5 trial, achieving the TtT thresholds proposed by Busetto et al, occurred with the specified clinical parameters
- Future research with a treat to target approach should include outcomes meaningful to patients to improve shared decision making.