

# Effect of weight loss on physical function measured by the 6-minute walking distance test in individuals with obesity: results from the SCALE IBT trial of liraglutide 3.0 mg

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Domenica Rubino,<sup>1</sup> Jena Shaw Tronieri,<sup>2</sup> Danny Sugimoto,<sup>3</sup> Michael Lund,<sup>4</sup> Altynai Satylganova,<sup>4</sup> Niels Zeuthen,<sup>4</sup> Tom Wadden<sup>2</sup>

<sup>1</sup>Washington Center for Weight Management and Research, Arlington, VA, USA; <sup>2</sup>Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; <sup>3</sup>Cedar Crosse Research Center, Chicago, IL, USA; <sup>4</sup>Novo Nordisk A/S, Søborg, Denmark

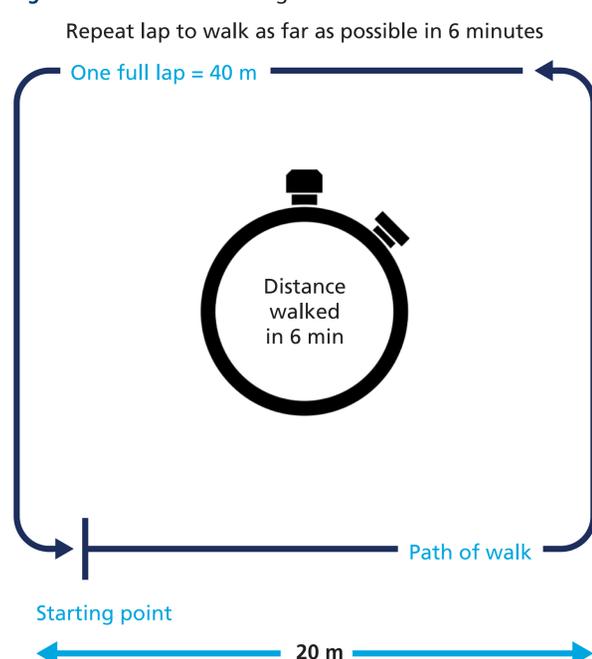
## Background

- Intensive behaviour therapy (IBT) can promote weight loss in patients with obesity, and alleviate functional impairments such as decreased mobility.<sup>1,2</sup> Adding weight-loss medication to IBT can allow patients to achieve an additional >5% weight loss.<sup>3</sup>
- In weight management clinical trials physical function is typically assessed with self-reported questionnaires, which are limited by their subjectivity.
- We present a *post hoc* analysis of the key secondary endpoint in the SCALE IBT trial: the effect of weight loss on walking capacity, as measured by the objective 6-minute walk test (6MWT). This test assesses cardiopulmonary and musculoskeletal systems by measuring the total distance walked along a 20 m walkway over 6 min.
- To our knowledge, this is the first pharmacological weight-loss trial to explore changes in 6-minute walking distance (6MWD).

## Methods

- The SCALE IBT trial (ClinicalTrials.gov: NCT02963935) was a 56-week, randomised, double-blind, placebo-controlled, two-armed multicentre trial in subjects with obesity who had not been diagnosed with type 1 or 2 diabetes mellitus.
- Key inclusion criteria: aged ≥18 years, body mass index (BMI) ≥30 kg/m<sup>2</sup> and maximum 5 kg self-reported weight change within the past 90 days since screening.
- Subjects were randomised 1:1 to receive either liraglutide 3.0 mg or placebo, as an adjunct to Centers for Medicare and Medicaid Services intensive behaviour therapy (CMS-IBT).
- IBT consisted of reduced caloric intake (based on body weight at randomisation), increased physical activity (walking or similar aerobic activity: min. 100 min/week, max. target 250 min/week) and 23 behaviour counselling visits.
- Weekly trial drug dose escalation was implemented during the first 4 weeks after randomisation in accordance with the Saxenda<sup>®</sup> EU summary of product characteristics.<sup>4</sup>
- Walking capacity was assessed at baseline and 56 weeks using the 6MWT (Figure 1).
- Missing observations were imputed based on a jump-to-reference multiple imputation (J2R-MI) approach.
- Week 56 responses were analysed using an analysis of covariance (ANCOVA) model with treatment, BMI groups, and sex as factors and baseline measurement of endpoint as covariate.
- Linear regression of 6MWD data vs. BMI data is based on observed data.
- We present a *post hoc* analysis of the key secondary endpoint of the SCALE IBT trial: the effect of weight loss on walking capacity.

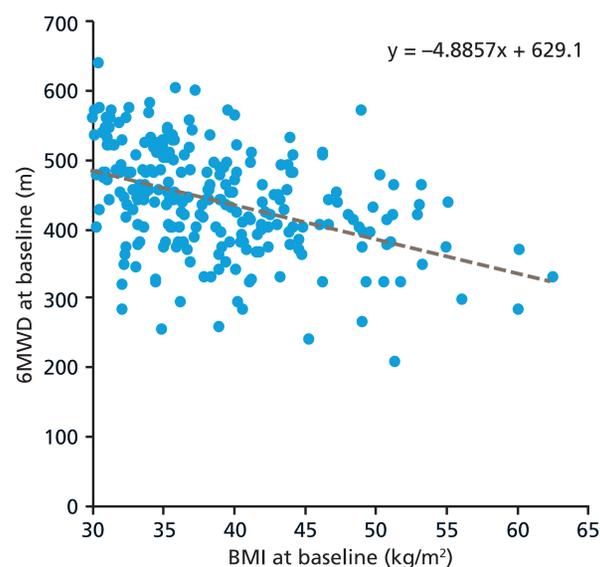
Figure 1: Six-minute walking test method



## Results

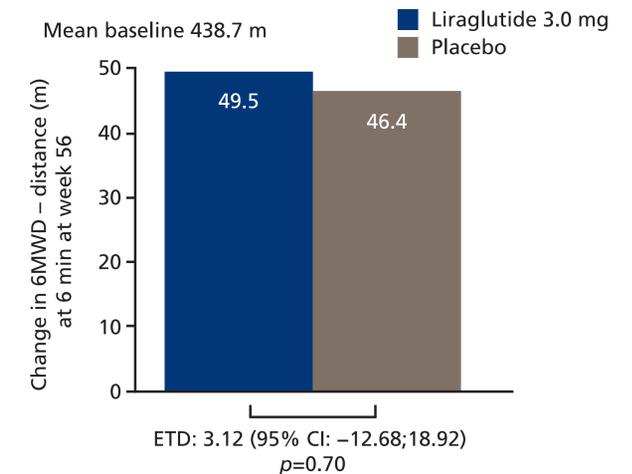
- 282 patients were randomised and included for analysis (liraglutide 3.0 mg n=142; placebo n=140).
- Baseline demographics and primary results of the trial can be found in posters P02.192; P02.196; P02.197.
- Mean weight loss was 7.5% with liraglutide 3.0 mg and 4.0% with placebo after 56 weeks (estimated treatment difference [ETD]: 3.5% [95% confidence interval (CI): 1.6;5.3];  $p=0.0003$ ).
- Mean 6MWD at baseline was 438.7 m (range: 207–637 m).
- Patients with lower BMIs at baseline tended to perform better on the 6MWT:
  - On average, a patient with a BMI 1 kg/m<sup>2</sup> lower than another patient was able to walk 4.9 m longer in 6 min ( $p<0.0001$ ) (Figure 2).
- After 56 weeks mean improvement in 6MWD was 49.5±5.5 m with liraglutide 3.0 mg and 46.4±5.8 m with placebo (ETD: 3.12 m [95% CI: -12.68;18.92];  $p=0.70$ ) (Figure 3).
- On average, a reduction of 1 BMI unit resulted in a 5-metre increase in 6MWD ( $p<0.0001$ ) (Figure 4).

Figure 2: BMI vs. 6MWD at baseline



6MWD, 6-minute walking distance; BMI, body mass index

Figure 3: Change in 6MWD from baseline to week 56

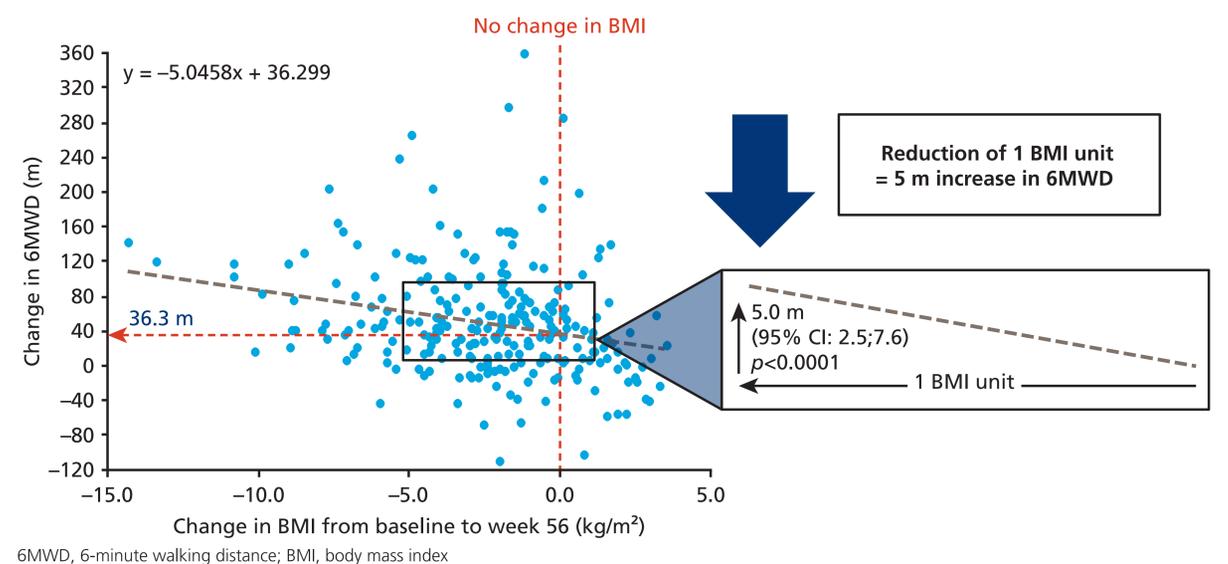


6MWD, 6-minute walking distance; CI, confidence interval; ETD, estimated treatment difference

## Discussion

- The similarity in the gradients of the regression line between BMI and 6MWD at baseline and change in BMI from baseline to week 56 and 6MWD indicates a robust association between BMI and 6MWD.
- Baseline 6MWD in this trial was lower than a previously reported mean reference value of 563.60±62.32 m, likely due to the older patient population in this trial (mean age 47.2 vs. 35.9 years).<sup>5</sup>
- Weight loss was associated with a mean 6MWD improvement of 11.3% in patients treated with liraglutide 3.0 mg. This compares with a range of 9–47% in the literature, with non-pharmacological interventions,<sup>6,7</sup> although comparisons are limited due to differing trial designs and populations.
- IBT recommended that participants perform aerobic activity for at least 100 min/week. This increased physical activity may have improved 6MWT performance independent of weight change, as reflected in Figure 4, where the intercept (change in 6MWD with no change in BMI) was 36.3 m.
- A 'practice effect' may also account for some of the improvement seen in 6MWD, although previous studies with repeated tests in patients with obesity<sup>8,9</sup> suggest that such an effect is likely to be small.
- Improvements in mobility in patients with obesity, as assessed by the 6MWT, could be indicative of improvements in quality of life.

Figure 4: Change in BMI vs. change in 6MWD at week 56



6MWD, 6-minute walking distance; BMI, body mass index

## Conclusion

- This *post hoc* analysis found objective improvement in walking capacity following weight loss achieved by a 56-week IBT programme (combined with liraglutide 3.0 mg or placebo), suggestive of improvements to the cardiopulmonary and musculoskeletal systems.
- Greater weight loss was associated with greater improvements in 6MWD in a linear manner.