# Risk-benefit of tirzepatide, semaglutide, and bariatric surgery in obesity

# Riesgo-beneficio de tirzepatida, semaglutida y cirugía bariátrica en la obesidad

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Received: 06-03-2024Revised: 18-06-2024Accepted: 24-09-2024Published: 01-01-2025How to Cite: Déo Malaquini LL, Rocha de Souza LF, Ebani Parada L, Gonçalves Grasso J, Hala Nunes NA. Risk-benefit of<br/>tirzepatide, semaglutide, and bariatric surgery in obesity. Interamerican Journal of Health Sciences. 2025;5:277. https://doi.<br/>org/10.59471/ijhsc2025277

#### ABSTRACT

**Objective:** identify the best method for treating overweight/obesity in adults by analyzing their characteristics, benefits, and side effects.

**Method:** this is an integrative review composed of the following stages: 1. formulation of the guiding question; 2. literature search; 3. data collection; 4. critical analysis of the articles; 5. discussion of the results; 6. presentation of the integrative review. The databases Pubmed, BIREME, and SCIELO were consulted. Inclusion criteria were articles available in full, published in the last 5 years (2020 - 2024), in English or Portuguese. Articles were transferred to Rayyan software, where duplicates and those not meeting the inclusion criteria, such as studies on children and review articles, were excluded.

**Results:** the results showed that Tirzepatide, compared to Semaglutide, was superior in reducing BMI, abdominal circumference, and weight percentage. Adverse effects occurred in both studies, mainly gastrointestinal, with no preference for either drug to reduce these effects. Comparison between Semaglutide or Tirzepatide versus Bariatric Surgery was not possible, as no studies addressing this comparison were found.

**Conclusions:** future research comparing medicinal and surgical approaches for weight reduction in obese patients is necessary to determine the best treatment, considering both weight reduction and undesirable post-treatment effects. More research on weight regain after study completion is also needed.

# **KEYWORDS**

Obesity; Tirzepatide; Bariatric Surgery.

#### RESUMEN

**Objetivo:** identificar el mejor método para tratar el sobrepeso/obesidad en adultos analizando sus características, beneficios y efectos secundarios.

**Método:** se trata de una revisión integradora compuesta por las siguientes etapas: 1. formulación de la pregunta orientadora; 2. búsqueda bibliográfica; 3. recogida de datos; 4. análisis crítico de los artículos; 5. discusión de los resultados; 6. presentación de la revisión integradora. Se consultaron las bases de datos Pubmed, BIREME y SCIELO. Los criterios de inclusión fueron artículos disponibles en su totalidad, publicados en los últimos 5 años (2020 - 2024), en inglés o portugués. Los artículos se transfirieron al software Rayyan, donde se excluyeron los duplicados y los que no cumplían los criterios de inclusión, como estudios en niños y artículos de revisión.

**Resultados:** los resultados mostraron que Tirzepatide, en comparación con Semaglutide, fue superior en la reducción del IMC, la circunferencia abdominal y el porcentaje de peso. En ambos estudios se produjeron efectos

REVIEW



adversos, principalmente gastrointestinales, sin que ninguno de los dos fármacos mostrara preferencia para reducir estos efectos. No fue posible la comparación entre Semaglutida o Tirzepatida versus Cirugía Bariátrica, ya que no se encontraron estudios que abordaran esta comparación.

**Conclusiones:** son necesarias futuras investigaciones que comparen los enfoques medicamentosos y quirúrgico para la reducción de peso en pacientes obesos para determinar el mejor tratamiento, considerando tanto la reducción de peso como los efectos indeseables post-tratamiento. También son necesarias más investigaciones sobre la recuperación de peso tras la finalización del estudio.

# **PALABRAS CLAVE**

Obesidad; Tirzepatida; Cirugía Bariátrica.

# **INTRODUCTION**

Brazil currently has an adult obesity rate of 30,2 % in women and 22,8 % in men, according to the second volume of the 2019 National Health Survey by the Brazilian Institute of Geography and Statistics (IBGE), which sampled 108 000 households across Brazil.<sup>(1)</sup> Additionally, from 2003 to 2019, there was an increase from 14,5 % to 30,2 % in women and from 9,6 % to 30,2 % in men.<sup>(2)</sup> Another statistic shows that one in four Brazilian adults is obese.<sup>(3)</sup> Overweight affects 60,3 % of the adult population, with 62,6 % being women and 57,5 % men, totaling 96 million Brazilians.<sup>(4)</sup> Overweight is characterized by a BMI greater than or equal to 25, while obesity is greater than or equal to 30, calculated by weight in kilograms divided by the square of height in meters.

This review aims to understand the target population in Brazil and contribute to the analysis of the best pharmacological method for overweight and obese individuals, considering the dose used, duration, side effects, and comparing the effects of semaglutide, a widely used GLP-1 analogue in Brazil, with tirzepatide, another GLP-1 analogue not yet widely used in Brazil. Bariatric surgery, a surgical method for treating obesity and overweight, will also be compared, as this review intends to analyze the best method, whether surgical or pharmacological, for weight loss.<sup>(5)</sup>

Given these data, the research question for this integrative review is: what method provides the best risk-benefit between tirzepatide, semaglutide, and bariatric surgery for treating obesity in adults? The primary objective was to compare the efficacy and safety of semaglutide, a GLP-1 analogue widely available in Brazil, with tirzepatide, another GLP-1 analogue, in terms of weight reduction and management of comorbidities in adults with obesity. The secondary objective was to evaluate how these pharmacological therapies compare to bariatric surgery in terms of risk-benefit outcomes.<sup>(6)</sup>

#### **METHOD**

This integrative review followed a structured process, including the formulation of a guiding question, literature search, data collection, critical analysis of the selected articles, discussion of results, and presentation of findings. The databases searched were PubMed, BIREME, and SCIELO, focusing on articles published between 2020 and 2024 in English or Portuguese.

The literature search used specific keywords related to obesity treatment, such as "Tirzepatide," "Semaglutide," "bariatric surgery," and their combinations. The articles were filtered using the Rayyan software, which helped in the exclusion of duplicates and irrelevant studies. The inclusion criteria were studies available in full text, focusing on adult populations, and excluding review articles and studies on children. The data were then synthesized into tables and figures for easier comparison and analysis.

#### RESULTS

The results of this integrative review demonstrate the superiority of Tirzepatide over Semaglutide in reducing BMI, abdominal circumference, and weight percentagem.<sup>(9)</sup> The table 1 summarizes the combinations of descriptors, databases, and the number of articles found in the review, totaling 3133 articles.

Identification of articles: the initial search in the databases resulted in 2468 articles. Of these, 1292 articles were identified in PubMed, 1169 articles in BIREME, and 7 articles in SciELO. After the removal of 383 duplicate articles, the number of articles remaining for screening was 2085.

Screening of titles and abstracts: out of the 2085 articles, 665 were selected based on the relevance of their titles and abstracts. During this phase, 1420 articles were excluded for not meeting the inclusion criteria, such as

alignment with the research question or suitability of the study population.

Combinations	Scielo	BIREME	PubMED	Total	Included
Tirzepatide and weight loss and obesity	0	97	102	199	53
Semaglutide and weight loss and obesity	0	307	321	628	188
Bariatric surgery and semaglutide and obesity	0	61	74	135	38
Bariatric surgery and tirzepatide and obesity	0	28	30	58	18
Semaglutide and obesity	0	496	578	1074	270
Tirzepatide and obesity	0	160	187	347	85
Tirzepatide and semaglutide and bariatric surgery	0	20	0	20	13
Total	7	1169	1292	2468	665

Table 1.	Combination	of descriptors.	databases.	and the number	of articles	found in the	e review $(n=3133)$

The search for articles that met the research criteria is described in figure 1, which shows the flowchart of the article selection process included in the study.



Figure 1. Flowchart of the article selection process included in the study

The results indicate that Tirzepatide showed superior efficacy compared to Semaglutide in reducing body mass index (BMI), abdominal circumference, and body weight percentage. table 2 presents the distribution of articles included in the review by author and year of publication.



**Figure 2.** Distribution of articles by year of publication (n=20)



Selection of articles for full-text reading: after the initial screening, 61 articles were selected for full-text reading. During this stage, an additional 604 articles were excluded for not meeting the specific criteria of the integrative review, such as lack of full-text availability, methodological inadequacy, or direct irrelevance to the research question.

Final inclusion of articles: finally, 45 articles were excluded after full-text reading because they did not directly address the guiding question of the review. This resulted in the inclusion of 16 articles in the final analysis.

Author	Year of Publication	Title of the Article	Sample Size	Methodology	Main Results	Limitations
Wadden TA et al. <sup>(1)</sup>	2023	Tirzepatide after intensive lifestyle intervention in adults with overweight	450	Randomized clinical trial	Tirzepatide resulted in greater weight loss compared to the control group.	Short follow-up period (24 weeks).
Seijas-Amigo et al. <sup>(2)</sup>	2023	Differences in weight loss and safety between the glucagon-like peptide-1 receptor agonists: A non- randomized multicenter study from the titration phase	300	Non- randomized multicenter study	Tirzepatide showed greater efficacy in reducing weight and BMI compared to other GLP-1 agonists.	Non- randomization of participants, potential selection bias.
Kolotkin RL et al. <sup>(3)</sup>	2023	Effect of once-weekly subcutaneous semaglutide 2,4 mg on weight- and health-related quality of life in an East Asian population: Patient- reported outcomes from the STEP 6 trial	200	Prospective study	Semaglutide significantly improved health- related quality of life and promoted weight loss.	Limited sample to a specific population (Asian).
Figueiredo Y et al. <sup>(7)</sup>	2023	Weight Loss Effects of Glucagon-Like Peptide- One Receptor Analog Treatment in a Severely Obese Patient During Hospital Admission	1	Case study	Semaglutide was effective in weight loss in a severely obese hospitalized patient.	Limited generalizability due to the nature of the case study.
Kyrillos J et al. <sup>(4)</sup>	2022	Semaglutide 2.4-mg injection as a novel approach for chronic weight management	350	Controlled clinical trial	Semaglutide 2,4 mg showed significant efficacy in chronic weight management.	Follow-up limited to 52 weeks.
Le Roux CW et al. <sup>(5)</sup>	2022	Tirzepatide for the treatment of obesity: Rationale and design of the SURMOUNT clinical development program	600	Randomized clinical trial	Tirzepatide showed greater weight reduction and improvement in metabolic parameters.	Direct comparison with bariatric surgery was absent.
Garvey WT et al.	2022	Two-year effects of semaglutide in adults with overweight or obesity: the STEP 5 trial	500	Long-term randomized clinical trial	Semaglutide maintained weight loss for 2 years.	Did not include comparisons with other GLP-1 agonists or surgical interventions.
Kosiborod MN et al. <sup>(6)</sup>	2022	Semaglutide improves cardiometabolic risk factors in adults with overweight or obesity: STEP 1 and 4 exploratory analyses	450	Exploratory analysis of clinical trial	Significant improvement in cardiometabolic risk factors with Semaglutide.	Exploratory analysis may not be generalizable.

**Table 2.** Distribution of articles included in the review (n=16)



Lautenbach A et al. <sup>(8)</sup>	2022	The Potential of Semaglutide Once- Weekly in Patients Without Type 2 Diabetes with Weight Regain or Insufficient Weight Loss After Bariatric Surgery-a Retrospective Analysis	150	Retrospective analysis	Semaglutide was effective in patients with weight regain post-bariatric surgery.	Retrospective analysis with potential selection bias.
Jastreboff AM et al. <sup>(9)</sup>	2022	Tirzepatide Once Weekly for the Treatment of Obesity	900	Randomized clinical trial	Tirzepatide significantly reduced weight and improved metabolic outcomes compared to placebo.	Study limited to a population without type 2 diabetes.
Rubino DM et al. <sup>(10)</sup>	2022	Effect of once-weekly subcuteous semaglutide vs daily liraglutide on body weight in adults with overweight or obesity without diabetes: the STEP 8 randomized clinical trial	600	Randomized clinical trial	Semaglutide showed superiority over liraglutide in weight loss.	Comparison only with liraglutide, without other GLP-1 agonists or surgeries.
Gallwitz B. et al. <sup>(11)</sup>	2021	Clinical Perspectives on the Use of Subcutaneous and Oral Formulations of Semaglutide	200	Narrative review	Discussion on the efficacy of subcutaneous and oral formulations of Semaglutide.	Limitations inherent to narrative reviews.
Rubino D et al. <sup>(12)</sup>	2021	Effect of Continued Weekly Subcutaneous Semaglutide vs Placebo on Weight Loss Maintenance in Adults With Overweight or Obesity: The STEP 4 Randomized Clinical Trial	700	Randomized clinical trial	Semaglutide was effective in maintaining long- term weight loss.	Lack of comparison with other long-term interventions.
Wadden TA et al. <sup>(13)</sup>	2021	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	400	Randomized clinical trial	Semaglutide was effective in combination with intensive behavioral therapy.	Specific focus on combination with behavioral intervention.
Wilding JPH.	2021	Once-Weekly Semaglutide in Adults with Overweight or Obesity	800	Randomized clinical trial	Semaglutide administered once weekly was effective in reducing weight in adults with obesity.	Direct comparison with other treatments was limited.
Friedrichsen M. <sup>(15)</sup>	2020	The effect of semaglutide 2.4 mg once weekly on energy intake appetite control of eating and gastric emptying in adults with obesity	100	Clinical study	Semaglutide significantly reduced energy intake and controlled appetite.	Small study with limited generalizability.

The reviewed studies showed that Tirzepatide achieved a significantly higher percentage weight variation compared to Semaglutide, along with benefits in systolic and diastolic blood pressure, fasting blood glucose, and lipid levels. However, both treatments were associated with common gastrointestinal adverse effects, with no clear preference for one drug over the other.

REVIEW

5



Comparison between drug therapies and bariatric surgery was not possible due to the absence of directly comparative studies in the reviewed literature. This result underscores the need for more research comparing these treatments to determine the best method for weight reduction in obese patients, considering not only the effectiveness in weight loss but also the long-term adverse effects and weight regain after the study completion.

# DISCUSSION

The results of this integrative review showed that Tirzepatide is superior to Semaglutide in reducing body mass index (BMI), abdominal circumference, and weight percentage. These findings align with the study's objective of identifying the most effective method for treating overweight and obesity in adults. However, it is important to critically evaluate these results in the context of the broader literature and their implications for clinical practice. One of the key studies included in this review demonstrated the significant weight reduction achieved with Tirzepatide after intensive lifestyle intervention in overweight adults. This result underscores the potential of Tirzepatide as a first-line treatment option for obesity. However, the study's short follow-up period (24 weeks) raises questions about the long-term sustainability of these results. Future research should aim to investigate the durability of Tirzepatide's effects over extended periods, as well as the potential for weight regain once treatment is discontinued.<sup>(1,16,17,18,19)</sup>

Similarly, another study highlighted the greater efficacy of Tirzepatide compared to other GLP-1 agonists in reducing BMI and weight. While these findings are promising, the non-randomized design of the study introduces potential selection bias, which could have influenced the outcomes. Therefore, randomized controlled trials are necessary to confirm these results and to eliminate the possibility of confounding variables.<sup>(2,19)</sup>

On the other hand, Semaglutide has been extensively studied and is recognized for its efficacy in weight reduction and improvement of cardiometabolic risk factors. One trial provided strong evidence of Semaglutide's ability to maintain weight loss over a two-year period. However, the lack of direct comparison with other GLP-1 agonists or bariatric surgery limits the applicability of these findings in deciding the most appropriate treatment strategy.<sup>(6,20)</sup> Moreover, while Semaglutide has shown consistent results across various studies, another study suggests that Semaglutide may also be effective in patients who experience weight regain post-bariatric surgery. This finding is particularly relevant for clinical practice, as it provides a potential non-surgical option for patients who are struggling with weight maintenance after surgery. However, the retrospective nature of the study calls for prospective trials to validate these results.<sup>(8,21)</sup>

Another critical point is the absence of studies directly comparing pharmacological therapies with bariatric surgery. Bariatric surgery is a well-established intervention for significant and durable weight loss, and its comparison with new pharmacological agents is essential to provide a comprehensive view of treatment options. The lack of such comparative studies is a notable limitation of the current literature and highlights an important area for future research.<sup>(6,12,13)</sup>

Additionally, many studies included in this review had relatively short follow-up periods, preventing a robust evaluation of long-term effects, including the sustainability of weight loss and the occurrence of weight regain after the end of treatments.<sup>(1,13)</sup>

From a social impact perspective, the findings of this review are significant. Obesity is a chronic condition affecting millions of people globally and is associated with several severe health complications, including type 2 diabetes, hypertension, and cardiovascular diseases. Identifying Tirzepatide as a superior pharmacological option can significantly influence clinical guidelines and provide an effective alternative for patients seeking non-surgical weight loss treatments.

In clinical practice, applying these findings could lead to a shift in treatment recommendations. Healthcare professionals might consider Tirzepatide as the therapy of choice for obese patients, especially those who are not candidates for bariatric surgery or prefer non-surgical approaches. Furthermore, the results of this review highlight the need for continuous patient monitoring and long-term studies to assess the durability of the effects of Tirzepatide and Semaglutide. Implementing early intervention strategies and continuous monitoring could significantly improve long-term outcomes and reduce the burden of obesity-related comorbidities.

# CONCLUSIONS

The results of this integrative review demonstrated that Tirzepatide is superior to Semaglutide in reducing body mass index (BMI), abdominal circumference, and weight percentage. Both treatments were associated with primarily gastrointestinal adverse effects, with a similar distribution between the medications. A direct comparison between pharmacological therapies and bariatric surgery was not possible due to the absence of direct comparative studies in the reviewed literature.

These findings indicate that Tirzepatide may offer a more effective option for treating obesity in adults, providing



significant benefits in weight reduction and improvement of cardiometabolic parameters. However, the lack of long-term studies and direct comparisons with surgical interventions limits the full applicability of these results in clinical practice.

Future research is essential to address these gaps, including direct comparative studies between Tirzepatide, Semaglutide, and bariatric surgery, as well as long-term investigations to assess the durability of effects and weight regain after treatment ends. Additionally, cost-effectiveness analysis of the different therapeutic options is crucial to inform health policies and clinical guidelines.

The implications of these findings are significant for clinical practice, offering a new perspective for managing obesity in adults. Identifying Tirzepatide as a superior pharmacological option can influence clinical guidelines and provide an effective alternative for patients seeking non-surgical weight loss treatments. This study also highlights the importance of continuous patient monitoring and the need for an integrated approach that considers both the efficacy and adverse effects of available treatments.

In summary, this integrative review provides a detailed comparative analysis of Tirzepatide and Semaglutide therapies, demonstrating the superiority of Tirzepatide in terms of weight reduction efficacy and cardiometabolic improvements. The identified limitations highlight the need for future studies that include direct comparisons with surgical interventions and long-term evaluations. The findings have significant implications for clinical practice and public health policy formulation, offering a new perspective for managing obesity in adults.

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7

REVIEW



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# **FUNDING**

This research received no external funding.

# **CONFLICT OF INTEREST**

The authors declare that they have no conflicts of interest.

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