Supplementary Material 2 - Efficacy and standard error of efficacy measurements of tirzepatide and semaglutide second stage

Outcome	Efficacy of Tirzepatide (Standard error)	Efficacy of Semaglutide (Standard error)
Proportion of individuals who achieved a weight reduction of ≥10%	81.60% (2.01)	60.50% (2.52)
Proportion of individuals who achieved a weight reduction of ≥15%	64.60% (2.47)	40.10% (2.53)
Proportion of individuals who achieved a weight reduction of ≥20%	48.40% (2.58)	27.30% (2.30)
Proportion of individuals who achieved a weight reduction of ≥25%	31.60% (2.40)	16.10% (1.90)

Based on: Aronne et al., 2025

Supplementary Material 3 - Certainty of evidence according to the GRADE system

Tirzepatide compared to Semaglutide of Obesity

Certainty Assessment							Summary of Results				
							Study event rates (%)			Potential absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirect evidence	Imprecision	Publication bias	Overall certainty of evidence	With Semaglutide	With Tirzepatide	Relative effect (95%CI)	Risk with Semaglutide	Risk difference with Tirzepatide
Least squares mean percentage change in body weight (follow-up: mean 72 weeks)											
750 (1 RCT)	Severe[a]	not serious	not serious	not serious	none	⨁⨁⨁◯ Moderate[a]			Difference between treatments = -6.5% (95% CI -8.1 to -4.9) Tirzepartide group = -20.2% (95% CI -21.4 to -19.1) Semaglutide group = -13.7% (95% CI -14.9 to -12.6)		
Least squares mean change in waist circumference - cm (follow-up: mean 72 weeks)											
750 (1 RCT)	Severe[b]	not serious	not serious	not serious	none	⨁⨁⨁◯ Moderate[b]			Difference between treatments = -5.4cm (95% CI -7.1 to -3.6) Tirzepartide group = -18.4cm (95% CI -19.6 to -17.2) Semaglutide group = -13.0cm (95% CI -14.3 to -11.7)		
Least squares mean change in body weight - kg (follow-up: mean 72 weeks)											
750 (1 RCT)	Severe[c]	not severe	not severe	not severe	none	⨁⨁⨁◯ Moderate[c]			Difference between treatments = -7.9 kg (95% CI -9.7 to -6.0) Tirzepartide group = -22.8 kg (95% CI -24.1 to -21.5) Semaglutide group = -15.0 kg (95% CI -16.3 to -13.7)		
Mean least squares change in Body Mass Index (BMI) (follow-up: mean 72 weeks)											
750 (1 RCT)	severe[d]	not severe	not severe	not severe	none	⨁⨁⨁◯ Moderate[d]			Between-group difference= -2.7 (95% CI -3.3 to -2.0) Tirzepartide group = -8.0 (95% CI -8.5 to -7.5) Semaglutide group = -5.3 (95% CI -5.8 to -4.8)		
Weight reduction of ≥10% (follow-up: mean 72 weeks)											
750 (1 RCT)	severe[d,c]	not severe	not severe	not severe	none	⨁⨁⨁◯ Moderate[d,c]	227/376 (60.4%)	304/374 (81.3%)	**RR 1.3** (1.2 to 1.5)	**Low** 0 per 1 000	**0 fewer per 1 000** (from 0 fewer to 0 fewer)
Weight reduction of ≥15% (follow-up: mean 72 weeks)											
750 (1 RCT)	severe[f]	not severe	not severe	not severe	none	⨁⨁⨁◯ Moderate[f]	151/376 (40.2%)	241/374 (64.4%)	**RR 1.6** (1.4 to 1.9)	151/376 (40.2%)	**241 more per 1 000** (from 161 more to 361 more)
Weight reduction of ≥20% (follow-up: mean 72 weeks)											
750 (1 RCT)	severe[g]	not severe	not severe	not severe	none	⨁⨁⨁◯ Moderate[g]	60/376 (16.0%)	118/374 (31.6%)	**RR 2.0** (1.5 to 2.2)	60/376 (16.0%)	**219 more per 1 000** (from 137 more to 329 more)
Weight reduction of ≥25% (follow-up: mean 72 weeks)											
750 (1 RCT)	severe[h]	not severe	not severe	not severe	none	⨁⨁⨁◯ Moderate[h]	60/376 (16.0%)	118/374 (31.6%)	**RR 2.0** (1.5 to 2.6)	60/376 (16.0%)	**160 more per 1 000** (from 80 more to 255 more)

Adverse events reported during treatment (%) (follow-up: mean 72 weeks)

750 (1 RCT)	not severe	not severe	not severe	not severe	none	⊕⊕⊕⊕ High	297/376 (79.0%)	287/374 (76.7%)	Not estimable	297/376 (79.0%)	

Serious adverse events (%) (follow-up: mean 72 weeks)

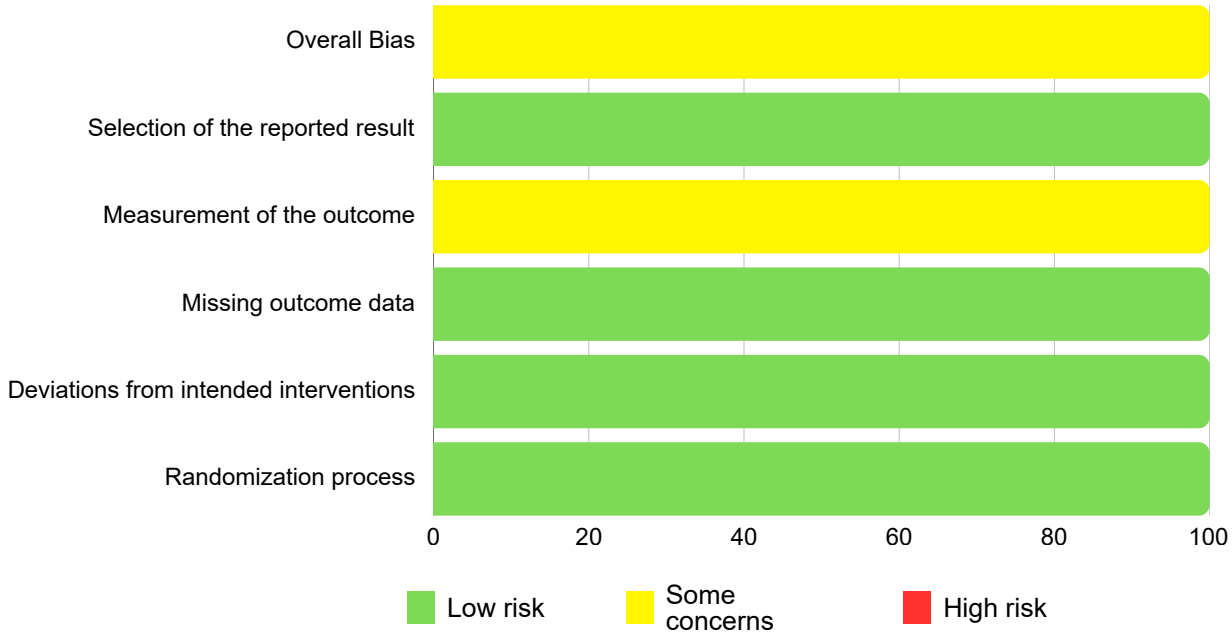
750 (1 RCT)	not severe	not severe	not severe	not severe	none	⊕⊕⊕⊕ High	13/376 (3.5%)	18/374 (4.8%)	Not estimable	13/376 (3.5%)	

Adverse events leading to study discontinuation (%) (follow-up: mean 72 weeks)

750 (1 RCT)	not severe	not severe	not severe	not severe	none	⊕⊕⊕⊕ High	6/376 (1.6%)	6/374 (1.6%)	Not estimable	6/376 (1.6%)	

Legend: a. The study was not blinded; b. Absence of blinding; c. Open study; d. Unblinded study; e. Absence of blinding; f. Absent blinding; g. Absent blindin; h. No blinding; CI. Confidence Interval; RR. Risk Ratio

Supplementary Material 4 - Assessment of methodological quality according to RoB2.0 for efficacy outcome



Supplementary Material 5 - Assessment of methodological quality according to RoB2.0 for safety outcome