Research-based Capstone - Epidemiology & Biostatistics Concentration, Master of Public Health

Comparative Effectiveness of Anti-Obesity Medications on Body Weight and Glycemic Control in Overweight/Obese Adults with Type 2 Diabetes: Systematic Review and Network Meta-Analysis of Randomized Controlled Trials

Chow Man Lok, Ko Lee Fong, Prof. Chenwen Zhong & Prof. Junjie Huang
The Jockey Club School of Public Health & Primary Care, The Chinese University of Hong Kong
Contact email: 1155009101@link.cuhk.edu.hk

Introduction

Background: Type 2 diabetes mellitus (T2DM) is closely linked to overweight and obesity, where weight reduction may lead to improved glycemic control and disease management.(1-3)

Aims: This study assessed the comparative effectiveness of six anti-obesity medications (AOMs) recommended by American Diabetes Association (ADA)—tirzepatide, semaglutide, liraglutide, orlistat, phentermine/topiramate, and bupropion/naltrexone—in overweight or obese adults with T2DM.(4)

Knowledge Gaps:

1. Existing reviews on AOMs evaluated efficacy without considering diabetes status and excluded tirzepatide.(5, 6)
2. Some studies assessed tirzepatide as a GLP-1 RA in diabetes, but none compared it to orlistat, phentermine /topiramate, or bupropion/ naltrexone in overweight or obese patients with diabetes.(7-10)

Methodology

A systematic review and network meta-analysis were performed using randomized controlled trials (RCTs) retrieved from PubMed, EMBASE, CENTRAL, and ClinicalTrials.gov through March 2025. RCTs with a follow-up duration of at least 12 weeks that meet all elements of the PICO framework are eligible for inclusion.

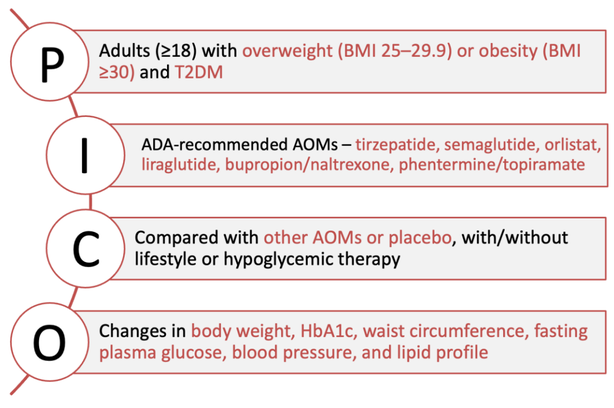


Figure 1. Details of PICO requirement adopted in this systemic review

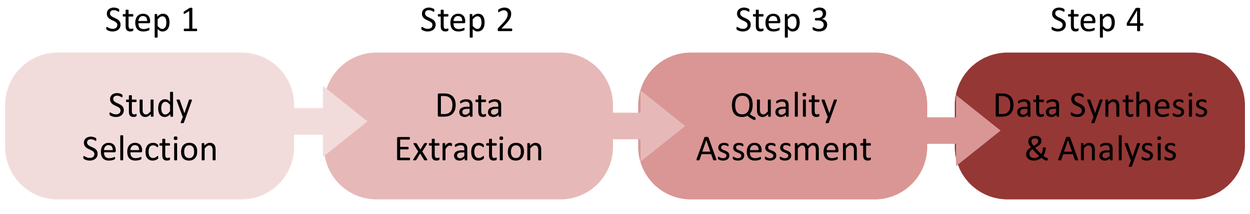


Figure 2. Flow chart of study methodology

Results

A total of 25 trials involving 10,403 participants were included:

- All AOMs were superior to placebo in reducing body weight, with tirzepatide demonstrating the largest effect (–10.16kg; 95% confidence interval –11.873 to –8.450), followed by phentermine/topiramate (–6.272kg (–9.644 to –2.899)) and semaglutide (-5.570kg (–6.788 to –4.353)).
- Tirzepatide also showed the greatest HbA1c reduction (–19.72mmol/mol (–23.856 to –15.580)), while orlistat showed favorable effects on lipid parameters. Phentermine/topiramate and naltrexone/bupropion showed minimal benefit in HbA1c reduction.
- Sensitivity analyses, and comprehensive dose-specific analysis supported the robustness of the findings.

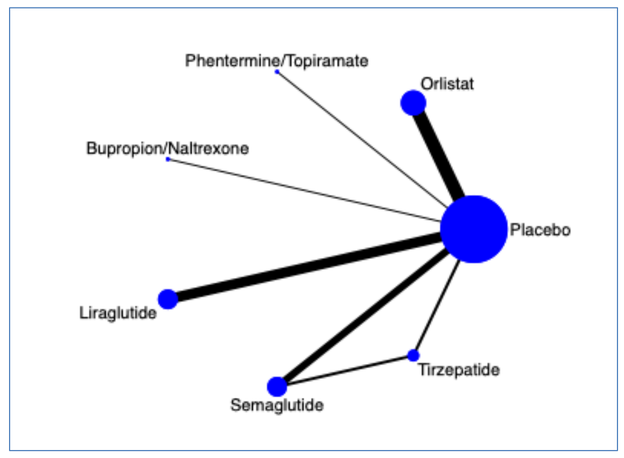
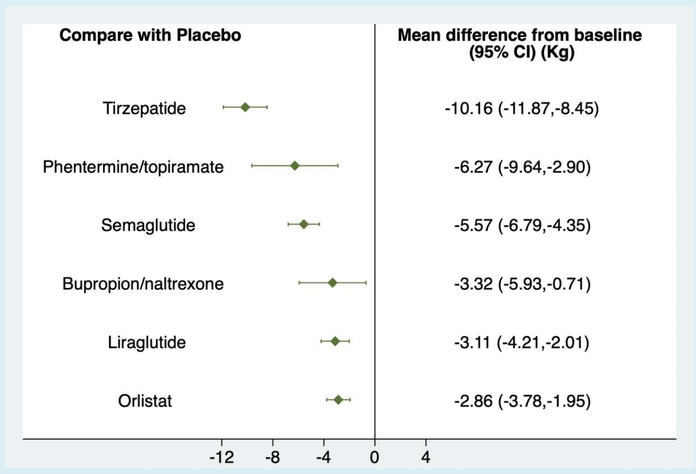
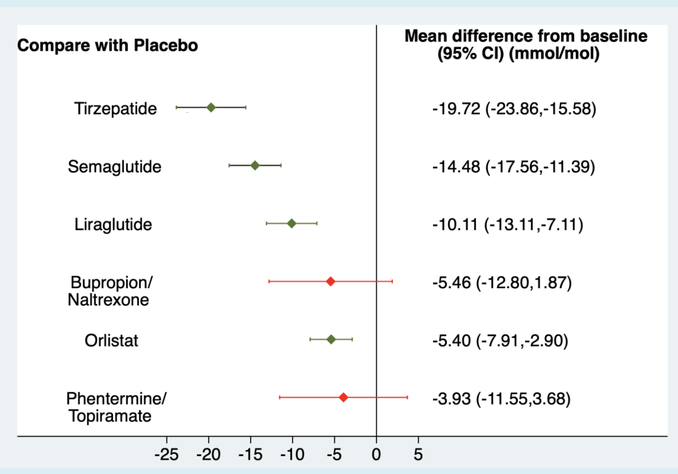


Figure 3. Network diagram of available comparisons for body weight and HbA1c



◄ Figure 4. Forest plot of effect sizes for body weight. All AOMs showed statistically significant reduction in body weight compared to placebo ($p < 0.05$). Treatments from most to least effective were: tirzepatide, phentermine / topiramate, semaglutide, bupropion / naltrexone, liraglutide, and orlistat



◄ Figure 5. Forest plot of effect sizes for HbA1c. Tirzepatide, semaglutide, liraglutide, and orlistat showed significant reductions in HbA1c compared to placebo ($p < 0.05$), whereas phentermine / topiramate and bupropion / naltrexone did not show significant effects ($p > 0.05$). Treatments from most to least effective were: tirzepatide, semaglutide, liraglutide, and orlistat.

Conclusion

This study offers comprehensive comparison of ADA-recommended anti-obesity medications in overweight or obese adults with T2DM. Tirzepatide and semaglutide emerged as effective options, while orlistat remains a cost-effective alternative with additional lipid-lowering benefits. These findings may guide personalized treatment in clinical practice.

References

1. Moosaie F, Ghaemi F, Mechanick JI, Shadnoush M, Firouzabadi FD, Kermanchi J, et al. Obesity and diabetic complications: a study from the nationwide diabetes report of the National Program for Prevention and Control of Diabetes (NPPCD-2021) implications for action on multiple scales. Primary Care Diabetes. 2022;16(3):422-9.

2. Lean ME, Leslie WS, Barnes AC, Brosnahan N, Thom G, McCombie L, et al. Durability of a primary care-led weight-management intervention for remission of type 2 diabetes: 2-year results of the DiRECT open-label, cluster-randomised trial. The lancet Diabetes & endocrinology. 2019;7(5):344-55.

3. Kahan S, Fujioka K. Obesity pharmacotherapy in patients with type 2 diabetes. Diabetes Spectrum: a Publication of the American Diabetes Association. 2017;30(4):250.

4. Care D. Standards of Care in Diabetes—2023. Diabetes care. 2023;46:S1-S267.

5. Singh AK, Singh R. Pharmacotherapy in obesity: a systematic review and meta-analysis of randomized controlled trials of anti-obesity drugs. Expert review of clinical pharmacology. 2020;13(1):53-64.

6. Iannone A, Natale P, Palmer SC, Nicolucci A, Rendina M, Giorgino F, et al. Clinical outcomes associated with drugs for obesity and overweight: A systematic review and network meta-analysis of randomized controlled trials. Diabetes, Obesity and Metabolism. 2023;25(9):2535-44.

7. Alhindi Y, Avery A. The efficacy and safety of oral semaglutide for glycaemic management in adults with type 2 diabetes compared to subcutaneous semaglutide, placebo, and other GLP-1 RA comparators: A systematic review and network meta-analysis. Contemporary clinical trials communications. 2022;28:100944.

8. Nuhoho S, Gupta J, Hansen BB, Fletcher-Louis M, Dang-Tan T, Paine A. Orally administered semaglutide versus GLP-1 RAs in patients with type 2 diabetes previously receiving 1–2 oral antidiabetics: systematic review and network meta-analysis. Diabetes Therapy. 2019;10:2183-99.

9. Caruso I, Di Gioia L, Di Molfetta S, Cignarelli A, Palmer SC, Natale P, et al. Glucometabolic outcomes of GLP-1 receptor agonist-based therapies in patients with type 2 diabetes: a systematic review and network meta-analysis. EClinicalMedicine. 2023;64.

10. Yao H, Zhang A, Li D, Wu Y, Wang C-Z, Wan J-Y, et al. Comparative effectiveness of GLP-1 receptor agonists on glycaemic control, body weight, and lipid profile for type 2 diabetes: systematic review and network meta-analysis. bmj. 2024;384.