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Trajectory of the body weight after drug discontinuation in the treatment of anti-obesity medications

Han Wu[1†], Wenjia Yang[1†], Tong Guo[1], Xiaoling Cai[1*] and Linong Ji[1*]

Abstract

Background Globally, obesity has emerged as a significant public health concern, imposing detrimental impacts on human health. The purpose of our study was to explore the long-term effects of anti-obesity medications (AOMs) on body weight and to draw the trajectory of weight change after discontinuation of AOMs.

Methods PubMed, Medline, Embase, the Cochrane Center Register of Controlled Trials for Studies, and Clinicaltrials.gov were searched from the inception to March 2024. Randomized controlled trials of AOMs conducted in population for at least 4 weeks and followed for 4 or more weeks after discontinuation were included. Weight change during treatment and after drug discontinuation was also reported. Random-effect model and meta-regression analysis were accordingly used.

Results At week 4 after discontinuation, compared with the control group, AOM treatment still had weight loss effect (WMD = −0.32 kg, 95% CI −3.60–2.97, $P = 0.85$, $I^2 = 83\%$). At 8 weeks after drug discontinuation, AOMs were associated with significant weight regain compared with the control group (WMD = 1.50 kg, 95% CI 1.32–1.68, $P < 0.0001$, $I^2 = 0.0\%$). The weight regain trend remained at 12 and 20 weeks (WMD = 1.76 kg, 95% CI 1.29–2.24, $P < 0.0001$, $I^2 = 72.0\%$; WMD = 2.50 kg, 95% CI 2.27–2.73, $P < 0.0001$, $I^2 = 0.0\%$). Among the different subgroups of AOMs, significant weight regain after 12 weeks of drug discontinuation was observed only in studies with glucagon-like peptide 1 receptor agonist (GLP-1 RA) related drugs. In addition, studies in which weight loss was greater during treatment than in the control group and studies in which lifestyle interventions were continued observed significant weight gain after drug discontinuation.

Conclusion Significant weight regain occurred 8 weeks after discontinuation of AOMs and was sustained through 20 weeks. Different weight regain was observed in subjects with different characteristics. Studies with longer follow-up duration are required to further investigate the potential factors associated with weight change after discontinuation of treatment.

Keywords Weight change trajectory, Treatment discontinuation, Anti-obesity medication, Meta-analysis

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Background

Obesity is an important issue of human health in the world today. By 2020, an estimated 2.2 billion adults worldwide were suffering from overweight and obesity, and it is predicted that this number will increase to 3.3 billion by 2035 [1]. Meanwhile, it was demonstrated that obesity was significantly associated with the increased risks of numerous complications, including cardiovascular disorders, diabetes mellitus, and certain cancers [2–5].

As recommended by the guidelines, lifestyle/behavioral therapy, pharmacotherapy, and bariatric surgery were of importance in the management of weight control [6], in which anti-obesity medications (AOMs) have been proved to be beneficial to obesity-related co-morbidity management [7]. There are currently 6 medications (orlistat, naltrexone-bupropion, liraglutide, semaglutide, tirzepatide, and phentermine-topiramate) that have been approved for the treatment of obesity in adults [8, 9].

It was shown that the long-term use of these AOMs in adults contributed to significant weight loss in many studies [10–15]. However, it was reported that there would be weight regain after discontinuation of AOMs. A European 2-year multicenter trial observed significant weight regain in patients who discontinued orlistat and switched to placebo compared with those who continued [16]. In a randomized controlled trial (RCT) evaluating the weight change using semaglutide, it was also found that after discontinuation of semaglutide, the patients gained weight significantly as well as a significant increase in blood pressure [17], which was a reminder that weight regain may have some adverse effects. Meanwhile, there were studies showing that weight regain can cause some metabolic indicators to revert back such as plasma lipids, blood pressure, fasting glucose, and insulin concentrations [18, 19].

However, current systematic conclusions about weight regain mostly came from the studies of bariatric surgery or behavioral interventions. So far, the long-term change of weight after discontinuation of AOMs is still lacking of systematic evaluation. Therefore, it is now timely to conduct a systematic review and meta-analysis to explore the long-term effects of AOMs on body weight after treatment discontinuation, and provide intuitive evidence by means of weight change trajectory.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement was used to conduct this meta-analysis [20]. The study protocol is available in the International Prospective Register of Systematic Reviews (registration No. CRD42023385404).

Data sources and search strategy

Systematic searches were conducted in PubMed, Medline, Embase, the Cochrane Center Register of Controlled Trials for Studies, and Clinicaltrials.gov last updated on March 8, 2024. Two investigators (HW and TG) independently searched for clinical trials aiming at weight management treatment. The search strategy details are provided in Additional file 1: Table S1.

Study selection

The criteria for including studies in this meta-analysis were as follows: (1) (i) randomized controlled trials (RCTs) comparing different AOMs with placebo, including glucagon-like peptide 1 receptor agonist (GLP-1 RA), dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 RAs, GLP-1 and glucagon receptor (GCGR) dual-agonist, orlistat, lorcaserin, naltrexone-bupropion, phentermine-topiramate, and bimagrumab; or (ii) RCTs comparing different AOMs with active drug control; (2) studies with treatment duration ≥ 4 weeks and with follow-up duration ≥ 4 weeks; (3) RCTs reporting both the body weight changes from baseline in the process of treatment and the body weight changes after treatment discontinuation in the follow-up study.

The criteria for exclusion are as follows: (1) studies that focus on non-adult individuals or pregnant adults; (2) studies with a duration of less than 24 weeks; (3) studies that did not report the change in weight after treatment discontinuation.

Outcome measures

In this meta-analysis, the primary outcome was the change in body weight at the specified cutoff point after treatment discontinuation as compared to the control group The secondary outcome was the change in BMI at the specified cutoff point after treatment discontinuation as compared to the control group. In the sensitivity analysis, we evaluate associations with weight change of the following subcategories: (1) different control groups, including placebo control and active control, (2) different baseline BMI, including BMI < 35 and BMI ≥ 35, (3) different indications, including obesity alone and obesity with type 2 diabetes, (4) GLP-1 related and non GLP-1 related treatments, (5) significant weight loss and not significant weight loss when AOMs compared to the controls, (6) different lifestyle intervention.

Data extraction and quality assessments

We removed the duplicates and screened the remaining articles at the title and abstract level according to the pre-determined inclusion and exclusion criteria for possible inclusions. The process of search and selection

was performed by two independent blinded investigators (HW and GT). If either investigator considered a study potentially eligible, we further obtained and screened the full text. We invited a third investigator (WY) to join the discussion and resolved discrepancies by consensus (Additional file 2: Fig. S1).

Two investigators (HW and TG) independently performed the data extraction from each publication using a standardized form: publication data, baseline characteristics of the study population (sample size, sex, age, body mass index (BMI), body weight, abdominal circumference, waist-to-hip ratio, visceral adipose tissue (measured by computed tomography, magnetic resonance imaging, or dual-emission X-ray absorptiometry)), duration of follow-up, weight change during treatment and after treatment discontinuation, description of the weight management group and control group. Disagreements or discrepancies were resolved by discussion between the two investigators and a third investigator (WY).

Two investigators (HW and TG) independently assessed the quality of each included study using Cochrane risk of bias instrument [21]. Each study is judged on seven items: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, selective outcome reporting, and other sources of bias.

Data synthesis and analysis

In this meta-analysis, weighted mean differences (WMDs) and 95% confidence intervals (CIs) were calculated for continuous measures. We used mean changes from the time of drug discontinuation to the specified cutoff point of follow-up (week 4, week 8, week 12, week 20, week 26, and week 52) and standard deviations (SDs) extracted from published data when reported. When SDs were missing, we estimated them from standard errors or confidence intervals. Meta-regression analysis was performed to evaluate the association between regain in body weight and participant characteristics. A P value < 0.05 was considered statistically significant.

Between-study heterogeneity was assessed using the Q test and I^2 statistic, with significance set at $P < 0.05$; heterogeneity was considered low, moderate, substantial, or considerable for estimated I^2 value of 0–40%, 30–60%, 50–90%, and 75–100%, respectively. The random-effect model was used in this meta-analysis. All analyses were conducted with Review Manager, version 5.4 (Nordic Cochrane Centre, Copenhagen, Denmark). Meta-regression analyses were conducted with STATA statistical software package, version 18.1 (Stata Corp, College Station, TX, USA).

Results

A total of 11 studies were included in this meta-analysis, including 6 studies on GLP-1 RA, 1 study on GLP-1 and GIP dual receptor agonists, 1 study on orlistat, 2 studies on phentermine-topiramate, and 1 study on naltrexone-bupropion (Additional file 1: Table S2) [22–32]. There were 8 placebo controls and 3 active drug controls studies with 1573 participants in the treatment group and 893 in the control group. The baseline characteristics and risk of bias evaluation for the included studies were summarized in Additional file 1: Tables S2 and S3. The overall risk of bias was low.

Trajectory of weight change after discontinuation of AOMs

Overall

Overall, compared with control groups, AOM treatment was significantly associated with greater weight regain which varied according to follow-up time point after treatment discontinuation (Fig. 1; Additional file 2: Fig. S2). At week 4, compared with control groups, AOM treatment still resulted in 0.32 kg (95% CI −3.60 to 2.97, $P = 0.85$, $I^2 = 83\%$) weight loss, while at weeks 8, 12, 20, 26, and 52, AOMs were associated with significant weight regain when compared with controls (WMD = 1.50 kg, 95% CI 1.32 to 1.68, $P < 0.0001$, $I^2 = 0.0\%$; WMD = 1.76 kg, 95% CI 1.29 to 2.24, $P < 0.0001$, $I^2 = 72.0\%$; WMD = 2.50 kg, 95% CI 2.27 to 2.73, $P < 0.0001$, $I^2 = 0.0\%$; WMD = 2.30 kg, 95% CI 0.53 to 4.07, $P = 0.01$, $I^2 = 0.0\%$; WMD = 2.47 kg, 95% CI 0.24 to 4.70, $P = 0.03$, $I^2 = 92.0\%$, respectively). Figure 2 shows the weight regain trajectory at different follow-up time points after treatment discontinuation. It can be seen from the figure that the weight had significantly regained in 8 weeks after treatment discontinuation, and showed a rising trend within 12 weeks and 20 weeks after treatment discontinuation, and then the weight regain gradually stabilized. Weight loss persisted 52 weeks after discontinuation of AOMs, as compared with baseline.

Stratified by baseline weight or BMI

Subgroup analyses were performed bounded by the weighted median of baseline weight (105.6 kg). Significant weight regain was observed in both subgroups (WMD = 1.45 kg, 95% CI 0.62 to 2.28, $P = 0.006$, $I^2 = 72\%$; WMD = 2.24 kg, 95% CI 1.94 to 2.54, $P < 0.001$, $I^2 = 0.0\%$), but no significant difference was observed between the two subgroups.

In the subgroup analyses that used a BMI cutoff of 35 kg/m^2, significant weight regain was only observed in the subgroup with lower BMI when compared to the control group (WMD = 1.66 kg, 95% CI 0.87 to 2.44, $P < 0.001$, $I^2 = 71\%$). Contrary to common knowledge, patients in the subgroup with a higher BMI did not show significant

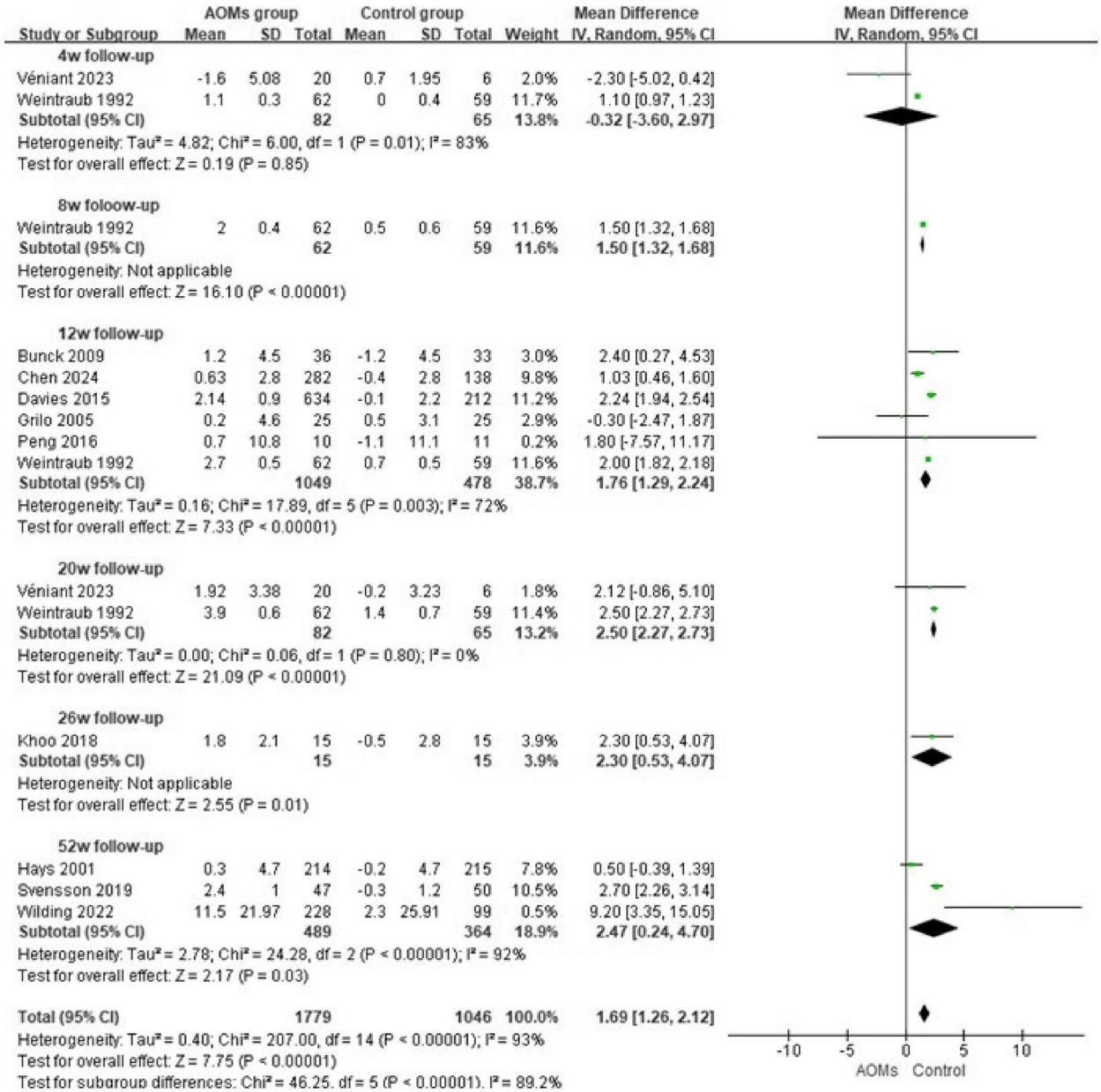

Fig. 1 Weight change at specific time point after treatment discontinuation. AOM: anti-obesity medication

weight gain (WMD = 1.21 kg, 95% CI −1.24 to 3.60, P = 0.33, I^2 = 72%) and there were no significant differences between the subgroups (P = 0.73) (Additional file 2: Fig. S3).

Stratified by placebo control or active control

Considering the RCTs including placebo and active control, we performed a subgroup analysis between them. When combined placebo controlled studies as a whole, significant weight regain was observed when compared with placebo group (WMD = 1.72 kg, 95% CI 1.20 to 2.23, P < 0.001, I^2 = 83%). The same result was obtained in the active controlled studies (WMD = 2.37 kg, 95% CI 0.30 to 4.44, P = 0.02, I^2 = 0%), while there is no statistically significant distinction observed between the two subgroups (P = 0.55) (Additional file 2: Fig. S3).

Stratified by different indications

For indication of obesity alone, AOMs resulted in 1.31 kg (95% CI 0.38 to 2.24, P = 0.006, I^2 = 73%) weight regain compared with control groups. With indication of diabetes, AOMs resulted in 2.24 kg (95% CI 1.94 to 2.54, P <

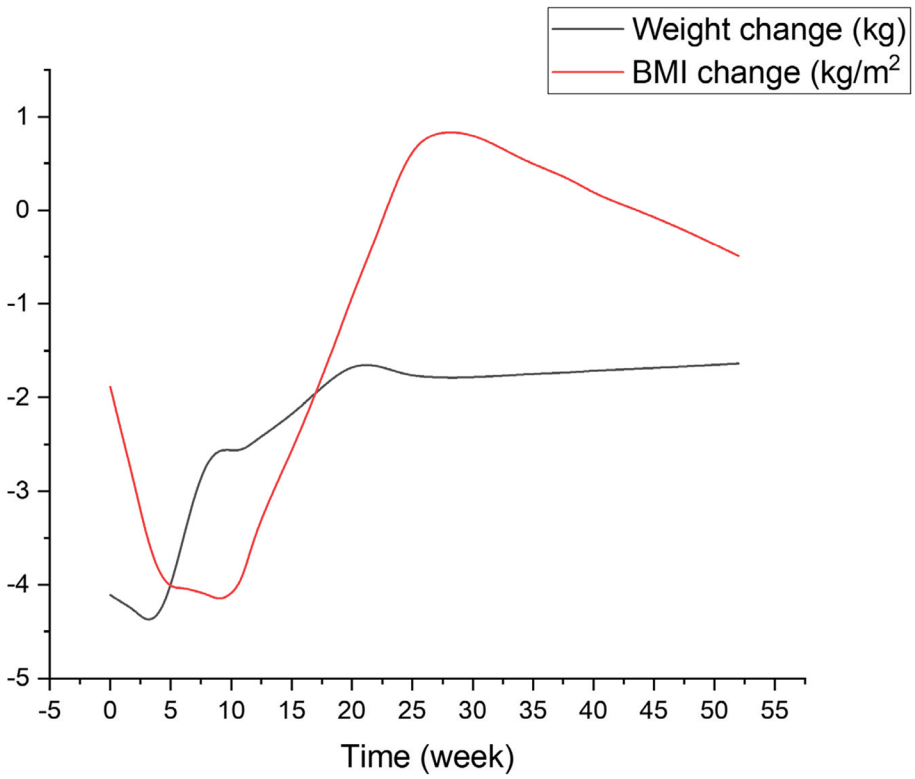

Fig. 2 Weight and BMI regain trajectory after treatment of AOM withdrawal. BMI: body mass index

0.001, I^2= 0%) weight change compared with control groups. There were no statistically significant differences observed between the two subgroups (P= 0.06) (Additional file 2: Fig. S3).

Stratified by GLP-1 related and non GLP-1 related treatments

In the included RCTs, GLP-1 related drugs (including liraglutide, semaglutide, beinaglutide, exenatide, and AMG133) showed significant weight regain compared with control group (WMD = 1.78 kg, 95% CI 0.76 to 2.80, P= 0.006, I^2= 85%). Regarding to the non GLP-1 related weight management strategies, no significant weight regain was observed (WMD = 1.23 kg, 95% CI −0.58 to 3.04, P= 0.18, I^2= 53%). There was no significant difference in weight regain between the two groups (P= 0.61) (Additional file 2: Fig. S3).

Stratified by lifestyle intervention

Continuation of lifestyle interventions after treatment discontinuation may affect the extent of weight regain. In the study, the subgroup with continuous lifestyle intervention showed significant weight regain (WMD = 1.83 kg, 95% CI 1.36 to 2.31, P< 0.001, I^2= 85%), whereas the subgroup without continuous lifestyle intervention did not (WMD = 1.1 kg, 95% CI −0.99 to 3.19, P= 0.30, I^2= 34%) (Additional file 2: Fig. S3).

Stratified by the level of weight reduction

To explore the relationship between significant weight loss during treatment and long-term weight loss maintenance, we performed subgroup analyses of whether significant weight loss was associated with weight regain. RCTs that showed significant weight loss during treatment periods compared with the control group and studies that did not show significant weight loss were divided into two subgroups. Compared to the control group, only the subgroup with significant weight loss during treatment periods demonstrated a substantial regain in weight (WMD = 1.76 kg, 95% CI 1.27 to 2.24, P< 0.001, I^2= 78%). The results suggested that at week 12 after treatment discontinuation, there was no significant difference in weight regain between significant and not significant weight loss subgroup (P= 0.99) (Additional file 2: Fig. S3).

Stratified by the rate of weight reduction

When subgroups were grouped by weighted median of the rate of weight reduction, significant weight regain was observed in both the faster and slower subgroups

compared with the control group (WMD = 1.94 kg, 95% CI 1.62 to 2.20, $P < 0.001$, $I^2 = 83\%$; WMD = 2.0 kg, 95% CI 1.83 to 2.18, $P < 0.001$, $I^2 = 0\%$, respectively). However, there were no significant differences between two groups ($P = 0.69$).

Trajectory of BMI change after discontinuation of AOMs

Regarding to BMI change, it was also different at specific follow-up time points after treatment discontinuation. BMI loss continued after treatment discontinuation of weeks 4 and 10 (WMD = − 1.77 kg/m^2, 95% CI −2.73 to −0.81, $P < 0.001$, $I^2 = 0.0\%$; WMD = − 0.21 kg/m^2, 95% CI −1.31 to 0.88, $P = 0.7$, $I^2 = 0.0\%$). At weeks 26 and 52, BMI regain was 0.70 kg/m^2 (95% CI 0.36 to 1.04, $P < 0.0001$, $I^2 = 0\%$) and 0.82 (95% CI 0.66 to 0.98, $P < 0.0001$, $I^2 = 83\%$), respectively. There was a turning point in BMI change trajectory at different follow-up time points after treatment discontinuation (Fig. 3).

Association between participant characteristics and weight change

Results of meta-regression indicated that the difference between participants including sex, age, indication, and BMI was not associated with the risk of weight regain, and the same is true of different control group. Meanwhile, the difference between treatment and follow-up duration was also not related to the weight regain and the level and rate of weight reduction did not either (Additional file 1: Table S4).

Discussion

According to this meta-analysis, AOMs resulted in significant weight loss while being used, followed by weight regain after treatment discontinuation. During the follow-up period, significant weight regain was observed from 8 to 52 weeks after treatment discontinuation (Figs. 4 and 5).

According to the trajectory of weight regain, body weight continued to decrease within 4 weeks after treatment discontinuation and then started to show a gradually increasing trend after 8 weeks. After 26 weeks of treatment discontinuation, the trajectory of weight regain leveled off, which implied that significant weight regain might happen at the first 6 months after discontinuation of AOMs. Weight regain was also found in other weight loss strategies. It was reported that patients who received gastric bypass, vertical-banded gastroplasty, or banding all regained an average of more than 5% from their lowest weight at 15 years of follow-up [33]. In terms of behavioral weight loss programs, it has been demonstrated that individuals in the behavioral intervention group experienced a more rapid weight regain compared to those in the minimal intervention group. This phenomenon could be correlated with the extent of their initial weight loss [34]. Moreover, a 10-year observational study suggested that only 25% of patients who lost weight on a low-calorie diet maintained weight loss [35]. Therefore, weight regain is common in various weight loss strategies and it is necessary to establish the long-term anti-obesity treatment in clinical practice.

According to the subgroup analysis, there was no association between the rate of the weight reduction and weight regain, with more significant weight regain observed in the slower rate subgroup. Though there were clinical studies consistent with our results [36], it has long been suggested that gradual weight loss is more beneficial for weight regain after treatment discontinuation [37]. As for the difference between our study and the previous understanding, it might be due to the fact that the weight loss strategy we focused on was AOMs, and there was no restriction on the degree of weight loss and weight regain when included. Therefore, the relationship between the rate of weight loss and the rate of weight regain remains inconclusive and a more comprehensive systematic analysis is still needed.

Furthermore, the relationship between the level weight loss during treatment and weight gain after discontinuation of treatment remains controversial. Although there was no significant difference between groups, our study observed weight regain only in the subgroup of higher level of weight loss compared with the control group. Previously, some studies have linked greater weight loss to better maintenance of weight loss, while others have linked it to more significant weight regain [38–40]. It was suspected that the latter may be driven by changes in body composition and psychology caused by the weight loss [41].

In the subgroup analysis, although no significant differences were observed among the subgroups based on different baseline weight, control groups, and indications, significant weight regain was observed in each subgroup compared with the control group, that is, the weight regain after treatment discontinuation was consistent in obese patients with different characteristics.

Baseline BMI is another indicator for obesity status. In our analysis, significant weight regain was observed only in the lower baseline BMI subgroups which did not conform to the common understanding, possibly because the enrolled patients were more severely obese and then not well differentiated by the BMI cutoff point, and the limited data in the analysis also reduced the confidence of the result. Additional data on weight change after treatment discontinuation in patients with various weight status groups including overweight or mild obesity still needed to be reported.

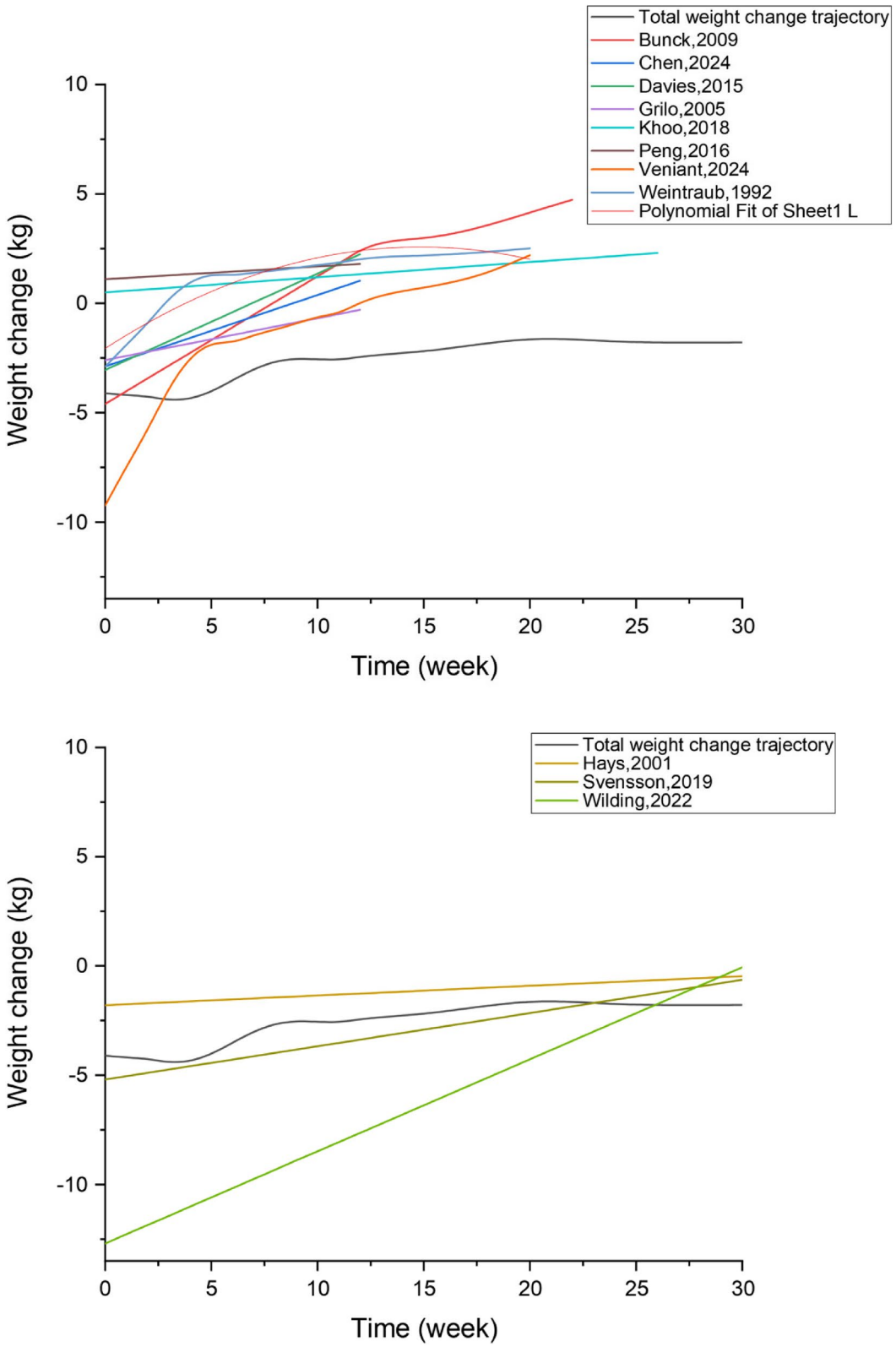

Fig. 3 Weight change trajectory of included studies after treatment of AOM withdrawal

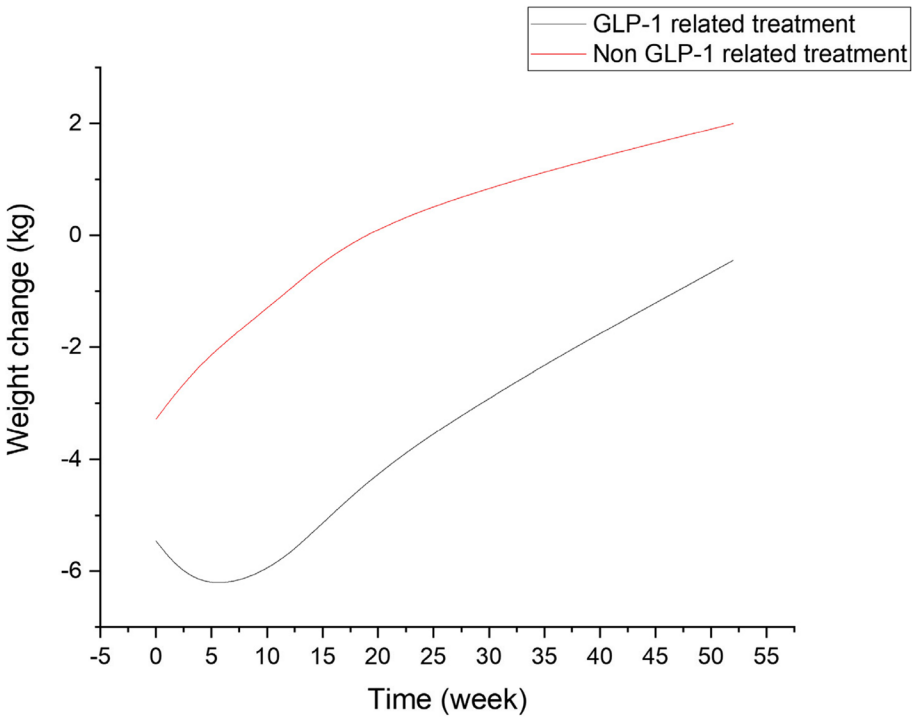

Fig. 4 Weight change in GLP-1 related and non GLP-1 related subgroup after 12 weeks of treatment discontinuation

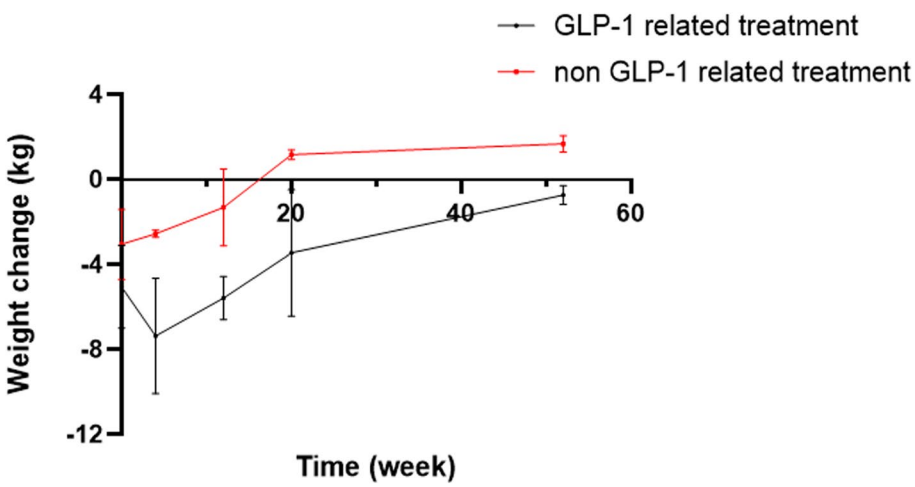

Fig. 5 GLP-1: glucagon-like peptide 1

At week 12 after discontinuation of AOMs, significant weight regain was observed in the GLP-1 related drug subgroup compared to the control group. GLP-1 receptors are abundantly expressed in the pancreas, intestine, and central nervous system. Among them, GLP-1 can increase satiation and reduce appetite by binding to receptors in the central nervous system [42]. In addition, GLP-1 causes delayed gastric emptying, which leads to weight loss [43]. At the same time, GIP exerts its weight-reducing effects by binding to its receptor—GIPR. The activation of GIPR can directly act on adipose tissue to increase energy expenditure and drive weight loss. It can also contribute to weight reduction through the central nervous system. GLP-1 and GIP receptor agonists seem to have a synergistic effect in weight reduction, although the mechanism is not yet clear [44]. In contrast,

discontinuation of GLP-1 and GIP related drugs attenuates these effects, and the reduction in GLP-1/GIP receptor agonist activity after treatment withdrawal may lead to weight regain. A study on the tirzepatide showed that after completing a 36-week induction treatment period with tirzepatide, participants who switched to a placebo almost regained half of the weight they had previously lost within a year [45], which was consistent with our research findings. Moreover, the patients included in the GLP-1 related subgroup all significantly lost weight during treatment, and therefore had a greater likelihood of weight regain.

The process of regaining weight after treatment discontinuation is called weight cycling. It has been theorized that weight cycling may be related to a variety of factors. A 10-week study with a very low energy diet shows that weight loss induces adverse gut hormonal changes that potentially affect weight regain and persist [46]. This adverse hormonal change in the gut causes an increase in hunger levels and urge to eat, which promotes weight regain. In addition, weight loss is associated with a reduction in resting energy expenditure due to changes in body composition, so-called metabolic adaptation, which has also been shown to be associated with weight regain [47]. At the same time, previous studies have proposed the physiological and behavioral factors of weight regain [48] may better complement the relationship between weight loss and weight regain. However, these results are mainly obtained from lifestyle and surgical weight loss strategies, and the mechanism of weight regain after AOM discontinuation needs to be further explored.

The effects of weight cycling on health and systemic metabolism are not thoroughly defined. There is some evidence suggesting that weight cycling has no effect on the risk of type 2 diabetes [49], and there is no conclusive evidence that previous weight cycling affects body composition or predisposition to obesity. A study compared weight-stable and weight-cycling groups and concluded that weight regain did not adversely affect body fat distribution [50]. However, a 9-year follow-up study of Finnish male smokers aged 50–69 years [51] showed that when compared with weight-stable subjects, subjects with greater weight fluctuations had a significantly increased risk of type 2 diabetes. The impact of weight cycling on obese patients has not been determined so far, so more individual level data may be more meaningful to clinical practice.

In our analysis, the subgroup with continuous lifestyle intervention showed significant weight regain, while the subgroup without the continuous lifestyle intervention did not. The results of subgroup analysis of whether the lifestyle intervention was sustained contrast with those of previous studies which have emphasized the importance of regular exercise for weight loss maintenance [52]. A meta-analysis also indicated that lifestyle interventions with frequent patient interactions sustained for a year or longer can achieve more significant weight loss after 1 year and 3 years [53]. Among several strategies for lifestyle intervention, regular exercise is conducive to the transformation of energy utilization, and the energy intake is more inclined to be consumed rather than stored, thus reducing weight regain. Furthermore, dietary interventions are recognized as a critical modality for the sustenance of weight reduction. Previous studies have emphasized that the energy deficit is a crucial factor for weight loss, characterized by the discordance between post-weight loss appetite and energy expenditure [54]. And a prolonged low-calorie diet effectively generated an energy deficit, thereby sustaining weight loss. In our analysis, there were only three studies in both subgroups, lowering the statistical power of this result. The specific pattern, intensity, and duration of lifestyle intervention in the included studies was not clear. Finally, in some included studies, the primary outcome was not aiming at the weight change after treatment withdrawal, so the information was incomplete. The above reasons may have interfered with the results of our study, which also suggested us to expand the number of included studies and further analyze the detailed intervention methods.

In the studies encompassed within our analysis, four studies provided descriptive data regarding adverse events. One of these studies revealed no significant disparity in the incidence of adverse events between AOM and control cohorts. Another study reported the absence of any participants who discontinued treatment permanently as a consequence of adverse events throughout the study's duration. The remaining two studies reported a higher prevalence of adverse events within the experimental group and instances of study withdrawal, which differed from the discontinuation requested by the researchers. Consequently, it is currently not possible to determine the correlation between adverse events experienced during the treatment period and subsequent weight regain after discontinuation. Furthermore, adverse events that emerged during the follow-up phase were not attributed to the study medication by the researchers. Whether discontinuation due to adverse events has affected the statistical analysis of weight regain still required further research for support.

Of course, this study has a number of limitations. First, due to the small number of included studies, the reported data at each follow-up time point after treatment discontinuation were limited and fewer studies were included in sensitive analyses, reducing the power of the test. Similarly, due to the limited availability of data, the analysis in this study was predominantly focused on weight and BMI

metrics. As a result, additional parameters indicative of weight loss efficacy were not included within the scope of this investigation. Secondly, we combined data from trials that varied in duration, baseline characteristics, and types of AOMs, which might result in heterogeneity to the meta-analysis, so we used a random-effects model for statistical analysis. Moreover, we did not include studies of lifestyle interventions and bariatric surgery, leading to the limitation of the trajectory describing weight change after discontinuation of the weight loss strategies. Finally, some of the included studies in this meta-analysis did not take weight change as the primary outcome, and some data were extracted from the appendix or from the Clinicaltrials.gov website, which may introduce potential inconsistencies.

Conclusions

Significant weight regain occurred 8 weeks after discontinuation of AOMs and was sustained through 20 weeks. Different weight regain was observed in subjects with different characteristics. Studies with longer follow-up duration are required to further investigate the potential factors associated weight change after discontinuation of treatment.

Abbreviations

AOM	Anti-obesity medication
WMD	Weighted mean difference
CI	Confidence interval
SD	Standard deviation
RCT	Randomized controlled trial
GLP-1 RA	Glucagon-like peptide 1 receptor agonist
GIP	Glucose-dependent insulinotropic polypeptide
GCCR	Glucagon receptor
BMI	Body mass index

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12916-025-04200-0.

Additional file 1: Tables S1–S4. Table S1 Searching details of the meta-analysis. Table S2 Baseline characteristics for included studies. Table S3 The risk of bias for included trials. Table S4 Meta-regression analysis for the overall association between characteristics of population and weight regain

Additional file 2: Figures S1–S3. Fig. S1 Flow diagram of included studies. Fig. S2 Overall analysis of weight change after drug withdrawal. Fig. S3 Subgroup analysis of weight change after drug withdrawal

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Authors' contributions

L.J. and X.C. conceptualized this study and designed the systematic review protocol; H.W. and TG performed the study selection and data extraction; X.C and W.Y. checked the data for accuracy; H.W. and W.Y. performed the statistical analyses; H.W., W.Y. and XC prepared the outlines and wrote the manuscript. All authors contributed to the critical revision of manuscript drafts and they read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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