RESEARCH ARTICLE

REVISED The short-term cost-effectiveness of once-weekly semaglutide versus once-weekly dulaglutide for the treatment of type 2 diabetes mellitus in Colombian adults [version 2; peer review: 2 approved]

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Abstract

Background

Type 2 Diabetes Mellitus (T2DM) is a highly prevalent disease worldwide and in Colombia, representing one of the main causes of death and placing a considerable burden on healthcare systems. 13 classes of drugs are approved for the treatment of T2DM, with Glucagon-like Peptide-1 (GLP-1) receptor agonists being a first-line treatment option for patients with or at high risk of certain cardiovascular diseases and chronic kidney disease. The objective of this study is to conduct a short-term cost-effectiveness analysis of once-weekly semaglutide versus once-weekly dulaglutide in Colombian adults with T2DM, from a third-party payer perspective.

Methods

Numbers needed to treat were calculated for different single and composite endpoints of the SUSTAIN 7 trial, annual costs for once weekly semaglutide 1.0 mg and dulaglutide 1.5 mg were extracted from the public SISMED database. With these inputs a cost of control model was developed, to obtain the annual cost of bringing one T2DM patient to relevant clinical outcomes by using semaglutide or dulaglutide.

Open Peer Review

Approval Status ✓ ✓

	1	2
version 2 (revision) 11 Dec 2023	✓ view	
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Any reports and responses or comments on the article can be found at the end of the article.

Results

Semaglutide was considered cost-effective compared to dulaglutide across all pre-specified endpoints, even in the different scenarios evaluated in the sensitivity analyses, and in a particularly pronounced manner for weight loss outcomes. Semaglutide at a dose of 1.0 mg once-weekly was cost-effective compared to dulaglutide 1.5 mg across all outcomes in the short-term, making it an appropriate first-line choice in the treatment of T2DM when deciding between these two GLP-1 receptor agonists.

Conclusions

This is the first short-term cost-effectiveness study of semaglutide and dulaglutide in T2DM Colombian patients. Our modeled results suggest that once-weekly semaglutide represents a cost-effective option for treating individuals with T2DM in Colombia who are not achieving glycaemia control with metformin, and it would be expected to improve HbA1C, promote greater weight loss and reduce costs from a third-payer perspective compared with treatment with dulaglutide.

Keywords
Semaglutide, Dulaglutide, Pharmacoeconomic, Cost-effectiveness

This article is included in the GDC Open Research in Latin America gateway.

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REVISED **Amendments from Version 1**

The new version contains the suggestions given by reviewer 2.

1. Adding a paragraph in the discussion: In Colombia, insurers (payers) are recognized as key players in the healthcare system. These payers have spent 30 years building their expertise in managing healthcare system resources and have had to adapt quickly to the inclusion of greater benefits, including the introduction of new medications, many of which are high-cost. This puts the short and long-term sustainability of health insurers in Colombia at risk. Payers in Colombia are gradually shifting towards a more detailed examination of the cost-effectiveness relationship of different health technologies. Due to operational issues, expertise, and human talent, these reviews have not yet been carried out in the long term. Additionally, due to operational considerations and variability in the insured population over time, there is currently no interest in conducting these analyses over long time horizons. In this line of thought, payers have an interest in short-term analysis and cost savings for the system. We believe that using this cost-control economic study design provides a valuable tool for these types of participants in the Colombian healthcare system in the short term (1 year), enabling them to make decisions regarding the prioritization of medications and the access granted to each molecule.

2. Reorganization of sections: methodology and results.

Any further responses from the reviewers can be found at the end of the article

Introduction

An estimated 537 million people were living with diabetes worldwide in 2021, and this number is expected to increase based on trends and future projections, suggesting that by 2045 the absolute number of people with diabetes will have increased by 46%.[1] The global prevalence of diabetes is estimated to be over 10%, with the highest prevalence rate observed in low and middle-income countries, meaning that three out of four adults with diabetes live in these regions.[2] In Colombia, the prevalence for type 2 diabetes mellitus (T2DM) ranges from 7.1%-8.5% overall, with wide variations between rural areas (1.4%-7.9%) and urban locations (1%-46%), representing the fifth leading cause of death with a rate of 15 deaths per 100,000 individuals.[3] This is a worrying finding, as the burden of diabetes is accompanied by large healthcare expenditures, accounting for 966 billion USD worldwide and 2.6 billion dollars annually in Colombia.[2,3]

Until recently, 12 classes of drugs were approved to treat T2DM, with a further option -the dual targeted tirzepatide-, receiving Food and Drug and Administration (FDA) approval in May 2022.[4,5] These treatments are either oral or injectable, aiming to prevent or delay the occurrence of microvascular and macrovascular complications, the main causes of morbidity and mortality in patients with diabetes.[5] Enhanced glycemic control can be achieved with glucagon-like peptide-1 (GLP-1) receptor agonists, recommended by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) as a first-line treatment option for individuals with T2DM with or at high risk for cardiovascular disease, heart failure, and/or chronic kidney disease. Furthermore, in these patients a GLP-1 receptor agonist is recommended over insulin when possible, and it is also the preferred addition to basal insulin for combined injection therapy.[6]

Multiple studies have shown robust evidence with this drug class for cardiovascular benefits among patients with T2DM. A systematic review with meta-analysis that included seven clinical trials showed that, overall, the GLP-1 receptor agonist family reduced major adverse cardiovascular events (MACE), including cardiovascular death, stroke, or myocardial infarction, by 12%.[7] Similar findings were also shown in another meta-analysis, demonstrating that GLP-1 receptor agonist treatment showed a significant 10% relative risk reduction in the three-point major adverse cardiovascular event primary outcome (cardiovascular mortality, non-fatal myocardial infarction, and non-fatal stroke), and a 12% relative risk reduction in all-cause mortality.[8] Once-weekly semaglutide and dulaglutide are GLP-1 receptor agonists approved for the treatment of T2DM by the FDA, European Medicines Agency (EMA) and the Colombia National Food and Drug Surveillance Institute (INVIMA),[9,10] with demonstrated efficacy in the SUSTAIN clinical trial program for the former and the AWARD trial program for the latter.[11,12]

The purpose of our study was to conduct a short-term cost-effectiveness analysis of once-weekly semaglutide versus once-weekly dulaglutide in Colombian adults with T2DM, from a third-party payer perspective, as has been recommended in multiple methodological guidelines for economic evaluations.[13]

Methods

Ethical compliance

This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors. It is considered research without ethical risks, in accordance with resolution 8430 of 1993 of the Colombian Ministry of Health.[13]

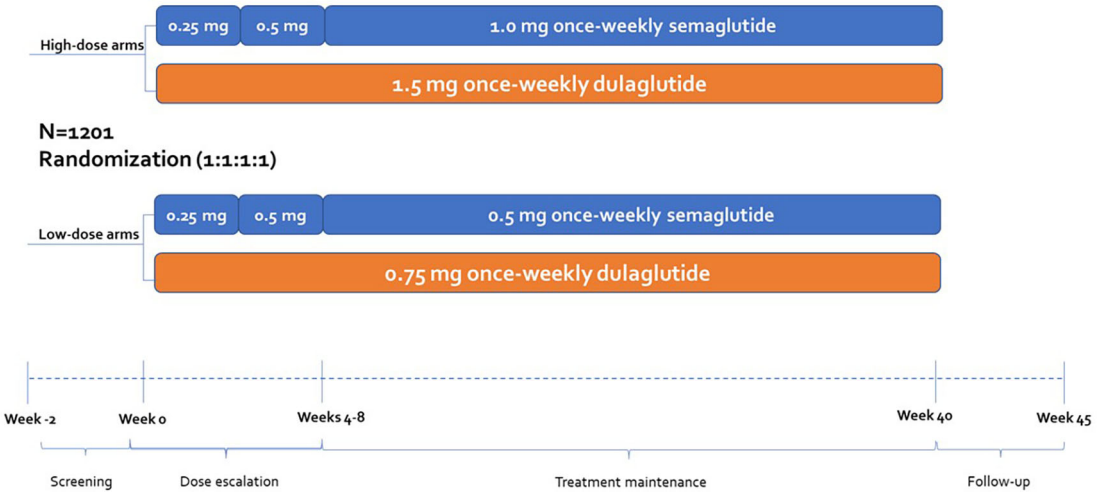

Figure 1. Design of the SUSTAIN 7 randomized controlled trial.

A cost of control model was created using Microsoft Excel to assess numbers needed to treat (NNT) as well as relative and absolute costs according to the criteria and results of SUSTAIN 7, randomized controlled trial (Figure 1 and Table 1). SUSTAIN 7 considers clinical parameters such as weight, glycated hemoglobin, and hypoglycemia results (Table 1). This clinical trial allowed a head-to-head comparison of semaglutide and dulaglutide in the primary clinical outcomes of interest for disease control and weight reduction.[14]

The analysis was conducted from the perspective of payers in Colombia, who bear 100% of the cost of these medications in the country, over a one-year time horizon. This time frame was selected for two main reasons: the low motivation of these actors in the Colombian health system for economic studies with longer time horizons, given the variability of the insured population over time that does not encourage the management of populations with chronic diseases with a long-term view, and the growing interest of payers in short-term studies with models that allow them to better manage available resources and generate savings for insurers.

For the time horizon selected, discount values were not used either. Likewise, 40 weeks of follow-up data from SUSTAIN 7 were considered to determine efficacy and were not extrapolated beyond the trial period. This allowed the reduction of the uncertainty of the modeled results. Drug prices for once weekly semaglutide 1.0 mg, and dulaglutide 1.5 mg were based on the 2021 costs derived from the SISMED database (Medication Price Information System, by its acronym in Spanish), which includes information on the prices of essential medicines in Colombia.[15] No other cost data was considered for the analysis in our study and 100% adherence was assumed for the two drugs once a week.

The higher doses contained in SUSTAIN 7 such as semaglutide 1 mg and dilaglutide 1.5 were used for modeling in this study (Table 2)[14] with n=600 patients. The NNT was calculated in absolute terms for each comparator. For placebos,

Table 1. Proportion of patients reaching target with once weekly semaglutide 1.0 mg, and dulaglutide 1.5 mg, all in combination with metformin, in the SUSTAIN 7 trial.

Endpoint	Once-weekly semaglutide 1.0 mg (%)	Once-weekly dulaglutide 1.5 mg (%)
HbA1c <7.0%	79	67
HbA1c ≤6.5%	67	47
HbA1c <7.0% without hypoglycemia, and no weight gain	74	58
Weight loss ≥5%	63	30
Weight loss ≥10%	27	8
≥1.0% HbA1c reduction and ≥3.0% weight loss	68	35

Table 2. Example cost of control calculation based on the proportion of patients achieving a HbA1c target <7%.

	Semaglutide 1.0 mg/once-weekly	Dulaglutide 1.5 mg/once-weekly	Interpretation
Drug cost (COP)/year	$ 5.843.354,89	$ 5.883.774,07	
Drug cost index	0,993130399	1,006917119	Price maintenance between semaglutide 1.0 mg versus dulaglutide 1.5 mg once weekly
NNT to achieve HbA1C <7.0%	1,27	1,49	
Cost per patient achieving control (COP)	$ 7.421.060,72	$ 8.766.823,37	
Amount spent (according to achieve target relative/once-weekly semaglutide)	1	1,181343706	The proportion of money spent is 1.18 times (18%) higher for delaglutide 1.5 mg compared to semaglutide 1.0. (Target patient HbA1C <7.0%). That is, for each $100.000 COP spent on semaglutide, $118.000 COP would be spent on dulaglutide to achieve this outcome.

Table 3. NNT calculation for one of the SUSTAIN 7 outcomes. ARR=Absolute Risk Reduction.

Example for HbA1C <7.0%	NNT calculation
Semaglutide 1.0 mg*	ARR=79% - 0%=79%|NNT=1/ARR=1/0.79=1.27
Dulaglutide 1.5 mg*	ARR=67% - 0%=67%|NNT=1/ARR=1/0.67=1.5

*Once-weekly.

NNTs are calculated assuming that zero patients in the group being compared achieve the specified outcome (Table 3). The absolute cost of control was calculated by multiplying the annual cost of treatment for each medication by the NNT of the selected data. The conservative approach was from the once-weekly semaglutide perspective, addressing a full year of treatment costs, thus extending beyond 40 weeks of SUSTAIN 7. Relative costs of control were calculated by reference to the cost of control at semaglutide 1.0 mg once a week.

One-way sensitive analyses were performed around the base case, such as varying the percentage of patients meeting each target by an approximation of the standard error (SE). This was done with the following formula in equation 1, where n is the number of patients in the arm of SUSTAIN 7 and p is the percentage of patients achieving each endpoint:

$$\sqrt{\frac{1}{n}p(1-p)} \tag{1}$$

Additionally, cost of control calculations were performed for the best- and worst-case pricing scenarios for semaglutide – the best scenario being when costs are the lowest possible for semaglutide and the highest for dulaglutide, and the worst being the opposite situation-, taking into account the range of prices (minimum and maximum) that were obtained from the SISMED database.

Results

Base case annual costs

The annual base cost for semaglutide and dulaglutide were calculated using the SISMED database, with similar costs per patient for both medications. Semaglutide 1.0 mg had a monthly cost of $486.946 Colombian pesos ($5.843.355 annually), while dulaglutide 1.5 mg had a monthly cost of $489.762 Colombian pesos ($5.877.144 pesos annually) (Table 4).[16]

Table 4. Colombian drug prices per month of treatment according to SISMED in 2021 Colombian pesos (COP) (December 2021).

Glucagon-like peptide 1 treatment	Pack contents (mg)	Number of pens	Base pack price (COP)	Minimum pack price (COP)	Maximum pack price (COP)
Semaglutide 1.0 mg	4	1	$ 486.946,24	$ 479.403,52	$ 503.170,95
Dulaglutide 1.5 mg	6	4	$ 489.762,03	$ 484.818,30	$ 490.314,51

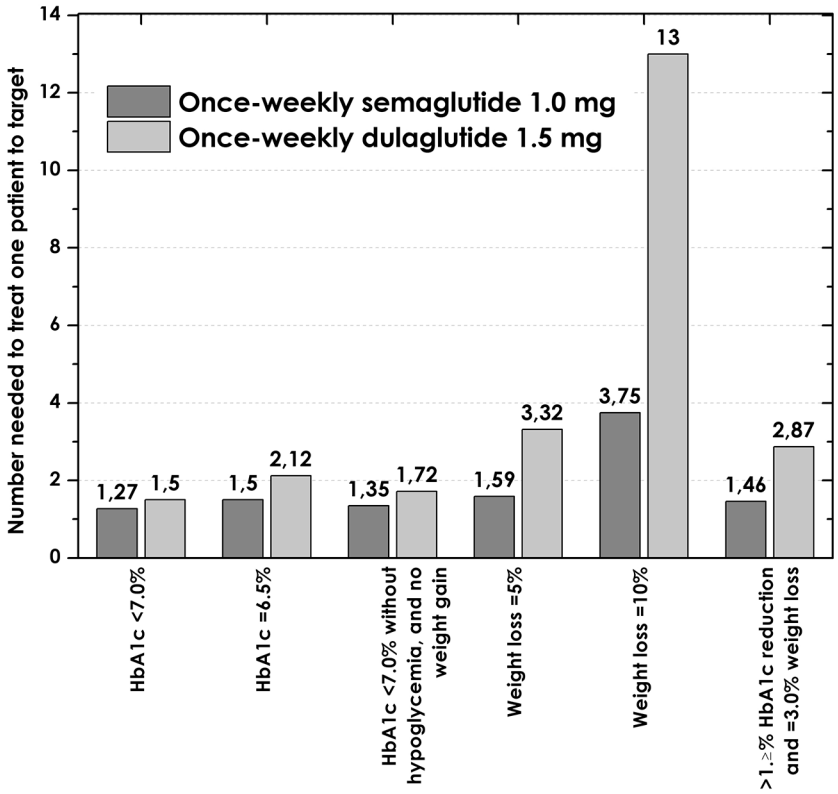

Figure 2. Numbers needed to treat to bring one patient to target with once-weekly semaglutide 1.0 mg, and dulaglutide 1.5 mg. HbA1C, glycated hemoglobin.

Numbers needed to treat (NNT)

The NNTs for all outcomes were larger for dulaglutide, with the most important differences compared to semaglutide being in the weight loss outcomes, particularly for achieving a weight loss ≥10%, with an NNT of 3.7 for semaglutide and 12.5 for dulaglutide (Figure 2).[16]

Cost of control

The previous values were used to estimate the cost per patient successfully reaching the SUSTAIN 7 outcomes. Six SUSTAIN 7 endpoints allowed calculation of the absolute cost of control for the high-dose arms of the drug. According to Table 5, the cost to achieve control was less for the drug semaglutide. Regarding the composite outcome of HbA1c <7%, no weight gain, and no hypoglycemia, which is particularly important -this HbA1C goal is considered appropriate for most T2DM patients by the ADA 2022 guidelines,[17] when it is not associated with significant hypoglycemia-, the cost per patient reaching this endpoint was $7.888.529 for semaglutide, compared to $10.108.687 with dulaglutide. This means that an expenditure 28% greater would have to be spent on dulaglutide to bring one patient to this target (Figure 3).[16]

Sensitivity analyses

Sensitivity analyses showed that variations in cost assumptions, where worst case scenarios for semaglutide (those where the price of this drug was highest and that of dulaglutide was lowest) were considered, did not change the finding that the cost of reaching the composite endpoint with semaglutide was lower than the cost with dulaglutide after one year of

Table 5. Absolute annual cost of control outcomes with once-weekly semaglutide 1.0 mg, and dulaglutide 1.5 mg in 2021 Colombian pesos (COP). Calculations in the base cost, best and worst scenarios for semaglutide.

Endpoint	Base cost		Best scenario for semaglutide		Worst scenario for semaglutide	
	Once-weekly semaglutide 1.0 mg (COP)	Dulaglutide 1.5 mg (COP)	Once-weekly semaglutide 1.0 mg (COP)	Dulaglutide 1.5 mg (COP)	Once-weekly semaglutide 1.0 mg (COP)	Dulaglutide 1.5 mg (COP)
HbA1c <7.0%	$ 7.421.060,85	$ 8.756.944,56	$ 7.306.109,67	$ 8.766.823,37	$ 7.668.325,21	$ 8.668.551,16
HbA1c ≤6.5%	$ 8.706.598,95	$ 12.518.316,72	$ 8.571.734,97	$ 12.532.438,78	$ 8.996.696,50	$ 12.391.955,68
HbA1c <7.0% without hypoglycemia, and no weight gain	$ 7.888.529,25	$ 10.108.687,68	$ 7.766.337,05	$ 10.120.091,41	$ 8.151.369,32	$ 10.006.649,66
Weight loss ≥5%	$ 9.290.934,45	$ 19.570.889,52	$ 9.147.019,20	$ 19.592.967,67	$ 9.600.501,64	$ 19.373.339,17
Weight loss ≥10%	$ 21.620.413,50	$ 73.464.300,00	$ 21.285.516,37	$ 73.547.175,94	$ 22.340.789,98	$ 72.722.744,62
≥1.0% HbA1c reduction and ≥3.0% weight loss	$ 8.589.731,85	$ 16.808.631,84	$ 8.456.678,13	$ 16.827.593,85	$ 8.875.935,48	$ 16.638.963,97

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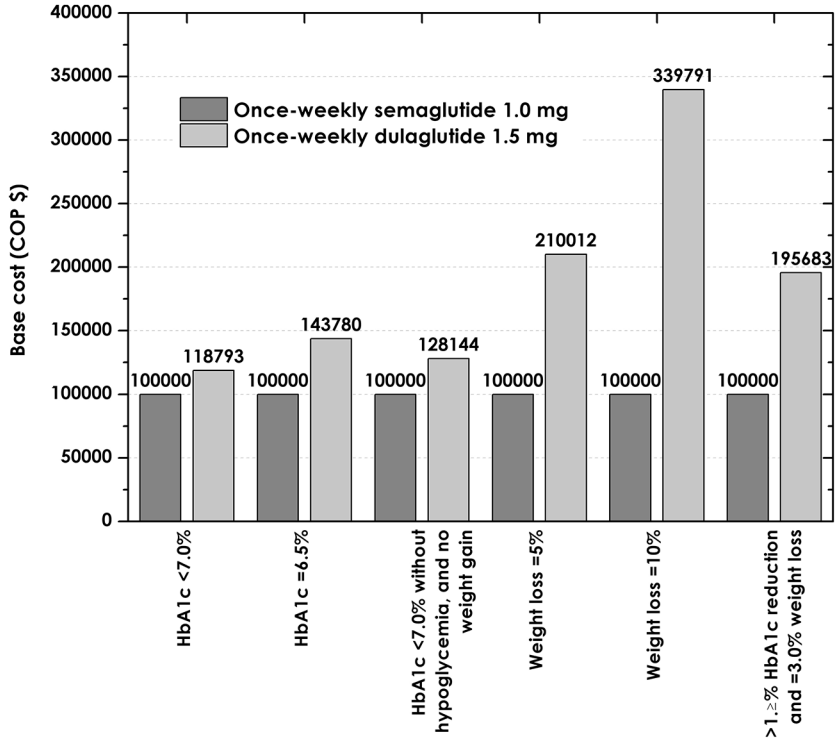

Figure 3. Relative cost once weekly for semaglutide 1.0 mg and dulaglutide 1.5 mg compared to base case (index=100,000) once weekly. HbA1C, glycosylated hemoglobin.

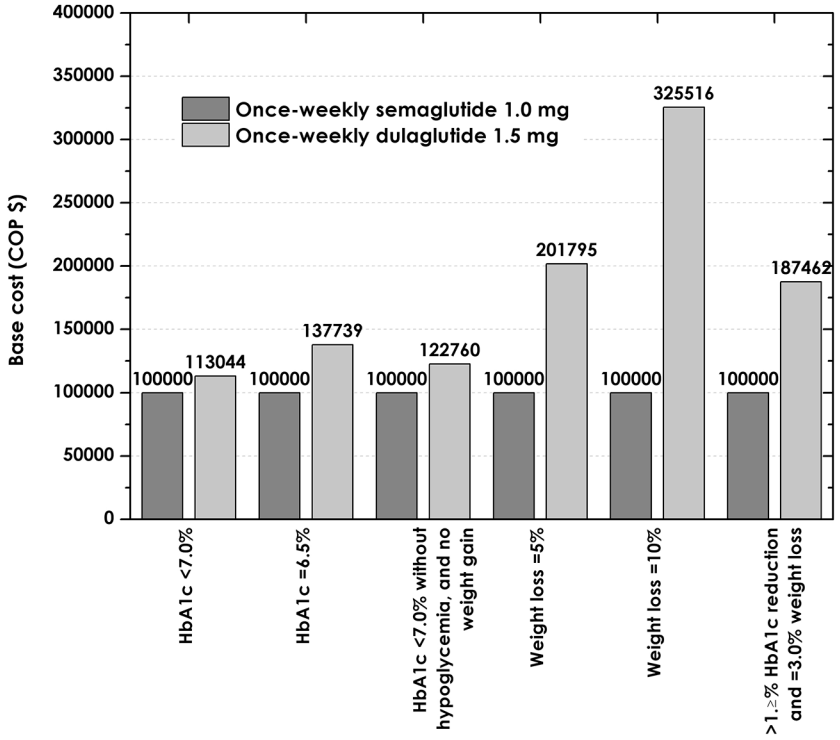

Figure 4. Relative cost of control with once-weekly semaglutide 1.0 mg and dulaglutide 1.5 mg versus once-weekly in the worst scenario of cost for semaglutide (index = 100.000). HbA1C, glycated hemoglobin.

treatment, with semaglutide having a cost per patient of $8.151.369, compared to $10.006.649 with dulaglutide, representing an expenditure 22% higher (Figure 4). Considering the one-way sensitivity, we reduced that by decreasing the proportion of patients reaching targets by one standard error (SE) with semaglutide once a week and increasing the patients reaching this target with dulaglutide by one SE, the cost of control of semaglutide once a week was lower by endpoints (Table 5). In this way, these analyzes support the conclusions of the base case analysis.

Discussions

We conducted an evaluation of the short-term cost-effectiveness of the GLP-1 receptor agonists semaglutide and dulaglutide, with cost-effectiveness assessed through the development of a cost of control model, in order to evaluate the numbers needed to treat (NNT) as well as the absolute and relative costs of bringing a single patient to each of the pre-specified composite and single endpoints in the SUSTAIN 7 trial, which demonstrated a higher efficacy with semaglutide for all outcomes.[14]

The calculations from our analysis suggest that achieving clinically relevant endpoints from SUSTAIN 7 would result in economic savings with once weekly semaglutide, compared to dulaglutide after one year of treatment. The annual drug cost for both medications was similar in the base case, with our results being consistent with previous studies that have also demonstrated that semaglutide is a cost-effective option when compared to dulaglutide.[18–22] In this study, we synthesized the effectiveness and expenditure evidence and found that semaglutide was associated with the lowest cost per patient reaching disease control for all endpoints, findings that were reaffirmed in our sensitivity analyses.

This study has important implications for stakeholders considering this is the first cost-effectiveness analysis to date comparing subcutaneous semaglutide and dulaglutide in the Colombian diabetic population, potentially allowing a better allocation of resources. Previous studies have demonstrated the superiority of semaglutide over dulaglutide in both short and long-term cost-effectiveness analyses, most of them being carried out in high-income countries.[18–22]

In Colombia, insurers (payers) are recognized as key players in the healthcare system. These payers have spent 30 years building their expertise in managing healthcare system resources and have had to adapt quickly to the inclusion of greater benefits, including the introduction of new medications, many of which are high-cost.[23] This puts the short and long-term sustainability of health insurers in Colombia at risk. Payers in Colombia are gradually shifting towards a more detailed examination of the cost-effectiveness relationship of different health technologies. Due to operational issues, expertise, and human talent, these reviews have not yet been carried out in the long term. Additionally, due to operational considerations and variability in the insured population over time, there is currently no interest in conducting these analyses over long time horizons. In this line of thought, payers have an interest in short-term analysis and cost savings for the system.[24,25] We believe that using this cost-control economic study design provides a valuable tool for these types of participants in the Colombian healthcare system in the short term (1 year), enabling them to make decisions regarding the prioritization of medications and the access granted to each molecule.

This study has several limitations. First, we restricted our comparison to semaglutide *versus* dulaglutide. It is important to acknowledge that there are other available molecules in the Colombian market. Second, we limited the costs in the analysis to drugs, as they were expected to be the major drivers of the cost-effectiveness of semaglutide and dulaglutide. Therefore, this model did not account for all potential costs. Third, the analysis takes a third-payer perspective over a short-term horizon. Alternative perspectives and time horizons may result in variable cost-effectiveness estimations, and as such, additional cost-effectiveness studies for these molecules with longer time horizons would be a welcome complement for our study. Fourth, we included prices disregarding potential discounts or refunds, which payers might need to consider in their decision-making processes.

Conclusions

This is the first short-term cost-effectiveness study of semaglutide and dulaglutide in T2DM Colombian patients. Our modeled results suggest that once-weekly semaglutide represents a cost-effective option for treating individuals with T2DM in Colombia who are not achieving glycaemia control with metformin, and it would be expected to improve HbA1C, promote greater weight loss and reduce costs from a third-payer perspective compared with treatment with dulaglutide. Additional cost-effectiveness studies are war-ranted to evaluate the long-term cost-effectiveness of these molecules in the Colombian diabetic population.

Data availability

Underlying data

All data underlying the results are available as part of the article and no additional source data are required.

Extended data

Zenodo: The short-term cost-effectiveness of once-weekly semaglutide versus once-weekly dulaglutide for the treatment of type 2 diabetes mellitus in Colombian adults. https://doi.org/10.5281/zenodo.7857437.[16]

This project contains the following underlying data:

- Final Data_F1000.xlsx. (Semaglutide and dulaglutide cost calculations for this study).

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Publisher Full Text

Open Peer Review

Current Peer Review Status: ✔ ✔

Version 2

Reviewer Report 19 December 2023

https://doi.org/10.5256/f1000research.159773.r229096

✔ **George Gourzoulidis**
Health Through Evidence, Athens, Greece

no other comments

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Economic EvaluationHealth Services ResearchOutcomes ResearchHealth Technology AssessmentHealthcare Economics

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 22 November 2023

https://doi.org/10.5256/f1000research.141032.r218541

✔ **Sajad Hamal**
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An interesting analysis, however, the generalizability may be limited, as the prices and cost basis for each therapy is based on prices in Columbia. Clearly, Semaglutide is more potent at the doses chosen, so will demonstrate dominance for each outcome, based on lower NNT and similar price structures. However, both Dulaglutide and Semaglutide come in higher doses now, so that is worthy of discussion and consideration of secondary analysis. At least discussing the more potent versions of each drug now available worldwide.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Cardiology

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 18 September 2023

https://doi.org/10.5256/f1000research.141032.r204359

?

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1. "An estimated 537 million people were living with diabetes worldwide in 2021, and this

number is expected to increase based on trends and future projections, suggesting that by 2045 the absolute number of people with diabetes will have increased by 46%". Please provide refs.

2. Why is a cost-effectiveness analysis of once-weekly semaglutide versus once-weekly dulaglutide in Colombian adults with T2DM necessary?

3. Cost of control model - figure of the model? Can the authors describe the model?

4. The study is weak in methods sections, the authors have to present the cost inputs of the model. Moreover, since this is a cost-effectiveness, the authors have to report why they do not take into account the QALYS?

5. Why the one-year horizon was selected?

6. The results have to be separated to clinical and cost outcomes.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
No

If applicable, is the statistical analysis and its interpretation appropriate?
Partly

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Economic EvaluationHealth Services ResearchOutcomes ResearchHealth Technology AssessmentHealthcare Economics

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 04 Dec 2023

Rosa Helena Bustos

Reply to the reviewers' comments- Reviewer 1
Original comments of the reviewer
Reply by the author(s)
Changes done on page number and line number

We would like to thank the reviewer for the painstaking review of our document and the suggestions made. We have taken the suggestions to heart and made the appropriate corrections and revision which have thereby strengthened and enriched our manuscript

1
An estimated 537 million people were living with diabetes worldwide in 2021, and this number is expected to increase based on trends and future projections, suggesting that by 2045 the absolute number of people with diabetes will have increased by 46%". Please provide refs.
Answer: The paragraph has been referenced.
Page 3
Line 14

2
Why is a cost-effectiveness analysis of once-weekly semaglutide versus once-weekly dulaglutide in Colombian adults with T2DM necessary?

Answer: In Colombia, health insurers play a crucial role in the healthcare system and have developed expertise over 30 years. The rapid inclusion of new, often expensive medications poses a risk to the sustainability of insurers in both the short and long term. Insurers in Colombia are gradually examining the cost-effectiveness of different health technologies in more detail. However, due to operational challenges and a lack of long-term reviews, there is a focus on short-term analysis and cost savings. The use of a cost-control economic study design is seen as a valuable tool for Colombian health insurers in the short term (1 year), aiding in decision-making on medication prioritization and access.

We added a new paragraph on discussion section to explain this point.
Page 3
Line 167-180

3
Cost of control model - figure of the model? Can the authors describe the model?

Answer: We have made a mistake in the order of paragraphs and the placement of titles in the methods and results sections. For this reason, you could not view the methodology section correctly. That's why we have moved some paragraphs and added some sentences and a complete paragraph to better organize and explain each section. This way, it will be easier for the reader to review how the cost control model was conducted and the sensitivity analysis.
Methods section

Page 4-7
Line: 42-93

4
The study is weak in methods sections, the authors have to present the cost inputs of the model. Moreover, since this is a cost-effectiveness, the authors have to report why they do not take into account the QALYS?
Answer: We have made a mistake in the order of paragraphs and the placement of titles in the methods and results sections. For this reason, you could not view the methodology section correctly. That's why we have moved some paragraphs and added some sentences and a complete paragraph to better organize and explain each section. This way, it will be easier for the reader to review how the cost control model was conducted and the sensitivity analysis.

For this particular study, the main outcomes of interest were related to the regulated costs of medications in Colombia and the main clinical outcomes of the SUSTAIN 7 trial (clinical and comparative study between both drugs). Since it is not a long-term cost-effectiveness study and we were not focused on life quality, QUALYs were not used as an outcome measure for this study. In the discussion section we highlight the importance of developing new long-term studies and cost-utility analysis.
Methods section
Page 4-7
Line: 42-93

5
Why the one-year horizon was selected?
Answer: The one-year time horizon was chosen for two reasons. Firstly, insurers in Colombia lack a strong interest in long-term studies because the variability in the insured population over time does not provide incentives for long-term population management efforts. The second reason is that most insurers in Colombia use annual performance results, and they are evaluated and audited by the national government only once a year. This is added in the new paragraph of the methods sections.
Page 5
Line 54-60

6
The results have to be separated to clinical and cost outcomes.
Answer: Since the extraction of clinical results was obtained from a primary study (SUSTAIN 7 trial), and the medication costs were also extracted from the SISMED database, these are not direct outcomes of our study. Therefore, they were recorded in the methods section. Consequently, in the results section, only the outcomes obtained from the model that combines costs with clinical outcomes were included, concluding with the sensitivity analysis.

In this section, we have reorganized it because of the mistake we made with the order of paragraphs and titles between methods and results sections, described previously.
Methods section

Page 4-7
Line: 42-93

Results:
Page 7-10
Line 96-144

Competing Interests: No competing interests were disclosed.