

REVIEW

Effect of Clinically Significant Weight Loss on Remission of Metabolic Complications: A Rapid Review and Meta-Analysis of Comparative Controlled Studies

Srividya Adapa¹  | Paul Fahey¹ | Milan Piya^{2,3}  | Frehiwot Birhanu¹ | Evan Atlantis¹

¹School of Health Sciences, Western Sydney University, Campbelltown, New South Wales, Australia | ²School of Medicine, Western Sydney University, Campbelltown, New South Wales, Australia | ³Campbelltown and Camden Hospitals, Campbelltown, New South Wales, Australia

Correspondence: Srividya Adapa (22069614@student.westernsydney.edu.au)

Received: 18 October 2024 | **Revised:** 28 October 2025 | **Accepted:** 24 December 2025

Keywords: meta-analysis | obesity | remission | weight loss

ABSTRACT

The strength of the association between achieving clinically significant weight loss and remission of metabolic complications remains unclear. This rapid review aimed to investigate the effect of weight loss on remission of metabolic risk factors. We searched Embase, Medline, Web of Science, and Google Scholar databases (up to June 2025) for studies comparing the effects of $\geq 5\%$ versus $< 5\%$ total weight loss (%TWL) for at least 12 months. Mean differences (MD) and risk ratios (RR) with 95% confidence intervals (95% CI) were calculated for the meta-analysis. A total of 43 comparative studies were reviewed. Compared to $< 5\%$ TWL, $\geq 5\%$ TWL had a higher RR of type 2 diabetes remission (RR = 7.88; 95% CI = 5.00, 12.43; $I^2 = 75.2\%$), hypertension remission (RR = 2.23; 95% CI = 1.06, 4.68; $I^2 = 70.5\%$), and metabolic syndrome remission (RR = 5.61; 95% CI = 1.62, 19.49; $I^2 = 70.2\%$). Compared to $< 5\%$ TWL, $\geq 5\%$ TWL participants achieved significant MDs in HbA1c (MD = -1.06; 95% CI = -1.40, -0.71), fasting plasma glucose (MD = -1.13; 95% CI = -1.84, -0.43), systolic blood pressure (MD = -3.65; 95% CI = -5.56, -1.74), diastolic blood pressure (MD = -3.26; 95% CI = -6.31, -0.20), triglycerides (MD = -0.26; 95% CI = -0.45, -0.06), and HDL-cholesterol (MD = 0.09; 95% CI = 0.04, 0.14). Remission of metabolic complications and improvements in HbA1c, blood pressure, lipids, and fasting insulin were observed following $\geq 5\%$ TWL in people with obesity in a dose-response manner. Factors like the %TWL achieved (particularly $\geq 15\%$), bariatric surgery, and duration of follow-up predict these outcomes.

1 | Introduction

Obesity, a chronic disease characterized by an excessive accumulation of adipose tissue leading to adverse health effects, results from a complex interaction of environmental, biochemical, and genetic factors that contribute to positive energy imbalance [1]. The global prevalence of obesity has more than doubled since 1990, with over one billion people now living with this chronic disease [2]. This epidemic has far-reaching consequences for societies worldwide, contributing significantly to the global burden of disease [3]. Obesity is associated with various chronic medical conditions including cardiovascular disease, hypertension, type

2 diabetes, nonalcoholic fatty liver disease, osteoarthritis, polycystic ovary syndrome, and sleep apnea [4]. Additionally, it is associated with mental, eating, and behavioral disorders, along with functional impairments [5, 6], underscoring its importance as a public health concern.

Furthermore, increased healthcare utilization and associated costs arising from obesity represent a significant financial burden on healthcare systems. Obesity imposes a substantial economic burden on societies worldwide. Direct medical costs alone account for a significant portion of healthcare expenditure, while indirect costs, such as lost productivity, further

exacerbate the financial impact [7]. The significant health and economic consequences associated with the obesity epidemic underscore the need for timely and effective solutions.

Clinical practice guidelines advocate weight loss to mitigate or resolve obesity-related complications. A modest 5% weight loss can lead to initial improvements in many of the obesity-related medical conditions, including type 2 diabetes, hypertension, and dyslipidemia [8, 9], and greater weight loss may offer additional benefits. Specifically, achieving reductions of 10% or 15% body weight has been associated with further significant improvements in various health outcomes such as obstructive sleep apnea, nonalcoholic fatty liver disease, and osteoarthritis [4, 8, 10]. While existing reviews primarily consist of narrative descriptions of the association between weight loss thresholds and disease remission, they lack quantitative meta-analyses to precisely estimate the effect size and investigate potential moderating factors.

This rapid review aims to quantitatively synthesize the evidence from studies of the effect of clinically significant weight loss on the remission of weight-related complications. Through this study, we hope to provide timely and robust evidence informing clinical decision-making and weight management strategies for improved patient outcomes.

1.1 | Research Question

What is the strength and size of the effect of clinically significant weight loss on remission of weight-related complications after a minimum of 1 year of treatment or follow-up?

2 | Methods

The development of this rapid review protocol was guided by previous research [11], the Centre for Review and Dissemination's Guidance for undertaking reviews in health-care, [12] the Joanna Briggs Institute methodology [13], the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols statement [14], and following updated Cochrane recommendations to provide timely synthesis of available evidence [15]. Our decision to conduct a rapid review was based on the need to synthesize emerging evidence on the health impacts of modest weight loss within a limited timeframe to inform ongoing clinical and policy discussions. As recommended by the updated Cochrane Rapid Review Methods Guidance [15], rapid reviews use streamlined systematic approaches, such as single-reviewer screening with verification and focused data extraction, to balance methodological rigor with timeliness.

2.1 | Eligibility Criteria

Using modified versions of the Population, Interventions, Comparators, and Outcomes [16] framework as shown in the Supplementary Table S1, we developed a research question and selected study eligibility criteria [17]. Inclusion criteria for studies appear in the Supplementary (Supplementary Table S1).

2.2 | Information Sources, Search Strategy, and Selection Process

The search strategy was developed in consultation with the subject experts (E.A., M.P.) and an academic librarian. Using keywords and phrases in specific fields including titles and abstracts, one author (S.A.) searched the recommended optimal combination of databases [18], including Embase, Medline, Web of Science, and Google Scholar databases, for potentially relevant articles up to April 2023. Although one author (S.A.) searched the recommended optimal combination of databases, the search strategy and its execution were verified by a second author (E.A.). An updated search was conducted from May 2023 to June 2025, with the updated search strategy detailed in Supplementary Table S3a. Filters were applied to limit the results to English language and adults (Supplementary Tables S2, S3). All records identified were exported from the databases into EndNote 20 reference manager and duplicate records were removed where possible. One reviewer (S.A.) first screened all titles and abstracts for eligibility against the inclusion criteria (Supplementary Table S1). Unclear abstracts and any uncertainties were resolved through discussion with the other authors (E.A., M.P., and P.F.). The available full-length reports retrieved from these records were screened by the initial reviewer (S.A.) for possible inclusion. A second reviewer (E.A.) independently verified all excluded full-text records to ensure that no relevant studies were omitted. Any conflicts were resolved through discussion and consensus. References from included studies were also searched. Reasons why studies identified in the second screen were excluded are provided in the Supplementary (Supplementary Table S4) and the reasons for exclusion of studies identified in the updated search are presented in Supplementary Table S4a.

2.3 | Data Extraction and Risk of Bias Assessment Process

We independently extracted and/or verified key characteristics (S.A., F.B., E.A.) and assessed the risk of bias (S.A., M.P.) of the studies included for review using the JBI's standardized critical appraisal checklists [19]. We used this information to assist our discussion on the strength of the body of evidence following our synthesis of results.

2.4 | Data Items

Our primary outcome of interest was remission of metabolic complications as defined by the studies themselves. The authors used different criteria, such as American Diabetes Association criteria [20, 21], or "Cleveland Clinic Bariatric Surgery Group criteria" [22], to define complete and partial remission of type 2 diabetes. American Diabetes Association 2009 Consensus Statement defined complete remission of type 2 diabetes as a fasting glucose level < 110 mg/dL, in addition to an HbA1c < 6.0% of total Hb, without use of any oral antidiabetic drugs or insulin. Partial remission was defined as a fasting glucose level between 110 and 126 mg/dL, in addition to an HbA1c level between 6.0% and 6.5% of total Hb, without use of any oral antidiabetic drugs or insulin. According to Cleveland

Clinic Bariatric Surgery group criteria, complete remission was defined as HbA1c < 6% and FPG < 100 mg/dL for 1 year in the absence of antidiabetic medications. Partial remission was defined as HbA1c 6%–6.4% and FPG 100–125 mg/dL for 1 year in the absence of antidiabetic medications. Two studies defined partial remission of diabetes as a transition from meeting diabetes criteria to a prediabetes level of glycemia (i.e., fasting plasma glucose level of 100–126 mg/dL and HbA1c of 5.7%–6.5%) with no antihyperglycemic medication and complete remission was defined as transition from diabetes criteria to full normalization of glucose (fasting plasma glucose level < 100 mg/dL and HbA1c < 5.7%) with no antihyperglycemic medications [23, 24]. Another two studies have defined diabetes resolution as HbA1c < 6.5% and FPG < 126 mg/dL with or without anti diabetes medication [25, 26]. Remission of hypertension was defined as a blood pressure less than 140/90 mmHg [27, 28] and stoppage of antihypertensive drugs for 6 months or more [27] or without current usage of antihypertensive drugs [28]. Patients were considered to have achieved remission of metabolic syndrome if they were no longer meeting the National Cholesterol Education Program Adult Treatment Panel III criteria [29–31]. We aimed to capture all available data on remission using these definitions as categorical outcomes. In addition to the primary outcome, we also extracted data on the mean differences between groups for continuous outcome variables. We aimed to collect all results compatible with this outcome domain in each study, including data from different time points and analyses. We also sought data on study characteristics, including population and setting, intervention groups ($\geq 5\%$ vs. $< 5\%$ weight loss groups), outcomes (remission or improvement in weight related complications), statistical methods, results/effect estimates, and author's conclusions. We assumed that missing data on outcomes or other variables indicated that the information was not reported in the study.

2.5 | Effect Measures

We categorized treatment groups based on percentage total weight loss (TWL). Groups with a mean TWL $\geq 5\%$ were compared to groups with a mean TWL $< 5\%$. For categorical outcomes (e.g., remission rates), we extracted the total number of participants and the number with the desired outcome (e.g., remission) for each treatment group. For continuous outcomes (e.g., blood pressure), we extracted the mean change from baseline and its associated standard deviation (SD) for each treatment group.

2.6 | Synthesis Methods

We used separate random-effects meta-analyses to pool the results for each clinical outcome. Pooled risk ratios (RRs) with 95% confidence intervals (CIs) were calculated for categorical outcomes, while pooled mean differences (MDs) with 95% CI were used for continuous outcomes. A detailed description of the methods used to prepare the data for synthesis, including handling of missing summary statistics and data conversions, is provided in the Supplementary (Supplementary Section 1). We employed inverse variance weights throughout

to minimize the influence of heterogeneity on the pooled estimates [32]. For meta-analyses including more than one comparison from the same study, we utilized a multivariate random-effects model to account for both within-study and between-study variations.

A meta-regression analysis was used to investigate how moderators, such as the difference in %TWL between two groups, weight loss categories ($\geq 15\%$ vs. $< 15\%$), intervention type (bariatric surgery vs. nonsurgery), length of follow-up (categorized as ≥ 36 and < 36 months), and risk of bias score (categorized as $\geq 75\%$ and $< 75\%$) might influence the overall effect size. This identified factors contributing to the variation in weight-loss treatment effectiveness on remission and improvement of metabolic disease outcomes observed across studies. Statistical significance was defined as $p < 0.05$, and clinical significance was determined based on conventional definitions of meaningful improvements in metabolic risk factors [33]. All analyses were conducted using the `metafor()` package in R. For the multivariate analysis, we calculated I^2 statistics and assessed publication bias using Egger's test implemented from first principles.

2.7 | Reporting Bias and Certainty Assessments

We employed meta-regression and sensitivity analyses to explore potential sources of heterogeneity (variation) in the effect sizes across studies. Meta-regression was only conducted when there were at least 10 between-group comparisons available for pooling, following recommendations from the Cochrane Handbook [34].

Forest plots are used to visually present both individual and pooled study results. Heterogeneity is quantified using the I^2 statistic (percentage of total variation attributable to between-study differences) and τ^2 statistic (measure of between-study variance). Additionally, we report p values from the chi-square test of heterogeneity to assess the statistical significance of the observed heterogeneity.

Publication bias, where studies with statistically significant results are more likely to be published, was evaluated using funnel plots and Egger's test. However, these analyses were only performed when there were at least 10 between-group comparisons available, as recommended by the Cochrane Handbook [34].

3 | Results

3.1 | Study Selection

A flow diagram of the study selection process is presented in the Supplementary (Supplementary Figure 1). Our search strategy identified 3460 records after the removal of 1828 duplicates. Out of these, 3312 records were excluded following the initial screening, and 12 records were excluded because of the unavailability of full-text versions, leaving 136 full-text articles for a second screening. Upon further evaluation, 99 additional records were excluded for reasons summarized in the

Supplementary (Supplementary Table S4). A flow diagram of the study selection process for the updated search is presented in the Supplementary (Supplementary Figure S1a). Our updated search strategy identified 1425 records after the removal of 315 duplicates. Out of these, 1388 records were excluded following the initial screening, and two records were excluded because of the unavailability of full-text versions, leaving 35 full-text articles for a second screening. Upon further evaluation, 29 additional records were excluded for reasons summarized in the Supplementary (Supplementary Table S4a).

3.2 | Study Characteristics

A detailed summary of the study characteristics is provided in Supplementary (Supplementary Table S5 and TS5a). We identified a total of 43 studies on weight management interventions for obesity published between 2003 and June 2025: 25 randomized controlled trials [20, 23–26, 31, 35–53], 13 observational studies [21, 22, 27, 28, 30, 54–61], four nonrandomized experimental studies [29, 62–64], and one cross-sectional study [65]. Geographically, studies originated from diverse locations, with the majority conducted in the United States ($n=22$) [20, 22–26, 28, 29, 35–40, 42, 44, 46, 51, 58, 61, 63, 65], followed by Australia ($n=4$) [31, 47, 48, 55], Italy ($n=3$) [43, 56, 62] and the United Kingdom ($n=3$) [41, 50, 59], and Brazil ($n=2$) [30, 52]. Notably, one study [64] encompassed 19 research sites across eight European countries, and another [49] spanned 129 research sites in 16 countries, as well as one study each from Pakistan [54], Taiwan [21], Kazakhstan [45], Norway [57], Egypt [27], South Korea [53], and China [60]. Sample sizes varied considerably, ranging from 18 to 4503 participants. Many studies ($n=24$) focused on individuals with a confirmed diagnosis of type 2 diabetes [20–26, 29, 31, 38, 41, 43, 44, 46–48, 51, 55, 56, 59, 60, 62, 63, 65]. Others studied populations included those with metabolic syndrome ($n=2$) [39, 45], and prediabetes ($n=1$) [39] and hypertension ($n=1$) [52] only. Notably, three studies [27, 57, 58] specifically recruited patients with severe obesity (body mass index [BMI] ≥ 40 kg/m² or ≥ 35 kg/m² with comorbidities) while four included individuals with a BMI of < 35 kg/m² [21, 54, 62, 63]. The remaining studies involved participants with a broader range of BMIs (25–45 kg/m²). Regarding intervention types, most studies ($n=24$) compared bariatric surgical interventions to nonsurgical approaches [20–22, 24–28, 30, 31, 43, 45–48, 52, 54, 57–60, 62, 63, 65]. Of these, three studies specifically compared laparoscopic sleeve gastrectomy (LSG) [27, 54, 62], seven compared Roux-en-Y gastric bypass (RYGB) [22, 25, 28, 30, 52, 57, 65], and four compared laparoscopic adjustable gastric banding (LAGB) to nonsurgical interventions [26, 31, 47, 48].

Several studies investigated various pharmacological and non-pharmacological interventions for weight management. Nine studies evaluated anti-obesity medications as an adjunct to lifestyle interventions compared to placebo and lifestyle interventions. These included the COR-11 study on naltrexone/bupropion [35], the BLOSSOM and the BLOOM-DM trials [37, 44] on lorcaserin, the QUEEN'S [53] the CONQUER and the SEQUEL trials [36, 39, 40] on phentermine and topiramate extended release. Additionally, the STEP 1 Trial assessed

semaglutide, A GLUCAGON LIKE PEPTIDE-1 (GLP-1) receptor agonist to placebo plus lifestyle interventions [49], while another study compared liraglutide, a GLP-1 analogue, to orlistat, a lipase inhibitor [64]. Six studies also compared the effectiveness of lifestyle interventions versus usual care for type 2 diabetes [23, 29, 38, 41, 42, 55]. Furthermore, one study investigated a very-low calorie ketogenic diet versus a standard low-calorie diet [56]. The included studies have a follow-up duration from 1 to 12 years.

3.3 | Risk of Bias in Studies

The results of our JBI risk of bias assessment of each study are presented in the Supplementary (Supplementary Table S6). All randomized controlled trial studies had at least 60% of the JBI risk of bias items clearly met, with 17 studies having one to three items unclear [20, 23, 24, 31, 35, 36, 38–40, 42–44, 46, 47, 49, 50]. Of the four nonrandomized experimental studies, two studies had 100% of the risk of bias items clearly met [62, 64] and two studies had 90% of the risk of bias items clearly met [29, 63]. Of the 13 cohort studies, 12 studies had at least 60% [21, 22, 27, 28, 30, 55–61], and one study had 45% [54] of the risk of bias items clearly met. One study, which is a cross-sectional design, had 100% of the risk of bias clearly met [65].

3.4 | Results of Syntheses

3.4.1 | Type 2 Diabetes Remission (Partial or Complete)

Pooled analysis of 25 pairs of comparison groups [20–29, 31, 41, 43, 48, 50, 57, 58, 61–63, 65] from 21 studies ($n=11,369$) showed a significantly increased RR of type 2 diabetes remission in groups achieving $\geq 5\%$ TWL compared to $< 5\%$ TWL (RR=7.88, 95% CI: 5.00, 12.43, Figure 1). Significant heterogeneity was present ($I^2=75.2\%$, $p<0.0001$). While visual inspection of funnel plot suggested asymmetry, Egger's test was not significant ($p=0.06$, Supplementary Figure 2). Meta-regression showed a higher difference in mean %TWL was associated with a greater RR of remission (RR=1.13, 95% CI: 1.09, 1.17, $I^2=76.8\%$). Further analysis revealed a stronger risk of remission for groups achieving $\geq 15\%$ TWL versus $< 15\%$ TWL (RR=5.02, 95% CI: 3.13, 8.06, $I^2=78.1\%$, Figure 2). Dichotomous meta-regressions revealed no significant associations for intervention type ($p=0.77$), follow-up length ($p=0.73$), or risk of bias score ($p=0.96$) with type 2 diabetes remission.

3.4.2 | HbA1c

Pooled analysis of 29 pairs of comparison groups [20–22, 24, 31, 38, 40–46, 48–51, 53–56, 59, 62] from 23 studies ($n=3964$) revealed a statistically and clinically significant MD in mean changes in HbA1c for groups achieving $\geq 5\%$ TWL compared to $< 5\%$ TWL (MD = -1.06%, 95% CI: -1.40, -0.71, Figure 3). There was substantial statistically significant heterogeneity ($I^2=99.4\%$). While visual inspection of funnel plot suggested asymmetry, Egger's test was not significant ($p=0.37$,

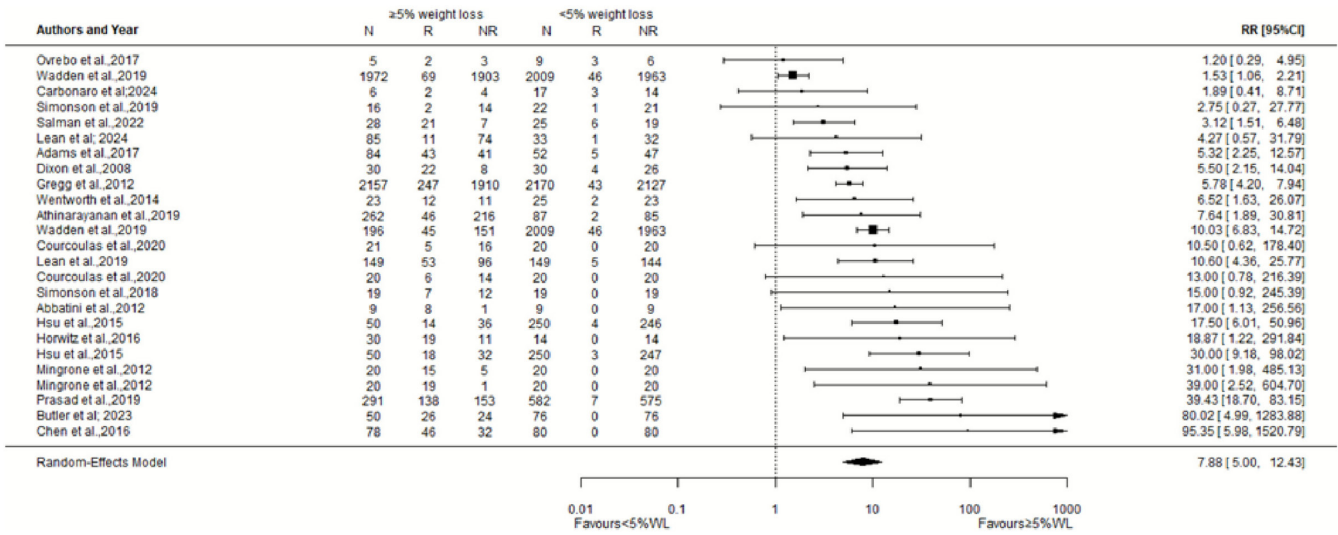


FIGURE 1 | Forest plot of comparison: < 5% WL versus ≥ 5%WL for T2D remission. *N* = sample size, *NR* = no. of patients not achieving remission of T2D, *R* = no. of patients achieving remission of T2D, RE Model = random effects model, *RR* = risk ratio. All the results are presented on logarithm scale.

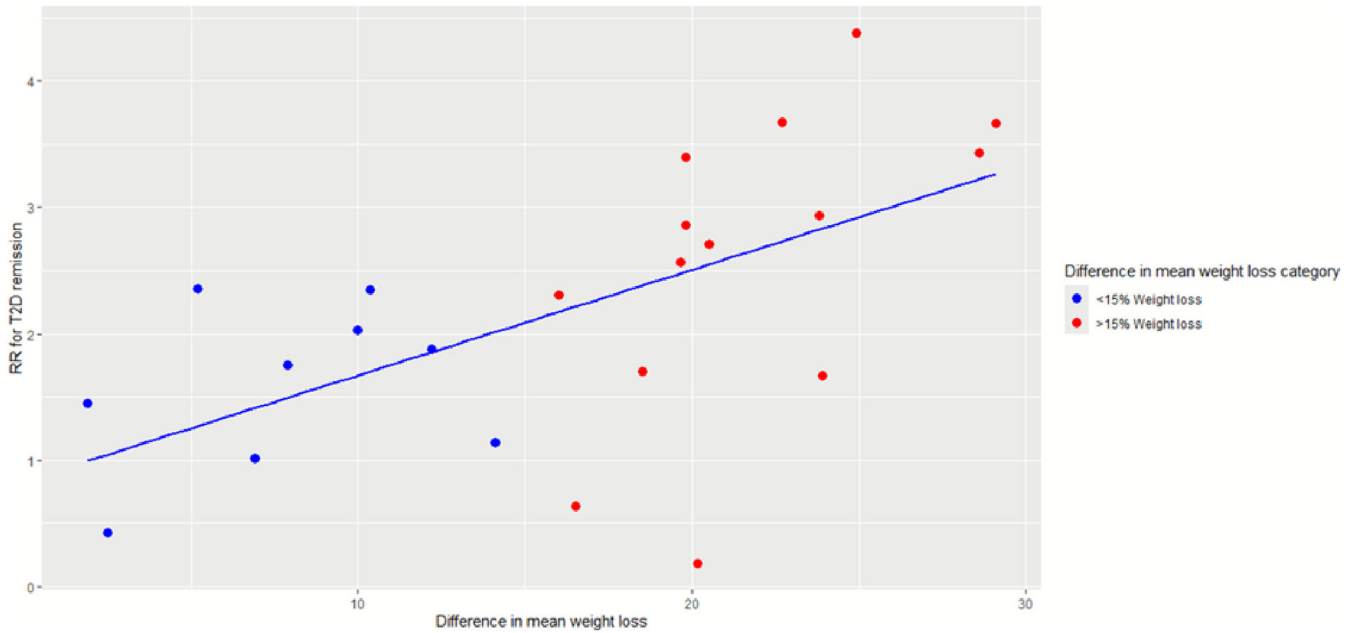


FIGURE 2 | Scatter plot >15%WL versus <15%WL for T2D remission.

Supplementary Figure 3). Meta-regression showed higher difference in mean %TWL was associated with a larger effect size for HbA1c reduction ($\beta = -0.08$, 95% CI: $-0.10, -0.06$). Further analysis revealed a stronger association for participants achieving $\geq 15\%$ versus $< 15\%$ TWL ($\beta = -0.89\%$, 95% CI: $-1.14, -0.64$, $I^2 = 98.1\%$, Figure 4). While intervention type ($\beta = -1.24$, 95% CI: $-1.71, -0.78$, $p < 0.0001$) and follow-up duration ($\beta = -0.92$, 95% CI: $-1.57, -0.27$, $p = 0.01$) were significant predictors, risk of bias score ($p = 0.30$) did not significantly influence HbA1c reductions. In one study which was not included in the meta-analysis, there was a significant increase in percentage of patients achieving HbA1c $< 7\%$ in those achieving $\geq 5\%$ TWL compared to those achieving $< 5\%$ TWL (60% vs. 43%, $p = 0.014$) [60].

3.4.3 | Fasting Plasma Glucose

Pooled analysis of 14 pairs of comparison groups [20, 27, 31, 40, 43–45, 48, 53, 57] from 10 studies ($n = 653$) revealed a statistically and clinically significant MD in mean changes in fasting plasma glucose for groups achieving $\geq 5\%$ TWL compared to $< 5\%$ TWL (MD = -1.13 , 95% CI: $-1.84, -0.43$, Figure 5). There was substantial statistically significant heterogeneity ($I^2 = 98.4\%$). Although visual inspection of funnel plot suggested asymmetry, Egger's test for publication bias was not significant ($p = 0.25$, Supplementary Figure 4). Meta-regression showed that a higher difference in mean %TWL was associated with a larger effect size for fasting plasma glucose ($\beta = -0.12$, 95% CI: $-0.17, -0.07$, $I^2 = 97.6\%$). Further analysis revealed a stronger association for

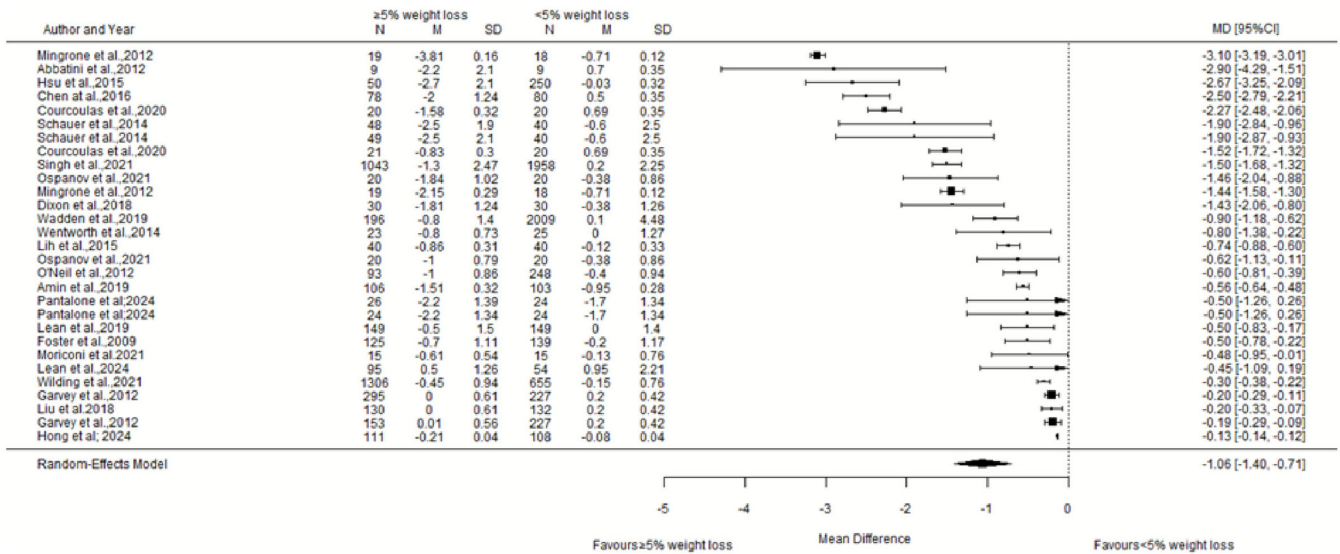


FIGURE 3 | Forest plot of comparison: <5% WL versus ≥5%WL for mean changes in HbA1c. M = mean change in HbA1c, MD = mean difference, N = sample size, RE model = random effects model, SD = standard deviation.

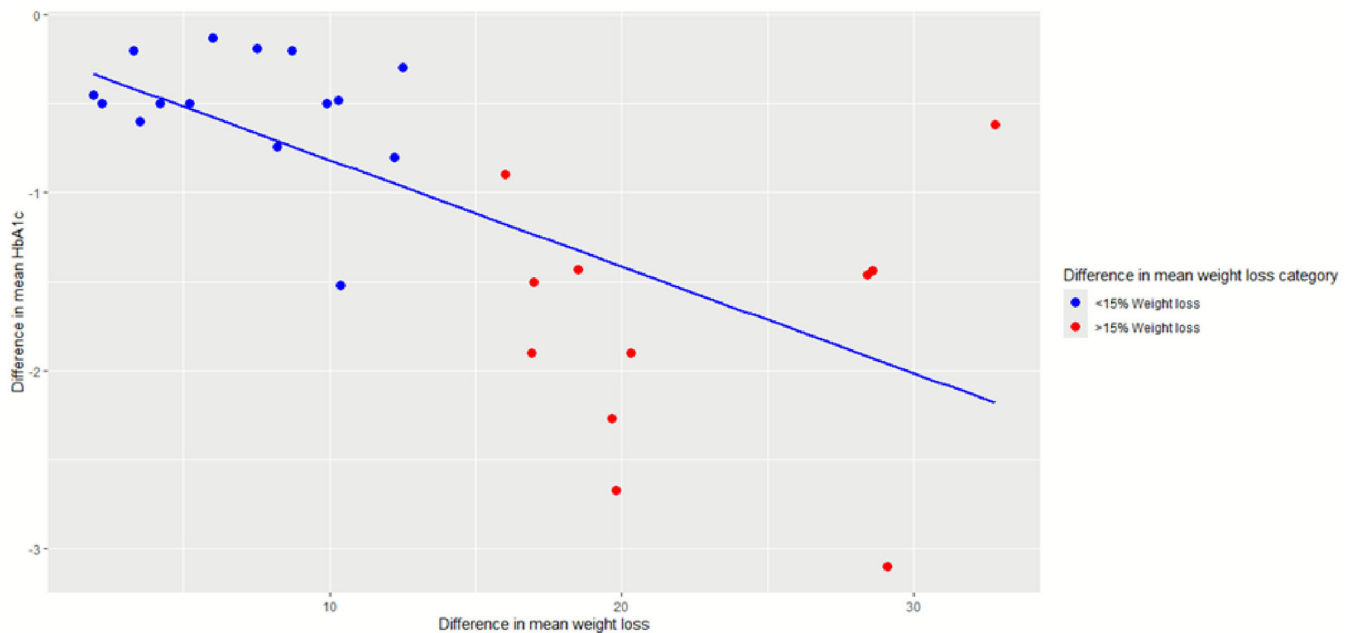


FIGURE 4 | Scatter plot >15%WL versus <15%WL for mean changes in HbA1c.

participants achieving ≥15%TWL versus <15%TWL ($\beta = -1.63$, 95% CI: $-2.20, -1.05$, $I^2 = 97.1\%$, Supplementary Figure S4a). While risk of bias score was a significant predictor ($\beta = 1.41$, 95% CI: $0.26, 2.56$, $I^2 = 96.9\%$), intervention type ($p = 0.16$) and follow-up length ($p = 0.56$) did not significantly influence fasting plasma glucose improvement.

3.4.4 | Fasting Insulin

Pooled analysis of three pairs of comparison groups [40, 44] from two studies ($n = 314$) revealed a significant MD in mean changes in fasting insulin for groups achieving ≥5%TWL compared to <5%TWL ($\beta = -1.99$, 95% CI: -3.79 to -0.19 , Supplementary Figure 5). There was moderate heterogeneity, which was not

statistically significant ($I^2 = 41.13\%$, $p = 0.4176$). One study [45] excluded from the meta-analysis showed significantly greater mean reductions in homeostasis model assessment for insulin resistance (HOMA-IR), among participants achieving ≥5%TWL with laparoscopic one anastomosis gastric bypass compared to those with <5%TWL with nonsurgical intervention (-7.67 vs. -1.56 , $p < 0.001$). Furthermore, another excluded study [47] reported significant changes in insulin sensitivity markers with median increase in fasting HOMA-S_{INSULIN} (47 vs. 4, $p = 0.0057$) and HOMA-S_{C-PEPTIDE} (29 vs. -1 , $p = 0.0006$) in the group achieving ≥5%TWL compared to the group with <5%TWL. There was a significant increase in median (interquartile range) area under the curve (AUC)_{C-PEPTIDE} after intravenous glucose tolerance test (IVGTT) from 2.11 (0.89, 5.19) nmol min⁻¹ at baseline to 3.60 (1.33, 8.23) nmol min⁻¹ at 2

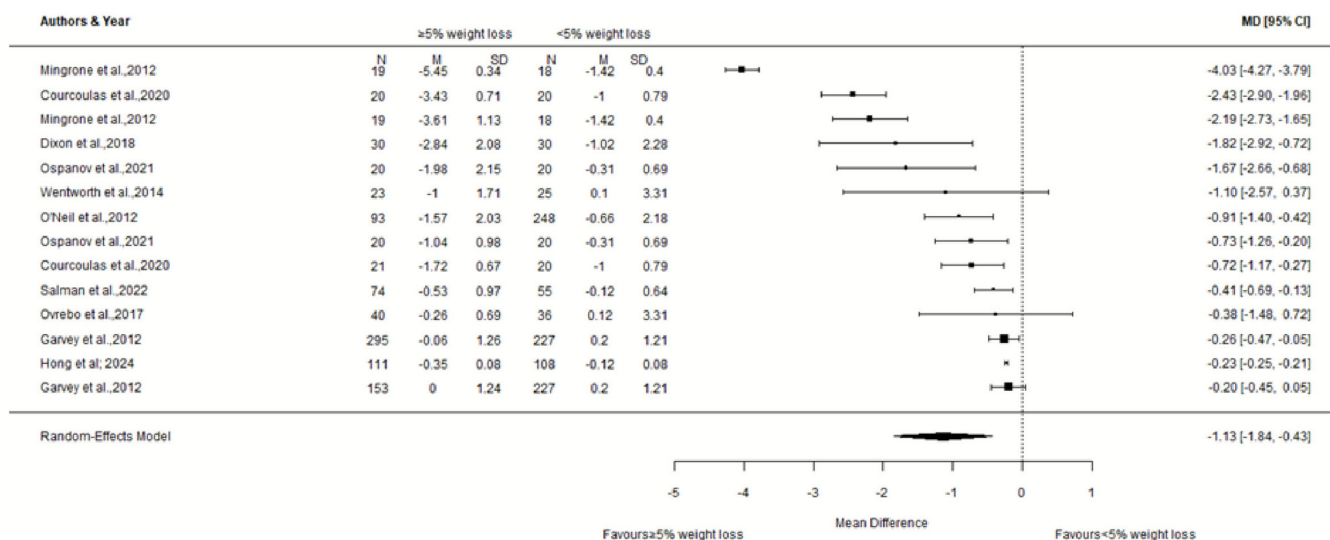


FIGURE 5 | Forest plot of comparison: <5% WL versus ≥5%WL for mean changes in FPG. M = mean change in FPG, MD = mean difference, N = sample size, RE model = random effects model, SD = standard deviation.

years in ≥5%TWL group, whereas $AUC_{C-PEPTIDE}$ did not change significantly in <5%TWL group, and there were no significant changes in glucose control and insulin response ($AUC_{GLUCOSE}$ and $AUC_{INSULIN}$) after IVGTT between two groups [47].

3.4.5 | Hypertension Remission

Pooled analysis of five pairs of comparison groups [27, 28, 57, 61] and four studies ($n=409$) showed a significantly increased RR of hypertension remission for groups achieving ≥5%TWL compared to <5%TWL (RR=2.23, 95% CI: 1.06,4.68, $I^2=70.5%$, Supplementary Figure S6). One study [36] excluded from the meta-analysis showed that, among participants with uncontrolled hypertension at baseline, rates of achieving blood pressure targets at follow-up were higher for those achieving ≥5%TWL compared to those achieving <5%TWL (75.0% vs. 52.9%, $p=0.003$) with the higher dose of phentermine and topiramate extended-release but not the lower dose medication (62.5% vs. 52.9%, $p=0.30$).

3.4.6 | Systolic Blood Pressure

Pooled analysis of 15 pairs of comparison groups [35, 37, 39, 41, 45, 48, 49, 52–56, 64] from 13 studies ($n=4165$) revealed a statistically significant MD in mean changes in systolic blood pressure for groups achieving ≥5%TWL compared to <5%TWL (MD=−3.65, 95% CI: −5.56, −1.74, Supplementary Figure S7). Substantial heterogeneity was present ($I^2=94.1%$), and a funnel plot suggested publication bias (Egger's test, $p=0.001$; Supplementary Figure S7a). Meta-regression showed a higher difference in mean %TWL was associated with a larger effect size for systolic blood pressure ($\beta=-0.42$, 95% CI: −0.64, −0.20, $I^2=79.4%$). Further analysis revealed a stronger association for groups achieving ≥15%TWL versus <15%TWL ($\beta=-7.86$, 95% CI: −13.95, −1.77, $I^2=90.1%$, Supplementary Figure S7b). While intervention type was a significant predictor ($\beta=-7.07$, 95% CI: −12.10, −2.03, $I^2=89.8%$, Supplementary Figure S7c),

meta-regression with risk of bias score ($p=0.39$) revealed no associations with systolic blood pressure improvement.

3.4.7 | Diastolic Blood Pressure

Pooled analysis of 11 pairs of comparison groups [35, 37, 39, 45, 48, 52, 53, 56, 64] from nine studies ($n=2564$) revealed a statistically significant MD in mean changes in diastolic blood pressure for groups achieving ≥5%TWL compared to <5%TWL (MD=−3.26, 95% CI: −6.31, −0.20, Supplementary Figure S8). Substantial heterogeneity was present ($I^2=98.7%$), and a funnel plot suggested publication bias (Egger's test, $p=0.02$; Supplementary Figure S8a). Meta-regression showed that a higher difference in mean %TWL was associated with a larger effect size for diastolic blood pressure ($\beta=-0.37$, 95% CI: −0.53, −0.22, $I^2=91.6%$, Supplementary Figure S8b). Further analysis revealed a stronger association with a larger effect size for groups achieving ≥15%TWL versus <15%TWL ($\beta=-8.24$ mmHg, 95% CI: −12.44, −4.05, $I^2=94.2%$, Supplementary Figure S8c). Intervention type was a significant predictor ($\beta=-7.73$, 95% CI: 12.48, −2.99, $I^2=95.7%$, Supplementary Figure S8d).

3.4.8 | Triglycerides

Pooled analysis of 11 pairs of comparison groups [20, 35, 37, 41, 43, 52, 53, 55] from eight studies ($n=2403$) revealed a statistically significant MD in mean changes in triglycerides for participants achieving ≥5%TWL compared to <5%TWL (MD=−0.26, 95% CI: −0.45, −0.06, Supplementary Figure S9). Substantial heterogeneity was present ($I^2=98.5%$) and a funnel plot suggested publication bias (Egger's test, $p<0.0001$; Supplementary Figure S9a). Meta-regression showed higher difference in mean %TWL was associated with a larger effect size for triglycerides ($\beta=-0.05$, 95% CI: −0.07, −0.04, $I^2=98.4%$, Supplementary Figure S9b). Further analysis revealed a stronger association with a larger effect size for groups achieving ≥15%TWL versus <15%TWL ($\beta=-0.59$, 95% CI: −0.74, −0.45,

$I^2 = 94.7\%$, Supplementary Figure S9c). Intervention type was a significant predictor ($\beta = -0.49$, 95% CI: $-0.74, -0.25$, $I^2 = 94.9\%$, Supplementary Figure S9d). Length of follow-up ($p = 0.21$) and risk of bias score ($p = 0.71$) showed no association with the improvement of triglycerides.

3.4.9 | HDL-Cholesterol

Pooled analysis of 12 pairs of comparison groups [20, 35, 37, 41–43, 51, 55, 64] from nine studies ($n = 2407$) revealed a statistically significant MD in mean changes in HDL-cholesterol for participants achieving $\geq 5\%$ TWL compared to $< 5\%$ TWL (MD = 0.09, 95% CI: 0.04, 0.14, $I^2 = 97.2\%$, Supplementary Figure S10). Funnel plot suggested insufficient evidence of publication bias (Egger's test, $p = 0.51$; Supplementary Figure S10a). Meta-regression showed higher difference in mean %TWL was associated with a larger effect size for HDL-cholesterol ($\beta = 0.01$, 95% CI: 0.01, 0.02, $I^2 = 96.7\%$, Supplementary Figure S10b). Further analysis revealed a stronger association with a larger effect size for groups achieving $\geq 15\%$ TWL versus $< 15\%$ TWL ($\beta = 0.19$, 95% CI: 0.15, 0.23, $I^2 = 90.5\%$, Supplementary Figure S10c). Intervention type was a significant predictor ($\beta = 0.14$, 95% CI: 0.07, 0.20, $I^2 = 83.6\%$, Supplementary Figure S10d). Length of follow-up ($p = 0.06$) and risk of bias score ($p = 0.12$) showed little evidence of association with the improvement of triglycerides.

3.4.10 | LDL-Cholesterol

Pooled analysis of eight pairs of comparison groups [20, 35, 37, 51, 55, 64] from six studies ($n = 2288$) revealed a statistically nonsignificant MD in mean changes in LDL-cholesterol for groups achieving $\geq 5\%$ TWL compared to $< 5\%$ TWL (MD = 0.04, 95% CI: $-0.07, 0.15$, $I^2 = 94.5\%$, Supplementary Figure S11).

3.4.11 | Metabolic Syndrome Remission

Pooled analysis of three pairs of comparison groups [29–31] from three studies ($n = 549$) showed a significantly increased RR of metabolic syndrome remission for participants achieving $\geq 5\%$ TWL compared to $< 5\%$ TWL (RR = 5.61, 95% CI: 1.62 to 19.49, $I^2 = 70.2\%$, Supplementary Figure S12).

4 | Discussion

This rapid review and meta-analysis investigated the impact of clinically significant weight loss on remission of metabolic complications in patients with obesity. The findings suggest that achieving clinically significant weight loss is associated with significant improvements in various metabolic risk factors and increased efficacy for disease remission in patients with obesity. Furthermore, meta-regression analysis showed factors like the %TWL achieved (particularly $\geq 15\%$), bariatric surgery, and duration of follow-up predict these outcomes.

We observed a significantly increased RR of type 2 diabetes remission in groups achieving $\geq 5\%$ TWL compared to those with lower weight loss (8-fold higher per percentage point TWL). This

effect strengthened for groups achieving $\geq 15\%$ TWL, demonstrating a dose-dependent relationship between weight loss and remission (5-fold higher per percentage point TWL). The findings on remission of type 2 diabetes with weight loss are strongly supported by the observed improvements in blood sugar control markers from systematic reviews. Groups achieving clinically significant weight loss ($\geq 5\%$ TWL) showed significantly greater mean reductions in HbA1c [66, 67], a key indicator of long-term blood sugar control [68], compared to the groups with lower weight loss. This effect was even more pronounced for groups achieving $\geq 15\%$ TWL [69] and is likely to be clinically significant [10, 66, 70, 71]. Similarly, weight loss led to significant decreases in mean fasting plasma glucose levels, a measure of blood sugar control [72]. These findings are highly consistent with the observed increase in diabetes remission rates, with a dose-dependent relationship between mean weight loss and risk of remission.

The meta-analysis revealed a positive and clinically significant association between weight loss and improved hypertension outcomes. Groups achieving $\geq 5\%$ TWL exhibited a significantly increased likelihood of achieving hypertension remission compared to those with lower weight loss as evident from other studies [67, 73]. Additionally, both systolic and diastolic blood pressure reductions were observed with weight loss, with a potentially clinically meaningful effect for those achieving $\geq 15\%$ TWL [69, 74]. The observed positive association between weight loss and improved hypertension outcomes is likely mediated through mechanisms such as reduced insulin resistance, decreased sympathetic nervous system activity, and alterations in the renin-angiotensin-aldosterone system [75]. While the mechanisms remain unclear, these findings align with the American Heart Association's Scientific Statement on weight-loss strategies for hypertension prevention and treatment, which emphasizes the importance of weight management for blood pressure control [76].

Weight loss also led to significant improvements in mean lipid profiles, with groups achieving $\geq 5\%$ TWL showing reductions in mean triglycerides and increases in mean HDL-cholesterol, both favorable changes [67, 73, 77]. This effect strengthened for groups achieving $\geq 15\%$ TWL, demonstrating a dose-dependent relationship between mean weight loss and improvements in mean HDL-cholesterol and triglycerides [69, 78]. Similarly, the study further suggests a potential benefit for metabolic syndrome remission. Groups achieving a mean $\geq 5\%$ TWL had a significantly increased RR of achieving metabolic syndrome remission compared to those with lower mean weight loss. However, the substantial heterogeneity across the comparison groups in the meta-analyses indicates that their clinical significance requires further exploration.

Mechanistically, weight loss, particularly a reduction in visceral adipose tissue, is postulated to improve insulin sensitivity [79, 80]. Insulin is a key hormone responsible for facilitating cellular glucose uptake [81]. Enhanced insulin sensitivity reduces the demand on pancreatic beta-cells for insulin production, potentially enabling functional recovery in some individuals with type 2 diabetes [82]. Additionally, weight loss may contribute to decreased systemic inflammation, another factor implicated in insulin resistance [83].

The mean weight loss thresholds used in the study ($\geq 5\%$ and $\geq 15\%$ TWL) provide a strong evidence-base for existing and recent clinical practice recommendations for weight management in patients with obesity [1, 84], as also reported in previous narrative reviews by experts [4, 10, 85]. Furthermore, our findings regarding the greater metabolic benefits associated with at least 15% TWL compared to less weight loss are consistent with recent studies published after the completion of our search strategy [70, 86]. Additionally, these findings are further supported by studies excluded from our analysis due to their control groups achieving more than 5% TWL [87, 88] and by another excluded study with only 20-week follow-up for mean changes in body weight for pooled tirzepatide group [73]. Overall, the results of this review demonstrate that clinically significant weight loss is associated with substantially improved metabolic markers and disease remission rates in a dose-dependent manner [20, 21, 24, 26–28, 31, 38, 41, 43, 44, 46, 48, 55, 58, 62].

5 | Limitations

While the observed trend in this study clearly demonstrates that clinically significant weight loss promotes metabolic improvements, some limitations exist. A fully independent duplicate screening process was not conducted. However, verification by a second reviewer, along with consensus resolution implemented as quality assurance measures, was consistent with current Cochrane Rapid Review Methods Guidance [15]. Substantial heterogeneity across studies (I^2 values $> 75\%$) suggests the potential influence of other unmeasured variables. This likely arises because the included studies varied in terms of weight loss interventions and follow-up periods, with a maximum of 12 years. A large-scale cohort study would be required to quantify the differences in effect sizes more accurately. It is possible that some relevant studies, such as the DROPLET trial [89], were not captured by our search strategy. However, the findings from DROPLET are consistent with the direction and magnitude of effects reported in our synthesis, supporting the robustness of our overall conclusions. Another limitation is the restriction of included studies to English-language publications, a decision necessitated by resource constraints. Furthermore, the certainty of the evidence was not formally graded using the GRADE framework, which represents another recognized limitation of the rapid review methodology.

The findings of this review have potential implications for healthcare and economic policy. Obesity and its complications impose significant economic burdens on healthcare systems [90]. Both surgical and nonsurgical weight loss have been shown to decrease the need for medications, hospital admissions, and other medical interventions for management of obesity and associated complications [91–93]. This likely translates to cost savings for both patients and healthcare providers [94]. For instance, effective diabetes management through weight loss can enhance patients' quality of life [8]. This can decrease absenteeism from work, increase productivity, and yield economic benefits [94]. Weight loss can also help prevent the development of other chronic conditions associated with obesity, including heart disease, stroke, and kidney disease [8, 59]. This can further reduce long-term healthcare costs [8].

6 | Conclusions

While it is well-established that clinically significant weight loss leads to improvements in metabolic health for patients with obesity in individual studies, this is the first rapid review to conduct a meta-analysis to generate the most reliable effect estimates of specific thresholds of %TWL associated with remission of metabolic risk factors. Our findings demonstrate that achieving $\geq 5\%$ TWL is associated with significant improvements in metabolic risk factors, with greater benefits observed at higher weight loss thresholds of $\geq 15\%$. These results not only reinforce the importance of weight loss in managing metabolic health but also offer clear, data-driven insights into the magnitude of these effects, supporting more precise clinical guidance for weight management in obesity.

Contributors

E.A. conceptualized this study. E.A., M.P., and P.F. designed this rapid review protocol. S.A. performed the literature search. S.A. and FB collected data. P.F. and S.A. performed data analysis and data interpretation. S.A. and M.P. assessed JBI risk of bias score for each included study. S.A. and E.A. prepared the outlines and wrote the manuscript. All authors contributed to the critical revision and editing of manuscript drafts and had final responsibility for the decision to submit for publication.

Conflicts of Interest

M.P. reports research grants from Translational Research Grant Scheme, NSW Health, Australia, and MTP Connect, Targeted Translational Research Accelerator Program; payments for educational events from Novo Nordisk, Eli Lilly, and Johnson and Johnson Medical Pty Ltd., support for attending meetings, payments for participation on a Data Safety Monitoring Advisory Board from Eli Lilly, Novo Nordisk, and INOVA pharmaceuticals; and is a current council member of ANZOS (Australia New Zealand Obesity Society). All declared interests relate outside the submitted manuscript. S.A., P.F., F.B., and E.A. declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. S. Wharton, D. C. W. Lau, M. Vallis, et al., "Obesity in Adults: A Clinical Practice Guideline," *CMAJ* 192, no. 31 (2020): E875–e891, <https://doi.org/10.1503/cmaj.191707>.
2. World Health Organisation, *Obesity and Overweight* (World Health Organisation, 2024), <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>.
3. R. G. Aboagye, E. Abu-Gharbieh, A. Adibi, et al., "Global Burden and Strength of Evidence for 88 Risk Factors in 204 Countries and 811 Subnational Locations, 1990–2021: A Systematic Analysis for the Global Burden of Disease Study 2021," *Lancet (British Edition)* 403, no. 10440 (2024): 2162–2203, [https://doi.org/10.1016/S0140-6736\(24\)00933-4](https://doi.org/10.1016/S0140-6736(24)00933-4).
4. D. B. Horn, J. P. Almandoz, and M. Look, "What Is Clinically Relevant Weight Loss for Your Patients and How Can It Be Achieved? A

- Narrative Review,” *Postgraduate Medicine* 134, no. 4 (2022): 359–375, <https://doi.org/10.1080/00325481.2022.2051366>.
5. D.-T. Chu, N. T. Minh Nguyet, V. T. Nga, et al., “An Update on Obesity: Mental Consequences and Psychological Interventions,” *Diabetes and Metabolic Syndrome: Clinical Research and Reviews* 13, no. 1 (2019): 155–160, <https://doi.org/10.1016/j.dsx.2018.07.015>.
6. E. Atlantis, M. Sahebolamri, B. S. Cheema, and K. Williams, “Usefulness of the Edmonton Obesity Staging System for Stratifying the Presence and Severity of Weight-Related Health Problems in Clinical and Community Settings: A Rapid Review of Observational Studies,” *Obesity Reviews* 21, no. 11 (2020): e13120, <https://doi.org/10.1111/obr.13120>.
7. M. A. Nagi, H. Ahmed, M. A. A. Rezq, et al., “Economic Costs of Obesity: A Systematic Review,” *International Journal of Obesity* 48, no. 1 (2024): 33–43, <https://doi.org/10.1038/s41366-023-01398-y>.
8. R. Walmsley and P. Sumithran, “Current and Emerging Medications for the Management of Obesity in Adults,” *Medical Journal of Australia* 218, no. 6 (2023): 276–283. Comment in: *Med J Aust.* 2023 Aug 21;219(4):187 PMID: 37402484 [<https://www.ncbi.nlm.nih.gov/pubmed/37402484>], <https://doi.org/10.5694/mja2.51871>.
9. D. A. Williamson, G. A. Bray, and D. H. Ryan, “Is 5% Weight Loss a Satisfactory Criterion to Define Clinically Significant Weight Loss?,” *Obesity (Silver Spring, Md)* 23, no. 12 (2015): 2319–2320, <https://doi.org/10.1002/oby.21358>.
10. A. A. Tahrani and J. Morton, “Benefits of Weight Loss of 10% or More in Patients With Overweight or Obesity: A Review,” *Obesity (Silver Spring, Md)* 30, no. 4 (2022): 802–840, <https://doi.org/10.1002/oby.23371>.
11. A. C. Tricco, J. Antony, W. Zarin, et al., “A Scoping Review of Rapid Review Methods,” *BMC Medicine* 13 (2015): 224, <https://doi.org/10.1186/s12916-015-0465-6>.
12. University of York Centre for Reviews and Dissemination, *Systematic Reviews: CRD’s Guidance for Undertaking Reviews in Health Care* (University of York Centre for Reviews and Dissemination, 2009).
13. L. Lizarondo, C. Stern, J. Carrier, et al., “Chapter 8: Mixed Methods Systematic Reviews,” in *JBI Manual for Evidence Synthesis*, eds. E. Aromataris and Z. Munn (JBI, 2020).
14. D. Moher, L. Shamseer, M. Clarke, et al., “Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 Statement,” *Systematic Reviews* 4 (2015): 1, <https://doi.org/10.1186/2046-4053-4-1>.
15. C. Garritty, C. Hamel, M. Trivella, et al., “Updated Recommendations for the Cochrane Rapid Review Methods Guidance for Rapid Reviews of Effectiveness,” *BMJ* 384 (2024): e076335, <https://doi.org/10.1136/bmj-2023-076335>.
16. J. Picot, J. Jones, J. L. Colquitt, et al., “The Clinical Effectiveness and Cost-Effectiveness of Bariatric (Weight Loss) Surgery for Obesity: A Systematic Review and Economic Evaluation,” *Health Technology Assessment (Winchester)* 13, no. 41 (2009): 1–iv, <https://doi.org/10.3310/hta13410>.
17. C. Schardt, M. B. Adams, T. Owens, S. Keitz, and P. Fontelo, “Utilization of the PICO Framework to Improve Searching PubMed for Clinical Questions,” *BMC Medical Informatics and Decision Making* 7, no. 1 (2007): 16, <https://doi.org/10.1186/1472-6947-7-16>.
18. W. M. Bramer, M. L. Rethlefsen, J. Kleijnen, and O. H. Franco Duran, “Optimal Database Combinations for Literature Searches in Systematic Reviews: A Prospective Exploratory Study,” *Systematic Reviews* 6, no. 1 (2017): 245–245, <https://doi.org/10.1186/s13643-017-0644-y>.
19. S. Moola, Z. Munn, C. Tufanaru, et al., “Chapter 7: Systematic Reviews of Etiology and Risk.” In *JBI Manual for Evidence Synthesis*, ed. E. Aromataris and Z. Munn (JBI, 2020), <https://synthesismanual.jbi.global>.
20. A. P. Courcoulas, J. W. Gallagher, R. H. Neiberg, et al., “Bariatric Surgery vs Lifestyle Intervention for Diabetes Treatment: 5-Year Outcomes From a Randomized Trial,” *Journal of Clinical Endocrinology and Metabolism* 105, no. 3 Comment in: *J Clin Endocrinol Metab.* 2020 Jun 1;105(6): PMID: 32270201 [<https://www.ncbi.nlm.nih.gov/pubmed/32270201>] (2020): 866–876, <https://doi.org/10.1210/clinem/dgaa006>.
21. C.-C. Hsu, A. Almulaifi, J.-C. Chen, et al., “Effect of Bariatric Surgery vs Medical Treatment on Type 2 Diabetes in Patients With Body Mass Index Lower Than 35: Five-Year Outcomes,” *JAMA Surgery* 150, no. 12 (2015): 1117–1124. Comment in: *JAMA Surg.* 2015 Dec;150(12):1124–5 PMID: 26375987 [<https://www.ncbi.nlm.nih.gov/pubmed/26375987>] Comment in: *JAMA Surg.* 2016 Apr;151(4):396 PMID: 26676447 [<https://www.ncbi.nlm.nih.gov/pubmed/26676447>] Comment in: *JAMA Surg.* 2016 Apr;151(4):396 PMID: 26676522 [<https://www.ncbi.nlm.nih.gov/pubmed/26676522>], <https://doi.org/10.1001/jamasurg.2015.2602>.
22. Y. Chen, L. Corsino, P. C. Shantavasinkul, et al., “Gastric Bypass Surgery Leads to Long-Term Remission or Improvement of Type 2 Diabetes and Significant Decrease of Microvascular and Macrovascular Complications,” *Annals of Surgery* 263, no. 6 (2016): 1138–1142. Comment in: *Ann Surg.* 2018 Feb;267(2):e25–e26 PMID: 27501168 [<https://www.ncbi.nlm.nih.gov/pubmed/27501168>] Comment in: *Ann Surg.* 2018 Feb;267(2):e26–e27 PMID: 27501177 [<https://www.ncbi.nlm.nih.gov/pubmed/27501177>] Comment in: *Ann Surg.* 2018 Feb;267(2):e26 PMID: 28118162 [<https://www.ncbi.nlm.nih.gov/pubmed/28118162>], <https://doi.org/10.1097/SLA.0000000000001509>.
23. E. W. Gregg, H. Chen, L. E. Wagenknecht, et al., “Association of an Intensive Lifestyle Intervention With Remission of Type 2 Diabetes,” *Journal of the American Medical Association* 308, no. 23 (2012): 2489–2496. Comment in: *Journal of the American Medical Association* 2012 Dec 19;308(23):2517–8 PMID: 23287825 [<https://www.ncbi.nlm.nih.gov/pubmed/23287825>] Comment in: *Dtsch Med Wochenschr.* 2013 Mar;138(11):514 PMID: 23463470 [<https://www.ncbi.nlm.nih.gov/pubmed/23463470>] Comment in: *Ann Intern Med.* 2013 May 21;158(10):JC4 PMID: 23689783 [<https://www.ncbi.nlm.nih.gov/pubmed/23689783>], <https://doi.org/10.1001/jama.2012.67929>.
24. T. A. Wadden, A. M. Chao, J. L. Bahnson, et al., “End-of-Trial Health Outcomes in Look AHEAD Participants Who Elected to Have Bariatric Surgery,” *Obesity (Silver Spring, Md)* 27, no. 4 (2019): 581–590. Comment in: *Obesity (Silver Spring).* 2019 Apr;27(4):534 PMID: 30900404 [<https://www.ncbi.nlm.nih.gov/pubmed/30900404>], <https://doi.org/10.1002/oby.22411>.
25. D. C. Simonson, F. Halperin, K. Foster, A. Vernon, and A. B. Goldfine, “Clinical and Patient-Centered Outcomes in Obese Patients With Type 2 Diabetes 3 Years After Randomization to Roux-en-Y Gastric Bypass Surgery Versus Intensive Lifestyle Management: The SLIMM-T2D Study,” *Diabetes Care* 41, no. 4 (2018): 670–679, <https://doi.org/10.2337/dc17-0487>.
26. D. C. Simonson, A. Vernon, K. Foster, F. Halperin, M. E. Patti, and A. B. Goldfine, “Adjustable Gastric Band Surgery or Medical Management in Patients With Type 2 Diabetes and Obesity: Three-Year Results of a Randomized Trial,” *Surgery for Obesity and Related Diseases* 15, no. 12 (2019): 2052–2059, <https://doi.org/10.1016/j.soard.2019.03.038>.
27. A. A. Salman, M. Matter, N. I. Fayad, et al., “Improvement of Coronary Calcium Scores After Bariatric Surgery in People With Severe Obesity,” *Obesity Surgery* 32, no. 2 (2022): 472–479. Comment in: *Obes Surg.* 2022 May;32(5):1750–1752 PMID: 35031953 [<https://www.ncbi.nlm.nih.gov/pubmed/35031953>] Comment in: *Obes Surg.* 2022 May;32(5):1748–1749 PMID: 35038112 [<https://www.ncbi.nlm.nih.gov/pubmed/35038112>], <https://doi.org/10.1007/s11695-021-05801-3>.
28. T. D. Adams, L. E. Davidson, S. E. Litwin, et al., “Weight and Metabolic Outcomes 12 Years After Gastric Bypass,” *New England Journal of Medicine* 377, no. 12 (2017): 1143–1155. Comment in: *Surg Obes Relat Dis.* 2018 Feb;14 (2):247 PMID: 29254688 [<https://www.ncbi.nlm.nih.gov/pubmed/29254688>] Comment in: *Am J Nurs.* 2018 Jan;118(1):56 PMID: 29280807 [<https://www.ncbi.nlm.nih.gov/pubmed/29280807>] Comment in: *N Engl J Med.* 2018 Jan 4;378(1):93

- PMID: 29298158 [<https://www.ncbi.nlm.nih.gov/pubmed/29298158>] Comment in: *N Engl J Med.* 2018 Jan 04;378(1):95 PMID: 29303539 [<https://www.ncbi.nlm.nih.gov/pubmed/29303539>] Comment in: *N Engl J Med.* 2018 Jan 04;378(1):93–4 PMID: 29303540 [<https://www.ncbi.nlm.nih.gov/pubmed/29303540>] Comment in: *MMW Fortschr Med.* 2018 Jan;160(1):35 PMID: 29335950 [<https://www.ncbi.nlm.nih.gov/pubmed/29335950>] Comment in: *JPEN J Parenter Enteral Nutr.* 2018 May;42(4):826–828 PMID: 29603283 [<https://www.ncbi.nlm.nih.gov/pubmed/29603283>], <https://doi.org/10.1056/NEJMoa1700459>.
29. S. J. Athinarayanan, R. N. Adams, S. J. Hallberg, et al., “Long-Term Effects of a Novel Continuous Remote Care Intervention Including Nutritional Ketosis for the Management of Type 2 Diabetes: A 2-Year Non-Randomized Clinical Trial,” *Frontiers in Endocrinology* 10 (2019): 10348, <https://doi.org/10.3389/fendo.2019.00348>.
30. H. Schmid, C. F. Goelzer Neto, L. S. Dias, et al., “Metabolic Syndrome Resolution by Roux-en-Y Gastric Bypass in a Real World: A Case Control Study,” *Revista Da Associacao Medica Brasileira (1992)* 61, no. 2 (2015): 161–169, <https://doi.org/10.1590/1806-9282.61.02.161>.
31. J. B. Dixon, P. E. O'Brien, J. Playfair, et al., “Adjustable Gastric Banding and Conventional Therapy for Type 2 Diabetes: A Randomized Controlled Trial,” *JAMA* 299, no. 3 (2008): 316–323. Comment in: *JAMA.* 2008 Jan 23;299(3):341–3 PMID: 18212321 [<https://www.ncbi.nlm.nih.gov/pubmed/18212321>] Comment in: *JAMA.* 2008 May 14;299(18):2146; author reply 2146–7 PMID: 18477778 [<https://www.ncbi.nlm.nih.gov/pubmed/18477778>] Comment in: *Nat Clin Pract Endocrinol Metab.* 2008 Aug;4(8):438–9 PMID: 18594488 [<https://www.ncbi.nlm.nih.gov/pubmed/18594488>] Comment in: *ACP J Club.* 2008 Jul;149(1):3 PMID: 18624371 [<https://www.ncbi.nlm.nih.gov/pubmed/18624371>] Comment in: *Arch Surg.* 2008 Jul;143(7):708–10 PMID: 18645115 [<https://www.ncbi.nlm.nih.gov/pubmed/18645115>] Comment in: *Evid Based Med.* 2008 Aug;13(4):108 PMID: 18667667 [<https://www.ncbi.nlm.nih.gov/pubmed/18667667>] Comment in: *Journal of the American Medical Association* 2010 Jun 16;303(323):2357 PMID: 20460606 [<https://www.ncbi.nlm.nih.gov/pubmed/20460606>], <https://doi.org/10.1001/jama.299.3.316>.
32. S. A. Doi, J. J. Barendregt, S. Khan, L. Thalib, and G. M. Williams, “Advances in the Meta-Analysis of Heterogeneous Clinical Trials I: The Inverse Variance Heterogeneity Model,” *Contemporary Clinical Trials* 45, no. Pt A (2015): 130–138, <https://doi.org/10.1016/j.cct.2015.05.009>.
33. R. R. Wing, W. Lang, T. A. Wadden, et al., “Benefits of Modest Weight Loss in Improving Cardiovascular Risk Factors in Overweight and Obese Individuals With Type 2 Diabetes,” *Diabetes Care* 34, no. 7 (2011): 1481–1486, <https://doi.org/10.2337/dc10-2415>.
34. J. Higgins James Thomas. *Cochrane Handbook For Systematic Reviews of Interventions Version 6.4.* (Cochrane, 2023), <https://training.cochrane.org/handbook/current>.
35. C. M. Apovian, L. Aronne, D. Rubino, et al., “A Randomized, Phase 3 Trial of Naltrexone SR/Bupropion SR on Weight and Obesity-Related Risk Factors (COR-II),” *Obesity* 21, no. 5 (2013): 935–943, <https://doi.org/10.1002/oby.20309>.
36. M. H. Davidson, S. Tonstad, S. Oparil, M. Schwiers, W. W. Day, and C. H. Bowden, “Changes in Cardiovascular Risk Associated With Phentermine and Topiramate Extended-Release in Participants With Comorbidities and a Body Mass Index ≥ 27 kg/m²,” *American Journal of Cardiology* 111, no. 8 (2013): 1131–1138.
37. M. C. Fidler, M. Sanchez, B. Raether, et al., “A One-Year Randomized Trial of Lorcaserin for Weight Loss in Obese and Overweight Adults: The BLOSSOM Trial,” *Journal of Clinical Endocrinology & Metabolism* 96, no. 10 (2011): 3067–3077, <https://doi.org/10.1210/jc.2011-1256>.
38. G. D. Foster, K. E. Borradaile, M. H. Sanders, et al., “A Randomized Study on the Effect of Weight Loss on Obstructive Sleep Apnea Among Obese Patients With Type 2 Diabetes The Sleep AHEAD Study,” *Archives of Internal Medicine* 169, no. 17 (2009): 1619–1626, <https://doi.org/10.1001/archinternmed.2009.266>.
39. W. T. Garvey, D. H. Ryan, R. Henry, et al., “Prevention of Type 2 Diabetes in Subjects With Prediabetes and Metabolic Syndrome Treated With Phentermine and Topiramate Extended Release,” *Diabetes Care* 37, no. 4 (2014): 912–921, <https://doi.org/10.2337/dc13-1518>.
40. W. T. Garvey, D. H. Ryan, M. Look, et al., “Two-Year Sustained Weight Loss and Metabolic Benefits With Controlled-Release Phentermine/Topiramate in Obese and Overweight Adults (SEQUEL): A Randomized, Placebo-Controlled, Phase 3 Extension Study,” *American Journal of Clinical Nutrition* 95, no. 2 (2012): 297–308, <https://doi.org/10.3945/ajcn.111.024927>.
41. M. E. J. Lean, W. S. Leslie, A. C. Barnes, et al., “Durability of a Primary Care-Led Weight-Management Intervention for Remission of Type 2 Diabetes: 2-Year Results of the DiRECT Open-Label, Cluster-Randomised Trial,” *Lancet Diabetes and Endocrinology* 7, no. 5 (2019): 344–355, [https://doi.org/10.1016/s2213-8587\(19\)30068-3](https://doi.org/10.1016/s2213-8587(19)30068-3).
42. J. Liu, J. G. Godino, G. J. Norman, et al., “Planned Care for Obesity and Cardiovascular Risk Reduction Using a Stepped-Down Approach: A Randomized-Controlled Trial,” *Preventive Medicine* 114 (2018): 223–231, <https://doi.org/10.1016/j.jypmed.2018.07.015>.
43. G. Mingrone, S. Panunzi, A. De Gaetano, et al., “Bariatric Surgery Versus Conventional Medical Therapy for Type 2 Diabetes,” *New England Journal of Medicine* 366, no. 17 (2012): 1577–1585. Comment in: *N Engl J Med.* 2012 Apr 26;366(17):1635–6 PMID: 22449318 [<https://www.ncbi.nlm.nih.gov/pubmed/22449318>] Comment in: *Nat Rev Endocrinol.* 2012 Jun;8(6):317 PMID: 22488643 [<https://www.ncbi.nlm.nih.gov/pubmed/22488643>] Comment in: *Ann Intern Med.* 2012 Jul 17;157(2):JC2–12 PMID: 22801703 [<https://www.ncbi.nlm.nih.gov/pubmed/22801703>] Comment in: *N Engl J Med.* 2012 Aug 2;367(5):473; author reply 474–6 PMID: 22853019 [<https://www.ncbi.nlm.nih.gov/pubmed/22853019>] Comment in: *N Engl J Med.* 2012 Aug 2;367(5):473–4; author reply 474–6 PMID: 22853020 [<https://www.ncbi.nlm.nih.gov/pubmed/22853020>] Comment in: *Expert Opin Pharmacother.* 2012 Oct;13(15):2249–53 PMID: 22957791 [<https://www.ncbi.nlm.nih.gov/pubmed/22957791>] Comment in: *Rev Clin Esp.* 2012 Oct;212(9):461 PMID: 23213657 [<https://www.ncbi.nlm.nih.gov/pubmed/23213657>] Comment in: *J Fam Pract.* 2013 Jan;62(1):30–2 PMID: 23326820 [<https://www.ncbi.nlm.nih.gov/pubmed/23326820>] Comment in: *Natl Med J India.* 2012 Sep-Oct;25(5):281–3 PMID: 23448628 [<https://www.ncbi.nlm.nih.gov/pubmed/23448628>] Comment in: *Internist (Berl).* 2013 May;54(5):639–44 PMID: 23568061 [<https://www.ncbi.nlm.nih.gov/pubmed/23568061>] Comment in: *Ann Intern Med.* 2013 Jun 4;158(11):821–4 PMID: 23580066 [<https://www.ncbi.nlm.nih.gov/pubmed/23580066>], <https://doi.org/10.1056/NEJMoa1200111>.
44. P. M. O'neil, S. R. Smith, N. J. Weissman, et al., “Randomized Placebo-Controlled Clinical Trial of Lorcaserin for Weight Loss in Type 2 Diabetes Mellitus: The BLOOM-DM Study,” *Obesity* 20, no. 7 (2012): 1426–1436, <https://doi.org/10.1038/oby.2012.66>.
45. O. Ospanov, A. Akilzhanova, J. N. Buchwald, et al., “Stapleless vs Stapled Gastric Bypass vs Hypocaloric Diet: A Three-Arm Randomized Controlled Trial of Body Mass Evolution With Secondary Outcomes for Telomere Length and Metabolic Syndrome Changes,” *Obesity Surgery* 31, no. 7 (2021): 3165–3176, <https://doi.org/10.1007/s11695-021-05454-2>.
46. P. R. Schauer, D. L. Bhatt, J. P. Kirwan, et al., “Bariatric Surgery Versus Intensive Medical Therapy for Diabetes - 3-Year Outcomes,” *New England Journal of Medicine* 370, no. 21 (2014): 2002–2013, <https://doi.org/10.1056/NEJMoa1401329>.
47. J. M. Wentworth, J. Playfair, C. Laurie, et al., “Gastric Band Surgery Leads to Improved Insulin Secretion in Overweight People With Type 2 Diabetes,” *Obesity Surgery* 25, no. 12 (2015): 2400–2407, <https://doi.org/10.1007/s11695-015-1716-5>.
48. J. M. Wentworth, J. Playfair, C. Laurie, et al., “Multidisciplinary Diabetes Care With and Without Bariatric Surgery in Overweight People: A Randomised Controlled Trial,” *Lancet Diabetes and Endocrinology* 2, no. 7 (2014): 545–552, [https://doi.org/10.1016/s2213-8587\(14\)70066-x](https://doi.org/10.1016/s2213-8587(14)70066-x).

49. J. P. Wilding, R. L. Batterham, S. Calanna, et al., "Once-Weekly Semaglutide in Adults With Overweight or Obesity," *New England Journal of Medicine* 384 (2021): 989–1002.
50. M. E. J. Lean, W. S. Leslie, A. C. Barnes, et al., "5-Year Follow-Up of the Randomised Diabetes Remission Clinical Trial (DiRECT) of Continued Support for Weight Loss Maintenance in the UK: An Extension Study," *Lancet Diabetes and Endocrinology* 12, no. 4 (2024): 233–246, [https://doi.org/10.1016/S2213-8587\(23\)00385-6](https://doi.org/10.1016/S2213-8587(23)00385-6).
51. K. M. Pantalone, B. Rogen, P. Zirm, et al., "An Obesity-Centric Approach With and Without Anti-Obesity Medications Compared to the Usual-Care Approach to Management of Patients With Obesity and Type 2 Diabetes in an Employer Setting: A Pragmatic Randomized Controlled Trial (EMPOWER-T2D)," *Diabetes Therapy* 15, no. 5 (2024): 1201–1214.
52. C. A. Schiavon, A. B. Cavalcanti, J. D. Oliveira, et al., "Randomized Trial of Effect of Bariatric Surgery on Blood Pressure After 5 Years," *Journal of the American College of Cardiology* 83, no. 6 (2023): 637–648, <https://doi.org/10.1016/j.jacc.2023.11.032>.
53. S. Hong, W. J. Kim, E. S. Kang, et al., "Evaluation of the Efficacy and Safety of Controlled-Release Phentermine/Topiramate in Adults With Obesity in Korea: A Randomized, Double-Blind, Placebo-Controlled, Phase 4 Trial (QUEEN's Study)," *Diabetes, Obesity and Metabolism* 27, no. 3 (2025): 1242–1250.
54. A. Amin, G. Siddiq, M. I. Haider, U. Khalid Choudry, and I. Nazir, "Laparoscopic Sleeve Gastrectomy Versus Lifestyle Modification in Class I Obesity in Pakistani Population: A Prospective Cohort Study," *Cureus* 11, no. 6 (2019): e5031, <https://doi.org/10.7759/cureus.5031>.
55. A. Lih, L. Pereira, R. H. Bishay, et al., "A Novel Multidisciplinary Intervention for Long-Term Weight Loss and Glycaemic Control in Obese Patients With Diabetes," *Journal of Diabetes Research* 2015 (2015): 729567, <https://doi.org/10.1155/2015/729567>.
56. E. Moriconi, E. Camajani, A. Fabbri, A. Lenzi, and M. Caprio, "Very-Low-Calorie Ketogenic Diet as a Safe and Valuable Tool for Long-Term Glycemic Management in Patients With Obesity and Type 2 Diabetes," *Nutrients* 13, no. 3 (2021): 758, <https://doi.org/10.3390/nu13030758>.
57. B. Ovrebø, M. Strommen, B. Kulseng, and C. Martins, "Bariatric Surgery Versus Lifestyle Interventions for Severe Obesity: 5-Year Changes in Body Weight, Risk Factors and Comorbidities," *Clinical Obesity* 7, no. 3 (2017): 183–190, <https://doi.org/10.1111/cob.12190>.
58. J. Prasad, E. Vogels, J. T. Dove, C. Wood, A. T. Petrick, and D. M. Parker, "Is Age a Real or Perceived Discriminator for Bariatric Surgery? A Long-Term Analysis of Bariatric Surgery in the Elderly," *Surgery for Obesity and Related Diseases: Official Journal of the American Society for Bariatric Surgery* 15, no. 5 (2019): 725–731, <https://doi.org/10.1016/j.soard.2018.12.019>.
59. P. Singh, N. Adderley, A. Subramanian, et al., "The Impact of Bariatric Surgery on Incident Microvascular Complications in Patients With Type 2 Diabetes: A Matched Controlled Population-Based Retrospective Cohort Study," *Diabetes Care* 44, no. 1 (2021): 116–124, <https://doi.org/10.2337/dc20-0571>.
60. T. Wu, S. K. H. Wong, B. T. T. Law, et al., "Five-Year Effectiveness of Bariatric Surgery on Disease Remission, Weight Loss, and Changes of Metabolic Parameters in Obese Patients With Type 2 Diabetes: A Population-Based Propensity Score-Matched Cohort Study," *Diabetes/Metabolism Research and Reviews* 36, no. 3 (2020): e3236, <https://doi.org/10.1002/dmrr.3236>.
61. J. Carbonaro, T. McLaughlin, R. Seip, et al., "Five-Year Outcomes of Revisional Bariatric Surgery: Gastric Band to Sleeve Gastrectomy or to Roux-En-Y Gastric Bypass," *Surgical Endoscopy* 38, no. 5 (2024): 2719–2725, <https://doi.org/10.1007/s00464-024-10764-4>.
62. F. Abbatini, D. Capoccia, G. Casella, F. Coccia, F. Leonetti, and N. Basso, "Type 2 Diabetes in Obese Patients With Body Mass Index of 30–35 kg/m²: Sleeve Gastrectomy Versus Medical Treatment," *Surgery for Obesity and Related Diseases: Official Journal of the American Society for Bariatric Surgery* 8, no. 1 (2012): 20–24, <https://doi.org/10.1016/j.soard.2011.06.015>.
63. D. Horwitz, J. K. Saunders, A. Ude-Welcome, et al., "Three-Year Follow-Up Comparing Metabolic Surgery Versus Medical Weight Management in Patients With Type 2 Diabetes and BMI 30–35. The Role of sRAGE Biomarker as Predictor of Satisfactory Outcomes," *Surgery for Obesity and Related Diseases: Official Journal of the American Society for Bariatric Surgery* 12, no. 7 (2016): 1337–1341. Comment in: *Surg Obes Relat Dis*. 2016 Aug;12 (7):1342 PMID: 27060880 [<https://www.ncbi.nlm.nih.gov/pubmed/27060880>], <https://doi.org/10.1016/j.soard.2016.01.016>.
64. A. Astrup, R. Carraro, N. Finer, et al., "Safety, Tolerability and Sustained Weight Loss Over 2 Years With the Once-Daily Human GLP-1 Analog, Liraglutide," *International Journal of Obesity* 36, no. 6 (2012): 843–854, <https://doi.org/10.1038/ijo.2011.158>.
65. A. E. Butler, M. Ramanjaneya, A. M. Moin, S. C. Hunt, and S. L. Atkin, "Clinical Improvement May Not Reflect Metabolic Homeostasis Normalization in Subjects With and Without Roux-En-Y Bariatric Surgery After 12 Years: Comparison of Surgical Subjects to a Lean Cohort," *Frontiers in Endocrinology* 14 (2023): 141228853, <https://doi.org/10.3389/fendo.2023.1228853>.
66. W. Qin, J. Yang, Y. Ni, et al., "Efficacy and Safety of Once-Weekly Tirzepatide for Weight Management Compared to Placebo: An Updated Systematic Review and Meta-Analysis Including the Latest SURMOUNT-2 Trial," *Endocrine* 86 (2024): 70–84, <https://doi.org/10.1007/s12020-024-03896-z>.
67. W. Qin, J. Yang, C. Deng, Q. Ruan, and K. Duan, "Efficacy and Safety of Semaglutide 2.4mg for Weight Loss in Overweight or Obese Adults Without Diabetes: An Updated Systematic Review and Meta-Analysis Including the 2-Year STEP 5 Trial," *Diabetes, Obesity & Metabolism* 26, no. 3 (2024): 911–923, <https://doi.org/10.1111/dom.15386>.
68. S. I. Sherwani, H. A. Khan, A. Ekhzaimy, A. Masood, and M. K. Sakharkar, "Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients," *Biomarker Insights* 11 (2016): 95–104, <https://doi.org/10.4137/bmi.S38440>.
69. J. C. Kim, M. G. Kim, J. K. Park, et al., "Outcomes and Adverse Events After Bariatric Surgery: An Updated Systematic Review and Meta-Analysis, 2013–2023," *Journal of Metabolic and Bariatric Surgery* 12, no. 2 (2023): 76–88, <https://doi.org/10.17476/jmbs.2023.12.2.76>.
70. A. P. Courcoulas, M. E. Patti, B. Hu, et al., "Long-Term Outcomes of Medical Management vs Bariatric Surgery in Type 2 Diabetes," *JAMA: The Journal of the American Medical Association* 331, no. 8 (2024): 654–664, <https://doi.org/10.1001/jama.2024.0318>.
71. M. E. J. Lean, W. S. Leslie, A. C. Barnes, et al., "Primary Care-Led Weight Management for Remission of Type 2 Diabetes (DiRECT): An Open-Label, Cluster-Randomised Trial," *Lancet (British Edition)* 391, no. 10120 (2018): 541–551, [https://doi.org/10.1016/S0140-6736\(17\)33102-1](https://doi.org/10.1016/S0140-6736(17)33102-1).
72. *Management of Type 2 Diabetes: A Handbook for General Practice* (Royal Australian College of General Practitioners (RACGP), 2020), accessed August 5, 2024, <https://www.racgp.org.au/getattachment/41fee8dc-7f97-4f87-9d90-b7af337af778/Management-of-type-2-diabetes-A-handbook-for-general-practice.aspx>.
73. M. Jastreboff Ania, J. Aronne Louis, N. Ahmad Nadia, et al., "Tirzepatide Once Weekly for the Treatment of Obesity," *New England Journal of Medicine* 387, no. 3 (2022): 205–216, <https://doi.org/10.1056/NEJMoA2206038>.
74. E. Climent, A. Oliveras, J. Pedro-Botet, A. Goday, and D. Benaiges, "Bariatric Surgery and Hypertension," *Journal of Clinical Medicine* 10, no. 18 (2021): 4049, <https://doi.org/10.3390/jcm10184049>.
75. J. E. Hall, J. M. do Carmo, A. A. da Silva, Z. Wang, and M. E. Hall, "Obesity-Induced Hypertension," *Circulation Research* 116, no. 6 (2015): 991–1006, <https://doi.org/10.1161/CIRCRESAHA.116.305697>.

76. M. E. Hall, J. B. Cohen, J. D. Ard, et al., "Weight-Loss Strategies for Prevention and Treatment of Hypertension: A Scientific Statement From the American Heart Association," *Hypertension* 78, no. 5 (2021): e38–e50, <https://doi.org/10.1161/HYP.0000000000000202>.
77. P. H. Wilding John, L. Batterham Rachel, S. Calanna, et al., "Once-Weekly Semaglutide in Adults With Overweight or Obesity," *New England Journal of Medicine* 384, no. 11 (2021): 989–1002, <https://doi.org/10.1056/NEJMoa2032183>.
78. L. Qi, Y. Guo, C.-Q. Liu, Z.-P. Huang, Y. Sheng, and D.-J. Zou, "Effects of Bariatric Surgery on Glycemic and Lipid Metabolism, Surgical Complication and Quality of Life in Adolescents With Obesity: A Systematic Review and Meta-Analysis," *Surgery for Obesity and Related Diseases* 13, no. 12 (2017): 2037–2055, <https://doi.org/10.1016/j.soard.2017.09.516>.
79. O. T. Hardy, M. P. Czech, and S. Corvera, "What Causes the Insulin Resistance Underlying Obesity?," *Current Opinion in Endocrinology, Diabetes, and Obesity* 19, no. 2 (2012): 81–87, <https://doi.org/10.1097/MED.0b013e3283514e13>.
80. I. J. Neeland, R. Ross, J. P. Després, et al., "Visceral and Ectopic Fat, Atherosclerosis, and Cardiometabolic Disease: A Position Statement," *Lancet Diabetes and Endocrinology* 7, no. 9 (2019): 715–725, [https://doi.org/10.1016/s2213-8587\(19\)30084-1](https://doi.org/10.1016/s2213-8587(19)30084-1).
81. G. Wilcox, "Insulin and Insulin Resistance," *Clinical Biochemist Reviews* 26, no. 2 (2005): 19–39.
82. R. Taylor, A. Ramachandran, W. S. Yancy, and N. G. Forouhi, "Nutritional Basis of Type 2 Diabetes Remission," *BMJ* 374 (2021): n1449, <https://doi.org/10.1136/bmj.n1449>.
83. V. E. Bianchi, "Weight Loss Is a Critical Factor to Reduce Inflammation," *Clinical Nutrition ESPEN* 28 (2018): 21–35, <https://doi.org/10.1016/j.clnesp.2018.08.007>.
84. T. P. Markovic, J. Proietto, J. B. Dixon, et al., "The Australian Obesity Management Algorithm: A Simple Tool to Guide the Management of Obesity in Primary Care," *Obesity Research & Clinical Practice* 16, no. 5 (2022): 353–363, <https://doi.org/10.1016/j.orcp.2022.08.003>.
85. D. H. Ryan and S. R. Yockey, "Weight Loss and Improvement in Comorbidity: Differences at 5%, 10%, 15%, and Over," *Current Obesity Reports* 6, no. 2 (2017): 187–194, <https://doi.org/10.1007/s13679-017-0262-y>.
86. S. E. Kahn, J. E. Deanfield, O. K. Jeppesen, et al., "Effect of Semaglutide on Regression and Progression of Glycemia in People With Overweight or Obesity but Without Diabetes in the SELECT Trial," *Diabetes Care* 47, no. 8 (2024): 1350–1359, <https://doi.org/10.2337/dc24-0491>.
87. A. P. Courcoulas, S. H. Belle, R. H. Neiberg, et al., "Three-Year Outcomes of Bariatric Surgery vs Lifestyle Intervention for Type 2 Diabetes Mellitus Treatment: A Randomized Clinical Trial," *JAMA Surgery* 150, no. 10 (2015): 931–940. Comment in: *JAMA Surg.* 2015 Oct;150(10):940 PMID: 26132502 [<https://www.ncbi.nlm.nih.gov/pubmed/26132502>] Comment in: *JAMA Surg.* 2016 Feb;151(2):196–7 PMID: 26465788 [<https://www.ncbi.nlm.nih.gov/pubmed/26465788>] Comment in: *JAMA Surg.* 2016 Feb;151(2):197 PMID: 26466125 [<https://www.ncbi.nlm.nih.gov/pubmed/26466125>] Comment in: *JAMA.* 2016 Mar 22–29;315(12):1276–7 PMID: 27002449 [<https://www.ncbi.nlm.nih.gov/pubmed/27002449>], <https://doi.org/10.1001/jamasurg.2015.1534>.
88. S. Ikramuddin, J. Korner, W. J. Lee, et al., "Durability of Addition of Roux-En-Y Gastric Bypass to Lifestyle Intervention and Medical Management in Achieving Primary Treatment Goals for Uncontrolled Type 2 Diabetes in Mild to Moderate Obesity: A Randomized Control Trial," *Diabetes Care* 39, no. 9 (2016): 1510–1518, <https://doi.org/10.2337/dc15-2481>.
89. N. M. Astbury, P. Aveyard, A. Nickless, et al., "Doctor Referral of Overweight People to Low Energy Total Diet Replacement Treatment (DROPLET): Pragmatic Randomised Controlled Trial," *BMJ* 362 (2018): k3760, <https://doi.org/10.1136/bmj.k3760>.
90. Health Aio, Welfare. *A Picture of Overweight and Obesity in Australia* (Australian Institute of Health and Welfare, 2017), <https://www.aihw.gov.au/reports/overweight-obesity/a-picture-of-overweight-and-obesity-in-australia>.
91. E. Migliore, A. Brunani, G. Ciccone, et al., "Effect of Bariatric Surgery on Survival and Hospitalizations in Patients With Severe Obesity. A Retrospective Cohort Study," *Nutrients* 13, no. 9 (2021): 3150, <https://doi.org/10.3390/nu13093150>.
92. A. Dohayan Al-Dohayan, D. F. Qamhiah, A. A. Abukhalaf, et al., "Cost Effectiveness of Bariatric Surgery in Patients With Obesity Related Comorbidities: A Retrospective Study," *Journal of Family Medicine and Primary Care* 10, no. 12 (2021): 4418–4422.
93. C. Ma, A. Avenell, M. Bolland, et al., "Effects of Weight Loss Interventions for Adults Who Are Obese on Mortality, Cardiovascular Disease, and Cancer: Systematic Review and Meta-Analysis," *BMJ* 359 (2017): j4849, <https://doi.org/10.1136/bmj.j4849>.
94. A. Okunogbe, R. Nugent, G. Spencer, J. Powis, J. Ralston, and J. Wilding, "Economic Impacts of Overweight and Obesity: Current and Future Estimates for 161 Countries," *BMJ Global Health* 7, no. 9 (2022): e009773, <https://doi.org/10.1136/bmjgh-2022-009773>.

Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Table S1:** Inclusion criteria for studies. **Table S2:** Keywords/synonyms/phrases in search fields. **Table S3:** Detailed search strategy used in each database. **Table S4:** List of excluded studies with reasons. **Table S4a:** List of studies excluded from the updated search with reasons. **Figure S1:** PRISMA flow diagram. **Figure S1a:** PRISMA flow diagram for the updated search. **Table S5:** Characteristics and summary of quantitative studies reviewed. **Table S5a:** Characteristics and summary of quantitative studies reviewed from the updated search. **Table S6:** Risk of bias assessment summary (JBI standardized critical appraisal tool). **Figure S2:** Funnel plot (T2D remission). **Figure S3:** Funnel plot (mean changes in HbA1c). **Figure S4:** Funnel plot (mean changes in fasting plasma glucose). **Figure S4a:** Scatter plot > 15% WL versus < 15% WL for mean changes in fasting plasma glucose. **Figure S5:** Forest plot of comparison: < 5%WL versus ≥ 5% WL for fasting insulin. **Figure S6:** Forest plot of comparison: < 5%WL versus ≥ 5% WL for Hypertension remission. **Figure S7:** Forest plot of comparison: < 5%WL versus ≥ 5% WL for mean changes in systolic blood pressure. **Figure S7a:** Funnel plot of comparison: < 5%WL versus ≥ 5% WL for systolic blood pressure. **Figure S7b:** Scatter plot > 15% WL versus < 15% WL for systolic blood pressure. **Figure S7c:** Meta regression of mean changes in SBP with intervention type as a predictor. **Figure S8:** Forest plot of comparison: < 5%WL versus ≥ 5% WL for mean changes in diastolic blood pressure.