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Efficacy of anti-obesity agents: a systematic review and network meta-analysis of randomized controlled trials

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ABSTRACT

Background: To conduct a network meta-analysis comparing the safety and efficacy of five anti-obesity drugs approved by the United States Food and Drug Administration (US FDA)-Bupropion/Naltrexone combination (BUP/NLX), Liraglutide (LIRA), Orlistat (ORLI), Phentiramine/Topiramate combination (PHEN/TPM) and Simaglutide (SGT) vs placebo.

Methods: The study's eligibility criteria include randomized controlled trials (RCTs) with a focus on obese patients receiving BUP/NLX or LIRA or ORLI or PHEN/TPM or SGT versus placebo. We conducted a comprehensive search of electronic databases (PubMed, Embase, Cochrane Library, and Scopus) to identify relevant randomized controlled trials published, with no restrictions on the publication language or year. Three reviewers independently screened the studies, extracted data, and assessed the risk of bias using the Cochrane Risk of Bias tool. Bucher's and Bayesian Meta-regression Simulation Method were used for indirect head-to-head comparison between various active drugs. RevMan Version 5.4® along with A Network Meta- Analysis Toolkit by Cochrane Methods were used. p-value less than 0.05 was considered significant.

Results: Total 28 studies were included in this meta-analysis. PHEN/TPM combination exhibited (odds ratio :0.568, p value <0.001, cl 95%) ORLI (odds ratio: 0.889, p value <0.001, cl 95%), SGT (odds ratio: 0.922, p value <0.001, cl 95%). BUP/NLX combination exhibited a high (odds ratio: 4.61, p value <0.001, cl 95%) LIRA displayed the lowest (odds ratio: 1.109, p value <0.001, cl 95%). Network meta-analysis revealed. BUP/NLX combination exhibited highest Efficacy. ORLI found as safest among the evaluated drugs. SGT had significant likelihood of adverse events (odds ratio = 1.328, p-value<0.0001, Cl 95%) compared to ORLI (odds ratio = 0.138, p-value<0.0001, Cl 95%), BUP/NLX (odds ratio = 0.197, p-value<0.0001, cl 95%), and LIRA (odds ratio = 0.456, p-value < 0.001, Cl 95%), PHEN/TPM (odds ratio = 0.456, p-value<0.0001, Cl 95%).

Discussion: These findings have important clinical implications for the management of obesity. The BUP/NLX , LIRA , and SGT can be considered as effective treatment options for weight reduction. However, healthcare providers need to carefully consider the safety profiles and potential side-effects of these medications when making treatment decisions. The study relied on aggregated data, which might introduce bias. High attrition rates and heterogeneity among studies limit the findings. It only compared common gastrointestinal side effects and didn't use the GRADE approach for evidence quality.

Conclusion: Study provides evidence supporting the efficacy of anti-obesity medications compared to placebo. BUP/NLX combination, LIRA, and SGT emerged as the most effective agents, considering safety profile. Findings can guide clinicians about options for obesity management.

Study Registration: The study is registered with PROSPERO (CRD42023465989).

KEYWORDS: Anti-obesity Agents, Obesity Management, Network Meta-analysis

INTRODUCTION

Over a third of the world's population is currently affected by obesity and overweight, which is a complex, multifaceted, and generally preventable condition. [1] According to estimates, 38% of adults worldwide will be overweight and another 20% will be obese by 2030 if secular trends continue. [2] While the general growth in obesity in the majority of affluent nations appears to have peaked. [3] By 2030, nearly 85% of adults in the United states of America(USA), according to the most catastrophic forecasts based on prior secular trends, will be overweight or obese, the rate of morbid obesity in many of these nations is still rising, notably among youngsters. [4] Additionally, obesity prevalence continues to rise in developing nations like India, mirroring the U.S.A.

Obesity is often characterized as having an excessive body weight for one's height, but this straightforward description conceals a complicated phenotype that is primarily caused by excessive adiposity, or body fatness, and that can express metabolically as well as physically. [5] Obesity significantly raises the risk of death and morbidity from chronic diseases, including those that cause incapacity, depression, type 2 diabetes, cardiovascular disease, and certain malignancies. The same disorders are brought on by childhood obesity, but they may manifest earlier or with more likelihood in adulthood. [6] As a result, both the financial and psychological costs of obesity alone as well as when these comorbidities and consequences are present, are startling.

Currently, drugs have been approved for the obesity by the the food and drug administration. While Naltrexone (NLX) can be used to suppress the autoinhibitory feedback linked to a fall in weight loss, bupropion (BUP) can be used for stimulating Pro-opiomelanocortin (POMC) neurons. [7] Liraglutide (LIRA) and Semaglutide (SGT)(GLP-1 Receptor agonist) effects on food intake, metabolism, and weight loss are primarily caused by its impacts on peripheral (vagal) and central pathways, as well as by the activation of the hindbrain and hypothalamus. [8] Orlistat (ORLI) acts by reversibly inhibiting gastric and pancreatic lipases. The inactivation of lipases prevents the hydrolysis of triglycerides, and thus free fatty acids are not absorbed. The maximum benefit of ORLI occurs when used in conjunction with diet and exercise. [9] FDA briefing does not specify the precise mechanism of weight loss with Phentermine (PHEN), but based on the package insert, it may be assumed that it functions as a sympathomimetic drug, which may reduce hunger as well as speed up metabolism. It is unknown how topiramate (TPM) works to cause people to lose weight. TPM is thought to cause weight loss by neurotransmitter-mediated appetite suppression and satiety augmentation. [10]

The objectives of the study is to assess the research comparing the effectiveness of these FDA approved anti-obesity medications to placebo. Additionally, we want to describe the major side effects associated with these medications and provide a comparison viewpoint. To Evaluate Comparative Effectiveness and Safety (in terms of Gastrointestinal side effects in form of (Nausea/Vomiting and Diarrhoea) of Phenteramine / Topiramate [PHEN/TPM], Orlistat (ORLI), Liraglutide [LIRA], Semaglutide (SGT), Bupropion /Naltrexone (BUP/NLX) for the treatment of Obesity by a Network — Meta-analysis.

Primary outcome: $\geq$5% reduction in weight loss.

Secondary outcome: Gastrointestinal related adverse drug effects in the form of vomiting and diarrhea.

METHODS

Inclusion criteria:

1. Randomized controlled trials with adequate method of concealment and single/double blind trials.
2. For this study, all Randomized controlled trials in which all participants who have obesity, with or without any comorbidities and who have been subjected to either one of these anti-obesity drugs namely (BUP/NLX), (LIRA), (ORLI), (PHEN/TPM), (SGT) versus placebo.

Exclusion criteria:

1. Those not fulfilling the inclusion criteria.
2. Studies with incomplete information.
3. Observational studies

Information sources: In this network meta-analysis, we considered Randomized Control Trials. The time frame for the inclusion of studies in this network meta-analysis extends from the inception of the earliest relevant studies till 2023. Studies published in the English language were included in this network meta-analysis. Only published studies were included.

Above Network Meta Analysis Plot (Figure 1) shows well connected Network of randomized Controlled Trials (RCTs) evaluating the FDA approved anti-obesity drugs.

Search strategy-

● We conducted a comprehensive search of electronic databases([PubMed, Embase, Cochrane Library, and Scopus) to identify relevant randomized controlled trials (RCTs])published, with no restrictions on the publication language or year.Figure 2

Selection of studies -

The abstracts of all the records that met our predefined inclusion criteria were screened by all the authors, and studies that entirely fulfilled our inclusion criteria, were retrieved with their supplementary appendix, for further analysis. Any ambiguity during the study selection has been resolved by mutual discussions and consensus.

Data collection process -

In this study, data collection from reports was conducted by two independent reviewers for each report. Three Reviewers have worked separately to minimize bias and enhance the reliability of data extraction. Any discrepancies or uncertainties in data extraction were resolved through discussion and consensus between the reviewers. To ensure data accuracy and completeness, we employed a process to contact study investigators when necessary. Any missing or unclear data points were clarified through direct communication with the investigators to ensure the integrity of the information collected. Additionally, automation tools were not used in the data collection process. Data extraction was performed manually by the reviewers to maintain the precision and accuracy of the collected information.

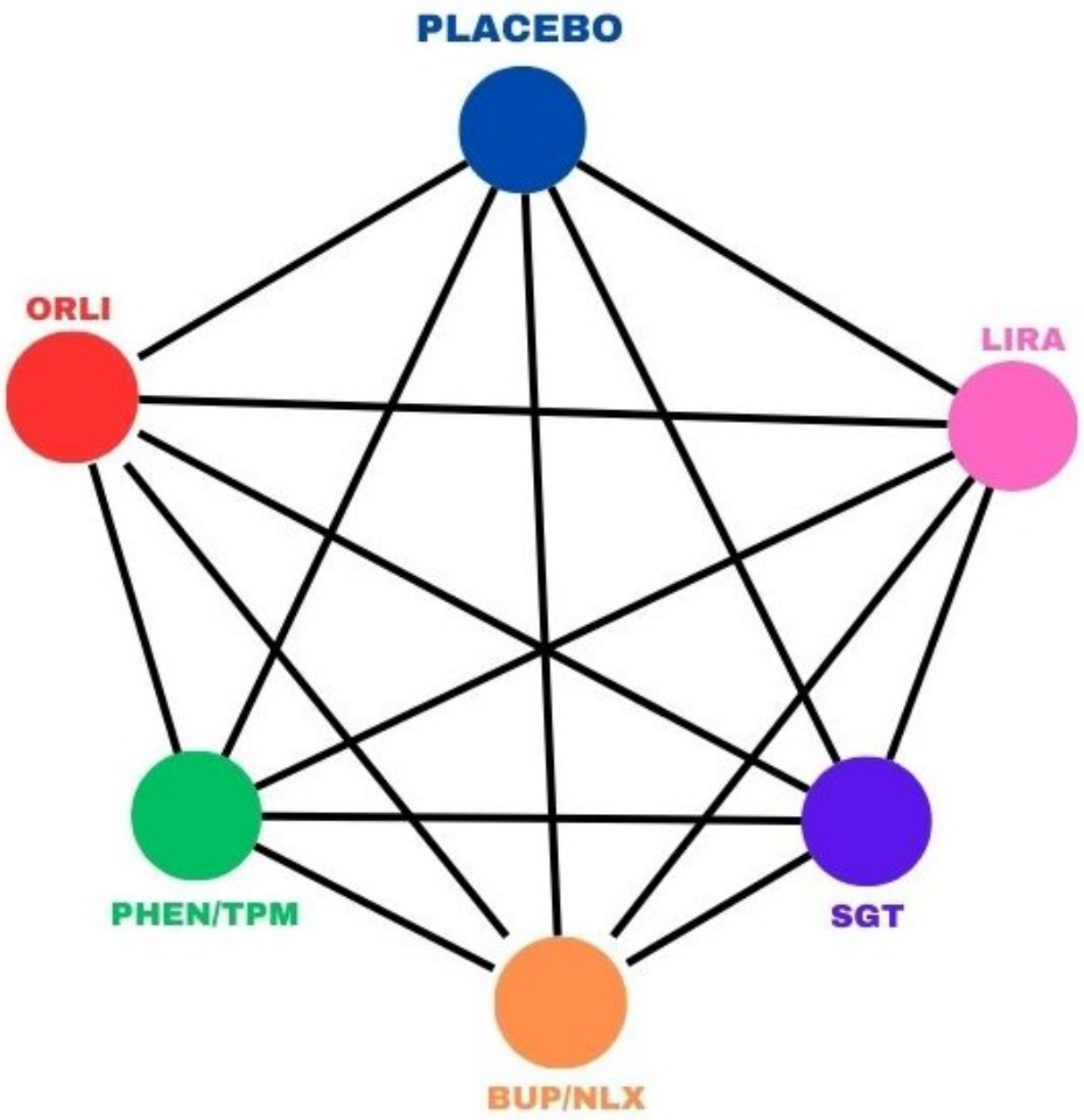

Figure 1: Network Meta Analysis of Anti-Obesity Drugs

Data abstraction-

Study design data including design synopsis, treatment comparators, dosage, titration schedule and duration of treatment were abstracted, along with baseline characteristics including summary statistics of BMI, age, and sex.

Data Items-

Study Settings:

In this network meta-analysis multiple research contexts were considered. These settings encompass clinical trials conducted within controlled clinical environments. The inclusion of studies from a range of settings will enhance the generalizability and applicability of the findings to both controlled experimental conditions and real-world clinical practice."

Time frame:

The time frame for the inclusion of studies in this network meta-analysis extends from the inception of the earliest relevant studies till 2023. This duration allows us to capture a comprehensive range of evidence while accommodating

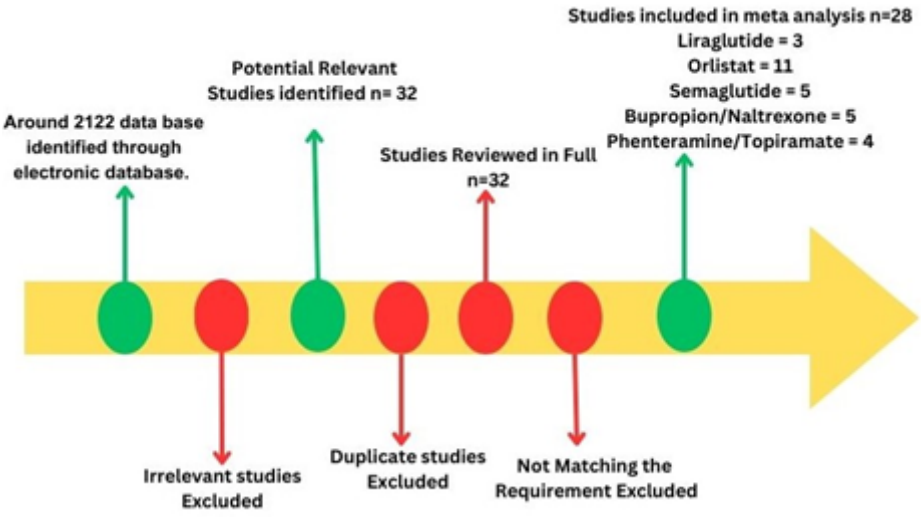

Figure 2: Prisma Flow Diagram (Information sources)

developments and changes in interventions and outcomes over time.

Language: Studies published in the English language were included in this network meta-analysis. The decision to limit the review to English language studies is based on resource constraints and the non-availability of qualified translators for other languages.

Publication Status: Only published studies are included in this network meta-analysis. The decision to exclude unpublished or grey literature is made to maintain a high standard of evidence and ensure the reliability of data sources.

Report Characteristics: Full-text articles are considered for inclusion in this network meta-analysis. Any study that fails to provide essential data was excluded from the analysis.

Risk Bias/Meta-bias(es):

We have assessed potential meta-biases in this network meta-analysis, including publication bias and selective reporting. Publication bias was evaluated using funnel plots, Egger's regression test and Begg's test. Selective reporting within studies was explored through visual inspection of forest plots and comparison of reported outcomes with pre-specified outcomes in the protocols."

Effect Measures :

In this network meta-analysis, we employed standardized mean Difference (SMD) as our Primary effect measure. The SMD was calculated by taking the Mean Difference (MD) between the intervention group and the placebo group and dividing it by the Standard Deviation (SD) of the Outcomes. We considered mainly the Odds ratio for Secondary effect measure.

Synthesis Methods: We conducted a comprehensive search of electronic databases (PubMed, Embase, Cochrane Library, and Scopus) to identify relevant randomized controlled trials (RCTs) published till 2023. Two reviewers independently screened the studies, extracted data and assessed the risk of bias using the Cochrane Risk of Bias tool. Bucher's and Bayesian Meta-regression Simulation Method were used for indirect head-to-head comparison between various active drugs. MedCalc® statistical software, RevMan Version 5.4 along with A Network Meta- Analysis Toolkit by Cochrane Methods were used. P-value< 0.05 was considered significant.

Reporting Bias assessment :

Visual Inspection of Funnel Plots: Funnel plots were visually inspected to assess the symmetry of data points, where each point represents an individual study's effect size plotted against its standard error. Asymmetry in the funnel plot can be indicative of publication bias, and we assessed the potential impact of this bias on our findings.

Egger's Test and Begg's test: Egger's and Begg's tests were conducted to quantify the degree of asymmetry in the funnel plot, providing statistical evidence for publication bias.

Certainty assessment:

We conducted sensitivity analysis to assess the influence of reporting bias on our findings. This involved comparing the outcomes of the primary analysis with adjusted estimates obtained through imputation of potentially missing studies, employing a graphical representation known as a "publication bias assessment plot" (Figure 3) and a "summary plot."(Figure 4)

Figures 3 and 4 shows results of the risk of bias Certainty assessment generated using robvis. Randomized Control Trial Studies were assessed using the ROB 2 tool.

Study characteristics:

Figure 3: Publication bias assessment plot

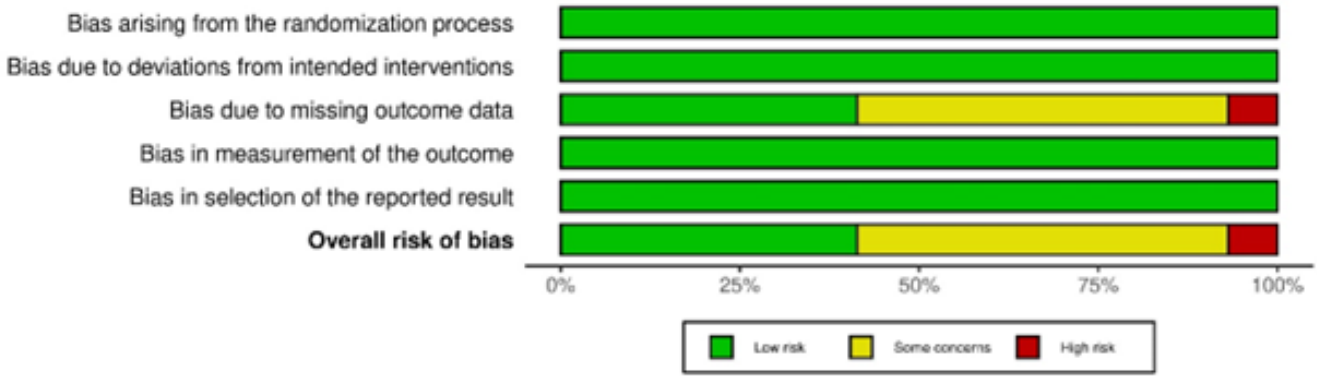

Figure 4: Publication Bias Summary Plot

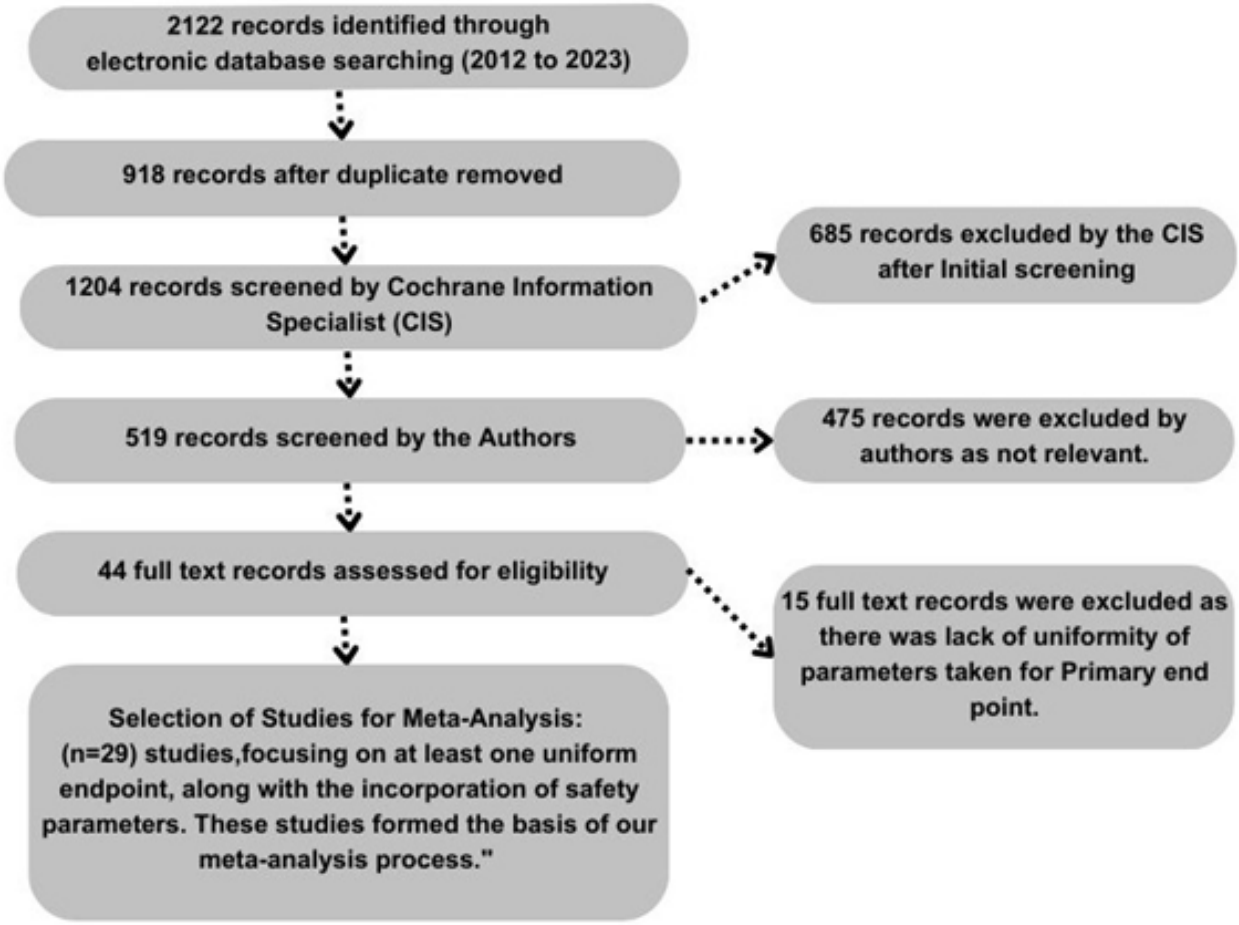

Figure 5: Flow chart-study selection

"Full-text articles" are considered for inclusion in this network meta-analysis.

Caroline et al. [11], Priscillia et al. [12], Frank et al. [13], Thomas et al. [14], Carel et al. [15], Dominica et al. [16], John et al. [17], Thomas et al. [18], Melanie et al. [19] ,Timothy et al. [20] , Kishore et al. [21], Daniel et al. [22], Davide et al. [23] ,Timothy et al. [24], Jart et al. [25] , Asghar et al. [26], Stephan et al. [27], Priscilla et al. [28], David et al. [29], Hanefeld et al. [30] , Michael et al. [31], Lindgrade et al. [32] , Keronff et al. [33] , Patrick et al. [34] , Swinburn et al. [35], Xavier et al. [36], Halawi H et al. [37], Melanie et al. [38], and Astrup et al. [39].

Any study that failed to provide essential data was excluded from the analysis. "Only Randomized control trials were included in our network Meta analysis. The abstracts of all the records that met our predefined inclusion criteria were screened by all the authors, and studies that entirely fulfilled our inclusion criteria, were retrieved with their supplementary appendix, for further analysis. Any ambiguity during the study selection has been resolved by mutual discussions and consensus. Two independent reviewers were involved in the study selection process. During the initial screening phase, both reviewers independently assessed titles and abstracts of retrieved studies for potential relevance based on the predefined eligibility criteria. Disagreements were resolved through discussion. In the eligibility phase, other three reviewers independently evaluated the full-text articles of potentially relevant studies to determine final inclusion. Consensus reached through discussion among all reviewers (Figure 5).

Egger's Test	PHEN/ TPM	ORLI	SGT	BUP/ NLX	LIRA
Intercept	0.98	-0.94	0.84	-6.84	0.07
Significance Level	0.34	0.84	0.39	0.11	0.93
Begg's test					
Kendall's Tau	0.01	-0.24	0.20	-0.20	0.33
Significance Level	1.00	0.31	0.62	0.62	0.50

Table 1: Risk of bias

The result for Table 1 is calculated from data extracted from studies [11–36] [37–39]

Egger's Test: Egger's test is used to assess the presence of publication bias in a meta-analysis. It tests funnel plot asymmetry, which can indicate bias in the reporting of studies. In Egger's test, the intercept is of primary interest. If the intercept is significantly different from zero, it suggests the presence of publication bias.

- For PHEN/TPM: The intercept is 0.9837, and the significance level is 0.3406. Since the p-value (0.3406) is greater than the typical significance level of 0.05, there is no strong evidence of publication bias for this treatment group.
- For ORLI: The intercept is -0.9458, and the significance level is 0.8439. Similarly, there is no strong evidence of publication bias for this treatment group.
- For SGT: The intercept is 0.8408, and the significance level is 0.3919. No strong evidence of publication bias.
- For BUP/NLX: The intercept is -6.8440, and the significance level is 0.1096. The p-value is relatively low but still above 0.05. It suggests some evidence of publication bias, but it's not very strong.
- For LIRA: The intercept is 0.06462, and the significance level is 0.9324. There is no strong evidence of publication bias.

Begg's Test: Begg's test is another test for publication bias in meta-analysis. It assesses the correlation between the effect sizes and their variances in the included studies. A significant p-value indicates the presence of publication bias.

- For PHEN/TPM: Kendall's Tau is 0.0124, and the significance level is 1.0000. The high p-value suggests no evidence of publication bias for this treatment group.
- For ORLI: Kendall's Tau is -0.2364, and the significance level is 0.3115. No strong evidence of publication bias.
- For SGT: Kendall's Tau is 0.2000, and the significance level is 0.6242. No strong evidence of publication bias.
- For BUP/NLX: Kendall's Tau is -0.2000, and the significance level is 0.6242. Similar to the previous tests, there is no strong evidence of publication bias.
- For LIRA: Kendall's Tau is 0.3333, and the significance level is 0.4969. Again, there is no strong evidence of publication bias.

In summary, based on the results of both Egger's and Begg's tests, there is generally no strong evidence of publication bias for the treatment groups you've analyzed. However, for BUP/NLX in Egger's test, there is some weaker evidence of publication bias, but it's not conclusive. Always consider the overall context of your meta-analysis and the characteristics of the included studies when interpreting these results.

Measurement of treatment effect

Direct comparison between active drug and placebo was done using random effect model and Odd's ratio was calculated.

Summary measures

The principal summary measure was the Odd's Ratio (at 95% Confidence Interval) and Funnel Plots as well as Forest Plots were represented. p-value less than 0.05 was considered significant.

Data synthesis and statistical analysis

Bucher's and Bayesian Meta-regression Simulation Method were used for indirect head-to-head comparison between various active drugs. RevMan Version 5.4® along with A Network Meta- Analysis Toolkit by Cochrane Methods were used. p-value less than 0.05 was considered significant.

RESULTS

Total 28 studies were included for the final analysis [9, 11–36] [37–39]Table 2 and Table 3 show direct and indirect comparison of drugs used in anti obesity.

Table 2. Efficacy (Direct comparison)					
Drugs	**PHEN/TPM**	**ORLI**	**SGT**	**BUP/NLX**	**LIRA**
Odd's Ratio	0.568	0.889	0.922	4.61	1.109
p-value	P < 0.001	P < 0.001	0.141	P < 0.001	0.118
Safety (Direct comparison)					
Odd's Ratio	0.456	0.138	1.328	0.197	0.456
p-value	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001

Table 2: Efficacy and safety (Direct Comparison) of anti-obesity drugs [11] - [39]

Efficacy and safety of anti-obesitydrugs [11–35] , [36–39]

The result for Table 2 is calculated from data extracted from [11] - [39] studies.

This network meta-analysis [using random effects model, based on heterogeneity] found a significant reduction in body weight (Table 2).

- Our network meta-analysis revealed the odds ratios for different drugs used in the treatment of obesity in relation to weight loss. The BUP/NLX combination exhibited the highest odds ratio (4.61), indicating a robust and significant association with weight loss. This finding suggests that the BUP/NLX combination is highly effective in promoting weight reduction compared to placebo.

- ORLI [odds ratio: 0.889, and LIRA (odds ratio: 1.109) also demonstrated substantial odds ratios, indicating significant efficacy in promoting weight loss, although slightly lower than that observed with the BUP/NLX combination.

- The PHEN/TPM combination exhibited an (odds ratio of 0.568), suggesting a relatively strong association with weight loss compared to placebo.

Efficacy (Indirect comparison)		
Drugs	**Odd's ratio**	**p value**
PHEN/TPM vs ORLI	2.1292	p < 0.0001
PHEN/TPM vs SGT	2.2166	p < 0.0001
PHEN/TPM vs BUP/NLX	3.8764	p < 0.0001
PHEN/TPM vs LIRA	0.3672	p < 0.0001
ORLI vs SGT	1.0411	P = 0.4667
ORLI vs BUP/NLX	1.8206	p < 0.0001
ORLI vs LIRA	0.1724	p < 0.0001
SGT vs BUP/NLX	1.7487	p < 0.0001
SGT vs LIRA	0.1656	p < 0.0001
BUP/NLX vs LIRA	0.09472	p < 0.0001
Safety (Indirect comparison)		
Drugs	**Odd's ratio**	**p value**
PHEN/TPM vs ORLI	0.4697	p < 0.0001
PHEN/TPM vs SGT	0.4511	p < 0.0001
PHEN/TPM vs BUP/NLX	0.258	p < 0.0001
PHEN/TPM vs LIRA	2.7237	p < 0.0001
ORLI vs SGT	0.9605	p = 0.4667
ORLI vs BUP/NLX	0.5493	p < 0.0001
ORLI vs LIRA	5.7992	p < 0.0001
SGT vs BUP/NLX	0.5718	p < 0.0001
SGT vs LIRA	6.0374	p < 0.0001
BUP/NLX vs LIRA	10.5579	p < 0.0001

Table 3: Efficacy and safety (Indirect Comparison) of anti-obesity drugs [11] - [39]

- On the other hand, SGT displayed the odds ratio, with a value of 0.922. This suggests a comparatively weaker association with weight loss, although still significant compared to placebo.

- To summarize, the ranking of the drugs based on their odds ratios for weight loss is as follows: BUP/NLX>LIRA>SGT>ORLI>PHEN/TPM. These findings provide valuable insights into the relative effectiveness of these drugs in promoting weight reduction and can inform clinical decision-making for the treatment of obesity.

This meta-analysis [using random effects model, based on heterogeneity] have shown the association of G.I. side effects [vomiting and diarrhea] (Table 2).

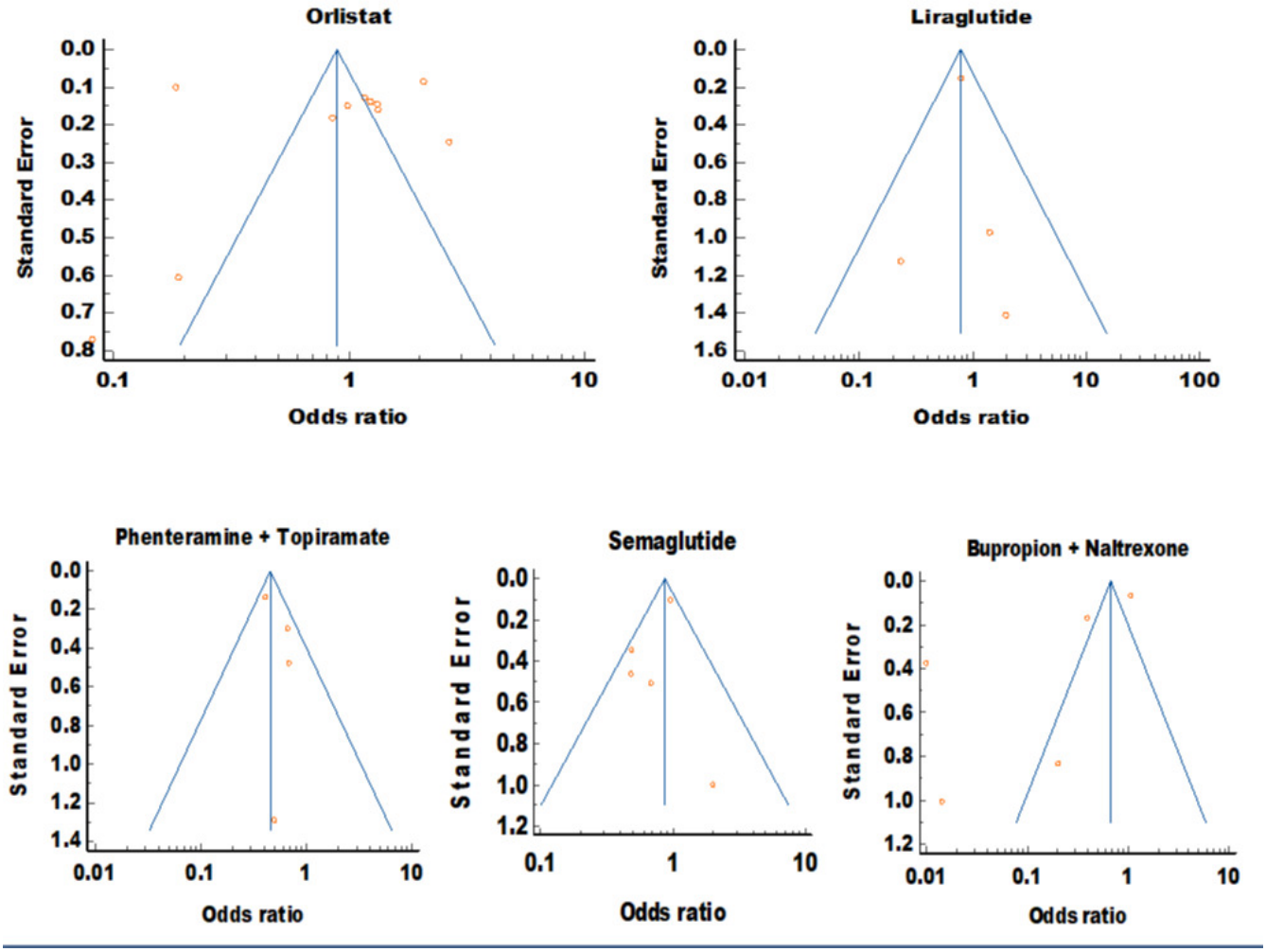

Figure 6: Funnel plot showing efficacy of five anti-obesity drugs [11] - [39]

• Our network meta-analysis also assessed the odds ratios for adverse events associated with the use of different drugs for obesity. The results indicate potential safety concerns for certain drugs.

• ORLI exhibited a relatively lowest odds ratio of 0.138, suggesting a safest. This indicates the lowest likelihood of adverse events associated with ORLI compared to placebo.

• PHEN/TPM combination displayed a relatively higher odds ratio of 0.465, indicating a potential safety concern when compared to some of the other drugs. This suggests a higher risk of adverse events associated with the PHEN/TPM combination compared to placebo.

• The BUP/NLX combination demonstrated an odds ratio of 0.198.

• SGT showed a moderate odds ratio of 0.138, indicating a potential safety concern. This suggests a moderate risk of adverse events associated with SGT compared to placebo.

• LIRA shows moderate odds ratio among the listed drugs, with a value of 0.456. This indicates a potential safety profile for LIRA compared to all the other drugs, with risk of adverse events.

• In summary, the ranking of the drugs based on their odds ratios for adverse events is as follows: ORLI>BUP/NLX>LIRA>PHEN/TPM>SGT. These findings provide important insights into the potential safety concerns associated with these drugs and can guide healthcare professionals in their decision-making process when selecting obesity treatment options.

DISCUSSION

The present study aimed to evaluate the efficacy and safety of five anti-obesity drugs through a meta-analysis of randomized controlled trials. The findings provide valuable insights into the comparative effectiveness and potential side effects of these medications.

The meta-analysis revealed that the BUP/NLX combination exhibited the highest efficacy among the evaluated drugs, followed by LIRA and SGT. These results can be compared with previous study Singh et al. Which also compared the efficacy and safety of these drugs. [40] Cichoń et al.have

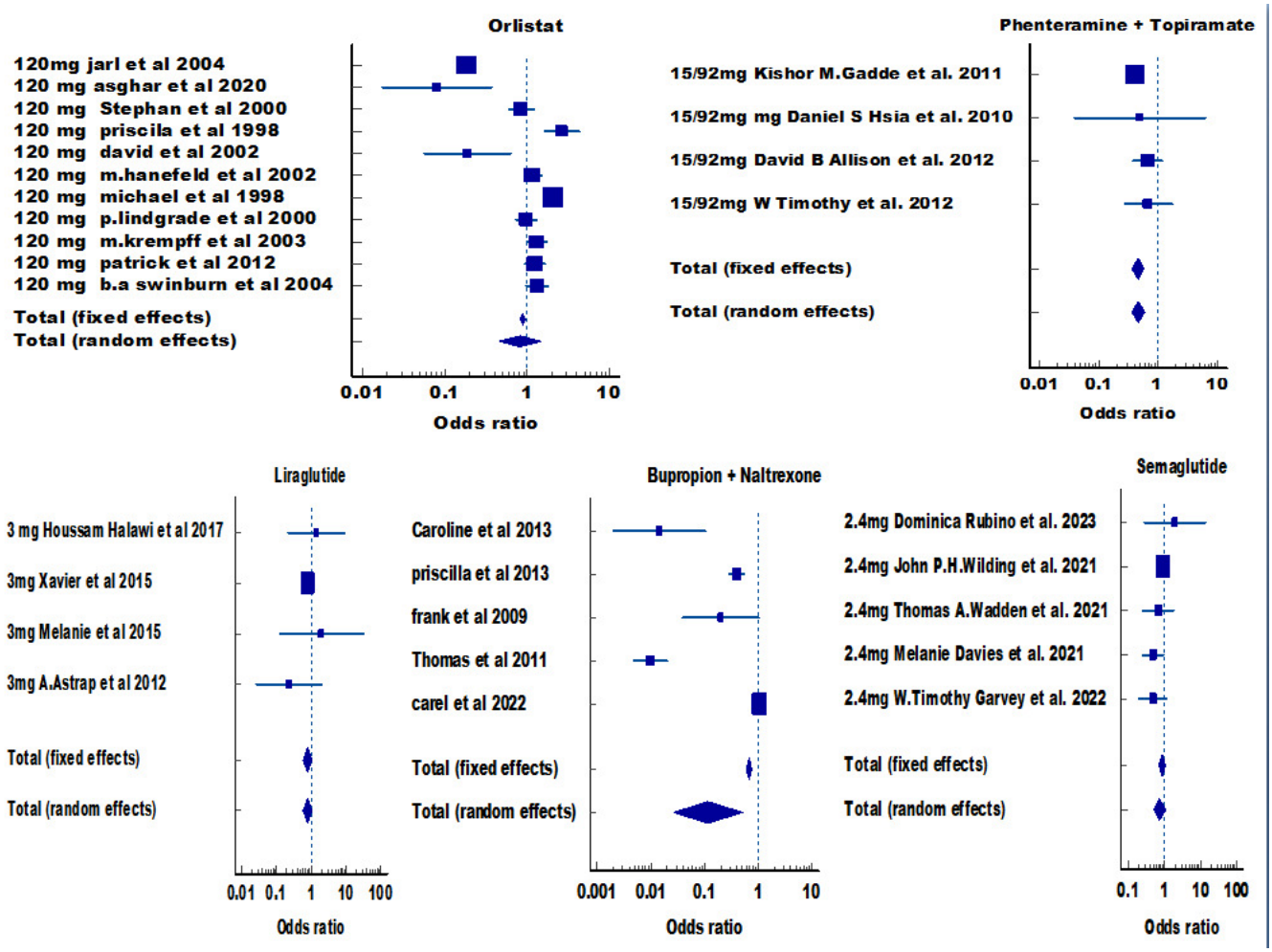

Figure 7: Forest Plot showing efficacy of five anti-obesity drugs [11] - [39]

demonstrated that among the currently available drugs for obesity, the most effective are PHEN/TPM combination and LIRA. [41]Calderon et al.has shown that the most prescribed medication was PHEN/TPM followed by LIRA but our study advises to choose a drug with a better safety profile and efficacious. [42]

The results have demonstrated the weight-reducing effects of these medications. The BUP/NLX combination has shown robust efficacy in promoting weight loss, which can be attributed to the combined mechanisms of action targeting appetite control and satiety. ORLI a lipase inhibitor, also demonstrated significant weight reduction, indicating its effectiveness in inhibiting fat absorption. LIRA, a glucagon-like peptide-1 [GLP-1] receptor agonist, showed moderate efficacy in weight loss compared to other drugs.

Qiucen et al. has done a meta-analysis of LIRA which has demonstrated a significant weight reduction with LIRA but patients has experienced at least one adverse event. [43]

A meta analysis by Viner RM et al. showed Orlistat modestly reduces BMI with a high prevalence of gastrointestinal adverse effects which can be compared with our study. [44]

In terms of safety, ORLI was found to have the lowest incidence of side effects among the evaluated drugs. This is consistent with the known safety profile, which has been extensively studied and utilized in clinical practice. [45]On the other hand, ORLI was associated with the lowest incidence of side effects, possibly due to its mechanism of action involving lipase inhibition. [46]

In comparison to other studies, our findings are consistent with the existing body of literature. The efficacy of the PHEN/TPM combination, ORLI and LIRA in promoting weight loss has been consistently reported across various studies. [47] [48] [49] [50]However, it is worth noting that variations in study designs, patient populations, and treatment duration can contribute to differences in the reported effectiveness and safety outcomes.

The primary strength of this study lies in its robust methodology, which involved a systematic assessment of data from randomized controlled trials conducted over a minimum duration of 6 months. It stands out as a unique study that comprehensively evaluates the efficacy and safety of five currently approved anti-obesity medications simultaneously. Notably, the study provides a comprehensive

perspective by specifically examining gastrointestinal [GI] related adverse events, adding valuable insights to the safety profile analysis.

However, there are a few limitations that need to be acknowledged. Firstly, the study relied on aggregated data rather than individual patient data, which may introduce inherent biases and limit the precision of the findings. Furthermore, the high attrition rates observed in some of the included trials may potentially introduce bias and impact the generalizability of the results. The considerable heterogeneity across the included studies may pose challenges in drawing definitive conclusions. we have only compared commonest adverse effect in terms of Gastrointestinal side effects in form of Nausea/Vomiting and Diarrhoea. There are other adverse drug reactions also associated with drugs but since there was no uniformity among them in studies, we have not included those. Additionally, it is important to note that the study did not employ the GRADE [Grading of Recommendations Assessment, Development, and Evaluation] approach for evaluating the quality of evidence.

Acknowledging these limitations, future research should aim to address these concerns by incorporating individual patient data, minimizing attrition rates, and considering the GRADE approach for a comprehensive assessment of the evidence. Despite these limitations, the current study provides valuable insights into the comparative efficacy and safety of the evaluated anti-obesity medications and offers a foundation for further investigations in this field.

These findings have important clinical implications for the management of obesity. The BUP/NLX , LIRA , and SGT can be considered as effective treatment options for weight reduction. However, healthcare providers need to carefully consider the safety profiles and potential side effects of these medications when making treatment decisions. Patient preferences, comorbidities, and individual response to treatment should also be taken into account.

CONCLUSION

The network meta-analysis revealed significant variations in the effectiveness and safety of the FDA approved medications used to treat obesity.

The combination has the highest odds ratio for efficacy, suggesting it may be more effective for weight loss. LIRA, SGT, also have relatively high odds ratios, indicating significant associations with weight loss. PHN/TPM combination has the lowest odds ratio among the listed drugs, suggesting a comparatively weaker association with weight loss.

BUP/NLX combination and LIRA emerged as the most effective medications for weight loss, indicating their potential as valuable therapeutic options. These medications, when prescribed under appropriate medical supervision, can lead to substantial weight reduction in individuals with obesity. However, they also get the top spot for maximum side effects. BUP/NLX combination also has moderate odds ratios, suggesting a potential for safety concerns. ORLI, and PHN/TPM have relatively lower odds ratios, indicating potentially better safety profiles.

It is important to note that medication selection should be individualized, considering patient characteristics, medical history, and potential contraindications. Furthermore, long-term safety and efficacy data are crucial in determining the sustained benefits and potential risks associated with these medications.

Overall, this network meta-analysis provides valuable insights into the comparative effectiveness and safety of the studied obesity medications. Healthcare professionals can utilize this information to make informed decisions when selecting pharmacological interventions for patients with obesity, aiming to achieve optimal weight management outcomes while prioritizing patient safety.

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