

Correlation Between Reduction in Total Body Weight and Change in Waist Circumference

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CONCLUSIONS

- In an era of unprecedented reductions in total body weight (TBW) with anti-obesity medications (AOMs), careful consideration of changes in body composition, including changes in lean muscle mass, is increasingly important
- Our analysis suggests that changes in waist circumference (WC) strongly correlate with AOM-induced changes in TBW in adults who participated in phase 3 obesity trials
- Anthropometric measures of central obesity, such as WC, which are good estimators of visceral adipose tissue volume, may serve as important indicators of therapeutic response to AOMs

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INTRODUCTION

- ▶ Obesity is a disease of excess or abnormal adipose tissue, the key driver of its pathogenic process¹⁻³
- ▶ Current guidance from the U.S. Food & Drug Administration (FDA) and European Medicines Agency recommends changes in baseline TBW as the primary efficacy measure in registrational clinical trials for overweight and obesity^{4,5}
- ▶ Currently approved AOMs achieve reductions in TBW based on a composite loss of fat mass and loss of lean mass; however, the loss of lean muscle mass with AOMs may have adverse long-term health consequences⁶⁻⁸
- ▶ Investigational therapies under development for the treatment of people living with overweight and obesity, such as anti-myostatin therapies (eg, taldefgrobep), may lead to clinically meaningful reductions in fat mass (including visceral adipose tissue and ectopic fat deposits) and improve metabolic parameters while increasing lean mass^{9,10}
 - Because investigational agents with the potential to reduce fat mass while increasing lean mass are expected to yield differentiated change in TBW relative to other AOMs, alternative clinical endpoints are necessary to properly evaluate the clinical efficacy of these novel therapies¹¹
- ▶ Visceral adipose tissue volume and anthropometric measures of central obesity (eg, WC and waist-to-height ratio) have proven to be better predictors of cardiometabolic risk than TBW and body mass index (BMI)¹¹⁻¹³
 - Changes in anthropometric measures of central obesity have been shown to correlate with changes in visceral adipose tissue volume^{13,14}
- ▶ Alternative clinical endpoints, such as change in anthropometric measures of central obesity, could be important for evaluating the clinical efficacy of AOMs with the ability to reduce fat mass while increasing lean mass

RESULTS

- ▶ The analysis included a total of 9938 participants from 6 clinical trials with study durations between 52 and 72 weeks (**Table 1**)
- ▶ Minimum BMI was 27 kg/m² across all studies, per eligibility criteria
- ▶ Participants were mostly female, comprising 67.1% to 85% of participants
- ▶ Mean age was between 43.8 and 51.1 years; minimum age across all studies was 18 years, per eligibility criteria
- ▶ Mean TBW loss ranged from 5.0% to 20.9%; corresponding mean reduction in WC ranged from 5.0 to 18.5 cm
- ▶ There was a strong linear relationship between changes in TBW and WC (**Figure 1**)
 - A 5% reduction in TBW was associated with an approximately 5 cm reduction in WC ($r=0.997$)

Table 1. Change in TBW and WC Across Adult AOM Trials

Drug	Dose	Sample Size ^a (n)	Study Duration (wk)	Mean Age (y)	Women (%)	TBW Loss (%)	Reduction in WC (cm)
Naltrexone SR/bupropion SR ¹⁵	16 mg/360 mg BID	471	56	44.4	85	5.0	5.0
Lorcaserin ¹⁶	10 mg BID	1538	52	43.8	82.9	5.8	6.8
Naltrexone SR/bupropion SR ¹⁵	32 mg/360 mg BID	471	56	44.4	85	6.1	6.2
Phentermine/topiramate ¹⁷	7.5 mg/46 mg QD	488	56	51.1	70	7.8	7.6
Liraglutide ¹⁸	3 mg SC QD	2437	56	45.2	78.7	8.0	8.2
Phentermine/topiramate ¹⁷	15 mg/92 mg QD	981	56	51.0	70	9.8	9.2
Semaglutide ⁷	2.4 mg SC QW	1306	68	46	73.1	14.9	13.5
Tirzepatide ¹⁹	5 mg SC QW	630	72	45.6	67.6	15.0	14.0
Tirzepatide ¹⁹	10 mg SC QW	636	72	44.7	67.1	19.5	17.7
Tirzepatide ¹⁹	15 mg SC QW	630	72	44.9	67.5	20.9	18.5

^aIncludes participants with data available for TBW and WC endpoints. BID, twice daily; QD, every day; QW, every week; SC, subcutaneous; SR, sustained release.

OBJECTIVE and METHODS

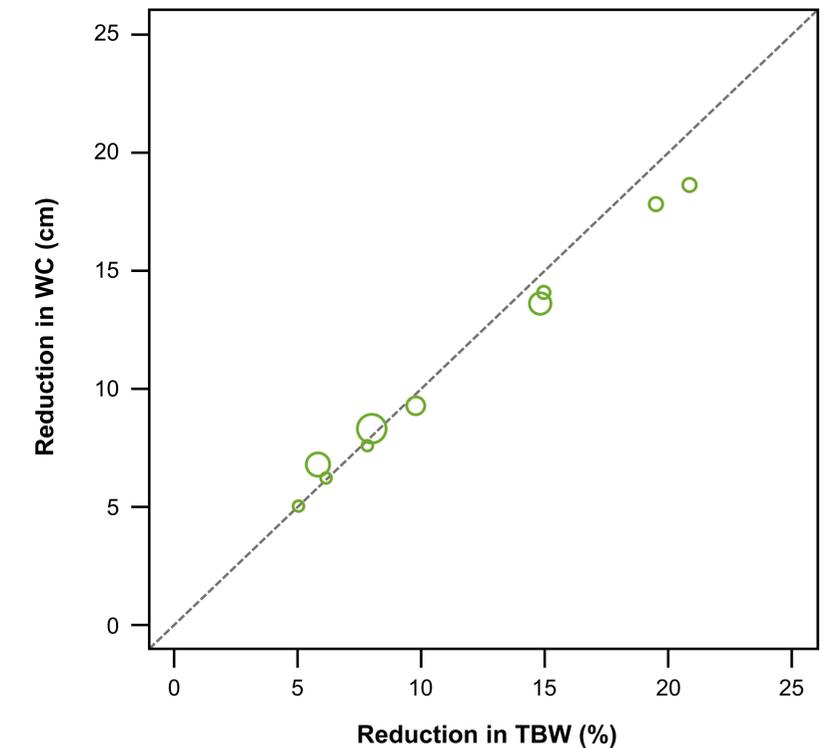
Objective

- ▶ Investigate the relationship between changes in TBW and WC in adults receiving AOMs in pivotal trials of the medications most recently approved by the FDA or those under review by the FDA

Methods

- ▶ This analysis included 6 phase 3 clinical trials conducted in adults living with overweight and obesity, comprising 10 dose groups from:
 - Semaglutide STEP 1 trial (NCT03548935)⁷
 - Naltrexone/bupropion COR-I trial (NCT00532779)¹⁵
 - Lorcaserin BLOOM trial (NCT00395135)¹⁶
 - Phentermine/topiramate CONQUER trial (NCT00553787)¹⁷
 - Liraglutide SCALE trial (NCT01272219)¹⁸
 - Tirzepatide SURMOUNT-1 trial (NCT04184622)¹⁹
- ▶ Placebo results were not included in the analysis
- ▶ A correlation was estimated with a weighted Pearson correlation coefficient, using weights proportional to the number of subjects in each dose group

Figure 1. Correlation Between Change in TBW and WC Across Adult AOM Trials



The dotted line represents the identity line. The size of each data point is proportional to the square root of the sample size.