Impact of Semaglutide on Body Composition in Adults with Overweight or Obesity: Exploratory Analysis of the STEP 1 Study

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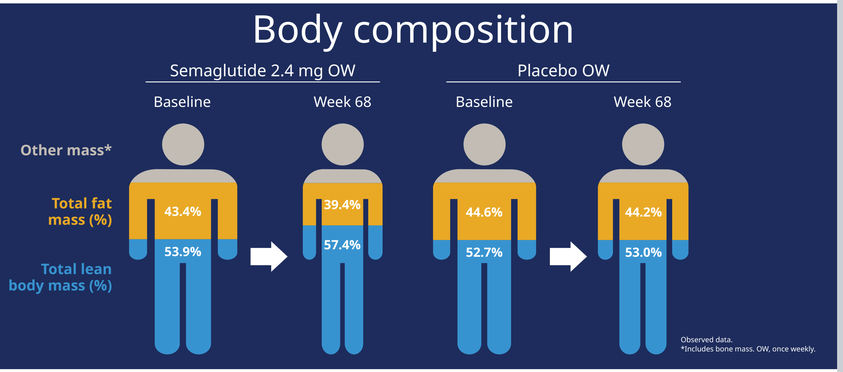
Semaglutide 2.4 mg reduces total fat mass and regional visceral fat mass, and increases the proportion of lean body mass in adults with overweight or obesity



Aim

- Central obesity is associated with increased risk of cardiometabolic disease.[1]
- Weight loss reduces lean muscle mass, potentially impacting resting energy expenditure and/or physical functioning.[2–4]
- This analysis of the randomised, double-blind STEP 1 study evaluated the impact of subcutaneous (s.c.) semaglutide, a glucagon-like peptide-1 analog, on body composition in adults with overweight/obesity using dual energy X-ray absorptiometry (DEXA).

Methods

- STEP 1 randomised 1,961 adults with body mass index (BMI) ≥30 kg/m², or ≥27 kg/m² with ≥1 weight-related comorbidity, without diabetes, to once-weekly s.c. semaglutide 2.4 mg or placebo (2:1), plus lifestyle intervention, for 68 weeks.
- A subset of 140 participants with BMI ≤40 kg/m² from 9 sites were included in the DEXA substudy.
- Change in body composition from baseline (BL) to week 68 was a supportive secondary endpoint.
- Visceral fat mass was calculated in the L4 region (both males/females), android region (males) or gynoid region (females), depending on site scanner methodology.
- Proportions of total fat and lean body mass were calculated relative to total body mass; proportions of visceral fat mass were calculated relative to the region assessed.
- Effects were assessed regardless of treatment adherence or initiation of other antiobesity therapies (treatment policy estimand).

Key results

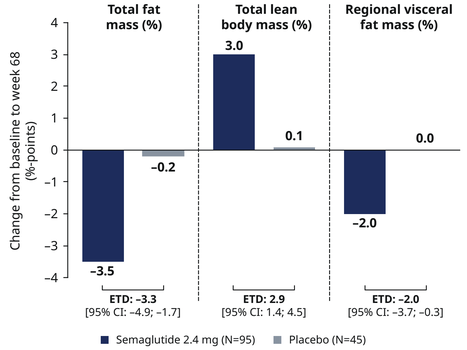
Table 1: Baseline characteristics in the DEXA subpopulation

	Semaglutide 2.4 mg (N=95)	Placebo (N=45)
Age, years	50 ± 12	52 ± 13
Female, n (%)	72 (75.8)	34 (75.6)
Body weight, kg	98.3 ± 15.9	98.7 ± 12.1
BMI, kg/m²	34.8 ± 3.6	35.0 ± 3.6
Waist circumference, cm	109.4 ± 10.6	111.0 ± 10.1
Body composition (DEXA)		
Total fat mass, kg	42.1 ± 10.1	43.3 ± 9.2
Total fat mass, %	43.4 ± 7.5	44.6 ± 8.1
Regional visceral fat mass, kg	1.3 ± 0.6	1.5 ± 0.7
Regional visceral fat mass, %	33.8 ± 9.9	36.3 ± 12.3
Total lean body mass, kg	52.4 ± 11.6	51.5 ± 10.8
Total lean body mass, %	53.9 ± 7.4	52.7 ± 7.7

Data are mean ± standard deviation unless indicated otherwise.

- BL body composition was similar in the treatment groups (Table 1).
- Change in body weight from BL to week 68 was –15.0% with semaglutide vs –3.6% with placebo.
- Weight loss with semaglutide resulted in reductions from BL in total fat mass of 19.3% and regional visceral fat mass of 27.4%, leading to 3.5%-point and 2.0%-point reductions in the proportions of total fat mass and visceral fat mass, respectively (Figure 1).
- Total lean body mass decreased from BL by 9.7% with semaglutide; however, relative to total body mass the proportion of lean body mass increased by 3.0%-points.

Figure 1: Change in body composition from baseline to week 68

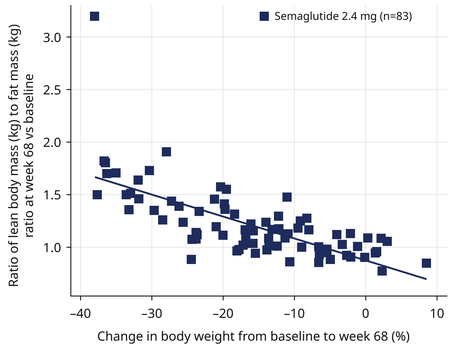


CI, confidence interval; ETD, estimated treatment difference.

- There were no major changes in body composition with placebo.
- By week 68, total fat mass and total lean body mass proportions were 39.4% and 57.4% with semaglutide vs 44.2% and 53.0% with placebo.
- Relative to the region assessed, the proportion of visceral fat mass at week 68 was 31.6% vs 35.6% in semaglutide and placebo groups.
- Total lean body mass to total fat mass ratio increased from BL to week 68 in the semaglutide group (Table 2).
- Greater improvements in lean body mass to fat mass ratio were observed with greater weight loss in the semaglutide group (Figure 2 and Table 2).

Key results

Figure 2: Change from baseline to week 68 in ratio of lean body mass to total body mass



Graph shows ratio of week 68 vs baseline lean body mass (kg) to total fat mass (kg) ratio plotted by change from baseline to week 68 in body weight. Observed data; no imputation for missing data. CI, confidence interval; Pt, participants.

Table 2: Lean body mass (kg) to total body fat mass (kg) ratio in the semaglutide group

	Mean [95% CI]
Baseline (n=83)	1.34 [1.22, 1.47]
Week 68 (n=83)	1.57 [1.44, 1.71]
Change from baseline to week 68	
Overall treatment group (n=83)	0.23 [0.14, 0.32]
Pts with weight loss ≥15% (n=44)	0.41 [0.28, 0.53]
Pts with weight loss <15% or not known (n=39)	0.03 [–0.05, 0.12]

Conclusions

- In adults with overweight/obesity, once-weekly semaglutide 2.4 mg was associated with reduced total fat mass and regional visceral fat mass, and a relatively increased proportion of lean body mass.
- Greater weight loss was associated with greater improvement in body composition (total lean body mass to total fat mass ratio).
- *Further results can be found in the STEP 1 primary publication.*[5]

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This trial was sponsored by Novo Nordisk and is registered with ClinicalTrials.gov (NCT03548935). Presenter Rhodri King has received speaker fees from Novo Nordisk, AstraZeneca and Lilly. The authors acknowledge the medical writing assistance of Paul Barlass of Axis, a division of Spirit Medical Communications Group Limited; and editorial updates by Ashfield Health.
First presented at ENDO, 20–23 March 2021, virtual meeting.
Presented at the Association of British Clinical Diabetologists (ABCD), 14 October 2021, virtual meeting.

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