Bayesian Network Meta-Analysis (NMA) of Weight Loss Efficacy for GLP-1 (Glucagon-like peptide-1) Receptor Agonists and Tirzepatide

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INTRODUCTION

- According to the World Obesity Atlas 2023, obesity (BMI ≥25 kg/m²) affected over 2.6 billion people globally in 2020 and is forecasted to exceed 4 billion by 2035 (1).
- GLP-1 receptor agonists (liraglutide, semaglutide) and the dual GLP-1/GIP (glucose-dependent insulinotropic polypeptide) agonist tirzepatide has shown significant weight reduction in clinical trials (2). However, head-to-head studies remain scarce, limiting the availability of comparative effectiveness evidence.
- A Bayesian NMA enables robust statistical framework to perform indirect comparisons across therapies and can yield a single, integrated estimate of their relative weight loss efficacy.

OBJECTIVE

This Bayesian NMA aims to compare the effectiveness of GLP-1 receptor agonists (liraglutide, semaglutide) and the dual GLP-1/GIP receptor agonist tirzepatide on weight loss.

METHOD

Study identification and data extraction:

- A systematic literature search was conducted across PubMed, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL).
- The search was restricted to randomized controlled trials (RCTs) and English-language publications.
- Data were extracted on study/trial name, full reference, study design, phase of the study, a summary of the study population characteristics, specific treatments administered, follow-up duration, and the effect size for the primary outcome (mean change in body weight from baseline).

Network meta-analysis model selection:

- A random-effects model was selected for this NMA considering the heterogeneity across studies. Although a random-effects model captures statistical heterogeneity, it does not automatically account for clinical or methodological differences that could compromise transitivity.

Bayesian model implementation:

- The Bayesian random-effects NMA was conducted using JAGS in R.
- Vague or non-informative normal priors were assigned for treatment effects and heterogeneity.

MCMC Simulation and Diagnostics:

- Three MCMC chains were run for 100,000 iterations with 50,000 burn-in.
- Model diagnostics were performed to assess the convergence and the overall quality of posterior samples via trace plots, Gelman-Rubin diagnostics, and effective sample size.

Output generation:

- Key outputs included pairwise comparisons of treatment with 95% credible intervals (CrI), along with league tables, forest plots, treatment ranking, and Surface Under the Cumulative Ranking Curve (SUCRA) values to summarize the relative weight-loss efficacy across interventions.

RESULTS

	Placebo	Liraglutide	Semaglutide	Tirzepatide
Placebo	-	5.35 (4.77, 5.95)	12.35 (11.66, 13.04)	22.10 (21.19, 23.01)
Liraglutide	-5.35 (-5.95, -4.77)	-	7.00 (6.13, 7.87)	16.75 (15.82, 17.68)
Semaglutide	-12.35 (-13.04, -11.66)	-7.00 (-7.87, -6.13)	-	9.75 (8.88, 10.61)
Tirzepatide	-22.10 (-23.01, -21.19)	-16.75 (-17.68, -15.82)	-9.75 (-10.61, -8.88)	-

Table 1. Mean difference in weight loss, kg (95% Credible intervals).

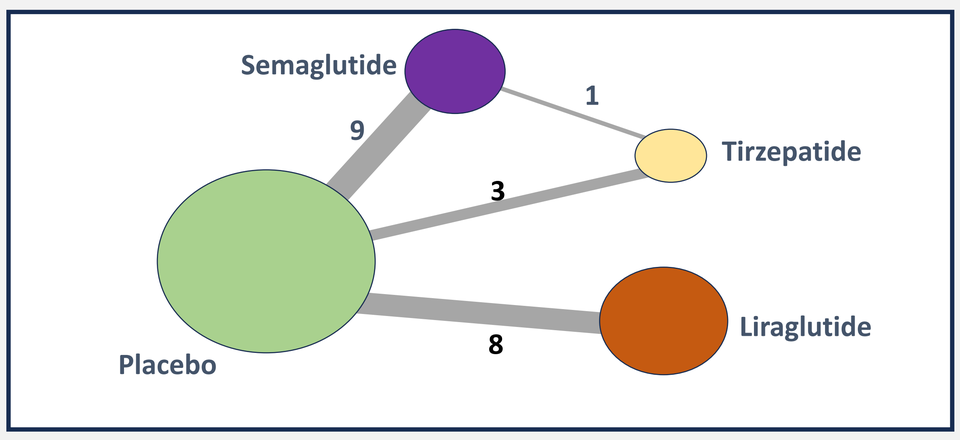

Figure 2. Network of Evidence for Weight Management Agents.

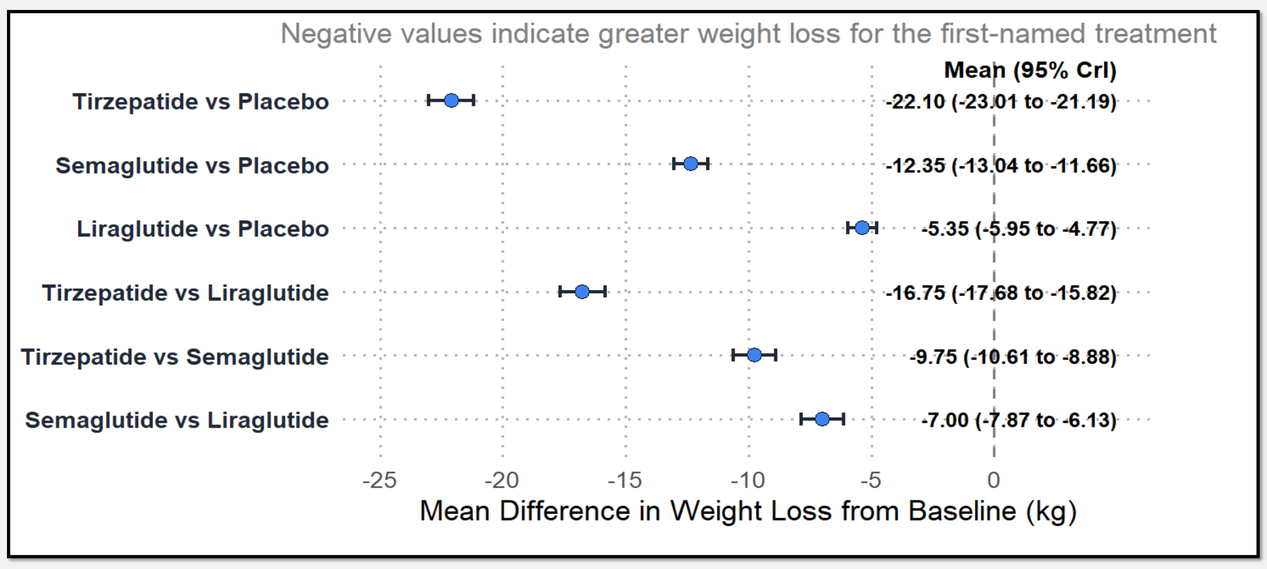

Figure 1. Network Meta-Analysis Forest Plot: Pairwise Mean Difference (kg).

- The network meta-analysis synthesized data from 21 different studies and included 21 treatment comparisons.
- Statistical diagnostics confirmed strong model reliability, with excellent convergence and minimal between-study heterogeneity measured at 0.29 kg (95% credible interval: 0.03 to 1.25 kg).
- Tirzepatide (pooled analysis) resulted in the greatest average weight loss vs. placebo, with a reduction of -22.10 kg (95% CrI: -23.01 to -21.19 kg).
- Semaglutide and Liraglutide also produced substantial weight loss compared to placebo: Semaglutide (-12.35 kg, 95% CrI: -13.04 to -11.66) and Liraglutide (-5.35 kg, 95% CrI: -5.95 to -4.77).
- Across all pairwise comparisons and SUCRA rankings, Tirzepatide consistently emerged as the most effective treatment option for weight loss.

CONCLUSIONS

In this Bayesian NMA Tirzepatide demonstrated the greatest average weight loss (-22.10 kg (95% CrI: -23.01, -21.19)) compared with liraglutide, semaglutide, dulaglutide, insulin degludec, and placebo. However, the analysis did not account for dose-dependent effects or adjust for differences among patients, which warrants further investigation.

LIMITATIONS

- This NMA considers a sole endpoint of mean weight loss from baseline and other outcomes such as waist circumference, proportion achieving a certain weight loss threshold, changes in metabolic parameters, adverse events and quality of life were not included.
- Publication bias and Risk of bias assessment weren't conducted.

REFERENCES

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