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Use of Tirzepatide in the Management of Obesity and Overweight: Feasibility Analysis for Incorporation into the Public Health System of Mato Grosso, Brazil

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Abstract

Background/Objectives: Obesity is a chronic disease with high prevalence in Brazil. Tirzepatide (a dual GIP/GLP-1 agonist) has emerged as a highly effective alternative, albeit with substantial costs. This study assessed the feasibility of offering tirzepatide within the public health system of Mato Grosso, Brazil.

Methods: A systematic review was conducted to evaluate the efficacy and safety of tirzepatide in head-to-head comparisons with other anti-obesity medications. Additionally, a 5-year budget impact analysis (from the payer perspective, State Health Secretariat) and a short-term cost-effectiveness analysis (72 weeks) were performed for weight loss targets of ≥10%, ≥15%, ≥20%, and ≥25%. Two population scenarios were considered: a broad scenario (overweight with comorbidities and obesity) and a restricted scenario (BMI ≥35 with multiple comorbidities), with progressive uptake rates (10–50%).

Results: A single randomized controlled trial (SURMOUNT-5, n=751) directly compared tirzepatide versus semaglutide. Tirzepatide was superior in percentage weight reduction (difference -6.5%; 95% CI -8.1 to -4.9; p<0.001), waist circumference (-5.4 cm; 95% CI -7.1 to -3.6), and BMI (-2.7 points; 95% CI -3.3 to -2.0) after 72 weeks. The annual cost per patient was US$ 5,445.96 for tirzepatide and ranged from US$ 2,855.29 (first year) to US$ 3,274.83 (subsequent years) for semaglutide. In the broad scenario, the 5-year cumulative budget impact was US$ 9.38 billion for tirzepatide and US$ 5.59 billion for semaglutide. In the cost-effectiveness analysis, semaglutide had a lower cost per responder for ≥10% and ≥15% targets; costs were similar for the ≥20% target, and tirzepatide was more efficient for the ≥25% target.

Conclusions: Despite tirzepatide's superior efficacy, particularly for more aggressive weight loss targets, both technologies impose a substantial financial burden. These findings support the recommendation against state-level incorporation, especially in the broad population scenario.

Introduction

Obesity is a disease characterized by excessive or abnormal fat accumulation that poses a health risk (1). The identification and stratification of obesity are primarily based on Body Mass Index (BMI) and waist circumference measurements, both validated anthropometric indicators. BMI enables the classification of overweight (BMI 25–29.9 kg/m²) and obesity (BMI ≥ 30 kg/m²). Complementarily, waist circumference serves as a clinically relevant marker by reflecting central adiposity, which is associated with increased cardiometabolic risk. Progression in these parameters elevates the risk of clinical complications, potentially triggering type 2 diabetes, hypertension, coronary heart disease, stroke, heart failure, kidney disease, dyslipidemia, fatty liver disease, sleep apnea, and other associated comorbidities. Such complications are associated with increased mortality, reduced life expectancy, and a diminished quality of life (2, 3).

In recent decades, obesity prevalence has consistently increased among adults, adolescents, and children, establishing itself as a global epidemic with significant clinical, social, and economic

repercussions for healthcare systems. Since 1990, obesity rates have more than doubled among adults and quadrupled among children and adolescents (4). In line with global trends, 61.4% of the adult population in Brazilian state capitals is overweight; within this figure, 37.1% are classified as having overweight and 24.3% as having obesity (5). In Cuiabá, 55.8% of the population is overweight, with 33.3% presenting overweight and 22.5% have obesity (6).

Like other chronic diseases, obesity requires an integrated, long-term approach that considers individual therapeutic goals and the balance between benefits and risks of available options. Accordingly, additional efforts are needed to define personalized therapeutic strategies encompassing lifestyle interventions, anti-obesity medications, and bariatric surgery, as these approaches enhance the maintenance of associated health gains. Sustained weight loss exceeding 10% of total body weight improves many obesity-related complications, including control of type 2 diabetes, hypertension, fatty liver disease, and obstructive sleep apnea, as well as quality of life (7, 8).

Pharmacological intervention plays a substantial role. Among the medications approved by the Brazilian Health Regulatory Agency (ANVISA) for obesity treatment, liraglutide and semaglutide stand out. In June 2025, tirzepatide received formal label indication for chronic weight management in adults with elevated BMI. The incorporation and use of these therapies must consider clinical criteria such as BMI, comorbidities, and safety profile, as well as aspects related to access and economic implications for the healthcare system (9). In the state of Mato Grosso, a state protocol has been in effect since 2004, which includes the use of sibutramine and orlistat for obesity; however, the use of sibutramine as a therapeutic option is not recommended, although it remains an alternative to GLP-1 (glucagon-like peptide-1) based therapies, which tend to have a greater effect on weight loss (10).

Given the high epidemiological burden of obesity and the current therapeutic limitations within the Brazilian Unified Health System (SUS), this study aims to assess the feasibility of incorporating tirzepatide as an obesity therapy in the state of Mato Grosso, Brazil, considering both the scientific evidence on its efficacy and safety, as well as the estimate of its economic impact and potential implications for the healthcare system.

Methods

Evidence Synthesis

To conduct the evidence synthesis, a systematic review was developed to answer the research question, structured using the PICO framework (Population, Intervention, Comparison, Outcome). A search strategy was developed and adapted for the main databases: PubMed, BVS, Embase, Cochrane, and Web of Science. No date or language restrictions were applied (Supplementary Material 1).

Study screening was also performed in this software, in a blinded manner by three independent researchers; any discrepancies were resolved by consensus. Only clinical trials evaluating tirzepatide for

individuals with obesity compared with another active treatment were considered. Pre-clinical studies, case series, reviews, post-hoc analyses, conference abstracts, and letters to the editor were excluded.

Data extraction was performed independently by two reviewers using a standardized form. This form included the following information: study title, objectives, type of research, country or location where the study was conducted, sample size, sociodemographic characteristics of participants, follow-up duration, study population, interventions and comparators used, inclusion and exclusion criteria, methods employed, outcomes analyzed, results obtained, authors' conclusions, and study funding source.

To assess the methodological quality of each study, the revised Cochrane risk-of-bias tool for randomized trials (RoB 2.0) tool was used (11). The Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) tool was employed to evaluate the certainty of the evidence (12).

Economic Evaluation

A short-term cost-effectiveness analysis was conducted, comparing treatment costs and clinical outcomes for semaglutide and tirzepatide. Although less commonly used, the short-term cost-effectiveness analysis was chosen because it allows for a direct assessment of the cost required to achieve a specific clinical outcome, serving as a powerful tool in resource-limited settings and having been previously employed to evaluate the technology selected in this study (13).

Additionally, a budget impact analysis was performed to assess the potential inclusion of tirzepatide in the public health system of Mato Grosso.

1. **Short-term cost-effectiveness analysis**

Semaglutide was selected as the comparator for the economic analyses, as it was the only drug directly compared to tirzepatide in randomized clinical trials. This comparison is based on the SURMOUNT-5 trial, a phase 3b, open-label, multicenter study (32 sites in the United States and Puerto Rico) that included 751 adult participants with obesity or overweight and weight-related comorbidities, without type 2 diabetes (14).

The cost-effectiveness analysis considered a 72-week time horizon based on the SURMOUNT-5 trial (14) and focused solely on direct medical costs associated with the Unified Health System of the state of Mato Grosso. The objective was to compare tirzepatide with semaglutide, assessing which is more efficient in terms of the cost required to achieve a specific clinical outcome: the mean percentage change in body weight, calculated by least squares means. This reduction was categorized as: weight reduction of ≥ 10%; weight reduction of ≥ 15%; weight reduction of ≥ 20%; weight reduction of ≥ 25%.

The choice of a short-term cost-effectiveness analysis is primarily justified by the current lack of sufficient data on the long-term effects of tirzepatide, which makes it difficult to estimate potential quality of life improvements or to better understand the magnitude of weight loss effects on reducing

other obesity-related diseases. The conduct of this short-term cost-effectiveness analysis was based on findings from analyses produced in Greece to inform decision-makers and budget managers regarding the use of tirzepatide and semaglutide in obesity (13), as well as in the United Kingdom for managing and allocating health budget within the National Health Service (NHS), and in the United States to inform treatment efficiency for diabetes (15, 16).

Intervention (tirzepatide) and control (semaglutide) costs were calculated using the standard doses indicated in the prescribing information for these medications, considering a 72-week period (17, 18). The prices used are those suggested by the manufacturers for the state of Mato Grosso (19, 20).

To calculate the cost required to achieve a specific clinical outcome within a 72-week timeframe, we divided the total medication expenditure by the proportion of individuals who achieved the weight reduction target. Relative costs, which indicate the expenditure required to achieve each target per currency unit ($), were calculated based on the cost of tirzepatide. A deterministic sensitivity analysis was performed by varying the efficacy rates for the assessed outcome—percentage weight reduction—taking into account the standard error of these measures (Supplementary Material 2) (14).

2. Budget Impact Analysis – BIA

The state of Mato Grosso, located in Brazil's Central-West region, has a territorial extension of approximately 903 208 km², representing 10.6% of the national territory. The state's Human Development Index (HDI) is 0.736. The estimated population for 2025 was 3.9 million inhabitants distributed across 142 municipalities. Population density is low, with approximately 4 inhabitants per km², due to extensive rural and agricultural areas (21). In 2023, the state recorded a Gross Domestic Product (GDP) approximate of $ 52,46 billion, representing approximately 2.5% of the national economy and one of the highest GDPs per capita in Brazil (22). However, according to information from the National Supplementary Health Agency (ANS), in 2025 Mato Grosso recorded 688 389 beneficiaries of private health care plans, corresponding to a coverage rate of 18.82% (23).

In line with national trends, in Cuiabá, the capital of Mato Grosso, 61.6% of the population was overweight in 2023, while 27.2% were classified as obese (24). Although a state protocol, funded by the public health system, exists for obesity treatment, data from the state pharmaceutical assistance indicate no adherence to the protocol that provides sibutramine and orlistat. Therefore, the budget impact analysis did not account for reference scenario costs. Consequently, the incremental budget impact reflected only the financial implications resulting from the adoption of the new technologies, tirzepatide and semaglutide.

The study was developed based on the Ministry of Health's Methodological Guidelines for Budget Impact Analysis (25), considering the perspective of the Mato Grosso State Health Secretariat. It analyzed two scenarios: one with the incorporation of tirzepatide and an alternative scenario using semaglutide, both with a five-year time horizon. The study population included adults with overweight and at least one related health condition, as well as individuals with obesity. A more restricted scenario was also created,

including only adults aged 18 years or older with a BMI of 35 or higher and multiple comorbidities, a population similar to that of the SURMOUNT-5 study (14).

To calculate the eligible population, epidemiological demand was considered, taking into account the following parameters: individuals aged 18 years or older; prevalence of overweight and obesity in the population; the trend of increasing obesity in Mato Grosso; and the proportion of individuals with comorbidities among those with overweight or obesity (26–28).

In the model, only direct medication costs were considered, calculated based on the manufacturer's prescribing information (17, 18). Accordingly, we considered the dosage regimen, dose escalation until reaching the maintenance dose in the first year, and in subsequent years, only the maintenance dose. The cost per dose was also considered. The prices used in the treatment calculation were those offered by the manufacturers Eli Lilly and Company (Indianapolis, Indiana, USA) for tirzepatide and Novo Nordisk A/S (Bagsvaerd, Denmark) for semaglutide (19, 20). The parameters used in the modeling are described in Table 1.

Given the high prevalence of obesity in the population, the limited number of pharmacological options available through the SUS for treating this condition, and market pressure for new obesity medications, a progressive uptake rate over the years was adopted. Thus, we assumed a market share of approximately 50% for both the tirzepatide intervention and the standard treatment. Uptake was planned to increase gradually, with rates of 10%, 20%, 30%, 40%, and 50% in years 1, 2, 3, 4, and 5, respectively.

Sensitivity analysis of tirzepatide introduction was performed by simulating a scenario with a slower diffusion rate of 5%, 10%, 15%, 20%, and 25% (conservative scenario) and a fixed 20% reduction in drug cost from the second year onward, simultaneously. This cost reduction refers to an assumed premise.

For the alternative scenario with semaglutide adoption, a conservative scenario was simulated with a slower diffusion rate of 5%, 10%, 15%, 20%, and 25% and simultaneous cost reduction. The variation in the cost parameter considered a semaglutide patent expiration in 2026; we adjusted the semaglutide price, varying it by -10%, -20%, -30%, and – 40% in years 2, 3, 4, and 5, respectively (28).

Results

Evidence Synthesis

The search strategy retrieved 723 records, of which 583 titles and abstracts were screened, and only one study was eligible—a phase 3, randomized, open-label, multicenter clinical trial (SURMOUNT-5) that compared once-weekly tirzepatide 15 mg versus once-weekly semaglutide 2.4 mg in 750 adults with obesity or overweight (BMI ≥ 30 kg/m² or ≥ 27 kg/m² with comorbidities), with 72 weeks of follow-up. Mean age was 44.7 ± 12.8 years, 64.7% were female, and mean BMI was 36.1 ± 4.1 kg/m².

Tirzepatide showed a higher probability of achieving weight reductions of ≥ 10%, ≥ 15%, ≥ 20%, and ≥ 25%, with risk ratios (RR) of 1.3 (95% CI: 1.2–1.5), 1.6 (95% CI: 1.4–1.9), 1.8 (95% CI: 1.5–2.2), and 2.0 (95% CI: 1.5–2.6), respectively. Greater absolute weight reduction (mean difference − 7.9 kg; 95% CI: −9.7 to − 6.0), greater reduction in waist circumference (mean difference − 5.4 cm; 95% CI: −7.1 to − 3.6), and greater reduction in body mass index (mean difference − 2.7; 95% CI: −3.3 to − 2.0) were also observed compared to semaglutide. Regarding safety, the frequency of adverse events was similar between groups (76.7% with tirzepatide versus 79% with semaglutide).

The certainty of evidence according to the GRADE system was classified as moderate for efficacy outcomes (percentage and absolute weight reduction, BMI, waist circumference, and weight loss targets of ≥ 10% to ≥ 25%) and high for safety outcomes (total adverse events, serious adverse events, and discontinuation), indicating reasonable confidence in the estimated results, although based on a single comparative study (Supplementary Material 3). Methodological assessment using the RoB 2.0 tool indicated low risk of bias for most domains evaluated, with some concerns related to the lack of blinding (Supplementary Material 4 and 5).

Economic Evaluation

Over the 72-week time horizon, the estimated total medication cost was US$ 7 540.56 for tirzepatide and US$ 4 114.84 for semaglutide (Table 2).

The short-term cost-effectiveness analysis (72 weeks) indicates that the cost to achieve a 10% or 15% weight reduction is lower with semaglutide than with tirzepatide (Table 3). For a 20% weight loss, costs are similar between the two technologies, while for a 25% reduction, tirzepatide proves more efficient.

In the univariate sensitivity analysis, even when considering the lowest and highest efficacy values for both medications, the amount invested to achieve the targets (cost per responder) remains very similar to the base case result. This demonstrates that the model is robust and does not change substantially even when these factors vary (Table 4).

Budget Impact

The results show that both tirzepatide and semaglutide would generate a very substantial impact on the health system budget of the state of Mato Grosso. However, between the two technologies, tirzepatide tends to have greater effects compared to semaglutide (Table 5).

In the bivariate sensitivity analysis for the broad population scenario, it was clear that the model is primarily influenced by technology costs and uptake rates. This means that depending on the values of these factors, results may vary considerably, as observed in the analysis of the more restricted population scenario (Fig. 1).

Discussion

In the short-term cost-effectiveness analysis for weight loss targets of ≥ 10% and ≥ 15%, semaglutide showed a lower cost per responder; for the ≥ 20% target, costs were similar; for the ≥ 25% target, tirzepatide was slightly more efficient. These findings help qualify decisions regarding clinical scope (which weight loss target is sought) versus budgetary constraints. These findings enable decision-making based on the desired clinical scope: for clinically significant but less extreme weight loss, semaglutide may be the more economical option; for very substantial weight loss goals, tirzepatide may offer a cost-per-responder advantage.

The evidence presented in this study refers to the use of tirzepatide and semaglutide, both at maximum dose, over a 72-week period. The product labels do not specify a determined treatment duration, and it remains unclear whether treatment should be continuous. Therefore, consideration must be given to whether treatment discontinuation with these drugs leads to weight regain. A systematic review indicated that discontinuation of GLP-1RA (glucagon-like peptide-1 receptor agonists) therapy resulted in weight recovery close to the original weight loss. Individuals who used semaglutide/tirzepatide regained 9.69 kg (95% CI 5.78 to 13.60). Regarding waist circumference, 32.7% and 47.7% of this measurement was regained after discontinuation of semaglutide and tirzepatide, respectively. Similarly, the mean BMI increase after discontinuation of semaglutide/tirzepatide was 3.59 kg/m² (29).

Similar results were reported in another systematic review including 37 randomized controlled trials (30), indicating that, on average, weight regain occurs at a rate of 0.4 kg/month following discontinuation of anti-obesity medications, meaning there is a trend toward returning to baseline weight within 1.7 years. Furthermore, although weight loss helped improve cardiometabolic markers, these return to pre-treatment values approximately 1.4 years after discontinuation. This evidence on post-discontinuation weight regain reinforces the need for continuous treatment to maintain benefits, which, in turn, further exacerbates the budget impact from a long-term perspective, exceeding the 5-year horizon evaluated in this study.

The Budget Impact Analysis demonstrated that even assuming gradual uptake, there are billion-dollar annual expenditures for the population considering the prevalence of overweight individuals with comorbidities or obesity in the state of Mato Grosso. The annual per-patient cost for tirzepatide was US$ 5 445.96, while semaglutide costs US$ 2 855.29 in the first year and US$ 3 274.83 in subsequent years. The estimated aggregate budget impact with tirzepatide incorporation ranges from over 598 million US dollars in the first year to 3 199 billion in the fifth year of implementation. This impact is very significant when compared, for example, with the entire pharmaceutical assistance budget of the state of Mato Grosso for the year 2025, which was just over 22 million dollars. This budgetary asymmetry points to substantial financial infeasibility for large-scale incorporation of these technologies from the current state payer perspective, without significant resource reengineering or identification of new funding sources.

When simulating a more conservative and restricted scenario, involving only individuals with BMI ≥ 35 and multiple comorbidities, a significant reduction in budget impact was observed. However, even in this scenario, the values remain substantial, suggesting that the issue of budget sustainability and cost-effectiveness persists. This finding fuels an essential debate regarding the definition of eligibility criteria for access to high-cost therapies in public health systems, requiring a delicate balance between pressing clinical need and sustainable financial capacity.

In Brazil, no other reports evaluating the budget impact of tirzepatide for obesity were found. International Health Technology Assessment agencies were consulted to verify their positions regarding tirzepatide use in obesity (31–35). Of the five agencies, two (ref. 31–32) issued favorable opinions for tirzepatide use in managing obesity or overweight, associated with weight-related comorbidities, and in conjunction with a reduced-calorie diet and physical exercise. One agency (33) presented search results for tirzepatide, but these were related only to its use for type 2 diabetes treatment, and no recommendations were found from the other agencies (34–35).

It is known that managing overweight and obesity through new, more accessible, and easy-to-use technologies has been of interest to industry, governments, and society. A search of the ClinicalTrials.gov database in September 2025, aiming to identify potential medications for the treatment of overweight with comorbidities and obesity that have tested or are testing technologies for obesity management, retrieved 1 284 phase 3 or 4 clinical studies of technologies for obesity management in adults, children, and adolescents, the majority being medications. This search identified other promising molecules for obesity treatment, such as retatrutide. Thus, the expansion of therapeutic options available for obesity management, as well as patent expirations such as that of semaglutide scheduled for March 2026 in Brazil, may alter the medication market in terms of prices and product availability. The entry of generics or biosimilars could, in theory, catalyze a reduction in treatment costs and, consequently, expand access to these therapies, mitigating part of the budget impact currently observed. This dynamic factor should be continuously monitored and considered in future reassessments of the scenario.

Among the limitations of this study, we can point out that the cost-effectiveness analysis was short-term (72 weeks) and based on intermediate weight loss targets, not incorporating relevant final outcomes such as major cardiovascular events, mortality, or improvement in health-related quality of life. This limitation restricts the ability to infer the full value of these therapies for patients and the health system from a broader, long-term perspective. Another limitation is the use of prevalence data from Vigitel 2023 for the capital, which were extrapolated to the entire state of Mato Grosso; although pragmatic, this decision may introduce representativeness bias. The budget impact assessment considered only direct medication acquisition costs; it did not incorporate costs of monitoring, adverse event management, consultations, tests, nor potential savings from comorbidity reduction.

This study has strengths – the choice of short-term cost-effectiveness analysis links costs to efficacy outcomes (responders), favoring discussion of "value per clinical target," offering pragmatic information

for decision-making in a more immediate horizon. The budget impact assessment was conducted in accordance with national methodological guidelines (Brazilian Ministry of Health), with a clear perspective, defined horizon, and transparent presentation of parameters and internal report sources. The inclusion of both broad and restricted populations (BMI ≥ 35 with multiple comorbidities) allows assessment of sensitivity to clinical criteria directly related to incorporation governance.

In the context of Brazilian recommendations for health technology incorporation, new technologies are evaluated considering not only their efficacy and safety, but also their cost-effectiveness ratio, budget impact, and strategic relevance to the SUS. Although tirzepatide and semaglutide appear effective in obesity management, their costs are high; thus, we conclude that the incorporation of tirzepatide for obesity management in the state of Mato Grosso, Brazil, faces many barriers, especially due to the high budget impact and the possibility of weight regain. Furthermore, we emphasize the importance of integrated and sustainable therapeutic strategies – pharmacological treatment of obesity should always be associated with structured physical activity programs, nutritional counseling, and psychosocial support, which are fundamental to enhancing clinical effectiveness and reducing the risk of weight regain.

Declarations

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Author Contributions

KCFN was responsible for project conceptualization and coordination; methodology definition; identification, extraction, analysis, and interpretation of economic data; search, screening, data extraction, and methodological quality assessment of studies included in the evidence synthesis; and manuscript writing. GYN was responsible for extraction, analysis, and interpretation of economic data, production of graphs and tables, and manuscript writing. LEGO and HCO were responsible for search, screening, data extraction, and methodological quality assessment of studies included in the evidence synthesis, and manuscript writing. TMG and ZQB were responsible for data extraction and manuscript writing. EHMT and CBP were responsible for critical analysis of the manuscript and writing. AKSC played an important role in interpreting the results; was responsible for manuscript writing and final technical review. PPSP co-participated in project coordination and methodology design; manuscript writing and final technical review. All authors approved the final version of the manuscript and agree to be responsible for all aspects of the work.

Competing interests

The authors declare no competing interests.

Data Availability Statement

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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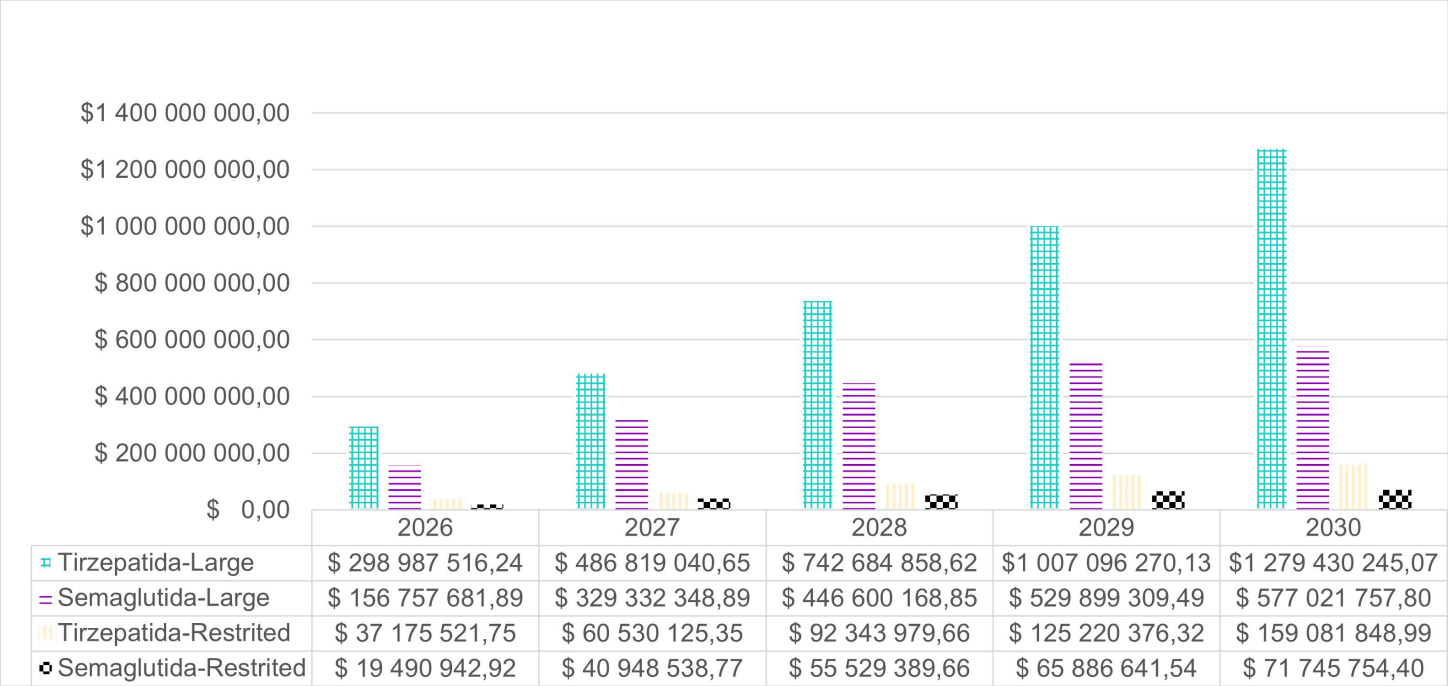
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Tables

Tables 1 to 5 are available in the Supplementary Files section.

Figures



	2026	2027	2028	2029	2030
Tirzepatida-Large	$ 298 987 516,24	$ 486 819 040,65	$ 742 684 858,62	$1 007 096 270,13	$1 279 430 245,07
Semaglutida-Large	$ 156 757 681,89	$ 329 332 348,89	$ 446 600 168,85	$ 529 899 309,49	$ 577 021 757,80
Tirzepatida-Restrited	$ 37 175 521,75	$ 60 530 125,35	$ 92 343 979,66	$ 125 220 376,32	$ 159 081 848,99
Semaglutida-Restrited	$ 19 490 942,92	$ 40 948 538,77	$ 55 529 389,66	$ 65 886 641,54	$ 71 745 754,40

Figure 1

Bivariate sensitivity analysis for large and restricted populations in US dollars $ (February 2026)

Legend: Restricted Population = Individuals with a BMI ≥35 with multiple comorbidities; Large Population = All individuals with obesity and individuals with overweight with at least 1 comorbidity.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Supplementary1.xlsx
- Suplementar2a5.pdf
- Table1.xlsx
- Table2.xlsx
- Table3.xlsx
- Table4.xlsx
- Table5.xlsx