REVIEW ARTICLE

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Efficacy and Safety of Semaglutide for Weight Loss in Obesity Without Diabetes: A Systematic Review and Meta-Analysis*

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Abstract

Background. The weight loss benefit of semaglutide in patients with diabetes is well-documented, but its clinical utility in treating obesity among patients without diabetes is less described. We therefore assessed the efficacy and safety of subcutaneous semaglutide as treatment for obesity in patients without diabetes.

Methodology. A comprehensive search of PubMed/MEDLINE, Cochrane and Google scholar was performed to identify trials on the efficacy and safety of subcutaneous semaglutide on patients with obesity without diabetes. Primary outcome was expressed as percent mean weight difference. Secondary outcomes including risk for gastrointestinal adverse events, discontinuation of treatment and serious adverse events were expressed as risk ratios. These were calculated using the random effects model.

Results. The study included 4 randomized controlled trials having a total of 3,613 individuals with obesity without diabetes. The mean difference for weight reduction was -11.85%, favoring semaglutide [95% confidence interval (CI) (-12.81,-10.90), p<0.00001]. Secondary outcomes showed that the risk of developing gastrointestinal adverse events was 1.59 times more likely with semaglutide (RR 1.59, 95%CI [1.34, 1.88], p<0.00001). Risk for discontinuation due to adverse events was twice as likely in the semaglutide group (RR 2.19, 95%CI [1.36,3.55], p=0.001) and the risk for serious adverse events was 1.6 times more likely for semaglutide (RR1.60, 95%CI [1.24, 2.07], p=0.0003). Serious events were mostly of gastrointestinal and hepatobiliary disorders such as acute pancreatitis and cholelithiasis.

Conclusion. Among individuals with obesity without type 2 diabetes, subcutaneous semaglutide is effective for weight loss with an 11.85% reduction from baseline compared to placebo. This supports the use of semaglutide for weight management in obesity. However, risk of gastrointestinal adverse events, discontinuation of treatment and serious adverse events were higher in the semaglutide group versus placebo.

Key words: obesity, Glucagon-like Peptide -1, weight loss, semaglutide

INTRODUCTION

Obesity is a chronic relapsing condition,[1] defined as excessive fat accumulation[2] with serious clinical complications such as diabetes mellitus, cardiovascular disease, musculoskeletal disorders and malignancy.[2,3] It is caused by an imbalance between energy intake and expenditure.[4] Obesity has tripled worldwide since 1975. In 2016, more than 1.9 billion adults older than 18 years were overweight and 650 million were obese.[2] Treatment options for obesity include bariatric surgery and nonsurgical treatment such as diet modification, behavioral therapy and pharmacologic therapy.[5]

Liraglutide, a glucagon-like peptide-1 receptor agonist (GLP1-RA), has been approved for the pharmacologic treatment of obesity, and is the only drug in its class approved for this indication.[6,7] GLP-1 RAs were developed for the treatment of diabetes since the incretin GLP-1 was shown to decrease blood glucose by stimulating insulin secretion and decreasing glucagon release. It also promotes weight loss by inducing satiety, leading to decreased caloric intake by delaying gastric emptying. In the brain, it decreases appetite through the stimulation of satiety centers indirectly through neural afferents and directly by crossing the blood brain barrier.[4] GLP-1 RAs available in the market have different duration of action, frequency of administration and dosing.[8] Dosing frequency

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affects adherence to therapy and studies show that a once weekly dosing was associated with significantly better adherence.[9,10] GLP-1 RAs available for once weekly dosing are exenatide, and the larger molecular weight dulaglutide and albiglutide. In a head-to-head review of GLP-1 RAs, albiglutide and dulaglutide were associated with less weight loss.[11] Large molecular weight GLP-1 RAs do not cross the blood brain barrier, which decreases its effect on stimulating the satiety center and leads to lesser weight loss compared with GLP-1 RAs with smaller molecular weight.[12] Semaglutide is a once weekly GLP-1 RA with smaller molecular weight[12] that is currently used for the treatment of type 2 diabetes mellitus (T2DM) and is associated with dose dependent reduction in glycosylated hemoglobin (HbA1c) as well as body weight in patients with diabetes.[6] It has not been approved for the treatment of obesity but the research study comparing a semaglutide to liraglutide in type 2 diabetics (SUSTAIN 10 trial) has shown that it was superior to liraglutide for weight reduction.[13]

Only a few drugs have been approved for treatment of obesity.[6,7] Some of these drugs include phentermine, bupropion/naltrexone and phentermine/topiramate. Safety has been a major concern since these drugs cause adverse psychological and physical effects.[7] It is therefore necessary to have an overall efficacy and safety evaluation of semaglutide as a promising option for the pharmacologic treatment of obesity. We conducted this systematic review and meta-analysis to present a comprehensive picture of the efficacy and safety of semaglutide for weight loss in obesity without diabetes.

Research question

Among individuals with obesity without T2DM, how effective and safe is semaglutide for weight loss?

Objectives

The objective of the study was to conduct a systematic review and meta-analysis on randomized controlled trials (RCT) of subcutaneous semaglutide on patients who are obese without T2DM. It aimed to determine the percent weight reduction from baseline after treatment with semaglutide. The study also aimed to determine the risk of gastrointestinal adverse events, risk for discontinuation and serious adverse events after treatment with semaglutide.

METHODOLOGY

Search strategy

This meta-analysis was performed in accordance to the PRISMA 2020 statement. A comprehensive systematic search of PubMed/MEDLINE, Cochrane and Google scholar was performed from inception to June 2021 to identify publications in the English or foreign language with adequate English translations on semaglutide versus placebo and other GLP-1 RAs for weight loss in obesity without T2DM. The search strategy was "semaglutide" AND "obesity." No filter was used. Ongoing trials were also sought in the relevant search. Two reviewers (HCT and MMM) independently searched the databases to identify all potentially eligible studies and reviewed the full articles for inclusion. Selected articles were then compared and the decision to include the article was reached through a consensus. Consult with the third author (OAD) was done when a consensus could not be made.

Types of studies and patient characteristics

RCTs were included in this review. Only published studies on adults with a BMI of ≥30 kg/m^2 or ≥27 kg/m^2 with at least one weight-related comorbidity were included. Patients with diabetes mellitus were excluded. The inclusion and exclusion criteria of each article were reviewed to confirm the target population.

Interventions/outcome

Studies that measured percent weight loss from baseline after treatment with semaglutide were included. Studies that compared semaglutide with medications other than GLP-1 RA or placebo were excluded.

Selection of studies

Two authors (HCT, MMM) independently screened and reviewed the abstracts and articles for inclusion. Articles were selected based on the inclusion criteria and decision to include the article was made through consensus. After removal of duplicates, the search yielded 945 publications. Based on title and abstract, 895 were either a clinical trial, review, meta-analysis, or cohort study and these were excluded. Full texts of 50 studies were reviewed and 4 were eligible for systematic review. Studies that had comparison groups and outcome not compatible with the goals of this review were excluded.

Data extraction and risk of bias assessment

Selected articles were downloaded and independently reviewed by the reviewers. Discrepancies in the selection process were resolved through discussion and reaching a consensus. Consultation with a third expert investigator was done when a consensus could not be reached. A data collection form was created and was used to extract information from each article. This included author, demographics of study population, inclusion and exclusion criteria, intervention and comparison methods, primary outcome of percent weight reduction and gastrointestinal adverse events. Quality assessment was done using the Cochrane Collaboration's tool for assessing risk of bias. Each article was critically appraised for risk of bias, which includes random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. These were graded

as high, low, or unclear, and discrepancies were settled through constructive discussion and reaching a consensus.

Data synthesis and analysis

Data synthesis and analysis were performed using Revman 5.4 for Mac. The effect measure was reported as percent mean weight change at 95% confidence interval. A p value < 0.05 was considered as statistically significant. Statistical heterogeneity between trials were assessed using the I^2 statistics. An I^2 value of 30 to 60% indicated moderate heterogeneity, 50 to 90% substantial heterogeneity, and 75 to 100% indicated considerable heterogeneity. Random effects model was used when heterogeneity was identified. When significant heterogeneity was detected even after using random effects model, a sensitivity analysis was performed. This was done by repeating the initial analysis, reviewing the inclusion and exclusion criteria and evaluating the methodology of each trial to see what could have contributed to the heterogeneity.

Registration

This study was registered with Prospero with ID CRD42021251299.

RESULTS

Study selection

The search yielded 1208 articles, of which 263 were duplicates. After removal of duplicates and 895 articles based on title and abstract alone, 50 full text articles were assessed for eligibility, of which 46 were excluded since the studies were either done in patients with diabetes or non-obese population, used an intervention other than semaglutide, or had an outcome that was not compatible with the goals of this review. After careful evaluation, 4 RTCs were included in the review (Figure 1). These trials measured the percent change in body weight after treatment with semaglutide versus placebo and reported the most common adverse effects associated with treatment. No ongoing similar studies were identified in the search.

Study characteristics

Across 4 trials, 3,613 individuals were included in the study (2,350 in the semaglutide group and 1,263 in the placebo group). Baseline characteristics were similar between both groups in the 4 individual trials. The mean weight, BMI, age and sex of the participants included in the trials are shown in Table 2. All were adults ≥18 years old with a BMI of ≥30 kg/m^2 or ≥27 kg/m^2 with at least 1 treated or untreated weight-related comorbidity without diabetes. The most common comorbidities were hypertension and dyslipidemia. The study of Wilding et al., used once weekly semaglutide injected subcutaneously starting at a dose of 0.25 mg and escalated every 4 weeks until the target dose of 2.4 mg was reached. However, unlike the other 2

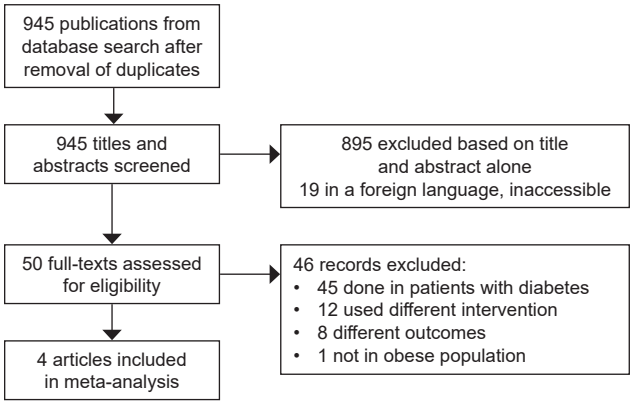

Figure 1. Flow diagram for systematic review and study selection of randomized controlled trials on semaglutide for weight loss in patients who are obese without diabetes.

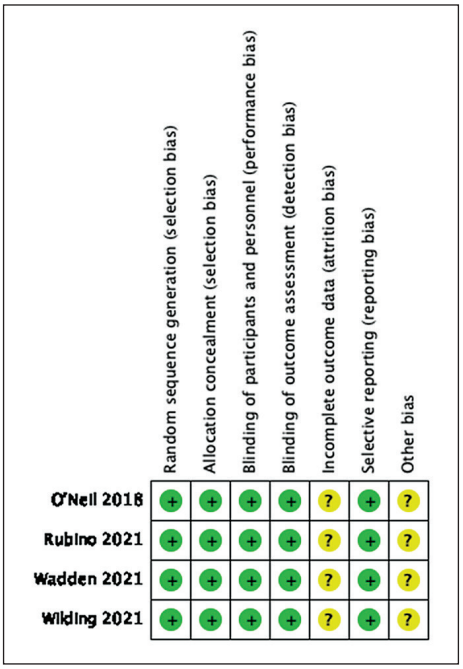

Figure 2. Risk of bias assessment of the included randomized controlled trials.

studies where participants were randomized to receive semaglutide or placebo at the start of study, Rubino's study randomized participants after the target dose was reached to continue with semaglutide or switch to matching placebo. O'Neil et al., used a smaller dose of semaglutide that was given once daily at 0.05 mg to 0.4 mg. The course of treatment was 68 weeks for Wilding, Rubino and Wadden et al., but only 52 weeks for O'Neil et al.'s study. All trials reported percent change in body weight from baseline until the end of study as well as most common adverse events associated with treatment (Table 1).

Risk of bias

Summary of the risk of bias is shown in Figure 2. The risk of bias is generally low for all studies. However, we deemed the risk of attrition bias questionable since in all 4 studies,

Table 1. Characteristics of the studies included in the systematic review and meta-analysis

First author, year	Study design	Study population	Inclusion criteria	Exclusion criteria	Interventions	Outcome
O'Neil, 2018	RCT	≥ 18 yo with BMI ≥30 kg/m^2	BMI ≥30 kg/m^2 with no weight fluctuation more than 5 kg in the 90 days before screening Undergone at least one unsuccessful non- surgical weight-loss attempt Free from major depressive symptoms	Diabetes	Semaglutide injected subQ once daily at one of the following doses (0.05 mg, 0.1 mg, 0.2 mg, 0.3 mg, 0.4 mg) or liraglutide (3.0 mg). Doses started at 0.05 mg and incrementally escalated every 4 weeks to the next level until reaching the final doses vs placebo of equal injection volume.	Percent change in bodyweight from baseline to week 52 most common reported adverse events
Rubino, 2021	RCT	≥ 18 yo with BMI ≥30 kg/m^2 or a BMI ≥27 kg/m^2 with at least 1 treated or untreated weight-related comorbidity	At least 1 self-reported unsuccessful dietary effort to lose weight BMI of 27 kg/m^2 or higher with at least 1 treated or untreated weight-related comorbidity (hypertension, dyslipidemia, obstructive sleep apnea, cardiovascular disease)	Diabetes, HbA1c 6.5% or greater More than 5 kg change in body weight within 90 days of screening.	Semaglutide started at 0.25 mg given subQ once weekly, increased every 4 weeks until 2.4 mg by week 16, and continued to week 20, then randomized, to continue semaglutide or switch to matching placebo for 48 weeks plus lifestyle intervention with monthly counseling, reduced calorie diet, increased physical activity	Percent change in body weight from randomization (week 20) to week 68 Most common reported adverse events
Wadden, 2021	RCT	≥ 18 yo with BMI ≥30 kg/m^2 or a BMI ≥27 kg/m^2 with at least 1 treated or untreated weight-related comorbidity	1 or more unsuccessful dietary effort to lose weight BMI of 27 kg/m^2 with at least 1 weight-related comorbidity (hypertension, dyslipidemia, obstructive sleep apnea, cardiovascular disease)	Diabetes, HbA1c 6.5% or greater More than 5 kg change in body weight within 90 days of screening prior or planned obesity treatment with surgery or a weight loss device	Semaglutide started at 0.25 mg given subQ once weekly, with dose escalation every 4 weeks until reaching target dose of 2.4 mg by week 16, continued until week 68 plus diet modification vs placebo	Percent change in body weight by week 68 Most common reported adverse events
Wilding, 2021	RCT	≥ 18 yo with BMI ≥30 kg/m^2 or a BMI ≥27 kg/m^2 with at least 1 treated or untreated weight-related comorbidity	1 or more unsuccessful dietary effort to lose weight BMI of 27 kg/m^2 with at least 1 weight-related comorbidity (hypertension, dyslipidemia, obstructive sleep apnea, cardiovascular disease)	Diabetes, HbA1c 6.5% or greater history of chronic pancreatitis, acute pancreatitis within 180 days before enrollment, previous surgical obesity treatment, and use of anti-obesity medication within 90 days before enrollment	Semaglutide started at 0.25 mg given subQ once weekly, with dose escalation every 4 weeks until reaching target dose of 2.4 mg by week 16, continued until week 68 plus counseling sessions every 4 weeks on adhering to a reduced calorie diet and increased physical activity vs placebo	Percent change in body weight from baseline to week 68 Most common reported adverse events

yo – year old, BMI – body mass index, subQ – subcutaneously

Table 2. Summary of the trial participants' baseline characteristics

First author, year	Mean weight semaglutide group (kg)	Mean weight placebo group (kg)	Mean BMI semaglutide group (kg/m^2)	Mean BMI placebo group (kg/m^2)	Mean Age semaglutide group (years)	Mean Age placebo group (years)	Female sex – no. (%) semaglutide group	Female sex – no. (%) placebo group
O'Neil, 2018	113.2	114.2	39.9	40.1	48	46	66/102 (65%)	88/136 (65%)
Rubino, 2021	96.5	95.4	34.5	34.1	47	46	429/535 (80.2%)	205/268 (76.5%)
Wadden, 2021	106.9	103.7	38.1	37.8	46	46	315/407 (77.4%)	180/204 (88.2%)
Wilding, 2021	105.4	105.2	37.8	38.0	46	47	955/1306 (73.1%)	498/655 (76%)

data for those who were lost to follow-up were included, which could affect the mean weight difference. As for other bias, it was also deemed questionable since all trials had confounding factors such as diet and exercise adherence that may have significantly affected the magnitude of weight loss.

All trials were double blinded, randomized, using interactive web-based response system with identically looking placebo and semaglutide. Hence, they are at low risk for selection, detection and performance biases.

Outcome of the meta-analysis

There was an 11.85% mean difference for weight reduction between the treatment groups, favoring semaglutide (mean difference -11.85, 95%CI [-12.81,-10.90], p<0.00001, I^2 43%) (Figure 3A). There is heterogeneity in between trials with an I^2 43%, P=0.16%. A sensitivity analysis was then performed, which decreased the heterogeneity to 0% after removing the study by Wadden et al. (Figure 3B). On review of the methodology, a possible cause of the heterogeneity is that in Wadden et al.,'s study, all participants received a very low calorie diet of 1000-1200 kilocalories per day (kcal/day) for the first 8 weeks followed by 1200-1800 kcal/day for the remainder of the study. They were also prescribed physical activity of 100 minutes per week that was slowly increased to reach 200 minutes per week. The other studies also prescribed reduced calorie diet and increased physical activity, but only a 500 kcal deficit per day and 150 minute of physical activity per week. The very low-calorie intake as well as increased minutes of physical activity in Wadden et al.'s study may have resulted in more weight loss especially in the placebo group, causing a smaller mean weight difference compared to the other studies.

Another outcome of this review is the risk for gastrointestinal adverse events (typically nausea, vomiting, diarrhea,

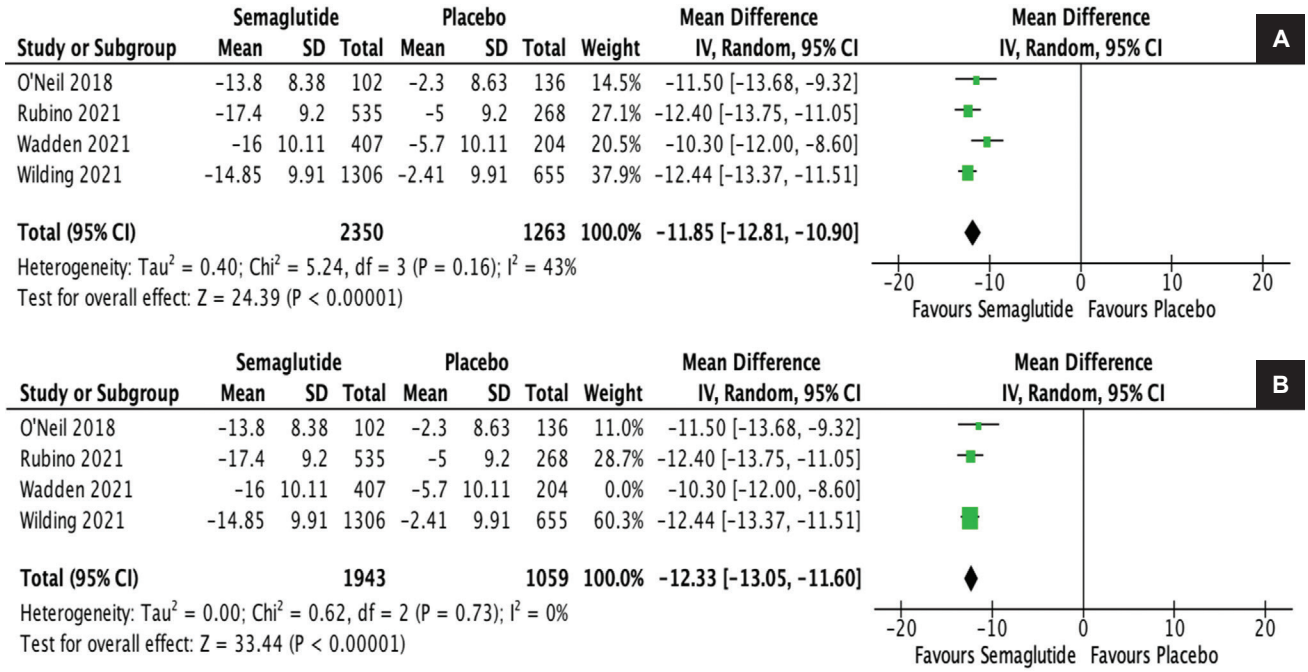

Figure 3. (A) Forest plot showing the effect of semaglutide on mean weight difference versus placebo. **(B)** Sensitivity analysis showing the effect of semaglutide on mean weight difference versus placebo.

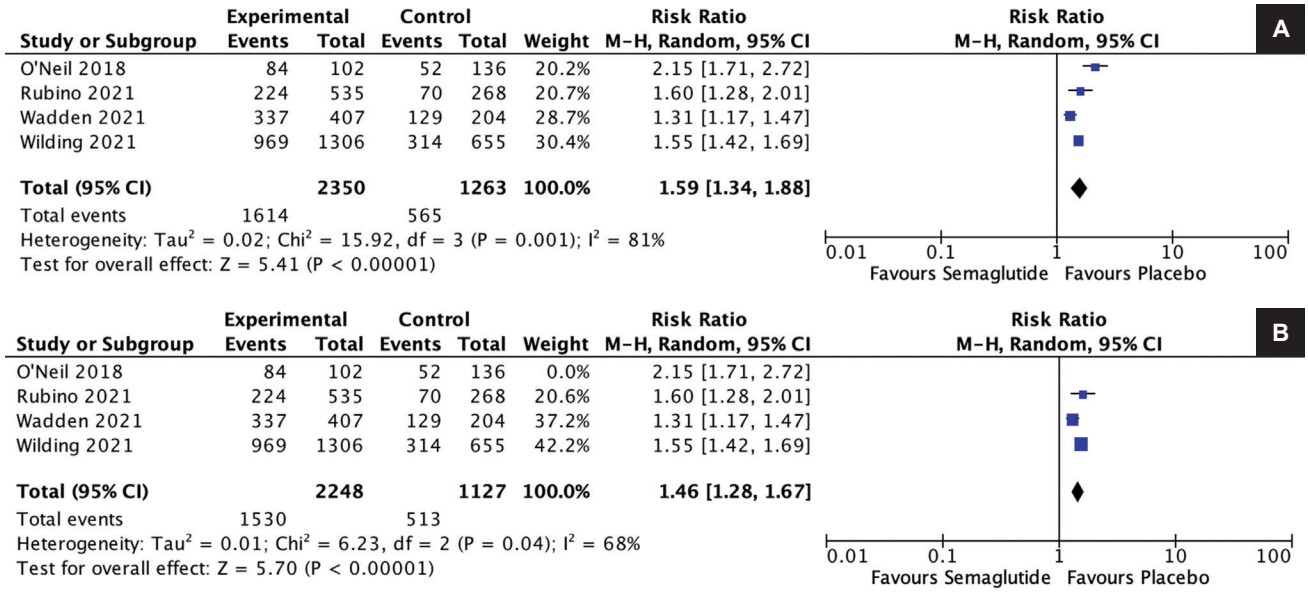

Figure 4. (A) Forest plot showing the risk of gastrointestinal adverse events with semaglutide treatment versus placebo. **(B)** Sensitivity analysis showing the risk of gastrointestinal adverse events with semaglutide treatment versus placebo.

constipation). The review showed that the risk of developing gastrointestinal adverse events was 1.59 times more likely with semaglutide treatment (RR 1.59, 95%CI [1.34, 1.88], p< 0.00001, I^2 81%) (Figure 4A). However, between-trial heterogeneity was high I^2 81%, which prompted a sensitivity analysis that decreased the heterogeneity to 68% (Figure 4B). The major source of heterogeneity was with the dose of semaglutide. Rubino, Wadden, and Wilding et al., all achieved a dose of 2.4 mg once weekly compared to O'Neil et al., where participants received only 0.4 mg once weekly subcutaneous injections.

Even though the risk for gastrointestinal adverse events was statistically significant, the studies of Rubino, Wadden and Wilding et al., reported that the duration of the adverse events was short, transient and resolved without discontinuation of treatment.

The consolidation of the 4 trials also showed that patients given semaglutide were twice as likely to discontinue treatment due to adverse events (RR 2.19, 95%CI [1.36,3.55], p=0.001, I^2 32%) (Figure 5A). Individually, the risk for discontinuation due to adverse events is 6% for semaglutide group and 2.9% for placebo group.

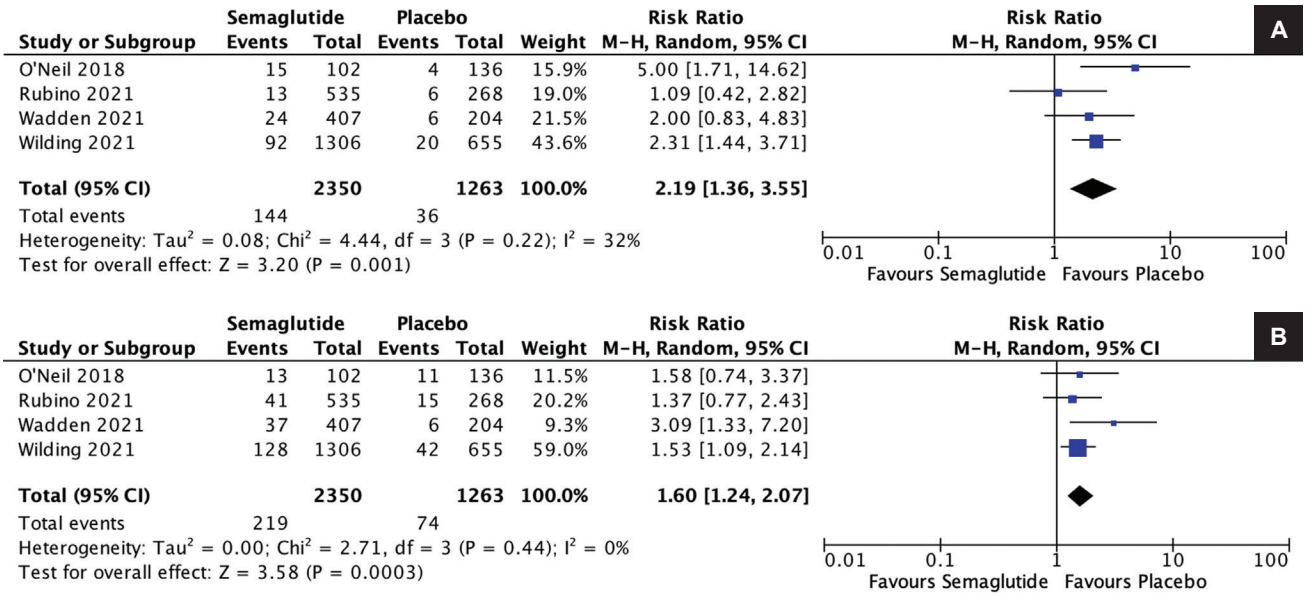

Figure 5. (A) Forest plot showing the risk of adverse events leading to discontinuation of treatment with semaglutide versus placebo. **(B)** Forest plot showing the risk of serious adverse events with semaglutide treatment versus placebo.

Serious adverse events were defined by the study of Rubino, Wadden and O'Neil et al., as life threatening, results in death, requires hospitalization or prolongation of existing hospitalization, results in persistent disability/incapacity, congenital anomaly/birth defect, important medical event (may jeopardize subject or may require medical/surgical intervention to prevent outcomes listed previously but may not be immediately life-threatening or result in death or hospitalization), as preventing daily activities by Wilding et al. These were reported to be uncommon. The risk for developing serious adverse events was 1.6 times more likely for semaglutide than placebo (RR1.60, 95%CI [1.24, 2.07], p=0.0003, I^2 0%) (Figure 5B). O'Neil, Wilding and Rubino et al.'s studies each mentioned that death was reported during the trial period, but was not considered to be related to semaglutide or placebo treatment. No death was reported in Wadden et al.'s study. Serious events were mostly of gastrointestinal disorders and hepatobiliary disorders such as acute pancreatitis and cholelithiasis.

DISCUSSION

Investigation for the use of semaglutide for obesity has been underway because trials in diabetic patients have shown that it is associated with weight loss. It is currently approved for the treatment of diabetes but not for obesity.[6] Patients with obesity sustain a 46% higher inpatient cost compared to normal weight individuals. They also have 27% more physician visits, outpatient costs and 80% higher expenses on prescription medications.[14]

Guidelines have recommended weight loss of 5 to 10% to improve metabolic function and health outcomes.[15,16] A 5% weight loss improves multi-organ insulin sensitivity[15] whereas, a 5 to 10% weight loss was associated with 0.6 to 1% reduction in HbA1c.[16] This review evaluated 4 double blind RCTs involving 3,613 participants between 2018 to 2021. Combining the results of the trials showed that semaglutide is indeed associated with weight loss with a mean difference of 11.85% compared with placebo. The subjects of the trials all had at least one unsuccessful non-surgical attempt to lose weight, and based on this meta-analysis, a 5 to 10% weight reduction could be achieved with semaglutide. However, it is important to consider that the Rubino study randomized participants to continue with semaglutide treatment or placebo after the target dose was reached. This could have affected the results because participants could have lost weight with initial treatment with semaglutide.

Patient adherence is an important factor in the treatment of obesity, and pharmacologic treatment has been associated with significant adverse events which lead to their discontinuation.[7] This prompted us to evaluate whether semaglutide was also associated with significant adverse events. Consolidating the trials showed nausea, vomiting, constipation and diarrhea to be the most common adverse events. The trials have reported that these were of mild to moderate severity and short duration that resolved without treatment. Moreover, adverse events leading to discontinuation and serious adverse events were uncommon. Dosing frequency is also a factor in adherence to treatment and once weekly dosing was associated with better adherence.[9] With its mild, transient adverse events and once weekly dosing, we can expect good adherence with semaglutide. We observed that aside from the administration of semaglutide, reduced calorie diet and increased physical activity were also part of the intervention. Hence, semaglutide alone probably will not be able to achieve an 11.85% weight loss. Despite these confounding factors, we still believe that semaglutide is a major factor in weight reduction because the subjects all attempted to lose weight prior to starting treatment but were unsuccessful.

Since obesity has been increasing in prevalence worldwide and can cause serious complications like cardiovascular disease and diabetes,[2,3] safe and acceptable treatments for this condition are crucial to prevent further health complications. However, since the trials were all done within a specified follow-up period, it is difficult to predict whether there will be weight gain following discontinuation of treatment, and whether continuous treatment will be necessary.

Strengths and limitations

The study presented a comprehensive systematic review and meta-analysis on semaglutide versus placebo for weight loss in patients who are obese without diabetes. It was able to show the percent mean weight loss after treatment with semaglutide as well as the risks for gastrointestinal adverse effects, discontinuation of treatment and serious adverse events. However, this review is limited to the 4 trials available for this meta-analysis and did not include unpublished literature. Bias may have occurred from these limitations. Furthermore, the studies included the weight for participants who were lost to follow-up and this could have affected the mean percent weight difference. The adherence of the participants to treatment during the trial is also a factor. Each study has their own diet plan and exercise program for the participants in addition to treatment, which could also have affected the magnitude of the effect estimate.

CONCLUSION AND RECOMMENDATIONS

In summary, among individuals with obesity without T2DM, subcutaneous semaglutide is effective for weight loss with an 11.85% reduction from baseline compared to placebo. This supports the use of semaglutide for weight management in obesity. However, risk of gastrointestinal adverse events, discontinuation of treatment, and serious adverse events were higher in the semaglutide group versus placebo. RCTs with longer follow-up are needed to determine long term efficacy, safety and risk for weight gain after treatment discontinuation. Subjects of the trials were also mostly of the white race, hence, future research can focus on its efficacy and safety on the Asian population.

Statement of Authorship
All authors certified fulfillment of ICMJE authorship criteria.

Author Contribution Statement
HCT, OAD, MMM conceived the study; developed the methodology; synthesized the data and prepared the original draft. HCT and OAD validated the research; reviewed and edited the manuscript. HCT and MMM conducted the research. HCT presented the data and coordinated the research activity planning. OAD supervised the research.

Author Disclosure
OAD reports receiving consulting fees from Eli Lilly and Novo Nordisk for service outside the submitted work, as well as honoraria for speaking engagements from Astra Zeneca, Novo Nordisk, and Eli Lilly outside the submitted work. HCT and MMM declare no conflict of interest in association with this study.

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References
1. Frühbeck G, Busetto L, Dicker D, et al. The ABCD of obesity: An EASO position statement on a diagnostic term with clinical and scientific implications. Obes Facts. 2019;12(2):131–6. PMID: 30844811. PMCID: PMC6547280. https://doi.org/10.1159/000497124.
2. World Health Organization. Obesity and overweight. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight. Accessed 15 May 2021.
3. Guh DP, Zhang W, Bansback N, Amarsi Z, Birmingham CL, Anis AH. The incidence of co-morbidities related to obesity and overweight: A systematic review and meta-analysis. BMC Public Health. 2009;9:88. PMID: 19320986. PMCID: PMC2667420. https://doi.org/10.1186/1471-2458-9-88.
4. van Bloemendaal L, ten Kulve JS, la Fleur SE, Ijzerman RG, Diamant M. Effects of glucagon-like peptide 1 on appetite and body weight: Focus on the CNS. J Endocrinol. 2014;221(1):T1-16. PMID: 24323912. https://doi.org/10.1530/JOE-13-0414.
5. Gloy VL, Briel M, Bhatt DL, et al. Bariatric surgery versus non-surgical treatment for obesity: A systematic review and meta-analysis of randomised controlled trials. BMJ. 2013;347:f5934. PMID: 24149519. PMCID: PMC3806364. https://doi.org/10.1136/bmj.f5934.
6. Christou GA, Katsiki N, Blundell J, Fruhbeck G, Kiortsis DN. Semaglutide as a promising antiobesity drug. Obes Rev. 2019;20(6):805–15. PMID: 30768766. https://doi.org/10.1111/obr.12839.
7. Ammori BJ, Skarulis MC, Soran H, Syed AA, Eledrisi M, Malik RA. Medical and surgical management of obesity and diabetes: What's new? Diabet Med. 2020;37(2):203-10. PMID: 31850536. https://doi.org/10.1111/dme.14215.
8. Dungan KM, Povedano ST, Forst T, et al. Once-weekly dulaglutide versus once-daily liraglutide in metformin-treated patients with type 2 diabetes (AWARD-6): A randomised, open-label, phase 3, non-inferiority trial. Lancet. 2014;384(9951):1349–57. PMID: 25018121. https://doi.org/10.1016/S0140-6736(14)60976-4.
9. Qiao Q, Ouwens MJNM, Grandy S, Johnsson K, Kostev K. Adherence to GLP-1 receptor agonist therapy administered by once-daily or once-weekly injection in patients with type 2 diabetes in Germany. Diabetes Metab Syndr Obes. 2016;9:201-5. PMID: 27418849. PMCID: PMC4934555. https://doi.org/10.2147/DMSO.S99732.
10. Johnston SS, Nguyen H, Felber E, et al. Retrospective study of adherence to glucagon-like peptide-1 receptor agonist therapy in patients with type 2 diabetes mellitus in the United States. Adv Ther. 2014;31(11):1119–33. PMID: 25408484. https://doi.org/10.1007/s12325-014-0166-0.
11. Madsbad S. Review of head-to-head comparisons of glucagon-like peptide-1 receptor agonists. Diabetes Obes Metab. 2016;18(4):317-32. PMID: 26511102. PMCID: PMC5064617. https://doi.org/10.1111/dom.12596.
12. Dhruv U, Gupta OP. Glucagon like peptide 1 receptor agonists: Glycaemic control and beyond. J Clin Diabetol. 2016;2(4):18–25. http://jcdonline.in/wp-content/uploads/2016/06/6.-JCD_Vol_2_No_4_Urman-Dhruv.pdf.
13. Capehorn MS, Catarig AM, Furberg JK, et al. Efficacy and safety of once-weekly semaglutide 1.0 mg vs once-daily liraglutide 1.2 mg as add-on to 1–3 oral antidiabetic drugs in subjects with type 2 diabetes (SUSTAIN 10). Diabetes Metab. 2020;46(2):100–9. PMID: 31539622. https://doi.org/10.1016/j.diabet.2019.101117.
14. Finkelstein EA, Trogdon JG, Cohen JW, Dietz W. Annual medical spending attributable to obesity: Payer-and service-specific estimates. 2009;28(5):w822-31. PMID: 19635784. https://doi.org/10.1377/hlthaff.28.5.w822.
15. Magkos F, Fraterrigo G, Okunade AL, et al. Clinical and Translational Report Effects of moderate and subsequent progressive weight loss on metabolic function and adipose tissue biology in humans with obesity. Cell Metab. 2016;23(24):591–601. PMID: 26916363. PMCID: PMC4833627. https://doi.org/10.1016/j.cmet.2016.02.005.
16. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS Guideline for the management of overweight and obesity in adults: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. J Am Coll Cardiol. 2014;63(25 Pt 5):2985–3023. PMID: 24239920. https://doi.org/10.1016/j.jacc.2013.11.004.
17. Rubino D, Abrahamsson N, Davies M, et al. Effect of continued weekly subcutaneous semaglutide vs placebo on weight loss maintenance in adults with overweight or obesity: The STEP 4 randomized clinical trial. JAMA. 2021;325(14):1414-25. PMID: 33755728. PMCID: PMC7988425. https://doi.org/10.1001/jama.2021.3224.
18. Wilding JPH, Batterham RL, Calanna S, et al. Once-weekly semaglutide in adults with overweight or obesity. N Engl J Med. 2021;384(11):989-1002. PMID: 33567185. https://doi.org/10.1056/nejmoa2032183.

19. Wadden TA, Bailey TS, Billings LK, et al. Effect of subcutaneous semaglutide vs placebo as an adjunct to intensive behavioral therapy on body weight in adults with overweight or obesity: The STEP 3 randomized clinical trial. JAMA - J Am Med Assoc. 2021;325(14):1403-13. PMID: 33625476. PMCID: PMC7905697. https://doi.org/10.1001/jama.2021.1831.

20. O'Neil PM, Birkenfeld AL, McGowan B, et al. Efficacy and safety of semaglutide compared with liraglutide and placebo for weight loss in patients with obesity: A randomised, double-blind, placebo and active controlled, dose-ranging, phase 2 trial. Lancet. 2018;392(10148):637-49. https://doi.org/10.1016/S0140-6736(18)31773-2.

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