Effects of gradual weight loss vs rapid weight loss on body composition and resting metabolic rate: A systematic review and meta-analysis

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Running title: Gradual vs rapid weight loss

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Abstract

This systematic review and meta-analysis compared the effects of different rates of weight loss (WL), but equivalent total WL, on body composition and resting metabolic rate (RMR). Studies examining gradual vs. rapid WL on body composition and RMR in participants with overweight/obesity published up to October 2019 were identified through PubMed, the Cochrane Library, Web of Science, Embase, SCOPUS, and Ovid databases. Meta-analysis was carried out using a fixed or random-effects model as appropriate. Although the magnitude of WL was similar (mean difference: 0.03 kg, 95% CI [-0.65, 0.71]), gradual WL promoted greater reductions in fat mass (FM) (-1 kg, 95% CI [-1.70, -0.29]) and body fat percentage (BFP) (-0.83%, 95% CI [-1.49, -0.17]). Gradual WL significantly preserved RMR compared with rapid WL (97.39 kcal, 95% CI [76.76, 118.01]). However, there was no significant difference in waist and hip circumferences, waist-to-hip ratio (WHR), and fat-free mass (FFM) between gradual and rapid WL. The present systematic review and meta-analysis indicates beneficial effects of gradual WL, as compared to rapid WL, on FM, BFP, and RMR in individuals with overweight/obesity. However, FFM changes and anthropometric indices did not significantly differ following different rates of WL.

**Keywords:** weight loss; obesity; fat free mass; fat mass; diet, body composition; resting metabolic rate; meta-analysis.
Introduction

Obesity is a major public health concern across the world\textsuperscript{(1)}. Based on the World Health Organization (WHO) reports, 39% of adults aged 18 years and older (38% of men and 40% of women) were overweight\textsuperscript{(2)}. The worldwide prevalence of obesity nearly doubled between 1980 and 2014, with 11% of men and 15% of women - equivalent to more than half a billion adults - classified as obese\textsuperscript{(2)}.

The definition of obesity is dependent upon the assessment method used (i.e. body mass index [BMI], waist circumference [WC], or body fat percentage [BFP]). BMI is the most common metric used for population and clinical screening for obesity\textsuperscript{(3; 4)}. However, it has been clearly demonstrated that obesity is characterized by an excess accumulation of body fat rather than excess body weight alone\textsuperscript{(5; 6)}. WHO defines obesity as an excessive accumulation of fat to the extent that health may be impaired\textsuperscript{(7)}. Therefore, in addition to weight loss (WL) in general, preferential reduction of fat mass (FM) may be the best way to manage obesity and its complications\textsuperscript{(8)}. As such, the relationships between FM and fat-free mass (FFM) during WL are worthy of consideration. Mathematical modeling by Hall expanded upon early attempts to quantify the proportion of body weight changes attributable to FFM and indicated a small effect of the magnitude of body weight change when initial FM is taken into account and changes in body weight are not large, such as is often observed in lifestyle interventions.\textsuperscript{(9)} However, the rate of body weight change was not considered in these models, and the importance of further longitudinal investigations was emphasized.

Dietary interventions for WL have always been considered the first step in obesity management\textsuperscript{(10)}. Accordingly, a variety of dietary interventions for WL have been suggested\textsuperscript{(11)}. Numerous strategies are based on the distribution of macronutrients such as low-carbohydrate/high-fat, high-carbohydrate/low-fat\textsuperscript{(12)}, or low-carbohydrate/high protein diet\textsuperscript{(13)}, as well as manipulation of energy balance to promote either gradual or rapid WL\textsuperscript{(8)}. Although rapid WL strategies remain appealing to individuals with obesity, it has been hypothesized that gradual WL may produce superior changes in body composition and anthropometric indices\textsuperscript{(8)}. In the scientific literature, some researchers and professional organizations\textsuperscript{(14; 15; 16)} have recommended a gradual WL approach, contending that gradual WL may produce better long-term weight management as compared to rapid WL, which is unlikely to be sustained. However, other researchers\textsuperscript{(17; 18; 19; 20)} have posited that larger calorie deficits and subsequent rapid WL are more likely to reinforce the weight-change process and produce superior long-term WL outcomes. As a result, uncertainty remains regarding the ideal energy intake and rate of WL needed for optimal obesity management. Additionally, other physiological variables could reasonably be influenced by the rate of WL and its potential effects on body composition. Resting metabolic rate (RMR), as the largest component of total energy expenditure, is a proxy indicator of FFM\textsuperscript{(21)}. Some studies showed that obese subjects decreased their RMR following
WL, which is influenced by a decrease in FFM\textsuperscript{(22; 23)}. Moreover, the existence of a low RMR is likely to contribute to reaching to a WL plateau and/or the high rate of weight regain\textsuperscript{(24; 25)}. Changes in RMR with WL could potentially be influenced by the rate of WL \textit{per se} or through effects on FFM.

It is hypothesized that slower WL leads to greater FM loss, and therefore gradual WL diets may better preserve FFM and RMR\textsuperscript{(26)}. Yet, the general impact of the WL rate on body composition changes is unsettled, demonstrating the need for comprehensive systematic reviews and meta-examinations of clinical trials on this topic. Therefore, the aim of this study was to conduct a systematic review and meta-analysis of the pooled data from controlled adult human trials to compare the efficacy of dietary WL with different rates in individuals with overweight and obesity for body composition variables including FM, FFM, BFP, WC, hip circumference (HC), and waist to hip ratio (WHR), as well as RMR.

**Experimental methods**

The present systematic review and meta-analysis adhered to the Preferred Reporting Items of Systematic Reviews and Meta-Analysis (PRISMA) statement guidelines\textsuperscript{(27)}.

**Data sources and search strategies**

A comprehensive literature search of six databases, including PubMed, the Cochrane Library, Web of Science, Embase, SCOPUS, and Ovid, was performed using the keywords “weight loss,” “rapid”, “quick,” “slow,” “gradual,” “rate of weight loss,” “weight reduction”, “diet”, and “caloric restriction” in combination with the keywords “body composition”, “fat mass”, “fat free mass” and “resting metabolic rate” to identify studies in English languages published up to October 10, 2019. The process of study selection is shown in the flow diagram (Figure 1).

**Study Selection and Quality Assessment**

Two authors independently assessed trial eligibility and quality. To be eligible for inclusion, dietary trials had to evaluate gradual vs. rapid WL in patients with overweight/obesity (BMI>25) and report at least one additional body composition parameter or RMR. Trials where both rapid and gradual WL groups lost similar weight (≤ 2 kg between-group differences\textsuperscript{(28; 29)} and/or no significant between-group differences) were included. The Cochrane Collaboration’s tool for assessing the risk of
bias was used to assess the risk of bias as previously described\(^{(30)}\). Briefly, nine items were scored, and these items were divided into 6 domains of bias with 3 rating categories available for each item: (1) low risk of bias; (2) unclear risk of bias; and (3) high risk of bias. All selected articles were scored by 2 authors (DAL and RB). The disagreement between the assessors was resolved by discussion, and in case of remaining discussion, a third assessor (AA) was consulted in order to make a final decision (Table 1).

**Inclusion and exclusion criteria**

Articles were included if they satisfied the following criteria: (1) original research article; (2) designed as a parallel or crossover trial; (3) conducted on humans 18 years of age or older; (4) used dietary-induced WL for interventions; (5) conducted on participants with overweight and/or obesity (6) assessed body composition parameters, anthropometric indices, or RMR; (7) intervention groups did not receive any food or supplement; and (8) similar total WL in both gradual and rapid WL group (<2kg between-group differences). Articles were excluded for: (1) unclear data; (2) lack of clear inclusion and exclusion criteria; (3) different amounts of WL and/or ≥ 2 kg differences between gradual and rapid WL groups; (4) inclusion of normal weight and/or athletic participants; and (5) short study durations (<2 weeks). For articles that contained unclear data, e-mail communications were sent to the corresponding authors to obtain additional information.

**Outcomes and Data Extraction**

Data from eligible studies were extracted by two investigators (DAL and MA) using an Excel form. The following data were extracted from each eligible study: first author, publication year, study location, study population, study design, sample size, type of body composition analysis, method of RMR measurement, age, sex ratio, measures of association, and brief results together with the adjusted covariates.

**Data synthesis and analysis**

Meta-analysis was carried out using Stata version 12.0 (Stata Corp., College Station, TX, USA). The fixed-effects model was used for the assessment of the pooled effect size. When heterogeneity was present, the random-effects model was used. Heterogeneity was tested using the I2 statistic, and an I2 value ≥50% with a level of significance of P<0.05 by the Cochran Q-test was interpreted as evidence of substantial heterogeneity. Publication bias was assessed by a funnel plot analysis, the Begg adjusted rank correlation test, and the Egger regression asymmetry test.
Additionally, the meaning test was used to assess the effect of individual studies by estimating the r values obtained when each study was omitted.

Results

Study selection

The first step of searching yielded 462, 47, 83, and 69 citations in PubMed, Cochrane Library, Web of Science and SCOPUS, respectively. Of these, 287 articles were excluded due to the duplication. The titles and abstracts of 338 articles were reviewed. Of these 323 studies were excluded due to the following reasons: animal model, reviews, non-dietary WL, and unrelated studies. Therefore, the full text of 15 studies assessed for eligibility. Eventually, 7 articles were included in this meta-analysis (8; 26; 31; 32; 33; 34; 35) (Figure 1). It should be noted that not all outcomes were reported in the 7 studies included.

Power analysis

A fixed-effect meta-analysis necessarily results in an increase in power (36). Therefore, we have performed a power analysis for random effect meta-analysis (37). According to the results, we used a random effect model only for FFM. The power calculated for FFM was 0.95.

Characteristics of included studies

All studies except for one were randomized-controlled studies. The intervention duration ranged from 9 to 36 weeks and 5 to 12 weeks in gradual and rapid groups, respectively. Pooled data included 167 participants from gradual WL intervention arms and 194 participants from rapid WL arms. The age range of the participants was 18 to 70 years old. All the included studies were parallel in design. Five studies were conducted on both sexes, and two other studies were performed on only females. Of seven studies were included in the systematic review and meta-analysis, all seven studies reported weight, FM and FFM (8; 26; 31; 32; 33; 34; 35), five studies reported WC (8; 26; 32; 33; 35), four studies reported BMI and HC (8; 26; 32; 33), RMR (8; 26; 31; 34), BFP (8; 26; 33; 34), and three studies reported WHR (8; 26; 33). The basis on the Cochrane Collaboration’s tool, four studies had a low risk of bias (≥4) and a quality score of three studies were lower than 4 (Table 1). The calorie intake also varied between studies. The characteristics of the included studies are summarized in Table 2.

Gradual Weight Loss vs. Rapid Weight Loss

Based on the analysis of 7 RCTs, gradual WL produced greater reductions in FM (weighted mean difference (WMD) kg: -1.00, 95% CI [-1.70, -0.29]) and BFP (WMD: -0.83%, 95% CI [-1.49, -
0.17]). Moreover, gradual WL significantly attenuated the reduction of RMR (WMD: 97.39 kcal, 95% CI [78.78, 118.01]) compared with rapid WL. However, there was no significant difference in body weight (WMD: 0.03 kg, 95% CI [-0.65, 0.71]), BMI (WMD: 0.14 kg/m², 95% CI [-0.25, 0.52]), HC (WMD: 0.21 cm, 95% CI [-1.20, 1.63]), WC (WMD: -0.32 cm, 95% CI [-1.80, 1.16]), FFM (WMD: 0.74 kg, 95% CI [-0.15, 1.64]) and WHR (WMD: -0.00, 95% CI [-0.02, 0.01]) between gradual and rapid WL (Figure 2-10). Mean changes in body composition and RMR in rapid and gradual WL, respectively are as follow: weight: -7.7 ± 3.5 and -7.5 ± 3.5; BMI: -3 ± 1.6 and -3 ± 1.5; FM: -5.6 ± 3.6 and -6.7 ± 3.7; PBF: -2.5 ± 1.8 and -3.8 ± 1.2; WC: -7.8 ± 4.5 and -8.7 ± 4.2; HC: -6.3 ± 4.7 and -7.4 ± 5; WHR: -0.04 ± 0.05 and -0.05 ± 0.5; FFM: -1.6 ± 1.3 and -0.6 ± 0.6; RMR: -136.9 ± 58.6 and -87.5 ± 74.3.

Publication Bias and sensitivity analysis

Publication bias as assessed by Egger's regression asymmetry test were as follows: RMR (p = 0.005), FFM (p = 0.327), HC (p = 0.004), WC (p = 0.093), BFP (p = 0.012), FM (p = 0.405), BMI (p = 0.093), body weight (p = 0.920). Results of the sensitivity analysis indicated that the elimination of each individual study did not change the pooled effect size (Supplementary File 1).

Discussion

In this meta-analysis, we compared the effects of gradual versus rapid WL on body composition in individuals with overweight and obesity. The main result of our analysis was that, when a similar magnitude of WL occurred, gradual WL was associated with greater declines in FM and BFP, as well as superior preservation of RMR. However, the rate of WL was not associated with differential changes in FFM, WC, HC, and WHR.

Previous studies have shown that obesity is a risk factor for all-cause mortality and fatal cardiovascular events\(^{38, 39}\). Moreover, increases in body fat may result in distinct disease risk as compared to increases in BMI alone\(^{40}\). It has been posited that gradual WL may increase the proportion of weight lost as FM. Although our results supported this contention by demonstrating that compared to rapid WL, gradual WL induced larger FM decrements, we did not detect significant differences in metrics of central obesity (i.e., WC and WHR). Several factors could be responsible for the disparity in whole-body FM and anthropometric measures related to central obesity. First, while WC and HC are well-known predictors of central obesity and decrease following dietary WL, they are not the best indices in terms of correlation with FM (as a criterion in obesity evaluation) during dietary WL\(^{8}\). Secondly, while the magnitude of WL observed in the present analysis (6.94 kg in gradual WL and 6.98 kg in rapid WL) elicited decreases in WC and HC, differences in these
anthropometric indicators of central obesity based on the rate of WL may not have been large enough to become distinguishable. Therefore, further studies with long-term interventions, greater magnitudes of WL, or more precise anthropometric measurement methods (41) may be needed to allow for additional evaluation of changes in surface anthropometric indices following gradual and rapid WL.

Preservation of muscle mass accompanied by FM loss is the ideal outcome following dietary WL. In practice, WL achieved through a calorie-reduced diet decreases both FM and FFM, the latter of which contains the majority of skeletal muscle (42). In individuals with overweight or obesity, FFM contributes approximately 20–30% to total WL (43; 44; 45; 46; 47; 48). It is well-established increasing dietary protein attenuates the weight-loss-induced reduction in muscle mass (49; 50; 51). However, the potential health benefits of WL could be attenuated by the WL-associated reduction of FFM (52; 53; 54), which when present along with other co-factors such as smoking and lack of exercise could increase the risk of additional disease states such as sarcopenia (54; 55; 56). Traditionally, a gradual WL has been suggested to be better preserve FFM. Some studies reported that rapid WL diets are suboptimal for FFM preservation (26; 33; 57). However, the present meta-analysis demonstrated that although rapid WL appeared to result in ~1 kg greater mean FFM loss than gradual WL, the difference between WL rates was not statistically significant. Several factors could be responsible for these results. First, it is well-established increasing dietary protein may attenuate the WL-induced reduction in muscle mass (58; 59). Some (two of seven) studies (31; 32) included in the meta-analysis did not report sufficient dietary information for these variables to be considered in the present analysis, meaning it is possible that the percentage of energy derived from different macronutrients, notably protein, could have differed between experimental arms or studies. Second, it has been suggested that the size of the calorie deficit determines the extent of FFM loss (60), and the calorie deficit varied widely in the included studies, even though all investigations implemented some form of a very low-calorie diet (VLCD). Third, although most of the included studies in our analysis directionally favored gradual WL for FFM preservation, the lack of a significant difference could be due to a relatively small magnitude of the effect and the limited duration of these studies. Fourth, studies measured body composition using different methods including bioelectrical impedance analysis (BIA), dual-energy X-ray absorptiometry (DXA), and air displacement plethysmography (ADP) using Bod Pod®. Previous reports have demonstrated that there are significant differences in FFM estimates obtained by these methods (61). Thus, the difference in techniques might explain some variability in the analyzed data. Conversely, only one of seven studies included in our analysis showed apparently superior FFM changes after rapid WL as compared to gradual WL (32). Since this study had a higher number of participants than any other investigation (n=127), the results had a large impact on the overall effect size. In contrast to our analysis, an earlier study that compared gradual and rapid WL, with body-weight reductions of 1.9 vs 1.1 kg/week over 8 weeks, demonstrated that the rapid WL group experienced a larger reduction in FFM (62). However, after adjusting for the magnitude of WL,
differences between groups no longer remained. In addition, Vink et al. (2016) showed during similar WL, rapid WL induced greater loss of FFM compared to gradual WL (1.8 vs 0.6 kg/week)\textsuperscript{(33)}. These contradictory findings indicate the need for more high quality and long-term research to determine if gradual WL is better suited for the preservation of FFM during WL in individuals with overweight and/or obesity. Additionally, despite the lack of statistical significance, the practical significance of the ~1 kg mean difference in FFM between gradual and rapid WL in the present analysis should be considered.

Decreases in RMR are a well-known consequence of WL \textsuperscript{(62; 63; 64; 65; 66)}. A prior investigation demonstrated reductions in RMR following WL occur as early as the first week, with a continued decline until the end of the 10 to 20-week intervention\textsuperscript{(31)}. Similarly, other studies observed a decline in RMR from the early portion of caloric restriction interventions\textsuperscript{(65; 67)}. It has been shown that both rapid and gradual WL may cause decreases in RMR\textsuperscript{(26)}. Our results showed that the rapid WL group presented a larger decrease in RMR. Since FFM contributes to metabolic rate, RMR decreases as FFM is decreased \textsuperscript{(68)}. However, given that changes in FFM do not fully explain the alteration in RMR after WL\textsuperscript{(69)}, it has been suggested that the metabolic, neuroendocrine, and autonomic systems regulating energy stores may be involved\textsuperscript{(70)}. The adipocyte secreted hormone leptin is one such factor, along with Peptide YY and thyroid hormones \textsuperscript{(71)}, which may mediate these adaptive changes in energy expenditure\textsuperscript{(70; 72)}. It has been shown that dietary WL may decrease the plasma levels of both, 3,5,3’ triiodo-L-thyronine (T3) \textsuperscript{(70; 73)} and leptin. Müller and Bosy-Westphal reported a trend for a decline in serum triiodothyronine concentrations (0.2 ± 0.4 ng/dL) that correlated (r = -0.56; p< 0.05) with the decrease in REE adjusted for FFM and FM following 3 weeks of calorie restriction\textsuperscript{(74)}. However, there are limited data concerning the differences in hormonal and neurological responses following slow and rapid WL. Nonetheless, modulation of these physiological factors could be a possible reason for the attenuation in RMR reduction with gradual WL compared to rapid WL despite no statistically significant differences in FFM changes in our analysis. However, only four studies measured RMR while all seven studies measured FFM. Because of limited data on the metabolic effect of the rate of WL, more studies are needed to determine the effects of gradual and rapid WL on RMR.

Our present analysis is not without its limitations. The meta-analysis was based on only seven trials, and some studies did not report dietary contents in each intervention. Thus, it is not possible to evaluate the effects of macronutrient composition or meal frequency on the observed results. Furthermore, since all but one trial lasted less than 4 months, our analysis is unable to show the long-term differences of gradual and rapid WL on anthropometric indices and RMR in individuals with overweight and/or obesity. Another limitation is the devices used for body composition analysis in the included studies. From seven studies, three studies measured body composition by BIA, two studies used DXA, and two other studies used Bod Pod. Although all three methods are established valid
methods of assessing body composition in certain contexts, they do not always reflect changes in body composition associated with WL similarly\textsuperscript{(61)}. Moreover, included studies provided different measures of non-fat tissue, i.e. lean body mass and FFM. It has been mentioned that the differences between LBM and FFM are about 2-3\% \textsuperscript{(75)}. Therefore, the terms LBM and FFM are often used interchangeably\textsuperscript{(76)}. Lastly, the lack of an energy deficit demarcation to define gradual and rapid WL is another limitation of our analysis. While future analyses could perform meta-regression to examine these effects, this is tenuous due to substantial concerns regarding self-reported dietary intake \textsuperscript{(77)} and was beyond the scope of the present analysis.

In conclusion, gradual WL is associated with greater loss of FM and BFP, as well as enhanced maintenance of RMR, in participants with overweight and obesity. However, the rate of WL was not associated with different changes in FFM, WC, HC, and WHR. Additional longer-term and high-quality clinical trials are needed to evaluate the differences of gradual and rapid WL, when similar WL is achieved, on body composition and physiological variables in individuals with overweight and/or obesity to further evaluate and confirm these findings.

Declaration of interest

The authors declare no conflict of interest.
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Figure legends:

**Figure 1.** Flow diagram of the literature search.
Figure 2. Forest plot of the fixed-effects meta-analysis of the effect of gradual vs. rapid weight loss on body weight.
Figure 3. Forest plot of the fixed-effects meta-analysis of the effect of gradual vs. rapid weight loss on fat mass.
**Figure 4.** Forest plot of the fixed-effects meta-analysis of the effect of gradual vs. rapid weight loss on body fat percentage.
Figure 5. Forest plot of the random-effects meta-analysis of the effect of gradual vs. rapid weight loss on fat free mass.
Figure 6. Forest plot of the fixed-effects meta-analysis of the effect of gradual vs. rapid weight loss on resting metabolic rate.
Figure 7. Forest plot of the fixed-effects meta-analysis of the effect of slow vs. rapid weight loss on body mass index.
**Figure 8.** Forest plot of the fixed-effects meta-analysis of the effect of slow vs. rapid weight loss on waist circumference.
Figure 9. Forest plot of the fixed-effects meta-analysis of the effect of slow vs. rapid weight loss on hip circumference.
Figure 10. Forest plot of the fixed-effects meta-analysis of the effect of slow vs. rapid weight loss on waist-hip ratio.