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DAKIN, Clarissa, BEAUMONT, Jordan <<http://orcid.org/0000-0002-9861-3379>> and O'HARA, Beverly

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Influence of GLP-1-Based Pharmacotherapies on Eating Behavior, Appetite, and Energy Intake in Adults With Overweight or Obesity: A Systematic Review and Meta-Analysis

Clarissa Dakin¹  | Jordan D. Beaumont²  | Beverley O'Hara³ 

¹School of Food Science and Nutrition, University of Leeds, Leeds, UK | ²Sheffield Business School, Sheffield Hallam University, Sheffield, UK | ³School of Health, Leeds Beckett University, Leeds, UK

Correspondence: Clarissa Dakin (c.dakin@leeds.ac.uk)

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ABSTRACT

Introduction: Although GLP-1-based pharmacotherapies achieve clinically significant weight loss, their influence on eating behavior is unknown.

Methods: This systematic review examined the effects of GLP-1-based pharmacotherapies on eating behavior, appetite, and energy intake in adults (≥ 18 years) with overweight or obesity ($\text{BMI} \geq 25 \text{ kg/m}^2$) without major comorbidities. MEDLINE, PsycINFO, EMBASE and Web of Science were searched on 4th November 2025. Risk of bias was assessed, and meta-analyses were conducted for energy intake and overall appetite suppression, with other outcomes synthesized qualitatively.

Results: Twenty-five articles involving 4060 participants were included (64% female, mean age = 44 years, mean BMI = 36.7 kg/m²). Four studies were deemed low risk of bias. A reduction in energy intake was observed ($\text{SMD} = -0.775$, 95% CI = -1.21 to -0.34 , $p = 0.002$), although heterogeneity was high ($I^2 = 82.7\%$) and the prediction interval included no effect. A small increase in appetite suppression was also observed ($\text{MD} = 7.800$, 95% CI = 3.74 to 11.86 , $p = 0.001$). Qualitative findings suggested reductions in food craving and some measures of food reward. Nausea was more frequent with active treatment and may have influenced the observed effects or increased awareness of treatment allocation.

Conclusion: GLP-1-based pharmacotherapies may reduce short-term energy intake and appetite. However, the magnitude and consistency of these effects remain uncertain because of substantial heterogeneity, imputation of variance data, and variability in outcome assessment. Evidence relating to food craving, food preferences and other eating behaviors requires further investigation.

Abbreviations: AUC, area under the curve; BES, Binge Eating Scale; BMI, body mass index; CoEQ, Control of Eating Questionnaire; DEBQ, Dutch Eating Behavior Questionnaire; EI, energy intake; ETD, estimated treatment difference; FCI, food craving inventory; FCQ-S, Food Craving Questionnaire State; FPQ, Food Preference Questionnaire; GLP-1, glucagon-like peptide-1; HEI, Healthy Eating Index; LFPQ, Leeds Food Preference Questionnaire; MD, mean difference; PFC, prospective food consumption; PFS, Power of Food Scale; RCT, randomized controlled trial; RoB, Cochrane risk of bias; ROBINS-I, Risk Of Bias In Non-randomized Studies—of Interventions; SE, standard error; SEM, standard error of the mean; SMD, standardized mean difference; TFEQ, Three Factor Eating Questionnaire; VAS, visual analogue scale; YFAS, Yale Food Addiction Scale.

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1 | Introduction

Glucagon-like peptide-1 (GLP-1)-based pharmacotherapies, including semaglutide and tirzepatide, represent a new generation of medications that achieve clinically significant weight loss, often exceeding 15%–20% of body weight [1]. GLP-1-based pharmacotherapies primarily act through gastrointestinal pathways to increase satiety and reduce appetite, leading to decreased energy intake and weight loss [2]. A recent systematic review and meta-analysis of 47 randomized controlled trials (RCTs) examined the effect of GLP-1-based pharmacotherapies on weight loss in adults with overweight/obesity or diabetes and found a mean reduction in weight of 4.57 kg compared with a placebo [3]. Confirming the efficacy of GLP-1-based pharmacotherapies for weight management, a systematic review of semaglutide used for weight loss in participants with obesity and without diabetes found a mean reduction in weight of 11.85% [4].

Although the effects on weight loss are established, less is known about the influence of GLP-1-based pharmacotherapies on eating behavior (e.g., motivation to eat, food preferences, and reward), appetite sensations, and objective measures of energy intake. These are all key factors that influence long-term weight management and may explain individual differences in responses to interventions [5–8]. The effect of GLP-1-based pharmacotherapies on eating behavior, appetite, and energy intake using different doses, duration, and assessment methods has been investigated in several studies [2, 9–11]. In a recent review of 12 studies examining the effects of GLP-1 infusion, liraglutide, or semaglutide, Aldawsari, Almadani, Almuhammadi, et al. [12] reported improvements in appetite sensations (measured using visual analogue scales [VAS]) and some changes in food preferences (measured using the Leeds Food Preference Questionnaire [LFPQ] and the Control of Eating Questionnaire [CoEQ]). However, only three of the studies in this review assessed food preferences, and broader aspects of eating behavior were not examined. Since this review, numerous new trials have been published, including studies investigating tirzepatide, which provides an opportunity for comprehensive synthesis.

Energy intake, appetite, eating behavior, food reward, food craving, and food preferences are related but distinct constructs. In this review, appetite refers to subjective motivation to eat and includes sensations such as hunger, satiation, satiety, fullness, desire to eat, and prospective food consumption, whereas energy intake reflects the amount of energy consumed [13, 14]. Food reward refers to the momentary value of a food to the individual at the time of ingestion [5]. In the literature, food reward includes separable hedonic and motivational components, commonly described as “liking” and “wanting,” which usually cohere but can also disassociate [15]. Food craving refers to a strong desire to eat a particular food and is related to but distinct from liking because many commonly craved foods are highly liked, but craving does not always result in eating [16–18]. The term “preference” refers to the selection of one item over others [19]. Food preferences are learned via experiences with food and eating and can refer to preferences for certain foods or predispositions for basic tastes (sweet, bitter, sour, and salty) [19, 20]. Eating behavior is used as a broader term encompassing food craving, food reward, food preferences, and other patterns of eating, all of which are influenced by psychological, environmental, and cultural factors [21].

Beyond weight management, there is emerging evidence that GLP-1-based pharmacotherapies may influence central reward pathways implicated in food motivation and addictive behaviors [22]. There is some evidence that GLP-1-based pharmacotherapy use alters food cravings, reduces “food noise,” and impacts the rewarding properties of food and substance use [22, 23]. Understanding these effects could provide insight into the broader behavioral influence of GLP-1-based pharmacotherapies and inform personalized approaches for weight management. Examining these behavioral mechanisms is essential, especially as 10%–30% of users may be nonresponsive to treatment (<5% weight loss) [24–26], and the factors that predict response versus nonresponse have not been identified.

The overall aim of this review is to synthesize evidence on how GLP-1-based pharmacotherapies used for weight loss or weight maintenance impact eating behavior, appetite, and energy intake in adults with overweight or obesity without major comorbidities. To our knowledge, no such systematic review and meta-analysis has been conducted. This review addresses that gap and looks to inform multilevel obesity treatment strategies that combine pharmacotherapy with evidence-based behavior change interventions through better identification of patients who may require additional support.

2 | Methods

2.1 | Information Sources and Search Strategy

Four electronic databases were searched on November 4, 2025: MEDLINE (Ovid), PsycINFO (Ovid), EMBASE (Ovid), and Web of Science (Core Collection). The MEDLINE, Embase, and PsycINFO strategies were run simultaneously as a multifile search in Ovid. Searches for all databases are included in Tables S1 and S2. Limits were set to include articles recruiting human populations and published in English, as translating studies into English could lead to relevant information being mistranslated. There were no search date restrictions. The search strategies were peer-reviewed by two authors (B.O. and J.B.) prior to execution using the PRESS checklist [27]. Additionally, reference lists, conference proceedings, and thesis databases were checked to identify other relevant articles. Duplicates were identified using Rayyan’s “deduplication” tool, manually checked by the team, and removed from the sample. This systematic review followed PRISMA guidelines [28] and was preregistered with PROSPERO (registration number: CRD420251182640).

2.2 | Study Selection, Inclusion, and Exclusion

Articles were included if they recruited adults (≥ 18 years) with a body mass index (BMI) of ≥ 25 kg/m² and without major comorbidities. Studies were excluded if participants were pregnant or presented with diabetes or major cardiovascular, hepatic, renal, gastrointestinal, endocrine, hematological, or neurological disorders that could affect drug metabolism or interpretation of outcomes. This included Parkinson’s disease, anorexia nervosa, bulimia nervosa, binge eating disorder, all cancers, inflammatory bowel diseases, intellectual deficiency, psychiatric conditions, sleep disorders, and weight loss surgery (e.g., gastric bypass or

bariatric surgery). Where trials included data for participants with and without diabetes, the authors were contacted to obtain data from the nondiabetes subgroup. Where these data were not available, the study was excluded. Studies recruiting participants with prediabetes or mild metabolic impairments (e.g., elevated waist circumference, low high-density lipoprotein cholesterol, triglycerides > 150 mg/dL, or impaired glucose tolerance) were included.

Trials were required to evaluate the effect of any GLP-1-based pharmacotherapy (e.g., exenatide, liraglutide, semaglutide, and tirzepatide) on weight loss or weight maintenance for a minimum of 1 week. Studies were excluded where interventions lasted less than 1 week. Interventions including standard wrap-around care, such as general lifestyle advice, nutritional guidance, and exercise recommendations, were permitted because these are typically mandated with GLP-1-based pharmacotherapy use. However, studies were excluded if they incorporated intensive lifestyle interventions likely to confound drug effects, including very-low-calorie diets (< 500 kcal/day), structured exercise programs exceeding standard recommendations (e.g., > 150 min/week supervised), or comprehensive behavioral programs (> 10 individualized sessions). Authors were contacted for further details about the intervention design if the methods section did not provide sufficient information to inform a decision about inclusion. Studies were eligible regardless of whether they included a comparator group.

Articles were included if they reported any eating behavior, appetite, or energy intake outcome, measured using any instrument, as change from baseline or change versus control/placebo. RCTs, nonrandomized trials, single-arm intervention studies, and observational studies (prospective or retrospective cohorts and case series) were included. Observational cross-sectional studies that do not assess changes in eating behavior, appetite, or energy intake and qualitative studies without quantitative outcomes were excluded. Alcohol intake was included as an outcome in the original protocol. However, only one eligible study reporting this outcome was identified. As this was insufficient to support a meaningful synthesis, alcohol intake was removed as an outcome from the revised review.

All titles and abstracts were assessed for eligibility by the main author (C.D.) and independently screened by two researchers (B.O. and J.B.), with uncertainty regarding eligibility discussed among the researchers. Full texts were retrieved and assessed for eligibility by C.D. and independently screened by B.O. and J.B., with uncertainty regarding eligibility discussed among the researchers. Eight authors were contacted to request additional data for the meta-analyses [29–36]. Six authors responded; however, data were only available for one study [31].

2.3 | Data Extraction

Data were extracted using the Cochrane group data collection form for intervention reviews of randomized and nonrandomized control trials [37] by one author (C.D.), and were cross-checked for errors by B.O. and J.B. The extracted characteristics of each included article consisted of the following: title, study ID, publication type, study design, study aim, ethical information, number of participants, population characteristics (age,

BMI, gender/sex, ethnicity, population description, method of recruitment, and inclusion/exclusion criteria), description of the intervention (number of participants randomized, type of GLP-1-based pharmacotherapy and dose used, and intervention length), description of outcomes (including measurement tool and unit of measurement), conflicts of interests, data and analysis (number of participants in analysis, means and standard deviations or equivalent, unit of analysis, statistical methods used, and appropriateness of these), key conclusions of study authors, and references to other available studies.

Where means and standard deviations were not reported, other relevant data were extracted (e.g., median and interquartile range [IQR], 95% confidence intervals [CI], and correlations). For the appetite outcome, only the overall appetite score (composite/aggregate score) was extracted, in line with recent recommendations [38]. If only separate appetite subscales were reported, these were extracted. If multiple energy intake outcomes were reported, only the *ad libitum* data were extracted.

2.4 | Data Synthesis

Meta-analyses were performed where ≥ 10 effect sizes were available. To avoid double counting participants and including statistically dependent effect estimates from the same study, only one effect estimate per study was included in each meta-analysis. Where outcomes were assessed at multiple time points, the latest available time point was included in the analyses. Where multiple doses were reported, the highest dose was included. This approach enabled a consistent study-level analysis but did not allow changes in behavioral effects over time or dose–response relationships to be examined. Effects on appetite and energy intake were examined using a random-effects meta-analysis as considerable between-study heterogeneity was expected. All analyses were carried out in the R environment, version 4.5.1 [39], using the following packages: *dmeter* [40], *esc* [41], *tidyverse* [42], *meta* [43], *metafor* [44], and *estmeansd* [45].

Overall postprandial appetite suppression was used as the primary outcome of appetite, assessed using a 100-mm VAS and calculated as the mean of satiety, fullness, inverted hunger (100 – hunger score), and inverted prospective food consumption (100 – prospective food consumption score). Higher scores indicate greater appetite suppression. This composite measure was selected because it was the most frequently reported appetite outcome across included studies. Effect estimates were pooled as between-group mean differences (MDs) in VAS units (mm). The use of MD was considered appropriate as all studies measured appetite using a standard 100-mm VAS scale. Standard errors (SEs) were extracted directly or derived from reported standard deviations or confidence intervals, according to Cochrane Handbook guidance [46]. In studies reporting appetite outcomes as area under the curve (AUC) over the postprandial period (mm·min), AUC values were converted to time-weighted mean VAS scores (mm) by dividing by the duration of the measurement period (e.g., 180 min), enabling pooling with studies reporting discrete VAS outcomes. Where necessary, between-group MDs and corresponding variances were derived from reported summary statistics. Of the 10 studies included, nine required imputations of missing SDs.

Only overall postprandial appetite suppression scores were included in the meta-analysis. Fasting appetite ratings, retrospective ratings covering the previous week, and individual appetite subscales were not pooled. The overall appetite suppression score was selected because it was the most consistently reported appetite outcome across studies and was measured using a standard 100-mm VAS. Where studies reported postprandial appetite as AUC, values were divided by the duration of the assessment period to derive a time-weighted mean VAS score. This conversion assumes that the reported AUC adequately represents the appetite response across the assessment period and may be influenced by differences in sampling frequency, the method used to calculate AUC, and assumptions regarding the response between measurement time points. This allowed outcomes to be expressed in a common unit but did not remove differences in meal conditions, assessment timings, or the duration over which appetite was measured.

A separate meta-analysis was conducted for energy intake. Studies were included if they reported between-group comparisons of energy intake for an intervention relative to a placebo or control condition. Energy intake data were extracted as sample size, means, and standard deviations for intervention and control groups. Given the heterogeneity in energy intake assessment methods across studies (e.g., single ad libitum test meals, total daily energy intake, and dietary recall), effect estimates were pooled using the standardized MD (SMD). Where studies reported energy intake as medians with interquartile ranges, these were converted to means and standard deviations using the “estmeansd” R package. Where 95% confidence intervals were reported in place of SDs, these were derived using the formula: $SD = \sqrt{(Upper - Lower) / 3.92}$. Of the 13 studies included, eight required imputations of SDs: four from 95% CIs, two from SEs, and two from medians and IQRs.

The restricted maximum likelihood estimator was used to calculate heterogeneity variance, and heterogeneity was also evaluated using the *I*-squared statistic (I^2), with values inferred as low (< 25%), moderate (25% to 75%), and high (> 75%). Knapp–Hartung adjustments [47] were used to calculate the confidence interval around the pooled effect, as this can reduce the chance of false positives, especially when the number of studies is small [48]. Prediction intervals were calculated to reflect the expected range of effects in future studies. The results of the meta-analyses are presented as forest plots. Sensitivity analyses were conducted excluding studies for which SDs were not reported directly, using the same random-effects models, restricted maximum likelihood estimators, and Knapp–Hartung adjustments as the primary analyses. For the appetite analysis, a sensitivity analysis was planned excluding studies for which the SE had to be derived or imputed from other reported summary statistics. However, this analysis could not be conducted because only one study reported the SE directly.

Leave-one-out analyses and influence diagnostics were used to identify potential outliers and influential studies, and analyses were repeated with these studies removed where appropriate. Sensitivity analyses excluding studies judged to be at high risk of bias were conducted to assess the robustness of the pooled estimates. For meta-analyses including at least 10 studies, small-study effects were assessed using funnel plots and Egger’s regression test for funnel plot asymmetry. Trim-and-fill analyses were also

conducted to explore the potential influence of missing studies on the pooled estimates. These findings were interpreted cautiously because funnel plot asymmetry may reflect publication bias, heterogeneity, or other methodological differences.

For both appetite and energy intake, subgroup analyses were conducted according to the type of GLP-1-based pharmacotherapy. Random-effects meta-regression analyses were also performed to examine the association between intervention duration and effect size. For energy intake, an additional subgroup analysis was conducted according to assessment method (ad libitum or dietary recall). Other potentially relevant moderators considered included baseline BMI, percentage of women, achieved weight loss, comparator type, and treatment dose. However, further subgroup or meta-regression analyses were not conducted because of the small number of studies.

2.5 | Study Quality Assessment

Risk of bias was assessed using the revised Cochrane risk of bias (RoB) tool (version 2) for parallel and crossover studies [49], and the Risk Of Bias In Non-randomized Studies—of Interventions (ROBINS-I) tool (version 2) [50]. Only full-text papers were assessed for risk of bias; due to lack of available information, conference abstracts were excluded [30, 33, 51, 52]. Judgments were made by two authors independently (JB and BO), with any discrepancies resolved through discussion between authors. The certainty of the evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach [53]. GRADE assessments were conducted for energy intake and appetite because these were the only outcomes with sufficient studies to permit meta-analysis. Only studies contributing to the respective meta-analyses were included in the GRADE assessments. Assessments were conducted independently by the review authors and subsequently discussed among all authors to reach consensus.

3 | Results

A total of 3620 articles were retrieved from the four databases. After removing duplicates, 3074 articles were screened (Figure 1); 25 articles were included in this review. There were very few studies that measured eating behavior; therefore, these outcomes are qualitatively summarized.

3.1 | Study Characteristics

Study characteristics are summarized in Table S3. A total of 4060 participants (64% female) were included in the reviewed studies, ranging from 14 to 1965 participants per study, with a mean age of 44 years (34.0–50.3 years) and a BMI of 36.7 kg/m² (33.8 to 43.7 kg/m²). Studies were published between 2010 and 2025 and were largely conducted in the USA ($n=12$), with a small number of studies conducted in Germany ($n=2$), the Netherlands ($n=2$), the United Kingdom ($n=1$), Denmark ($n=1$), Russia ($n=1$), Spain ($n=1$), Switzerland ($n=1$), Malaysia ($n=1$), and Greece ($n=1$). These studies used the following GLP-1-based pharmacotherapies: liraglutide ($n=15$), semaglutide ($n=7$), tirzepatide ($n=4$),

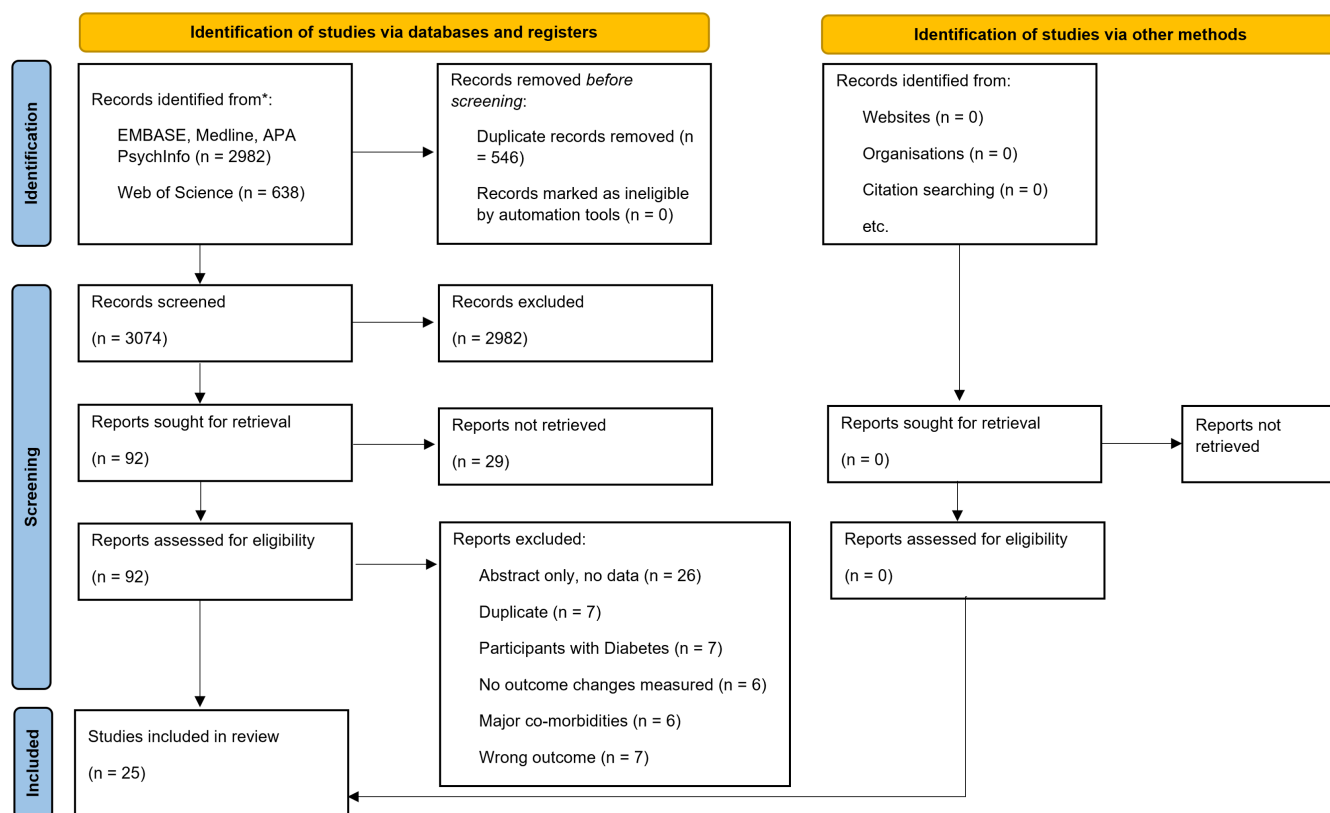


FIGURE 1 | Flow diagram of study selection. *Note:* Alcohol intake was specified as an outcome in the original protocol, but this outcome was excluded as only one eligible study reported it.

exenatide ($n=3$), and survodutide ($n=1$). The average duration of treatment length was 18.73 weeks, ranging from 4 to 52 weeks. Study comparators included placebo ($n=14$), none/observational ($n=6$), control ($n=3$), lifestyle ($n=2$), and exercise ($n=1$).

Outcomes measured included energy intake ($n=15$), appetite ($n=14$), and eating behavior ($n=13$). Energy intake was assessed using a range of objective and self-reported methods. Most commonly, studies measured energy intake during controlled ad libitum test meals, including buffet meals, vending machine paradigms, or standardized laboratory-based lunch or dinner meals. Several studies assessed total daily energy intake, estimated using 24-h dietary recalls, food diaries, or image-based food logging applications. Appetite-related outcomes were assessed using VAS presented on 100-mm lines. Studies typically measured individual subscales of appetite (hunger, fullness, satiety, desire to eat, and prospective food consumption) under fasting and/or postprandial conditions following standardized meals, with several studies calculating an overall appetite suppression score. One study also measured appetite retrospectively, using appetite ratings over the previous week to calculate an average retrospective overall appetite score [54].

Eating behavior and food reward were examined using multiple validated questionnaires, including the CoEQ, LFPQ, Food Craving Inventory (FCI), Food Craving Questionnaire State (FCQ-S), Three Factor Eating Questionnaire (TFEQ), Power of Food Scale (PFS), Dutch Eating Behavior Questionnaire (DEBQ), Binge Eating Scale (BES), Yale Food Addiction Scale (YFAS), and the Healthy Eating Index (HEI).

3.2 | Study Quality

3.2.1 | Risk of Bias

Only four studies were deemed low risk of bias. Most studies were rated ‘some concern’ ($n=10$). Two studies were rated as having serious risk of bias and six studies were rated as having a high/critical risk of bias (Figures S1, S2, and S3). There were no concerns regarding randomization for the RCTs. Lack of blinding may be a concern across all trials, as participants could potentially discern their treatment allocation through the presence (or absence) of characteristic side effects of GLP-1-based pharmacotherapies. Only one study informed all participants that they would experience nausea to maintain blinding [31]. Therefore, there was some concern that detection bias could be present in self-reported measurement of outcomes. One nonrandomized study reported departure from the protocol, where participants were able to switch between treatment options [55]. Across all studies, the most serious sources of bias were judged to be incomplete reporting of outcome data and lack of adjustment for confounders, for example, physical activity [56].

Excluding scheduling issues as a reason for withdrawal, median attrition rates for the parallel trials were 9% for active treatment versus 4% for placebo (data available for $n=10$) (Table S5). Inadequate reporting of reasons for withdrawal may mean the assumption of “missing at random” was violated in some studies (Tables S6 and S7). Most studies did not analyze data according to a predefined data analysis plan;

TABLE 1 | Quality of evidence included in the systematic review and meta-analysis based on GRADE approach.

Outcome	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Decision
Energy Intake	Some concerns ^a	Considerable ^b	No serious indirectness ^c	No serious imprecision ^d	Undetected ^e	Moderate ⊕⊕⊕○
Appetite	Some concerns ^f	Substantial ^g	No serious indirectness ^h	Moderate imprecision ⁱ	Possible ^j	Low ⊕⊕○○

Note: Only studies included in the corresponding meta-analysis were considered. Study-level concerns were considered collectively when judging each outcome-level GRADE domain.

^aEnergy intake risk of bias: Four studies were at low risk of bias, eight had some concerns, and one was at high risk. The outcome was downgraded for concerns relating to selection of the reported result.

^bEnergy intake inconsistency: Considerable heterogeneity was present across study estimates ($I^2 = 82.7\%$).

^cEnergy intake indirectness: No overall downgrade was applied. One study recruited a selected sample of adults with accelerated gastric emptying, which may not be generalizable to the broader population, but all other studies had no serious indirectness concerns.

^dEnergy intake imprecision: No overall downgrade was applied. Four studies had study-level imprecision concerns: Acosta, Camilleri, Burton, et al. [29] included a small sample and a very wide confidence interval; Basolo, Burkholder, Osgood, et al. [31] showed a clear reduction at 2 weeks, but the 24-week result was nonsignificant with wide confidence intervals; Richardson, Schembre, Jospe, Widmer, and Silver [57] underpowered to detect small-to-moderate effects and did not report confidence intervals; and Silver, Olson, Mayfield, et al. [58] had limited power and large standard deviations relative to the effect sizes.

^eEnergy intake publication bias: Publication bias was considered undetected based on the funnel plot and Egger's test.

^fAppetite risk of bias: One study was at low risk of bias, eight had some concerns and one was at high risk. The outcome was downgraded for concerns relating to selection of the reported result.

^gAppetite inconsistency: Substantial heterogeneity was present across study estimates ($I^2 = 67.5\%$).

^hAppetite indirectness: No overall downgrade was applied. In Jensen, Janus, Lundgren, et al. [56], participants underwent an 8-week low-calorie diet prior to randomization, which may have influenced any observed effects of liraglutide on appetite. All other studies had no serious indirectness concerns.

ⁱAppetite imprecision: Four studies were downgraded at study level. The confidence intervals crossed zero in two studies [9, 32], one study had wide confidence intervals [59], and one study was not powered for appetite outcomes and reported limited quantitative information [34].

^jAppetite publication bias: Publication bias was considered possible based on the funnel plot and Egger's test.

however, it was judged that there was low risk of selective reporting overall. Four out of 13 studies (30.7%) that reported effects on energy intake were judged to be at low risk of bias, compared with two out of 10 (20%) for studies that reported effects on appetite. Conversely, two out of 13 (15.4%) and one out of 10 (10%) papers were judged to be at high risk of bias for energy intake and appetite, respectively. The nonrandomized studies were judged to be at risk of significant bias due to poor control of confounding variables, incomplete outcome data, and issues with measurement of the outcome variables (e.g., nonvalidated tools and subjective measures). Ten out of the 17 randomized studies included in the review were funded by pharmaceutical companies.

3.2.2 | Grade

The certainty of evidence assessed using GRADE is summarized in Table 1. Overall, the certainty of evidence was rated as moderate for energy intake and low for appetite. For energy intake, certainty was limited by concerns regarding risk of bias, particularly the selection of reported results, and considerable between-study heterogeneity ($I^2 = 82.7\%$). However, no serious overall concerns were identified for indirectness or imprecision, and publication bias was not detected. For appetite, certainty was limited by concerns regarding risk of bias, substantial heterogeneity ($I^2 = 67.5\%$), imprecision in several study estimates, and possible publication bias.

3.3 | Study Findings

Table S4 summarizes the direction and statistical significance of reported effect, split by outcome (energy intake, appetite, and eating behavior).

3.3.1 | Energy Intake

Meta-analysis of 13 studies ($n = 809$, GLP-1-based pharmacotherapy, $n = 420$, control/placebo group $n = 389$) showed a negative effect of GLP-1-based pharmacotherapies on energy intake (SMD = -0.775 , 95% CI = -1.21 to -0.34 , $p = 0.002$; Figure 2), indicating that GLP-1-based pharmacotherapies decrease energy intake versus control. The between-study heterogeneity variance was estimated at $\tau^2 = 0.42$ (95% CI = 0.17 – 1.33), with an I^2 value of 82.70% (95% CI = 71.70%–89.40%). The prediction interval ranged from SMD -2.25 to 0.70 , indicating that although most future studies are expected to show reductions, effects compatible with little to no reduction are also plausible in some contexts. Leave-one-out and influence diagnostics identified two studies as influential contributors to between-study heterogeneity and possible outliers [34, 59]. With these studies removed, the effect size slightly decreased (SMD = -0.767 , 95% CI = -1.17 to -0.36 , $p = 0.001$). Heterogeneity also decreased ($I^2 = 76.00\%$, 95% CI = 56.90–86.70).

In a sensitivity analysis restricted to the five studies that reported SDs directly ($n = 258$), the pooled estimate remained in the direction of reduced energy intake but was smaller and no longer statistically significant (SMD = -0.478 , 95% CI = -1.53 to 0.57 , $p = 0.276$). Heterogeneity remained substantial ($I^2 = 87.2\%$, 95% CI = 72.3% to 94.0%), and the prediction interval was wide (SMD -2.91 to 1.95).

Visual inspection of the funnel plot did not suggest evidence of publication bias (Figure S4), and Egger's test did not indicate the presence of funnel plot asymmetry ($p = 0.705$). Trim-and-fill analysis did not identify any missing studies, and the pooled effect estimate was unchanged.

There was evidence of subgroup differences by drug ($p < 0.001$, Table 2). An additional subgroup analysis found significant

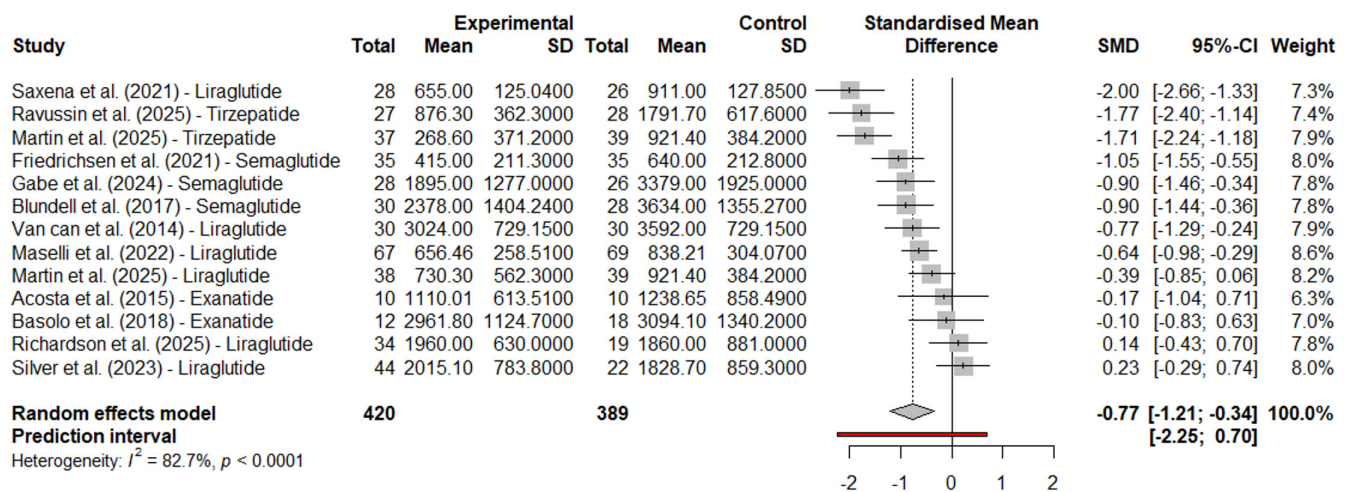


FIGURE 2 | Forest plot of the effect of GLP-1-based pharmacotherapies on energy intake.

differences by method of energy intake ($p < 0.001$). When measuring energy intake using diet recall, there was a small positive effect of GLP-1-based pharmacotherapies on intake ($k = 2$, $SMD = 0.18$, 95% $CI = -0.40$ to 0.77 , $I^2 = 0.00$). In comparison, when measuring energy intake using an ad libitum study design, there was a negative effect of GLP-1-based pharmacotherapies ($k = 11$, $SMD = -0.95$, 95% $CI = -1.37$ to -0.54 , $I^2 = 76.10$). Lastly, there was no significant influence of intervention length (weeks) on energy intake ($p = 0.609$).

Five studies reported changes in macronutrient intake alongside energy intake. Basolo, Burkholder, Osgood, et al. [31] found that treatment with exenatide was associated with larger decreases in energy intake from all three macronutrients compared with placebo, indicating consistent reductions across macronutrients. Similarly, Ravussin, Sanchez-Delgado, Martin, et al. [54] reported that, after 18 weeks, tirzepatide produced large reductions in energy intake from all macronutrients during ad libitum test meals (lunch and dinner). Orban, Kanehl, Stoll, et al. [33] reported small but consistent reductions in refined carbohydrate consumption in both the liraglutide and control groups. Consumption of dairy products was reported more frequently among the GLP-1-based pharmacotherapy group. However, energy intake from dairy was lower, suggesting that participants were choosing lower-calorie dairy products or smaller portions.

Based on a 24-h recall, Richardson, Schembre, Jospe, Widmer, and Silver [60] reported very small effects of GLP-1-based pharmacotherapies on carbohydrate intake (0.4% vs. 2.9% of kcals, adjusted $p = 0.019$) and protein intake (1.4% vs. -0.3% of kcals, adjusted $p = 0.037$). Based on an average of three 24-h recalls, Silver, Olson, Mayfield, et al. [59] reported that liraglutide produced no differences in macronutrient intakes compared with the control group (fat -1.2% vs. -1.4%, $p = 0.57$; carbohydrate -0.2% vs. 2.4%, $p = 0.18$).

3.3.2 | Appetite

Meta-analysis of 10 studies ($n = 321$) showed a significant positive effect of GLP-1-based pharmacotherapies and

TABLE 2 | Subgroup analysis on the effect of drug type on energy intake.

Drug type	k	SMD	95% CI	I^2
Exenatide	2	-0.13	-0.53 to 0.27	0.00
Liraglutide	6	-0.55	-1.36 to 0.26	85.30
Semaglutide	3	-0.95	-1.17 to -0.73	0.00
Tirzepatide	2	-1.74	-2.15 to -1.33	0.00

overall appetite suppression score ($MD = 7.800$, 95% $CI = 3.74$ to 11.86 , $p = 0.001$; Figure 3), indicating that GLP-1-based pharmacotherapies suppress appetite compared with control/placebo. The between-study heterogeneity variance was estimated at $\tau^2 = 21.52$ (95% $CI = 4.51$ – 96.30), with an I^2 value of 67.50% (95% $CI = 36.90\%$ – 83.30%). The prediction interval ranged from $MD -3.47$ to 19.07 , indicating that although the average effect favors GLP-1-based pharmacotherapies, future studies may observe little or no appetite suppression in some contexts. Leave-one-out analysis and influence diagnostics indicated that no single study had a disproportionate impact on the pooled effect size or between-study heterogeneity. Formal outlier detection did not identify any outliers. The funnel plot did suggest evidence of publication bias (Figure S5), and Egger's test indicated evidence of small study effects ($p = 0.027$). Trim-and-fill analysis imputed four missing studies to the left, resulting in an attenuated and no longer statistically significant pooled estimate (adjusted $MD = 4.30$, 95% $CI = -0.33$ to 8.93 , $p = 0.066$). Excluding the study at high risk of bias did not materially change the pooled effect estimate for GLP-1-based pharmacotherapies on overall appetite suppression score ($MD = 7.901$, 95% $CI = 3.27$ – 12.53 , $p = 0.004$), and heterogeneity remained similar ($I^2 = 71.00\%$, 95% $CI = 42.70\%$ – 85.40%).

A subgroup analysis found that the type of drug did not significantly influence the effect of GLP-1-based pharmacotherapies on appetite ($p = 0.064$). Additionally, a random effects meta-regression found that intervention length had no significant effect on the studies' effect size ($p = 0.403$).

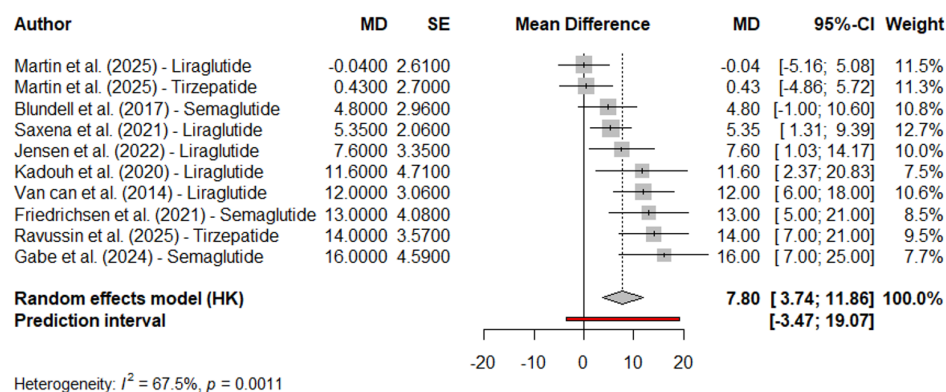


FIGURE 3 | Forest plot of the effect of GLP-1-based pharmacotherapies on appetite suppression. Note: A positive mean difference (MD) indicates greater appetite suppression or less appetite; a negative MD indicates lower appetite suppression or more appetite.

3.3.3 | Eating Behavior

Martin, Carmichael, Carnell, et al. [32] found a decrease in TFEQ susceptibility to hunger at week six in the liraglutide (-1.8 AU, 95% CI = -3.2 to -0.3 AU, $p = 0.016$) and tirzepatide (-3.7 AU, 95% CI = -5.2 to -2.3 AU, $p < 0.001$) groups versus placebo. When compared with the CoEQ, three studies found lower hunger and higher craving control in those treated with semaglutide [9, 11, 61]. Although Gabe, Breitschaft, Knop, et al. [61] found lower craving for sweet and savory foods, Blundell, Finlayson, Axelsen, et al. [9] found only lower craving for sweet foods. Conversely, Friedrichsen, Breitschaft, Tadayon, Wizert, and Skovgaard [11] found lower craving for savory foods. Only two studies specifically measured the effects of GLP-1-based pharmacotherapies on food craving, with both using the FCI [32, 62], and one of these studies also using the FCI-State [32]. Those receiving tirzepatide reported lower overall food craving after 18 weeks of treatment (-0.35 AU, 95% CI = -0.61 to -0.09 AU, $p = 0.010$) [62], with reductions specifically for sweet foods, carbohydrates, and fast food fats. Martin, Carmichael, Carnell, et al. [32] similarly found that overall FCI scores decreased at 6 weeks in both the liraglutide (0.3 AU, 95% CI = -0.6 to -0.1 AU, $p = 0.008$) and tirzepatide groups (-0.6 AU, 95% CI = -0.9 to -0.4 AU, $p < 0.001$) compared with placebo. Specifically, those receiving GLP-1-based pharmacotherapies showed lower craving for sweet foods, high-fat foods, fast food fats, and carbohydrates. Furthermore, there was a reduction in FCI-State scores for both liraglutide (-0.6 AU, 95% CI = -0.9 to -0.3 AU, $p = 0.001$) and tirzepatide (-1.1 AU, 95% CI = -1.4 to -0.8 AU, $p < 0.001$) groups versus placebo. Both groups showed reductions in hunger, lack of control, anticipation of negative reinforcement, anticipation of positive reinforcement, and desire.

Three studies explored food preferences; two using the LFPQ [9, 57], and one used the Food Preference Questionnaire (FPQ) [62]. One study measured desire to consume only [59]. Blundell, Finlayson, Axelsen, et al. [9] reported reductions in explicit liking and implicit wanting for high-fat savory foods and an increase in implicit wanting for low-fat and sweet foods after 12 weeks of treatment with semaglutide compared with placebo. Jensen, Janus, Lundgren, et al. [57] also found reductions in explicit liking and implicit wanting for high-fat savory foods and reductions in explicit liking and implicit wanting for high-fat sweet foods with liraglutide compared with placebo. In contrast, Silver, Olson, Mayfield, et al. [59]

found no significant differences in desire to consume sweet or savory foods between the liraglutide and control groups. Findings from Kennedy, Knights, Ravussin, et al. [62] showed decreases in food preferences across multiple food categories, including high fat foods, low fat foods, high sugar foods, low carbohydrate/high protein foods, and low fat/low carbohydrate foods.

Two studies reported changes in metrics of disordered eating, using the BES [63] and YFAS [64]. Participants treated with liraglutide showed reductions in binge eating score, from 20 AU (IQR 18 to 27 AU) to 11 AU (IQR 7 to 16 AU) ($p < 0.001$) [63], and scores for food addiction were reduced in those receiving semaglutide (57.5% – 4.2% after 4 months, $p < 0.001$) [64]. However, most studies detected no differences across measures of restraint/restrictive eating [32, 57], uncontrolled eating [57], emotional eating [57, 58], or external eating [58] when measured through either the TFEQ or DEBQ. Only two reductions in scores were observed; Mosikian, Golikova, Martjanova, and Babenko [58] found lower DEBQ restrictive eating scores following 6 months of treatment with liraglutide (78.6 – 50.0 AU, $p = 0.010$), and Martin, Carmichael, Carnell, et al. [32] found a decrease in TFEQ disinhibition at Week 6 in those receiving tirzepatide (-3.8 AU, 95% CI = -5.2 to -2.4 AU, $p < 0.001$) but not liraglutide ($p = 0.071$). Martin, Carmichael, Carnell, et al. [32] additionally found that treatment with liraglutide (-0.5 AU, 95% CI = -0.8 to -0.2 , $p = 0.004$) and tirzepatide (-1.0 AU, 95% CI = -1.3 to -0.7 AU, $p < 0.001$) increased overall power of food scores compared with placebo. Finally, two studies used the HEI [51, 60]. Cardel, Foster, Heinberg, Richardson, and Lee [51] found that participants treated with semaglutide or tirzepatide improved their HEI scores from 55.0 to 65.1 AU at 6 months ($p < 0.001$). However, Richardson, Schembre, Jospe, Widmer, and Silver [60] found no difference in total HEI score between the liraglutide and control groups.

3.3.4 | Adverse Events and Potential Influence of Nausea

The most commonly reported side effect of treatment with GLP-1-based pharmacotherapies was nausea. Only 10 out of 23 studies reported detailed information about the prevalence of nausea as a side effect. Across these 10 studies, nausea was

reported in 51% of participants receiving a GLP-1-based pharmacotherapy, versus 16% of participants receiving placebo (Table S4). Only one study reported the results of a sensitivity analysis of nausea on study outcomes. The authors reported that overall study conclusions were similar when participants who experienced nausea or vomiting were excluded; however, some measurements of nausea were measured using retrospective VAS [32]. One study tested for an association between presence of nausea and reduction in food intake and reported no association [31].

4 | Discussion

The long-term use, tolerability, and safety of pharmacotherapy for weight loss remain a significant challenge [65]. Although recent clinical trials using GLP-1-based pharmacotherapies show promise for weight management [66], the effect of these medications on eating behavior is not well understood. The aim of this systematic review and meta-analysis was to evaluate the effects of GLP-1-based pharmacotherapies used for weight loss on eating behavior, appetite, and energy intake in adults with overweight/obesity and without major comorbidities. Twenty-six studies were identified, assessing the impact of five different GLP-1-based pharmacotherapies for weight loss. The meta-analyses suggest that GLP-1-based pharmacotherapies have a negative effect on energy intake and are associated with a reduction in some measures of motivation to eat and food reward. The effects on appetite suppression are uncertain. These findings should be interpreted cautiously due to some use of nonstandard methodologies and the presence of bias in the majority of the included studies.

Most studies used an appropriate methodology (i.e., test meals) to determine energy intake. Two studies used 24-h recalls; these studies both reported lower energy intake compared with baseline, but higher energy intake at postintervention compared with control [59, 60]. A variety of measures used to assess eating behavior were identified. However, there were not enough studies using comparable tools or outcomes to enable a quantitative synthesis, meaning that a meta-analysis of eating behavior was not conducted. Overall, the available evidence remains too limited and heterogeneous to draw conclusions about how GLP-1-based pharmacotherapies influence eating behavior, particularly in populations without diabetes.

4.1 | Energy Intake

Several GLP-1-based pharmacotherapies are now approved for weight management, all of which increase the effects of GLP-1, a hormone secreted by the gut that stimulates the secretion of insulin [67]. These agents may promote weight loss through multiple mechanisms, including increased satiety, reduced appetite, and reduced food intake, and emerging evidence suggests that they may also alter food reward pathways [68]. The pooled analysis suggested that GLP-1-based pharmacotherapies reduce energy intake on average. However, the substantial heterogeneity and prediction interval crossing the null indicate that the magnitude and presence of this effect may vary across populations and treatment settings. Interestingly,

a subgroup analysis suggested a progressive increase in the effect size of energy intake reduction across the GLP-1-based pharmacotherapies, with small effects observed for exenatide and increasingly larger effects for liraglutide, semaglutide, and tirzepatide. Both semaglutide and tirzepatide were associated with larger reductions in energy intake, whereas earlier agents showed smaller and more heterogeneous effects. These findings support current evidence that next-generation GLP-1-based pharmacotherapies are more effective for weight loss than older molecules [69]. These findings should be interpreted cautiously given the limited number of studies with varying doses, populations, and protocols within the subgroup analyses. However, it appears that higher-potency and multi-receptor agonists are associated with stronger effects on energy intake.

An additional subgroup analysis identified differences in the effect on energy intake depending on the method used to measure energy intake. When energy intake was assessed via dietary recall, GLP-1-based pharmacotherapies had no meaningful effect. Studies that used an ad libitum design (e.g., test meal or vending machine paradigm) demonstrated a large reduction in energy intake. This discrepancy could be due to the methodological limitations of measuring energy intake. Although research has not directly compared ad libitum test meals with dietary recall methods, dietary assessment methods that rely on self-report and recall have many limitations [70]. Notably, self-report methods of dietary intake are known to under-report energy intake by up to 47% [71–74]. Ad libitum test meals enable more controlled measurements of energy intake. However, studies reviewed in the present work captured only acute effects on eating at a single meal or within 24 h rather than habitual intake across weeks or months. Although ad libitum test meals are reproducible, they also have challenges such as the importance of prior diet standardisation [75]. The subgroup results may reflect acute reductions in energy intake in controlled conditions and failure to detect real changes in everyday energy intake. It remains unclear whether these reductions are sustained over the extended periods required to achieve negative energy balance and, ultimately, weight loss. Furthermore, although the use of the SMD allowed energy intake outcomes reported using different scales to be pooled, it does not make laboratory-based and self-reported assessments clinically equivalent. The overall pooled estimate should therefore be interpreted as an average across different aspects of energy intake rather than as a single estimate of habitual energy intake reduction. The subgroup findings suggest that reductions may be more apparent under controlled laboratory conditions than in free-living settings. However, this comparison is uncertain because only two studies used dietary recall.

Only five studies reported changes in macronutrient intake with GLP-1-based pharmacotherapy use, which provides a limited understanding of how GLP-1-based pharmacotherapies influence the composition of participants' diets. This finding is consistent with a recent narrative review which found that differences in methodology and reliance on standardized test meals mean that changes in macronutrient or micronutrient intake remain to be identified [76]. Two ad libitum studies [31, 54] found that exenatide and tirzepatide produced reductions in energy intake across all macronutrients, which suggests that GLP-1-based pharmacotherapies reduce total energy intake and do not

alter macronutrient preference. Studies using dietary recall also found no meaningful differences in macronutrient composition between GLP-1-based pharmacotherapy and control groups [59, 60]. Orban, Kanehl, Stoll, et al. [33] reported increased dairy consumption among GLP-1-based pharmacotherapy users. However, participants appeared to select lower calorie dairy products or consume smaller portions. Taken together, these findings suggest that GLP-1-based pharmacotherapies may reduce energy intake under controlled, acute conditions. It remains unclear whether these effects lead to long-term reductions in free-living energy intake and their effects on habitual macronutrient intake. Further research is needed to examine how free-living dietary patterns change over time with GLP-1-based pharmacotherapy use.

4.2 | Appetite

The pooled analysis suggested a small increase in appetite suppression with GLP-1-based pharmacotherapies. However, the prediction interval crossed the null, and the adjusted estimate following trim-and-fill was no longer statistically significant, indicating that little or no effect may be observed in some settings. Confidence in the appetite estimate was further limited by the extensive imputation of variance data. Nine of the 10 included studies did not report the SE directly, meaning that a sensitivity meta-analysis restricted to directly reported variance data was not possible. Consequently, although there is evidence to suggest that increases in satiety and decreases in hunger are a main mechanism through which GLP-1-based pharmacotherapy impacts weight loss [68], the current data are not sufficient to support this premise. It is possible that current methods to measure appetite are not sufficiently sensitive to detect real changes; laboratory approaches to measuring appetite have known limitations in their ability to capture environmental or temporal influences [77].

This meta-analysis assessed overall postprandial appetite suppression. Fasting appetite, 24-h appetite, and studies reporting a retrospective appetite suppression score were not included. Consequently, the pooled appetite estimate should be interpreted cautiously because the included studies differed in their postprandial assessment conditions. Although outcomes were expressed using the same 100-mm VAS scale, studies used different standardized meals, assessment time points, and postprandial measurement periods. Converting AUC values into time-weighted mean VAS scores provided a common unit for analysis but did not make the underlying measurements clinically equivalent. The pooled estimate therefore represents an average across heterogeneous postprandial conditions rather than a single standardized appetite construct. This clinical and methodological heterogeneity limits the interpretability and generalisability of the pooled effect.

It is possible that the observed effect is only representative of acute and context-specific changes in appetite which may not reflect changes in appetite over many days and weeks. Appetite sensations are dynamic and, as such, measuring appetite over a single test meal may not fully capture how GLP-1-based pharmacotherapies influence appetite during everyday behavior. Ravussin, Sanchez-Delgado, Martin, et al. [54] assessed

retrospective appetite over the previous week and found that appetite suppression scores significantly increased from baseline to day 123 in the tirzepatide group, indicating that appetite suppression attenuates over the long term. It should be noted however that use of retrospective VAS scores has not been validated in appetite research, and their reliability is unknown. A paucity of studies exists that validate self-reported appetite measurements in nonmonitored free-living settings relative to clinical environments [78]. Ecological momentary assessment (EMA) is one approach that aims to address the limitations of laboratory methods by focusing on an individual's current feelings, behavior, and their surrounding environment. Measurements are taken repeatedly in the individual's natural environment and may better capture how appetite sensations fluctuate across time and context [79]. Further research that tracks appetite scores over time is needed to better understand the effect of GLP-1-based pharmacotherapies.

Importantly, there were no subgroup differences in appetite by drug type or any evidence that the intervention duration moderated the effect of GLP-1-based pharmacotherapies on appetite. However, the small number of studies limited the power of these analyses to detect moderator effects. Overall, these findings suggest a possible small reduction in appetite, although the magnitude and consistency of this effect remain uncertain and do not adequately explain the large reduction in energy intake found in the ad libitum studies.

GLP-1-based pharmacotherapies may influence weight loss partly through changes in eating behavior that are not captured by VAS measures of appetite or that the current findings are relevant only to acute and postprandial measures of appetite under controlled conditions. In the current study, appetite ratings were predominantly exploratory outcomes; however, understanding how changes in appetite interact with energy intake to drive weight loss in GLP-1-based pharmacotherapy treatment is important. Future studies should use standardized meals, assessment periods and time points, report both individual appetite sensations and a validated overall appetite suppression score to improve comparability across trials, and utilize more ecologically valid methods, such as EMA, to assess longitudinal changes in appetite.

4.3 | Eating Behavior

A main aim of this review was to examine how GLP-1-based pharmacotherapies used for weight loss affect eating behavior. Unfortunately, a meta-analysis could not be conducted due to heterogeneity of the studies, using different measurements of eating behavior that are not comparable. However, the limited available evidence suggests that GLP-1-based pharmacotherapies may influence some aspects of eating behavior, which merits further investigation. Across the included studies, treatment with GLP-1-based pharmacotherapies was associated with reductions in food craving, especially craving for sweet foods, with no changes observed for craving for fruits and vegetables [9, 11, 32, 61, 62]. Additionally, studies found changes in food preferences and reward, with reductions in explicit liking and implicit wanting for high-fat savory foods [9, 57, 62].

Appetite suppression, food craving, and food reward are related but distinct constructs and should not necessarily be interpreted as manifestations of a common pharmacological effect. GLP-1 receptor activation engages distinct and overlapping neural circuits involved in eating behavior [80]. The anorectic effects of GLP-1 receptor activation involve homeostatic pathways in the hypothalamus and brainstem, including the nucleus tractus solitarius and arcuate nucleus [80, 81]. However, GLP-1 signaling may also influence limbic and mesolimbic pathways involved in food motivation and reward. Preclinical evidence suggests that amylin receptor signaling can modulate mesolimbic circuitry, including pathways involving the ventral tegmental area and nucleus accumbens, which influence hedonic eating, food motivation, and reward [82, 83]. Although the amylin analogue cagrilintide was outside the scope of this review, these findings illustrate how next-generation obesity pharmacotherapies may engage partly distinct pathways involved in eating behavior. Reductions in appetite should therefore not be considered physiologically equivalent to changes in food craving, liking or wanting. This distinction may provide context for the findings of the current review, in which effects on appetite suppression were small and uncertain, whereas some studies reported reductions in food craving, explicit liking and implicit wanting.

Modulation of both homeostatic and reward-related pathways may provide some biological context for reported reductions in “food noise,” although this is an inconsistently defined construct. GLP-1-based pharmacotherapies may influence reward-related behavior, including neural responses to food cues and highly rewarding foods [84]. In a qualitative analysis of patient experiences using semaglutide for weight loss, users have reported significant reductions in “food noise,” which is characterized by reductions in food-related intrusive thoughts and maladaptive eating behaviors [85]. The analysis found that users believed they were able to regain control over their eating habits, which in some circumstances led to reductions in binge eating and emotional eating. In the current review, Robert, Rohana, Shah, et al. [63] found that treatment with liraglutide reduced binge eating disorder symptoms, and Nicolau, Pujol, Tamayo, et al. [64] found that treatment with semaglutide reduced food addiction scores, aligning with previous evidence that GLP-1-based pharmacotherapies affect “food noise” [85]. However, findings relating to other maladaptive eating behaviors such as emotional eating, external eating, and disinhibition are less conclusive. Based on the limited data available, studies using highly cited and validated questionnaires of eating behavior found no significant differences in cognitive restraint [32, 57], uncontrolled eating [57], emotional eating [57, 58], or external eating [58] between GLP-1-based pharmacotherapy groups and placebo after treatment.

Understanding how GLP-1-based pharmacotherapies change food preferences remains challenging, and the existing evidence cannot establish whether GLP-1-based pharmacotherapies selectively alter food preferences. Although some studies reported reductions in explicit liking and implicit wanting for specific food categories including high-fat savory foods [9, 57], another study found broader reductions in food preferences across multiple food categories [62]. This also included reductions in preferences for nutritionally opposing foods (e.g., high-fat and low-fat foods), and categories that comprise a healthy diet (e.g., low carbohydrate/

high protein and low fat-low carbohydrate/high protein). These findings suggest that GLP-1-based pharmacotherapies are associated with reductions in overall motivation to eat rather than selectively altering food preferences, which is in contrast to the current view that GLP-1-based pharmacotherapies decrease preference for energy-dense foods specifically [9, 86].

In the current review, reductions in food preference scores may reflect reductions in reward responsiveness in general rather than changes in preferences for specific foods. Therefore, it cannot be assumed that pharmacological treatment alone will result in improvements in diet quality, which has important implications for clinical practice and intervention design. Reductions in food preferences in general and reductions in nutritionally beneficial categories (e.g., protein) may result in macronutrient or micronutrient deficiencies if individuals are not offered appropriate nutritional support during treatment. This highlights the importance of providing wrap-around care alongside GLP-1-based pharmacotherapy [87]. Nutritional guidance and behavior change strategies are needed to ensure individuals maintain adequate diet quality and consume sufficient protein intake while in an energy deficit.

The differences in findings relating to food preferences and food craving could also be due to the different methods used to measure these outcomes. Food preference tasks like the LFPQ and FPQ assess a wider range of food categories, for example, “low-carbohydrate/high protein.” In contrast, food craving measures (e.g., FCI) focus on a different set of food groups (e.g., sweets and fast-food fats) and do not include a protein-specific category. Potentially, the specific reduction in food craving for sweets and fast-food fats, alongside no change in craving for fruits and vegetables, could reflect differences in the scope of measurements to assess craving versus preferences. It also could reflect a reduction in overall interest in eating rather than changes to the reward of specific foods. This distinction is important because changes in overall food motivation are conceptually different from changes in food preferences, but in the existing literature on food preferences, reward and craving are often viewed as similar constructs.

These findings suggest that GLP-1-based pharmacotherapies are associated with changes in some aspects of eating behavior, such as reductions in food craving, particularly for highly palatable, energy-dense foods. Although evidence for selective changes in food preferences is mixed, it appears that GLP-1-based pharmacotherapies may reduce preference for high-fat, energy-dense foods. Differences in outcome measures and nutritional equivalence of food category characteristics limit the extent to which current findings can be interpreted as true preference shifts as a result of GLP-1-based pharmacotherapy treatment.

4.4 | Methodological Comments

Several methodological limitations exist across the included studies that warrant cautious interpretation of findings. Clinical and methodological heterogeneity was substantial, with studies differing in pharmacotherapy, dose, route of administration, treatment duration, comparator, and the

behavioral or nutritional support provided alongside treatment. Heterogeneity was explored according to pharmacotherapy type, intervention duration, and, for energy intake, assessment method. However, other potential moderators such as baseline BMI, percentage of women, and achieved weight loss were not examined. The subgroup and meta-regression findings should therefore be considered exploratory and interpreted cautiously.

Outcome assessment methods also varied considerably. Energy intake was assessed using controlled ad libitum meals, buffet or vending-machine paradigms, dietary recalls and food-logging methods. These approaches measure different aspects of energy intake, ranging from acute consumption under controlled laboratory conditions to habitual intake in free-living environments. Although the appetite meta-analysis was restricted to overall postprandial appetite suppression measured using a 100-mm VAS, studies differed in their standardized meals, assessment timings, and postprandial measurement periods. These differences mean that the pooled estimates represent average effects across heterogeneous interventions and assessment conditions rather than the effect of a single pharmacotherapy or standardized protocol. The pooled estimates, particularly for energy intake, should therefore not be assumed to apply consistently across drugs, doses, treatment settings, or assessment methods.

Intervention duration varied substantially, ranging from very short-term studies of 4–6 weeks [29, 32, 34, 36] to longer trials lasting up to 1 year [57]. This meta-analysis showed no moderating effect of intervention length. However, the wide variation limits direct comparison across studies; observed changes in behavior may be due to acute versus sustained effects of GLP-1-based pharmacotherapy treatment, meaning behavioral responses may change over time. The decision to include only the latest time point and highest dose from each study was also a limitation. This approach was used to avoid double-counting participants and including nonindependent estimates. However, it assumes that a single assessment represents the treatment effect. It is possible that responses may have changed during treatment, particularly as doses are increased, because participants adapt to the treatment or any adverse effects such as nausea. Additionally, effects that were observed at the highest dose may not represent experiences at a lower dose or participants who were unable to tolerate the maximum dose.

The included studies were not designed to distinguish direct pharmacological effects on appetite and eating behavior from changes occurring secondary to weight loss, improvements in metabolic health, or changes in dietary habits over time. The observed reductions in appetite, energy intake, and food craving should not necessarily be interpreted as independent direct effects on appetite and reward pathways. Behavioral changes may have resulted partly from weight loss itself or changes in metabolic health and dietary habits. Few studies assessed weight loss as a mediator; therefore, this could not be examined.

Nausea is a widely reported side effect of GLP-1-based pharmacotherapies [88], but most studies included in this review did

not present detailed information on prevalence or investigate its effect on outcomes. Nausea was more frequently reported in participants receiving GLP-1-based pharmacotherapies than in those receiving placebo. For the 10 studies that reported prevalence of nausea, median rates were 51% in active treatment arms versus 16% in placebo arms. In some cases, participants with nausea experienced greater weight loss [35]. Rather than acting solely as a confounder, nausea may lie on the causal pathway between treatment and reduced appetite or energy intake. Nausea and other gastrointestinal symptoms may reduce motivation to eat and could therefore mediate part of the observed treatment effect [89, 90]. However, GLP-1-based pharmacotherapies may also influence appetite through homeostatic and reward-related pathways independently of nausea, although the included studies did not allow these mechanisms to be distinguished [80, 81]. The greater prevalence of nausea in active-treatment groups may also have increased participants' awareness of treatment allocation. Therefore, participants who experienced nausea could reasonably be assumed to be, consciously or subconsciously, aware of allocation. This functional unblinding could influence subjective ratings of appetite and eating behavior through expectancy or demand effects. Subconscious demand characteristics may play a role in biasing the results away from the null to an unknown degree. Study duration may be relevant, as it is reported that nausea and gastrointestinal symptoms diminish over time [91, 92].

Interpretation was limited by incomplete and inconsistent adverse-event reporting, including differences in definitions, assessment methods, severity thresholds, and reporting time points. Self-report tools for monitoring the frequency and severity of nausea have poor validity and reliability, meaning that it is difficult to evaluate the effects of the most common side effects of treatment with GLP-1-based pharmacotherapies [93]. Few studies assessed whether nausea was associated with appetite or energy intake outcomes. Attrition may have introduced further bias, as nausea and other gastrointestinal adverse events contributed to withdrawal in some studies, although the magnitude and direction of this effect remain uncertain. Consequently, it was not possible to determine the extent to which the observed effects reflected direct pharmacological effects on appetite regulation, indirect effects mediated through nausea, or bias arising from awareness of treatment allocation and treatment-related withdrawal. Future trials should assess adverse events prospectively using standardized measures and conduct mediation or sensitivity analyses to distinguish effects associated with nausea from appetite-related effects occurring independently of gastrointestinal symptoms.

There is also limited evidence on the effect of GLP-1-based pharmacotherapies following discontinuation or during weight maintenance. None of the included studies reported outcomes postintervention, which leaves a gap in our understanding of whether changes in energy intake, appetite, and eating behavior persist after treatment and for how long. A posttreatment analysis of the trial by Jensen, Janus, Lundgren, et al. [57] found that during the year after termination of treatment (Weeks 51–104), weight re-gain was 6.0 kg greater after discontinuing liraglutide compared with termination of supervised exercise [94]. Although the analyses reported posttreatment changes in body composition, physical activity, and sedentary time, there were no analyses of changes in eating behavior, energy intake,

or appetite. Given the growing evidence that weight regain is common after discontinuation with GLP-1-based pharmacotherapies, there is a critical need to examine eating behavior after termination of treatment to inform longer term obesity management. One recent meta-analysis found that patients gained 0.4 kg per month after discontinuation of GLP-1-based pharmacotherapies, resulting in a return to baseline weight in under 2 years [95]. Future research should examine the degree to which changes in eating behaviors, appetite, and energy intake are associated with any weight re-gain.

4.5 | Strengths and Limitations

To our knowledge, no systematic review and meta-analysis has been conducted to examine the influence of GLP-1-based pharmacotherapies used for weight loss on eating behavior, appetite, and energy intake in adults with overweight or obesity without major comorbidities. This review was able to quantitatively synthesize the effect of GLP-1-based pharmacotherapies on energy intake and overall appetite suppression using a random-effect meta-analysis. Subgroup analyses were also conducted, which enabled a more in-depth examination of drug type and method used to assess energy intake.

A key value of this review lies in its identification of the need for enhanced quality in primary evidence. Perceptions of appetite, hunger, and fullness are subjective sensations. Investigators should, where possible, standardize conditions (e.g., time since last meal and time of day), use standardized instruments (e.g., 100-mm VAS with appropriate anchors [13]) and combine these with objective measures (e.g., subsequent energy intake in a test meal) to triangulate findings. Validation of methodologies to assess the most common side effects of GLP-1-based pharmacotherapy treatment, in particular nausea, is also required to increase methodological rigor in GLP-1-based pharmacotherapy trials.

Risk of bias was rigorously assessed across studies, with emphasis placed on relevant sources of material bias, specifically the potential effects of nausea and other gastrointestinal adverse effects. Many systematic reviews exaggerate estimates of effects due to inclusion of small, poor-quality or single-center trials [96]. The incorporation of risk of bias assessments into synthesis is therefore crucial to ensure that conclusions drawn from systematic reviews are based on the strongest evidence, yet this requirement is often disregarded [97, 98]. To our knowledge, this is the first systematic review and meta-analysis of the effects of GLP-1-based pharmacotherapy treatment on energy intake, appetite and eating behavior to produce a comprehensive and credible synthesis, which takes into account the strength of the available evidence.

The aim of this review was to isolate the effect of GLP-1-based pharmacotherapies in the context of weight management for adults without major comorbidities, which limited the number of eligible studies that could be synthesized. Due to small numbers and incomplete reporting, it was not possible to explore side effects or attrition rates by drug. Other limitations of the work are that only English-language papers were retrieved and that the process of assessing bias is inherently subjective.

4.6 | Conclusions

In adults with overweight or obesity, and without diabetes, psychiatric conditions, eating disorders, or other major comorbidities, GLP-1-based pharmacotherapies may reduce short-term energy intake and appetite. However, confidence in the magnitude and consistency of these effects is limited by substantial clinical and methodological heterogeneity, wide prediction intervals, imputation of variance data, variability in outcome assessment, and the small number of studies judged to be at low risk of bias. Evidence relating to food preferences and other eating behaviors remains limited and heterogeneous. Nausea may contribute to reductions in appetite and energy intake and may increase participants' awareness of treatment allocation, particularly where outcomes are self-reported. As adverse events were incompletely and inconsistently reported, the extent to which the observed effects occurred independently of nausea remains uncertain. Larger, well-controlled trials are needed to elucidate effects of GLP-1-based pharmacotherapies on appetite and eating behavior, with more transparent and clear reporting of analyses and participant flow. Extensive efforts should be made to improve retention; in the case of withdrawal, detailed reporting of side effects and adverse events is required to allow readers to form judgments on whether the assumption "missing at random" is satisfied. Such rigor is essential to advance understanding of the effects of GLP-1-based pharmacotherapies on eating behavior, thereby enabling the development of appropriate evidence-based weight management support for individuals who discontinue treatment.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Extracted outcome data and analytic code supporting the findings of this study are available from the corresponding author upon reasonable request.

References

1. Q. Qi, A. Cox, S. McNeil, and P. Sumithran, "Obesity Medications: A Narrative Review of Current and Emerging Agents," *Osteoarthritis and Cartilage Open* 6 (2024): 100472.

2. C. Cheney, K. Hunter, and M. Klein, "Impact of GLP-1 Receptor Agonists on Perceived Eating Behaviors in Response to Stimuli," *Diabetes, Metabolic Syndrome and Obesity* 18 (2025): 1411–1418, <https://doi.org/10.2147/dmso.S488806>.
3. H. J. Wong, B. Sim, Y. H. Teo, et al., "Efficacy of GLP-1 Receptor Agonists on Weight Loss, BMI, and Waist Circumference for Patients With Obesity or Overweight: A Systematic Review, Meta-Analysis, and Meta-Regression of 47 Randomized Controlled Trials," *Diabetes Care* 48, no. 2 (2025): 292–300.
4. H. C. Tan, O. A. Dampil, and M. M. Marquez, "Efficacy and Safety of Semaglutide for Weight Loss in Obesity Without Diabetes: A Systematic Review and Meta-Analysis," *Journal of the ASEAN Federation of Endocrine Societies* 37, no. 2 (2022): 65–72.
5. P. J. Rogers and C. A. Hardman, "Food Reward. What It Is and How to Measure It," *Appetite* 90 (2015): 1–15.
6. P. J. Teixeira, E. V. Carraca, M. M. Marques, et al., "Successful Behavior Change in Obesity Interventions in Adults: A Systematic Review of Self-Regulation Mediators," *BMC Medicine* 13 (2015): 84, <https://doi.org/10.1186/s12916-015-0323-6>.
7. J. Stubbs, D. Brogelli, C. Pallister, A. Avery, A. McConnon, and J. Lavin, "Behavioural and Motivational Factors Associated With Weight Loss and Maintenance in a Commercial Weight Management Programme," *Population* 6, no. 18 (2012): 19.
8. R. Stubbs, G. Finlayson, and J. Blundell, "Appetite: Psychobiological and Behavioral Aspects," (2023).
9. J. Blundell, G. Finlayson, M. Axelsen, et al., "Effects of Once-Weekly Semaglutide on Appetite, Energy Intake, Control of Eating, Food Preference and Body Weight in Subjects With Obesity," *Diabetes, Obesity & Metabolism* 19, no. 9 (2017): 1242–1251, <https://doi.org/10.1111/dom.12932>.
10. J. S. Tronieri, T. A. Wadden, O. Walsh, et al., "Effects of Liraglutide on Appetite, Food Preoccupation, and Food Liking: Results of a Randomized Controlled Trial," *International Journal of Obesity* 44, no. 2 (2020): 353–361, <https://doi.org/10.1038/s41366-019-0348-6>.
11. M. Friedrichsen, A. Breitschaft, S. Tadayon, A. Wizer, and D. Skovgaard, "The Effect of Semaglutide 2.4 mg Once Weekly on Energy Intake, Appetite, Control of Eating, and Gastric Emptying in Adults With Obesity," *Diabetes, Obesity & Metabolism* 23, no. 3 (2021): 754–762, <https://doi.org/10.1111/dom.14280>.
12. M. Aldawsari, F. A. Almadani, N. Almuhammadi, S. Algabsani, Y. Alamro, and M. Aldhwayan, "The Efficacy of GLP-1 Analogues on Appetite Parameters, Gastric Emptying, Food Preference and Taste Among Adults With Obesity: Systematic Review of Randomized Controlled Trials," *Diabetes, Metabolic Syndrome and Obesity* 16 (2023): 575–595.
13. C. Gibbons, M. Hopkins, K. Beaulieu, P. Oustric, and J. E. Blundell, "Issues in Measuring and Interpreting Human Appetite (Satiety/Satiation) and Its Contribution to Obesity," *Current Obesity Reports* 8, no. 2 (2019): 77–87, <https://doi.org/10.1007/s13679-019-00340-6>.
14. L. Cifuentes and A. Acosta, "Homeostatic Regulation of Food Intake," *Clinics and Research in Hepatology and Gastroenterology* 46, no. 2 (2022): 101794, <https://doi.org/10.1016/j.clinre.2021.101794>.
15. I. Morales and K. C. Berridge, "'Liking' and 'Wanting' in Eating and Food Reward: Brain Mechanisms and Clinical Implications," *Physiology & Behavior* 227 (2020): 113152.
16. W. Sun and H. Kober, "Regulating Food Craving: From Mechanisms to Interventions," *Physiology & Behavior* 222 (2020): 112878.
17. M. L. Pelchat, "Of Human Bondage: Food Craving, Obsession, Compulsion, and Addiction," *Physiology & Behavior* 76, no. 3 (2002): 347–352.
18. A. J. Hill, "The Psychology of Food Craving*: Symposium on 'Molecular Mechanisms and Psychology of Food Intake'," *Proceedings of the Nutrition Society* 66, no. 2 (2007): 277–285.
19. L. L. Birch, "Development of Food Preferences," *Annual Review of Nutrition* 19, no. 1 (1999): 41–62.
20. A. K. Ventura and J. Worobey, "Early Influences on the Development of Food Preferences," *Current Biology* 23, no. 9 (2013): R401–R408.
21. C. Dakin, G. Finlayson, and R. J. Stubbs, "Exploring the Underlying Psychological Constructs of Self-Report Eating Behavior Measurements: Toward a Comprehensive Framework," *Psychological Review* 132 (2024): 1241–1265.
22. M. K. Klausen, M. Thomsen, G. Wortwein, and A. Fink-Jensen, "The Role of Glucagon-Like Peptide 1 (GLP-1) in Addictive Disorders," *British Journal of Pharmacology* 179, no. 4 (2022): 625–641.
23. D. Arillotta, G. Floresta, A. Guirguis, et al., "GLP-1 Receptor Agonists and Related Mental Health Issues: Insights From a Range of Social Media Platforms Using a Mixed-Methods Approach," *Brain Sciences* 13, no. 11 (2023): 1503.
24. 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, no. 11 (2021): 989–1002.
25. D. Weghuber, T. Barrett, M. Barrientos-Pérez, et al., "Once-Weekly Semaglutide in Adolescents With Obesity," *New England Journal of Medicine* 387, no. 24 (2022): 2245–2257.
26. W. Garvey, J. Frias, A. Jastreboff, et al., "Tirzepatide Once Weekly for the Treatment of Obesity in People With Type 2 Diabetes (SURMOUNT-2): A Double-Blind, Randomised, Multicentre, Placebo-Controlled, Phase 3 Trial," *Lancet* 402, no. 10402 (2023): 613–626.
27. J. McGowan, M. Sampson, D. M. Salzwedel, E. Cogo, V. Foerster, and C. Lefebvre, "PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement," *Journal of Clinical Epidemiology* 75 (2016): 40–46.
28. M. J. Page, J. E. McKenzie, P. M. Bossuyt, et al., "The PRISMA 2020 Statement: An Updated Guideline for Reporting Systematic Reviews," *BMJ* 372 (2020): n71.
29. A. Acosta, M. Camilleri, D. Burton, et al., "Exenatide in Obesity With Accelerated Gastric Emptying: A Randomized, Pharmacodynamics Study," *Physiological Reports* 3, no. 11 (2015): e12610, <https://doi.org/10.14814/phy2.12610>.
30. W. Al-Najim, N. Kapoor, A. Mangan, et al., "The Use of Direct Measures of Behaviour to Predict Weight Loss in Patients With Obesity," *Irish Journal of Medical Science* 188, no. Supplement 9 (2019): S210. 43rd Annual Meeting of the Irish Endocrine Society. Galway Ireland., <https://doi.org/10.1007/s11845-019-02073-w>.
31. A. Basolo, J. Burkholder, K. Osgood, et al., "Exenatide Has a Pronounced Effect on Energy Intake but Not Energy Expenditure in Non-Diabetic Subjects With Obesity: A Randomized, Double-Blind, Placebo-Controlled Trial," *Metabolism, Clinical and Experimental* 85 (2018): 116–125, <https://doi.org/10.1016/j.metabol.2018.03.017>.
32. C. K. Martin, O. T. Carmichael, S. Carnell, et al., "Tirzepatide on Ingestive Behavior in Adults With Overweight or Obesity: A Randomized 6-Week Phase 1 Trial," *Nature Medicine* 31, no. 9 (2025): 3141–3150, <https://doi.org/10.1038/s41591-025-03774-9>.
33. F. Orban, P. Kanehl, M. Stoll, et al., "Inferring Dietary Patterns in People With Obesity Participating in a Remote Weight Management Programme With or Without Adjunctive GLP-1RA Pharmacotherapy," *Diabetes Technology & Therapeutics* 27, no. Supplement 2 (2025): e293. 18th International Conference on Advanced Technologies and Treatments for Diabetes, ATTD 2025. Amsterdam Netherlands, <https://doi.org/10.1089/dia.2024.78502.abstracts>.
34. A. R. Saxena, A. Banerjee, K. D. Corbin, S. A. Parsons, and S. R. Smith, "Energy Intake as a Short-Term Biomarker for Weight Loss in Adults With Obesity Receiving Liraglutide: A Randomized Trial," *Obesity Science and Practice* 7, no. 3 (2021): 281–290, <https://doi.org/10.1002/osp4.486>.

35. D. Maselli, J. Atieh, M. M. Clark, et al., "Effects of Liraglutide on Gastrointestinal Functions and Weight in Obesity: A Randomized Clinical and Pharmacogenomic Trial," *Obesity* 30, no. 8 (2022): 1608–1620, <https://doi.org/10.1002/oby.23481>.
36. J. Van Can, B. Sloth, C. B. Jensen, A. Flint, E. E. Blaak, and W. H. M. Saris, "Effects of the Once-Daily GLP-1 Analog Liraglutide on Gastric Emptying, Glycemic Parameters, Appetite and Energy Metabolism in Obese, Non-Diabetic Adults," *International Journal of Obesity* 38, no. 6 (2014): 784–793, <https://doi.org/10.1038/ijo.2013.162>.
37. Cochrane, "Data Extraction Forms," accessed 21/03/2022, <https://dplp.cochrane.org/data-extraction-forms>.
38. C. A. Dakin, C. Duarte, K. Beaulieu, et al., "Examining the Structure of Visual Analogue Scales to Capture Motivation to Eat in Fasting and Post-Meal Conditions," *Appetite* (2026): 108457.
39. R: A Language and Environment for Statistical Computing. Version 4.5.1, (2021), <https://www.R-project.org/>.
40. M. Harrer, P. Cuijpers, T. Furukawa, and D. Ebert, "Companion R Package for the Guide 'Doing Meta-Analysis in R,'" (2019), <http://dme-tar.protectlab.org/>.
41. D. Lüdtke, "esc: Effect Size Computation for Meta Analysis (Version 0 (Version 0.5.1)," (2019), <https://doi.org/10.5281/zenodo.1249218> <https://CRAN.R-project.org/package=esc>.
42. H. Wickham, M. Averick, J. Bryan, et al., "Welcome to the Tidyverse," *Journal of Open Source Software* 4, no. 43 (2019): 1686.
43. S. Balduzzi, G. Rücker, and G. Schwarzer, "How to Perform a Meta-Analysis With R: A Practical Tutorial," *Evidence-Based Mental Health* 153 (2019): 153–160, <https://doi.org/10.1136/ebmental-2019-300117>.
44. W. Viechtbauer, "Conducting Meta-Analyses in R With the Metafor Package," *Journal of Statistical Software* 36, no. 3 (2010): 1–48.
45. Estimating the Sample Mean and Standard Deviation From Commonly Reported Quantiles in Meta-Analysis, Version 1.0.1. (2023), <https://github.com/stmcg/estmeansd>.
46. J. Chandler, M. Cumpston, T. Li, M. J. Page, and V. Welch, *Cochrane Handbook for Systematic Reviews of Interventions*, vol. 4 (Wiley, 2019) (1002):14651858.
47. G. Knapp and J. Hartung, "Improved Tests for a Random Effects Meta-Regression With a Single Covariate," *Statistics in Medicine* 22, no. 17 (2003): 2693–2710.
48. J. IntHout, J. Ioannidis, and G. F. Borm, "The Hartung-Knapp-Sidik-Jonkman Method for Random Effects Meta-Analysis Is Straightforward and Considerably Outperforms the Standard DerSimonian-Laird Method," *BMC Medical Research Methodology* 14, no. 1 (2014).
49. J. A. Sterne, J. Savović, M. J. Page, et al., "RoB 2: A Revised Tool for Assessing Risk of Bias in Randomised Trials," *BMJ* 366 (2019): 14898.
50. J. A. Sterne, M. A. Hernán, B. C. Reeves, et al., "ROBINS-I: A Tool for Assessing Risk of Bias in Non-Randomised Studies of Interventions," *BMJ* 355 (2016): i4919.
51. M. Cardel, G. D. Foster, L. Heinberg, K. Richardson, and A. M. Lee, "Improvements in Dietary Quality and Health Behaviors in Telemedicine Patients Taking GLP-1's Within a GLP-1 Specific Behavioral Program," *Current Developments in Nutrition* 9 (2025): 107206, <https://doi.org/10.1016/j.cdnut.2025.107206>.
52. E. Ekinici, D. M. Bushnell, C. W. Le Roux, et al., "Treatment With Dual Agonist Improves Eating Behaviour in People Living With Overweight/Obesity," *Obesity Research & Clinical Practice* 18, no. 5 Supplement 1 (2024): S9–S10, <https://doi.org/10.1016/j.orcp.2024.09.022>.
53. G. Guyatt, T. Agoritsas, R. Brignardello-Petersen, et al., "Core GRADE 1: Overview of the Core GRADE Approach," *BMJ* 389 (2025): 389.
54. E. Ravussin, G. Sanchez-Delgado, C. K. Martin, et al., "Tirzepatide Did Not Impact Metabolic Adaptation in People With Obesity, but Increased Fat Oxidation," *Cell Metabolism* 37, no. 5 (2025): 1060–1074.e4, <https://doi.org/10.1016/j.cmet.2025.03.011>.
55. M. S. Welling, C. J. de Groot, M. Mohseni, et al., "Treatment With Liraglutide or Naltrexone-Bupropion in Patients With Genetic Obesity: A Real-World Study," *EClinicalMedicine* 74 (2024): 102709, <https://doi.org/10.1016/j.eclinm.2024.102709>.
56. N. A. King, P. P. Caudwell, M. Hopkins, J. R. Stubbs, E. Naslund, and J. E. Blundell, "Dual-Process Action of Exercise on Appetite Control: Increase in Orexigenic Drive but Improvement in Meal-Induced Satiety," *American Journal of Clinical Nutrition* 90, no. 4 (2009): 921–927, <https://doi.org/10.3945/ajcn.2009.27706>.
57. S. B. K. Jensen, C. Janus, J. R. Lundgren, et al., "Exploratory Analysis of Eating- and Physical Activity-Related Outcomes From a Randomized Controlled Trial for Weight Loss Maintenance With Exercise and Liraglutide Single or Combination Treatment," *Nature Communications* 13, no. 1 (2022): 4770, <https://doi.org/10.1038/s41467-022-32307-y>.
58. A. A. Mosikian, T. I. Golikova, M. V. Martjanova, and A. Y. Babenko, "Prediction Scale of Response to Liraglutide Therapy as the Method for Increase of Treatment Efficacy in Type 2 Diabetes," *Future Science OA* 8, no. 3 (2022): FSO779, <https://doi.org/10.2144/fsoa-2021-0070>.
59. H. J. Silver, D. Olson, D. Mayfield, et al., "Effect of the Glucagon-Like Peptide-1 Receptor Agonist Liraglutide, Compared to Caloric Restriction, on Appetite, Dietary Intake, Body Fat Distribution and Cardiometabolic Biomarkers: A Randomized Trial in Adults With Obesity and Prediabetes," *Diabetes, Obesity & Metabolism* 25, no. 8 (2023): 2340–2350, <https://doi.org/10.1111/dom.15113>.
60. K. M. Richardson, S. M. Schembre, M. R. Jospe, A. Widmer, and H. J. Silver, "The Influence of the Glucagon-Like Peptide-1 Receptor Agonist, Liraglutide, on Dietary Patterns and Nutrient Intakes in Patients With Obesity and Prediabetes: A Secondary Analysis of a Randomized Controlled Trial," *Diabetes, Obesity & Metabolism* 27, no. 7 (2025): 3725–3735, <https://doi.org/10.1111/dom.16395>.
61. M. B. N. Gabe, A. Breitschaft, F. K. Knop, et al., "Effect of Oral Semaglutide on Energy Intake, Appetite, Control of Eating and Gastric Emptying in Adults Living With Obesity: A Randomized Controlled Trial," *Diabetes, Obesity & Metabolism* 26, no. 10 (2024): 4480–4489, <https://doi.org/10.1111/dom.15802>.
62. S. F. Kennedy, A. Knights, E. Ravussin, et al., "Impact of Tirzepatide Treatment on Participant-Reported Food Craving and Food Preference: Secondary Analyses of a Phase 1 Randomised Controlled Trial in People With Obesity With Dietary Restriction," *Diabetes, Obesity & Metabolism* 27, no. 11 (2025): 6784–6789, <https://doi.org/10.1111/dom.70063>.
63. S. A. Robert, A. G. Rohana, S. A. Shah, K. Chinna, W. N. Wan Mohamud, and N. A. Kamaruddin, "Improvement in Binge Eating in Non-Diabetic Obese Individuals After 3 Months of Treatment With Liraglutide—A Pilot Study," *Obesity Research & Clinical Practice* 9, no. 3 (2015): 301–304, <https://doi.org/10.1016/j.orcp.2015.03.005>.
64. J. Nicolau, A. Pujol, M. Tamayo, et al., "Short Term Effects of Semaglutide Among Patients With Obesity and Food Addiction," *Obesity Facts* 17, no. Supplement 1 (2024): 430–431, <https://doi.org/10.1159/000538577>.
65. T. Müller, C. Clemmensen, B. Finan, R. DiMarchi, and M. Tschöp, "Anti-Obesity Therapy: From Rainbow Pills to Polyagonists," *Pharmacological Reviews* 70, no. 4 (2018): 712–746.
66. T. D. Müller, M. Blüher, M. H. Tschöp, and R. D. DiMarchi, "Anti-Obesity Drug Discovery: Advances and Challenges," *Nature Reviews Drug Discovery* 21, no. 3 (2022): 201–223.
67. L. Collins and R. A. Costello, "Glucagon-Like Peptide-1 Receptor Agonists," StatPearls [Internet]. StatPearls Publishing, (2024).

68. J. Ard, A. Fitch, S. Fruh, and L. Herman, "Weight Loss and Maintenance Related to the Mechanism of Action of Glucagon-Like Peptide 1 Receptor Agonists," *Advances in Therapy* 38, no. 6 (2021): 2821–2839.
69. D. J. Drucker, "GLP-1-Based Therapies for Diabetes, Obesity and Beyond," *Nature Reviews. Drug Discovery* 24 (2025): 1–20.
70. N. V. Dhurandhar, D. Schoeller, A. W. Brown, et al., "Energy Balance Measurement: When Something Is Not Better Than Nothing," *International Journal of Obesity* 39, no. 7 (2015): 1109–1113.
71. S. S. Jonnalagadda, D. C. Mitchell, H. Smiciklas-Wright, et al., "Accuracy of Energy Intake Data Estimated by a Multipass, 24-Hour Dietary Recall Technique," *Journal of the American Dietetic Association* 100, no. 3 (2000): 303–311, [https://doi.org/10.1016/S0002-8223\(00\)00095-X](https://doi.org/10.1016/S0002-8223(00)00095-X).
72. C. A. Blanton, A. J. Moshfegh, D. J. Baer, and M. J. Kretsch, "The USDA Automated Multiple-Pass Method Accurately Estimates Group Total Energy and Nutrient Intake," *Journal of Nutrition* 136, no. 10 (2006): 2594–2599, <https://doi.org/10.1093/jn/136.10.2594>.
73. T. L. Burrows, Y. Y. Ho, M. E. Rollo, and C. E. Collins, "Validity of Dietary Assessment Methods When Compared to the Method of Doubly Labeled Water: A Systematic Review in Adults," *Frontiers in Endocrinology* 10 (2019): 850.
74. R. S. Gibson, U. R. Charrondiere, and W. Bell, "Measurement Errors in Dietary Assessment Using Self-Reported 24-Hour Recalls in Low-Income Countries and Strategies for Their Prevention," *Advances in Nutrition* 8, no. 6 (2017): 980–991.
75. N. T. Gregersen, A. Flint, C. Bitz, J. E. Blundell, A. Raben, and A. Astrup, "Reproducibility and Power of ad Libitum Energy Intake Assessed by Repeated Single Meals," *American Journal of Clinical Nutrition* 87, no. 5 (2008): 1277–1281.
76. S. Christensen, K. Robinson, S. Thomas, and D. R. Williams, "Dietary Intake by Patients Taking GLP-1 and Dual GIP/GLP-1 Receptor Agonists: A Narrative Review and Discussion of Research Needs," *Obesity Pillars* 11 (2024): 100121.
77. M. Randle, A. L. Ahern, E. Boyland, et al., "A Systematic Review of Ecological Momentary Assessment Studies of Appetite and Affect in the Experience of Temptations and Lapses During Weight Loss Dieting," *Obesity Reviews* 24, no. 9 (2023): e13596.
78. S. Åberg, M. Palmnäs-Bédard, T. Karlsson, T. Hjorth, K. N. Iversen, and R. Landberg, "Evaluation of Subjective Appetite Assessment Under Free-Living vs. Controlled Conditions: A Randomized Crossover Trial Comparing Whole-Grain Rye and Refined Wheat Diets (VASA-Home)," *Nutrients* 15, no. 11 (2023): 2456.
79. S. Shiffman, A. A. Stone, and M. R. Hufford, "Ecological Momentary Assessment," *Annual Review of Clinical Psychology* 4 (2008): 1–32.
80. E. Hwang, B. Portillo, and K. W. Williams, "Glucagon-Like Peptide 1 (GLP-1) Action on Hypothalamic Feeding Circuits," *Endocrinology* 166, no. 10 (2025): bqaf125.
81. A. Kabahizi, B. Wallace, L. Lieu, et al., "Glucagon-Like Peptide-1 (GLP-1) Signalling in the Brain: From Neural Circuits and Metabolism to Therapeutics," *British Journal of Pharmacology* 179, no. 4 (2022): 600–624.
82. C. E. Geisler, L. Décarie-Spain, M. K. Loh, et al., "Amylin Modulates a Ventral Tegmental Area-To-Medial Prefrontal Cortex Circuit to Suppress Food Intake and Impulsive Food-Directed Behavior," *Biological Psychiatry* 95, no. 10 (2024): 938–950.
83. R. V. Bhimani, L. Rzepecki, J. Park, and E. G. Mietlicki-Baase, "Ventral Tegmental Area Amylin Receptor Activation Differentially Modulates Mesolimbic Dopamine Signaling in Response to Fat Versus Sugar," *eNeuro* 11, no. 6 (2024): ENEURO. 0133-24.2024.
84. S. Badulescu, A. Tabassum, G. H. Le, et al., "Glucagon-Like Peptide 1 Agonist and Effects on Reward Behaviour: A Systematic Review," *Physiology & Behavior* 283 (2024): 114622.
85. E. Plenn, D. Amin, J. Henry, G. Leavitt, J. Walker, and T. Soleymani, "A Qualitative Analysis of Patient Experiences Using Semaglutide 2.4 mg for Weight Loss," *Obesity Science and Practice* 11, no. 4 (2025): e70085.
86. C. Gibbons, J. Blundell, S. T. Hoff, K. Dahl, R. Bauer, and T. Bækdal, "Effects of Oral Semaglutide on Energy Intake, Food Preference, Appetite, Control of Eating and Body Weight in Subjects With Type 2 Diabetes," *Diabetes, Obesity and Metabolism* 23, no. 2 (2021): 581–588, <https://doi.org/10.1111/dom.14255>.
87. D. Mozaffarian, M. Agarwal, M. Agarwal, et al., "Nutritional Priorities to Support GLP-1 Therapy for Obesity: A Joint Advisory From the American College of Lifestyle Medicine, the American Society for Nutrition, the Obesity Medicine Association, and The Obesity Society," *Obesity Pillars* 15 (2025): 100181.
88. L. Liu, J. Chen, L. Wang, C. Chen, and L. Chen, "Association Between Different GLP-1 Receptor Agonists and Gastrointestinal Adverse Reactions: A Real-World Disproportionality Study Based on FDA Adverse Event Reporting System Database," *Frontiers in Endocrinology* 13 (2022): 1043789.
89. M. Lean, R. Carraro, N. Finer, et al., "Tolerability of Nausea and Vomiting and Associations With Weight Loss in a Randomized Trial of Liraglutide in Obese, Non-Diabetic Adults," *International Journal of Obesity* 38, no. 5 (2014): 689–697.
90. R. J. Jalleh, C. K. Rayner, T. Hausken, K. L. Jones, M. Camilleri, and M. Horowitz, "Gastrointestinal Effects of GLP-1 Receptor Agonists: Mechanisms, Management, and Future Directions," *Lancet Gastroenterology & Hepatology* 9, no. 10 (2024): 957–964.
91. T. D. Filippatos, T. V. Panagiotopoulou, and M. S. Elisaf, "Adverse Effects of GLP-1 Receptor Agonists," *Review of Diabetic Studies* 11, no. 3 (2015): 202–230.
92. J. J. Gorgojo-Martínez, P. Mezquita-Raya, J. Carretero-Gómez, et al., "Clinical Recommendations to Manage Gastrointestinal Adverse Events in Patients Treated With GLP-1 Receptor Agonists: A Multidisciplinary Expert Consensus," *Journal of Clinical Medicine* 12, no. 1 (2022): 145.
93. J. M. Wood, K. Chapman, and J. Eilers, "Tools for Assessing Nausea, Vomiting, and Retching: A Literature Review," *Cancer Nursing* 34, no. 1 (2011): E14–E24.
94. S. B. K. Jensen, M. B. Blond, R. M. Sandsdal, et al., "Healthy Weight Loss Maintenance With Exercise, GLP-1 Receptor Agonist, or Both Combined Followed by One Year Without Treatment: A Post-Treatment Analysis of a Randomised Placebo-Controlled Trial," *EClinicalMedicine* 69 (2024): 1–69.
95. S. West, J. Scragg, P. Aveyard, et al., "Weight Regain After Cessation of Medication for Weight Management: Systematic Review and Meta-Analysis," *BMJ* 392 (2026): 392.
96. I. Roberts and K. Ker, "How Systematic Reviews Cause Research Waste," (2015).
97. S. V. Katikireddi, M. Egan, and M. Petticrew, "How Do Systematic Reviews Incorporate Risk of Bias Assessments Into the Synthesis of Evidence? A Methodological Study," *Journal of Epidemiology and Community Health* 69, no. 2 (2015): 189–195.
98. D. Zeraatkar, A. Bhasin, R. E. Morassut, et al., "Characteristics and Quality of Systematic Reviews and Meta-Analyses of Observational Nutritional Epidemiology: A Cross-Sectional Study," *American Journal of Clinical Nutrition* 113, no. 6 (2021): 1578–1592.

Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Table S1:** Search terms used for Ovid, MEDLINE, PsychINFO, and EMBASE. **Table S2:** Search terms used for Web of Science. **Table S3:** Characteristics of included studies. **Table S4:**

Summary of included study outcomes. **Table S5:** Reported nausea and attrition for parallel trials. **Table S6:** Reported side effects, adverse effects and attrition for energy intake studies. **Table S7:** Reported side effects, adverse effects and attrition for appetite studies. **Figure S1:** Risk of bias assessment for randomized crossover trials. **Figure S2:** Risk of bias assessment for randomized parallel trials. **Figure S3:** Risk of bias assessment for nonrandomized trials. **Figure S4:** Funnel plot for studies measuring energy intake. **Figure S5:** Funnel plot for studies measuring appetite.