

Comment on: “Relative Effectiveness and Safety of the GLP-I Receptor Agonists, Semaglutide and Liraglutide in the Treatment of Obese Type 2 Diabetics” [Letter]

Huina Zhu¹, Haoyue Jin², Binru Wang²

¹Department of Critical Care Medicine, Shaoxing Central Hospital Affiliated to China Medical University, Shaoxing, Zhejiang, 312030, People's Republic of China; ²Department of Clinical Medicine, North Sichuan Medical College, Nanchong, Sichuan, 637000, People's Republic of China

Correspondence: Haoyue Jin, Department of Clinical Medicine, North Sichuan Medical College, Nanchong, Sichuan, 637000, People's Republic of China, Email 3241615021@qq.com

Dear editor

Hoffmann et al's comparison of semaglutide and liraglutide offers important insights for managing obese T2DM patients.¹ The inclusion of waist circumference as a visceral adiposity marker is particularly useful for clinical practice. That said, we believe several public health dimensions merit further consideration to enhance the work's translational impact.

First and foremost, health equity issues must be addressed. The advantages of semaglutide in terms of BMI reduction ($\Delta=0.96$ kg/m², $p=0.017$) and waist circumference improvement (-10.7 cm vs -7.2 cm, $p=0.002$) must be weighed against its significantly higher cost.² In healthcare systems with limited resources, such as those in Eastern Europe, this may inadvertently exacerbate treatment inequalities. Future research could strengthen this issue by quantifying the cost-effectiveness ratio (eg, the cost per unit BMI/waist circumference improvement in euros €/kg/m²) and examining prescribing differences across different income/education levels.

Secondly, the clinical significance of the observed differences needs further clarification. Although changes in BMI and waist circumference were statistically significant (Δ BMI ≥ 0.96 kg/m², waist circumference change -10.7 cm vs -7.2 cm), they still raise important clinical questions: Does this BMI change translate into a clinically meaningful reduction in risk? Presenting the data in reference to established standards (such as the $\geq 5\%$ weight loss threshold proposed in the ADA 2025 guidelines³) would be more valuable; while the improvement in waist circumference suggests potential for cardiovascular risk regulation, an absolute risk assessment model would be more effective in supporting policy decisions.

Third, the potential for preventing comorbidities has not been fully explored. Current research has not evaluated whether the improvement of anthropometric indicators (such as BMI and waist circumference) is associated with the following clinical outcomes: including a reduction in components of metabolic syndrome (eg, a decrease in the incidence of new-onset hypertension), as well as gender-specific health outcomes—particularly the fact that the predictive value of waist circumference changes for female cardiovascular risk is significantly stronger.⁴

Public Health Recommendations

At the policy level, it is recommended that the National Drug Catalog explore a tiered pricing mechanism for semaglutide, prioritizing coverage for high-risk subgroups (specific criteria: waist circumference >102 cm for men or >88 cm for women). The research focus should concentrate on three dimensions: first, conducting direct efficacy comparison trials in diverse populations with recently approved drugs (eg, tirzepatide); second, using electronic health

records to track cardiovascular events for long-term prognosis assessment; and third, identifying systemic barriers to GLP-1 receptor agonist use in primary care through implementation research.

Conclusion

This study advances our understanding of GLP-1 RAs in real-world settings. To maximize public health impact, subsequent work should address cost barriers, clarify clinical thresholds, and evaluate comorbidity prevention – aligning with WHO diabetes reduction targets.

A Data Availability Statement

The authors confirm that the data supporting the findings of this study are available within the article [and/or] its supplementary materials.

Author Contributions

Huina Zhu: Writing – original draft.

Binru Wang: Data curation, Visualization.

Haoyue Jin: Conceptualization, Supervision, Writing – review & editing.

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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