PHARMACOECONOMIC ANALYSIS OF SITAGLIPTIN/METFORMIN FOR THE TREATMENT OF TYPE 2 DIABETES MELLITUS: A COST-EFFECTIVENESS STUDY

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Running title: Pharmacoeconomic analysis of sitagliptin/metformin

Precis: Assessment of the cost-effectiveness and cost-utility of sitagliptin/metformin for the treatment of type 2 diabetes mellitus compared to those of glibenclamide/metformin in a semi-private hospital.

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SUMMARY

Objective: To assess the cost-effectiveness and cost-utility of sitagliptin/metformin for the treatment of type 2 diabetes mellitus compared to those of glibenclamide/metformin in a semi-private hospital and to compare the cost-effectiveness and cost-utility of sitagliptin/metformin in a semi-private hospital to those in the public health system (Sistema Público de Salud [SPS]) of Ecuador in 2019.

Methods: A cost-effectiveness study considering the probability of cardiovascular death as the outcome and quality-adjusted life-year (QALY) as a measure of utility, estimating direct medical costs in US$ by a "model case" from the perspective of the third payer. The results will be presented as an incremental cost-effectiveness ratio (ICER). One-way and two-way sensitivity analyses with tornado diagrams were performed.

Results: Direct medical costs were lower at the hospital than from the SPS in Ecuador. Considering the drugs metformin/sitagliptin, the total cost was US$ 35.69 lesser in the hospital (US$ 880.38) than from the comparator (US$ 916.07). The highest percentage of direct medical costs corresponded to drugs (between 63.94% and 84.65%). An ICER of US$ –19,131.61 was obtained at the Hospital Un Canto a la Vida (HUCV) and US$ –1,621.85 at SPS. In addition, the cost per QALY earned was US$ 611.11. Sensitivity analysis showed that the probability of drug use and the relative risk of cardiovascular death associated with such prescription were parameters that most affected the model.

Conclusions: The combination therapy metformin/sitagliptin compared to metformin/glibenclamide was shown not to be cost-effective in the HUCV, and highly cost-effective in the SPS.

Keywords: sitagliptin, cost-effectiveness, cost-utility, QALY, type 2 diabetes mellitus.

INTRODUCTION

The International Diabetes Federation (IDF) estimates in its 2019 report that 9.3% of adults (approximately 463 million) worldwide have diabetes. Seventy-nine percent of these adults live in low and middle-income countries, and if the growth trend continues, an estimated 700 million adults will have diabetes by 2045, mostly in countries with the incomes described above. Spending on diabetes has a significant impact on health budgets worldwide[1]. The economic burden of diabetes mellitus is significant in health systems. The evidence reports that this economic impact is greater in developing countries than in developed countries.

In Latin America and the Caribbean, medical care costs for these patients are reported to be between 2.5% and 15% of the total health expenditure[2]. Of these costs, drugs are among the most representative. In one Latin American study, drugs corresponded to 43% of the direct costs of care for these patients. By 2019, it is estimated that the total health care expenditure related to diabetes in the South American and Caribbean region will be US$ 69.7 billion, equivalent to 9.2% of the global total. These values are likely to increase in the region to 15.3% by 2030 and 22.9% by 2045. This region spends an average of 19.4% of its total health expenditure on diabetes, the highest percentage among the IDF regions. The economic impact of diabetes is expected to continue to grow.

Diabetes can be seen as an example of global inequity, where people in many high-income countries can access the latest advances in drugs, tools and care at little or no immediate cost, while those in low and middle-income countries still face excessive difficulties in access. The availability of medicines is only one factor affecting access; the cost of medicines influences people's ability

to pay for their treatment. Different studies have shown that the cost of diabetes medicine is increasing[4].

In the pharmacological treatment of type 2 diabetes mellitus there are sufficient evidence-based recommendations that metformin is the first choice drug[5,6]; however, some controversy persists regarding the drug of choice to be administered in conjunction with metformin when control goals are not achieved in these patients. A meta-analysis that compared nine families of antidiabetics considering clinical outcomes such as cardiovascular mortality, as well as their adverse reactions (hypoglycemia and effects on body weight), did not show significant differences between them; thus, it is recommended to rely on the specific characteristics of the patients to prescribe a second antidiabetic[7].

There are arguments for and against the use of sulfonylureas[8,9]. Thus, the clinical practice guide for type 2 diabetes mellitus published by the Ministry of Public Health of Ecuador recommends prescribing a second- or third-generation sulfonylurea (such as glyclazide or glimepiride) as a second oral antidiabetic. One drug in this family that is included in this chart is glibenclamide, which is associated with a higher risk of hypoglycemia, and should not be used on patients over 65 years of age or with renal and/or hepatic alterations[5].

The American Diabetes Association's recommendations for the treatment of patients with type 2 diabetes mellitus in 2019 and 2020[6,10] state that the addition of a second drug will be based on the patient's clinical characteristics (presence of cardiovascular disease or high risk of it, other comorbidities): risks for specific adverse effects of certain drugs (safety and tolerability), cost, and patient preferences. Drugs such as sodium-glucose co-transporter 2 (SGLT-2) inhibitors or

glucagon-like peptide type 1 (GLP-1) inhibitors are recommended preferentially in patients with established cardiovascular disease or high risk of disease; however, their higher cost would limit their access. In this sense, drugs such as dipeptidyl peptidase 4 (DPP-4) inhibitors, sulfonylureas, and thiazolinediones are shown to be cheaper alternatives.

Cost-effectiveness studies conducted in Colombia, Switzerland, and Belgium estimated the cost-effectiveness and cost-utility of DPP-4 inhibitors versus sulfonylureas: they showed that the former had better results[11–13]. In the Colombian study, linagliptin was the drug that showed the best performance; while in the Swiss and Belgian studies, sitagliptin had the best cost-effectiveness, in addition to using the quality-adjusted life-year (QALY) as the main outcome.

Thus, this study seeks to establish the cost-effectiveness of sitagliptin associated with metformin for the treatment of type 2 diabetes mellitus at the Hospital Un Canto a la Vida (HUCV), Quito, Ecuador in relation to the combination of metformin/glibenclamide by 2019. As an additional finding, the cost-utility of metformin/sitagliptin will be determined in relation to the prescription made in the Public Health System (Sistema Público de Salud [SPS]) of Ecuador. This article is the final part of a research project in a Pharmacoeconomics and Health Technology assessment.

METHODS

Studio design

The DPP-4 inhibitors were studied because they are the second-line drugs with the lowest cost outside sulphonylureas; within them, sitagliptin was studied because it is the one with the most evidence in the literature. A cost-effectiveness study was conducted, considering—as the main

outcome—the probability of cardiovascular death associated with the prescription of sulfonylureas or DPP-4 inhibitors in conjunction with metformin as reported in the literature[7]. The QALY was used as the denominator for cost-effectiveness determination. In both cases, the guidelines of Rascati[14] and Drummond et al.[15] were followed. The recommendations of the CHEERS[16] initiative were considered for the presentation of the results.

Cost estimates

Initially, a partial economic evaluation was carried out (analysis of direct medical costs for outpatient care, measured in US dollars); following the cost classification exposed by Rascati[14] and under the guidelines of Drummond et al.[15]; where the "model case" was considered for which the recommendations of the Clinical Practice Guide for the care of patients with diabetes mellitus type 2 in Ecuador[5,17] were used. Each event was considered to be of recent diagnosis and with a one-year follow-up.

Perspective

Patient care costs were estimated from the perspective of the third party payer, that is, from the point of view of the provider and financer of health benefits (the benefits rate of the HUCV, which is classified as a semi-private NGO hospital), and compared to the costs of care in the SPS through its rate[18]. The values of the drugs were extracted from the prices of the hospital pharmacy (for the HUCV), and the database of the National Council for Setting and Reviewing Drug Prices for Human Use and Consumption (for the SPS), updated in August 2019[19].

To establish the cost of the medicines, the defined daily dose (DDD) by the World Health

Organization, understood to be the average maintenance dose assumed per day for a medicine used for its main indication in adults, was used[20,21]. In the case of metformin, it was assumed that the case-type started this drug from diagnosis, while for glibenclamide and sitagliptin, it was assumed that the drug was started after at least three months of follow-up, as established by the respective clinical guidelines[5,6]. The values obtained were recorded in the Microsoft Excel® database designed for the study.

Data analysis

The results will be presented as cost-effectiveness and incremental cost-utility indices (ICER and ICUR, respectively), for which the methods of Drummond et al.[15] and on the website of the NATS-INC[22] were used for calculation, respectively, according to the following formula:

Incremental cost-utility ratio (ICER) = ([Cost of the intervention – cost control]/[Intervention outcome – Control outcome]) × *t*,

where *t* represents the time at which the values will be measured.

To estimate the time horizon of the calculations, recent data on the life expectancy of the Ecuadorian population published by the World Bank[23], which corresponds to 76.8 years, was taken into account, as well as the average age of the diabetic patients treated in the hospital base of this study (67.77 years), which were quantified in another study of the authors that has not yet been published[24]. The reduction in this life expectancy based on the presence of diabetes was also

considered, and that in people aged 65 years is equivalent to 4.8 years according to DiAngelantonio et al.[25] Thus, the life expectancy for the respective calculations was estimated at 4.23 years.

The decision tree chosen as the analysis model was developed using Microsoft Excel® with the addition of the TreePlan® add-in. In each decision branch, the values of costs, utility measured as QALY, probability of receiving the intervention, and—as the main measure of effectiveness—the risk of cardiovascular mortality of the interventions reported in the meta-analysis by Palmer et al.[7] were included. This model considered the following possible scenarios for both HUCV and SPS patients: 1) type 2 diabetic patients treated with metformin/glibenclamide, 2) type 2 diabetic patients treated with metformin/sitagliptin, and 3) type 2 diabetic patients not receiving these treatments.

In each decision node, the costs of each scenario were included (except for those who would not receive any of the proposed therapeutic alternatives), the probabilities of receiving each of the interventions taken from a previous study carried out by the authors (awaiting publication)[24], plus those reported in a medical graduation thesis that was carried out in a hospital with similar technical characteristics to those of the SPS[26]. In addition, usefulness values estimated as the QALY in each possible scenario were included; both those obtained by the authors in the project being published (described above), and those published in a medical specialty thesis on patients with type 2 diabetes mellitus treated in ambulatory health units belonging to Ecuador's public health system[27].

To identify the efficiency threshold for the calculated incremental rates, a criterion of "willingness to pay" for the benefits of new interventions was used in accordance with the criteria of the World

Health Organization (WHO) Commission on Macroeconomics and Health, which relates them to each country's per capita gross domestic product (GDP)[28].

A sensitivity analysis of one-way and two-way analyses with tornado diagrams was carried out considering all of the factors that would determine the ICER in both the HUCV and SPS scenarios. For costs, a 5% discount rate was considered; while for relative risks and prescription probabilities of the studied alternatives, the 95% confidence intervals calculated from the available data in the respective references were used as limits.

RESULTS

In terms of direct health care costs without considering drugs, this value was found to be US$ 8.31 higher in the HUCV (US$ 148.88) than in the SPS (US$ 140.57). This cost included both medical consultations and complementary and laboratory studies required to follow up a typical patient according to the recommendations of the clinical guidelines taken as a reference. The greatest differences were found when treatment costs were considered in the total value.

The metformin/sitagliptin combination cost US$ 35.69 less in the HUCV (US$ 880.38 total cost) than in the SPS (US$ 916.07 total cost). Similarly, a lower cost (US$ 46.49) was found for the metformin/glibenclamide combination in the HUCV (US$ 412.88 total cost) compared to that in the SPS (US$ 459.57 total cost). This shows that the largest percentage of the total direct medical cost of a patient with type 2 diabetes mellitus who begins treatment and subsequently requires a second drug is found in the cost of the drugs. In the HUCV, this value corresponded to 63.94% and 83.09% depending on whether metformin/glibenclamide or metformin/sitagliptin was used,

respectively. In contrast, in the SPS, the cost of drugs corresponded to 69.41% or 84.65%, depending on whether metformin/glibenclamide or metformin/sitagliptin was prescribed, respectively.

By calculating the incremental cost-effectiveness index for each scenario (HUCV and SPS), according to the decision tree model constructed for this study (Figure 1), and considering the changes in the risk of cardiovascular death associated with prescribing the respective drug combinations as a result of the proportion of prescriptions expected in each scenario, an ICER of US$ –19,131.61 was obtained for the respective risk reduction in the HUCV, while the ICER was US$ –1,621.85 in the SPS (Table 1). For these calculations, the decision branch regarding the use of other treatments was not considered; it was not part of the objectives of this research.

According to the Commission of Macroeconomics and Health of the WHO, the thresholds of cost-effectiveness of each country or region should be directly related to the value of its gross domestic product (GDP) per capita; considering this, it has been defined that a therapy would be highly cost-effective if its ICER/ICUR is below the value of the GDP per capita[28]. The last per capita GDP figure reported by the World Bank for Ecuador was US$ 6,344.90 for the year 2018[29], the maximum threshold for accepting a health technology is estimated at US$ 19,034.70. Thus, for the HUCV, the prescription of metformin/sitagliptin would not be a cost-effective alternative, while for the SPS, it would be.

To perform the cost-utility analysis and estimate the incremental cost-utility ratios (ICUR), the total utility for patients with type 2 diabetes who would receive care at the HUCV is 2.9948 QALY,

while that of those who receive care at the SPS would be 2.9187 QALY. In addition, it was calculated that US$ 611.11 more would be spent on the HUCV than on the SPS for each QALY gained over the estimated life expectancy, making it a highly cost-effective intervention based on the criteria of the respective WHO commission (Table 2).

In the one-way sensitivity analysis, the probability of using the combination metformin/sitagliptin and the relative risk of death from cardiovascular causes associated with this prescription were estimated as the parameters that most affected the model in the HUCV scenario (Figure 2). In the two-way analysis for this scenario, it is observed that variations in both the prescription probabilities of the metformin/sitagliptin and metformin/glibenclamide association are those that would most modify the ICER values (Supplementary Table 2 and Supplementary Figure 1).

In the SPS-use scenario, the relative risk of cardiovascular death associated with metformin/glibenclamide prescription versus a DPP-4 inhibitor and the probability of metformin/glibenclamide use were the variables that most modified the model (Figure 3). In the two-way analysis, the modifications in the two variables described above were maintained as those that most affected the value of the ICER in this scenario (Supplementary Table 3 and Supplementary Figure 2).

DISCUSSION

In determining the cost-effectiveness of the therapeutic combination of metformin/sitagliptin compared to metformin/glibenclamide in the HUCV as measured by the ICER, this combination was shown to be not cost-effective as it exceeded the WHO suggested ceiling of three times a

country's GDP per capita. While applying the cost-effectiveness model for a similar scenario in SPS, the metformin/sitagliptin alternative was highly cost-effective. In the two-way sensitivity analysis, the variable that modified the ICER in both scenarios was the probability of using the metformin/glibenclamide combination. In the comparison of the two scenarios to determine the cost-utility, the metformin/sitagliptin combination proved to be highly cost-efficient according to the same WHO criteria. As additional data, it was confirmed that the highest direct medical cost of care for diabetic patients is in the prescribed drugs.

Afroz et al. in their study in Bangladesh reported that medication constituted 60.7% of the direct costs of diabetes patient care; with an average annual cost of US$ 864.70 per patient per year in 2017[30]. In the cost description of patients not requiring hospitalization, medication represented 83.5% of the total direct cost of US$ 409.80 per patient per year, with direct medical costs of US$ 357.80 (equivalent to approximately US$ 372 in 2019). The percentage of the cost attributed to medication is similar to that found in this study; however, direct medical costs are much lower than those reported by the authors. This difference may be due to the more accurate methodology used by Afroz to estimate costs.

In a study by Barceló et al. on the costs of diabetes in Latin America and the Caribbean in 2015[31], based on the use of metformin, the total cost of this medication for the region was estimated to be between US$ 11 and US$ 18 million, and modifications in its price could result in up to a 50% reduction in the direct costs. A limitation in the comparison of these specific data in our study is that it did not consider the value of drugs in combination therapy or new drugs. This could justify the fact that in our research, the cost of metformin/sitagliptin in particular represented more than 80% of the direct costs reported. In addition, the Barceló study considered the costs of emergency care and complications, parameters that were not evaluated in this study.

There are studies that do consider sitagliptin in their cost-effectiveness analysis. Cazarim et al. conducted a cost-effectiveness analysis in 2013 in Brazil to evaluate the effectiveness of four DPP-4 inhibitors (sitagliptin, saxagliptin, vildagliptin, and linagliptin) with a reduction in glycosylated hemoglobin (HbA1c) as the outcome[32]. In this study, linagliptin was reported as the cheapest drug, while the metformin/sitagliptin combination reported a cost of US$ 598.12 per patient per year. This value for 2019 would be the approximate equivalent of US$ 654, which is at least US$ 77 less than the value reported in this study. This difference may be due to the fact that in Cazarim's study, the direct costs were not considered in relation to complementary studies and medical care (only the costs of adverse drug effects were used). Furthermore, in our study, the DDD was used to estimate the amount of drugs prescribed. In addition, after sensitivity analysis and with an incremental cost-effectiveness of US$ 1,506.75 per patient per year to reduce HbA1c by 1%, the metformin/sitagliptin combination was the most cost-effective. In our study, the cost-effectiveness of this combination was evidenced only in the SPS setting and depends on the prescription frequency of the comparator (metformin/glibenclamide) and the risk of cardiovascular death associated with this prescription.

In a systematic review on the cost-effectiveness of sodium-glucose co-transporter 2 inhibitors (SGLT-2), glucagon-like peptide inhibitors (GLP-1) and dipeptidyl peptidase-4 inhibitors (DPP-4) conducted by Hong et al.[33], it was reported that in 13 of 15 studies reviewed, the new drugs were cost-effective relative to sulfonylureas. In addition, seven studies directly referenced DPP-4 inhibitors: five reported that they were cost-effective strategies for sulfonylureas, and two studies reported that they were not. For sitagliptin versus sulfonylureas, an incremental effectiveness of 0.031 QALYs and a cost-incremental effect of THB 141,806 (Thai currency) was reported: the

equivalent of an ICER (ICUR) of US$ 139,102 per QALY earned after currency conversion for the study year (2014). Our study reported a slight increase in profit and a largely cost-effective ICER (ICUR), but with a higher value per QALY earned. Regarding limitations of the referred systematic review to consider, we mention that there could be some biases in the studies because they were funded by the pharmaceutical industry, besides the fact that they could not perform a meta-analysis because of the differences in methodologies.

To the best of our knowledge, this study constitutes the first report in Ecuador to establish the cost-effectiveness of sitagliptin as a combination therapy with metformin for patients with type 2 diabetes mellitus. By identifying the incremental cost-effectiveness indices for this therapeutic combination and correlating them with the economic standard of efficiency established by the WHO, it provides the participating institution with information to make decisions regarding whether or not it is worth recommending this therapeutic alternative to its patients. It also provides data that will allow for the replication of these results in similar scenarios.

Among the limitations of this analysis, we used utility measures obtained from another study with a limited number of patients; therefore, this measure could have been underestimated or overestimated. By using the case-type methodology to estimate costs, the real use of resources by patients is not evident, as other methodologies, such as micro-costing, do. In addition, since the comparison was made only with sitagliptin, a new study could be carried out that includes other DPP-4 inhibitors marketed in Ecuador to whether this drug is the most cost-effective in this pharmacological group or not.

CONCLUSIONS

The generalization of these results should be performed with caution; the model was specifically designed considering the characteristics of the institution (especially in terms of costs and utility measures) and its comparator (SPS). Therefore, differences in the costs, prescription frequency of the drugs studied here, or number of services provided for the care of diabetic patients in other instances would make the data obtained in this study less extrapolatable. We recommend following the general guidelines for transferring the results of economic evaluations from one scenario to another, such as those suggested by Drummond et al., through the development of decision models adapted to the context of the application[15,34].

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Table 1 – Incremental cost-effectiveness of the two combined therapeutic alternatives for the treatment of type 2 diabetes mellitus.

Scenary	Costs without drugs	Cost Met+sit*	Cost Met+glib†	Cardiovascular death risk with Met+sit[1]	Cardiovascular death risk with Met+glib[1]	Cost increase ΔC	Effectiveness increase ΔE	ICER ΔC/ΔE
Hospital UCV	148.88	731.50	264.00	0.83*0.1228	1.2*0.1053	467.50	-0.024436	-19131.61
Public Health System	140.57	775.50	319.00	0.83*0.0164	1.2*0.2459	456.50	-0.281468	-1621.85

* Met/sit: Metformin plus sitagliptin.

† Met/glib: Metformin plus glibenclamide

[1] Data calculated from references 7 and 26, and from the article Quality of life in patients with type 2 diabetes mellitus prepared by the authors, not yet published. Risk calculated between the RR of each pharmacological combination and the frequency of use.

Table 2 – Incremental cost-utility of metformin - sitagliptin.

Scenary	Cost increase between Met+sit* vs Met+glib†	Qality of life[1]	Life expectancy (model time horizon)	Cost increase HUCV vs SPS ΔC	Utility increase ΔU	ICUR ΔC/ΔE
Hospital UCV	467.50	0.708 QALY	4.23 years	46.53	0.07614	611.11
Public Health System	456.50	0.69 QALY	4.23 years			

* Met/sit: Metformin plus sitagliptin.

† Met/glib: Metformin plus glibenclamide

[1] Data calculated from references 21 and 22, and from the article Quality of life in patients with type 2 diabetes mellitus prepared by the authors, not yet published. The total profit is obtained by multiplying the QALY of each scenario by the life expectancy.

Figure 1 - Decision tree.

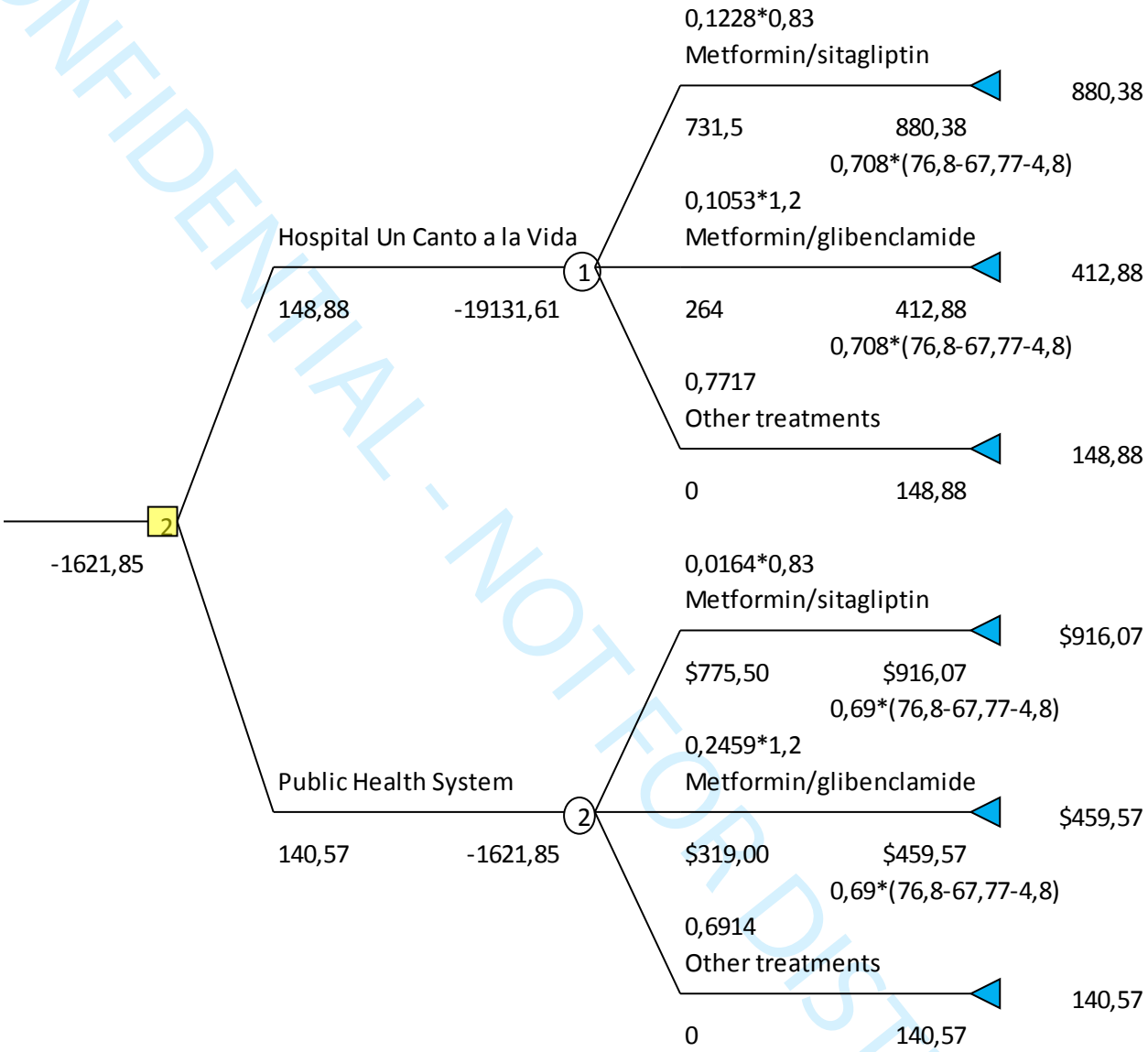


Figure 2 – One-way sensitibity analysis: Tornado diagram, Hospital Un Canto a la Vida.

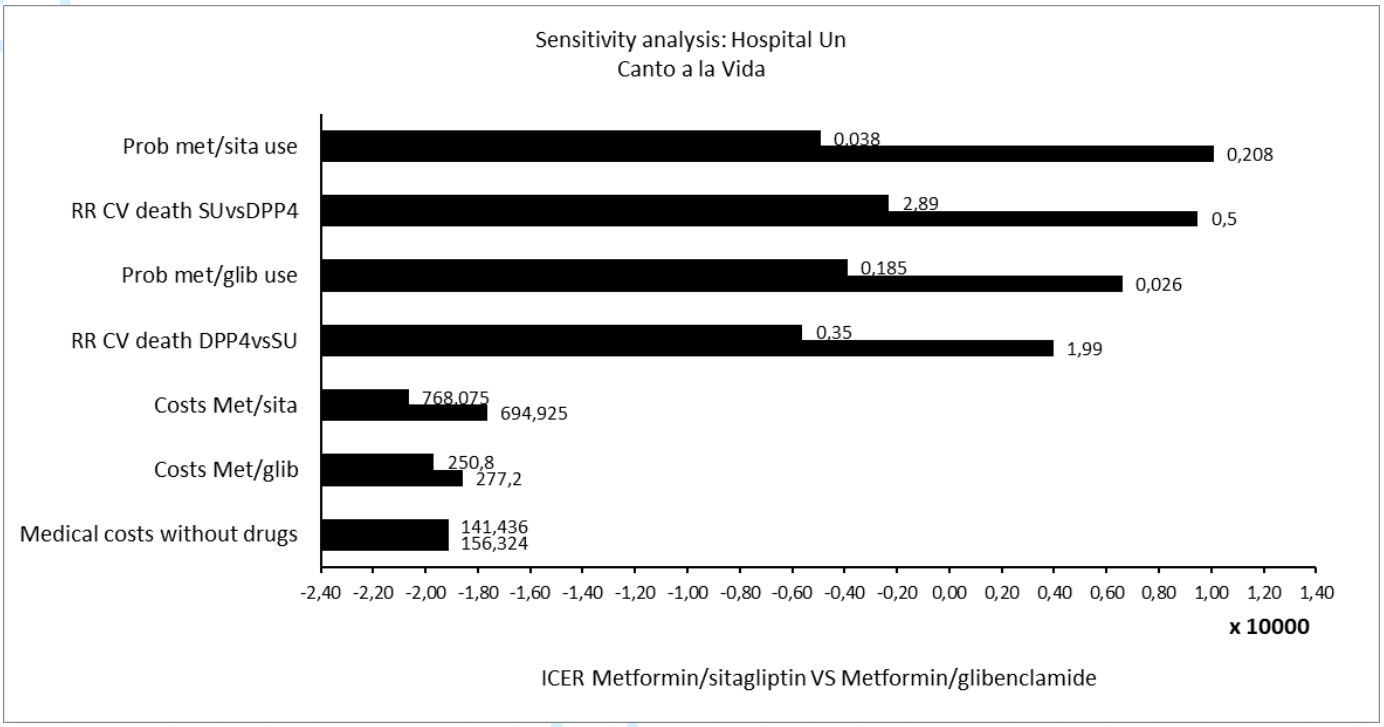
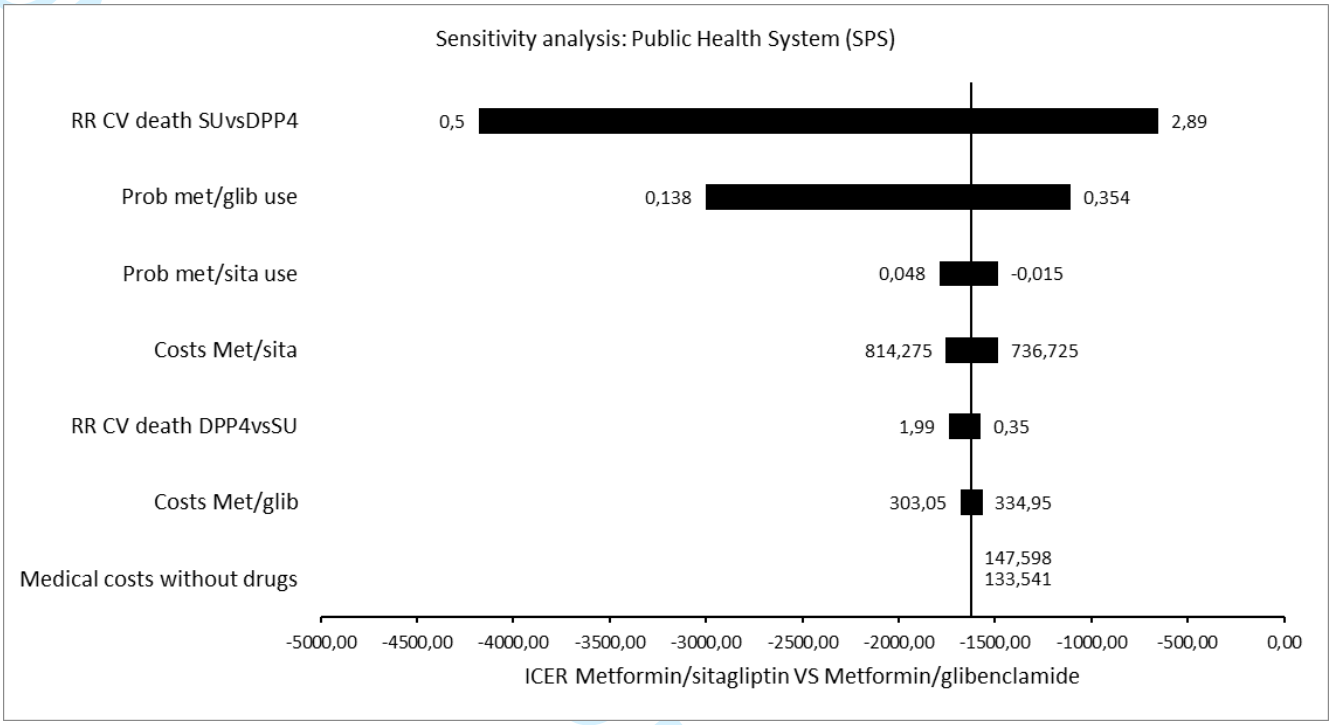


Figure 3 - One-way sensitibity analysis: Tornado diagram, Public Health System.



MATERIAL SUPLEMENTARIO

Tabla suplementaria 1 - Costos directos de la atención de pacientes diabéticos.

Costos médicos directos	Hospital Un Canto a la Vida		Sistema público de salud	
	Costo unitario	Costo anual	Costo unitario	Costo anual
Consulta externa inicial de 20 minutos (1 prestación anual)	12 US$	12 US$	12,73 US$	12,73 US$
Consulta externa subsecuente de 15 minutos (4 por año*)	12 US$	48 US$	12,06 US$	48,24 US$
Laboratorio que incluye:				
Biometría hemática	3,41 US$	3,41	2,73	2,73
Glucosa en ayunas	2,12 US$	2,12	1,86	1,86
Colesterol HDL-LDL	9 US$	9	7,89	7,89
Triglicéridos	2,06 US$	2,06	2,42	2,42
ALT	3,65 US$	3,65	4,28	4,28
AST	4 US$	4	2,05	2,05
Creatinina	3 US$	3	3,29	3,29
TSH	7,19 US$	7,19	6,83	6,83
Elemental y microscópico de orina (EMO)	3,45 US$	3,45	3,04	3,04
Hemoglobina glicosilada[&]	9,75 US$	39 US$	7,45	29,80
Electrocardiograma	12 US$	12 US$	15,41 US$	15,41 US$
Metformina 500mg[a] DDD 2g	0,21 US$	231 US$	0,25 US$	275 US$
Glibenclamida 5mg DDD 10mg	0,06 US$	33 US$	0,08 US$	44 US$
Sitagliptina 100mg[b] DDD 100mg	1,82 US$	500,50 US$	1,82 US$	500,50 US$
Total atención médica (sin fármacos)		148,88 US$		140,57 US$
Total con metformina/glibenclamida		412,88		459,57
Total con metformina/sitagliptina		880,38		916,07

DDD: Dosis diaria definida

***** La guía recomienda una segunda consulta al mes de la primera, y después cada 3 meses.

[&] Realizada al diagnóstico y después cada 3 meses

[a] Se realiza el cálculo del valor total, considerando inicio de medicación a partir del 4 mes de tratamiento (275 días de tratamiento anual).

[b] Puesto que al momento de realizar este estudio no se comercializa este principio activo de manera individual sino en combinación con otros; para ambos escenarios se utilizó el precio techo establecido por el Consejo Nacional de Fijación y Revisión de Precios de Medicamentos de Uso y Consumo Humano de Ecuador.

Tabla suplementaria 2 - Datos para el análisis de sensibilidad, Hospital Un Canto a la Vida

	Corresponding Input Value			ICER HUCV Output Value				
Input Variable	Low Output	Base Case	High Output	Low	Base	High	Swing	Percent Swing ^2
Prob uso met/sita	0,038	0,1228	0,208	-4930,39	-19131,61	10101,56	15031,95	39,2%
RR muerte CV SUvsDPP4	0,5	1,2	2,89	-2309,86	-19131,61	9487,76	11797,62	24,1%
Prob uso met/glib	0,026	0,1053	0,185	-3893,37	-19131,61	6610,20	10503,57	19,1%
RR muerte CV DPP4vsSU	0,35	0,83	1,99	-5606,86	-19131,61	3961,46	9568,32	15,9%
Costos Fárm Met/sita	694,925	731,5	768,075	-20628,38	-19131,61	-17634,84	2993,53	1,6%
Costos Fárm Met/glib	250,8	264	277,2	-19671,80	-19131,61	-18591,42	1080,37	0,2%
Costos de atención sin fármacos	141,436	148,88	156,324	-19131,61	-19131,61	-19131,61	0,00	0,0%

Tabla suplementaria 3 - Datos para el análisis de sensibilidad, escenario Sistema Público de Salud.

	Corresponding Input Value			ICER en cada escenario				
				Output Value				Percent
Input Variable	Low Output	Base Case	High Output	Low	Base	High	Swing	Swing ^2
RR muerte CV SUvsDPP4	0,5	1,2	2,89	-4175,13	-1621,85		3520,21	76,6%
Prob uso met/glib	0,138	0,2459	0,354	-3003,53	-1621,85	-1110,20	1893,33	22,1%
Prob uso met/sita	-0,015	0,0164	0,048	-1788,51	-1621,85	-1484,41	304,10	0,6%
Costos Fárm Met/sita	736,725	775,5	814,275	-1759,61	-1621,85	-1484,09	275,52	0,5%
RR muerte CV DPP4vsSU	0,35	0,83	1,99	-1739,42	-1621,85	-1577,73	161,69	0,2%
Costos Fárm Met/glib	303,05	319	334,95	-1678,52	-1621,85	-1565,19	113,33	0,1%
Costos de atención sin fármacos	133,541	140,57	147,598	-1621,85	-1621,85	-1621,85	0,00	0,0%

Figura suplementaria 1 - Análisis de sensibilidad de dos vías: Diagrama de tornado, Hospital Un Canto a la Vida.

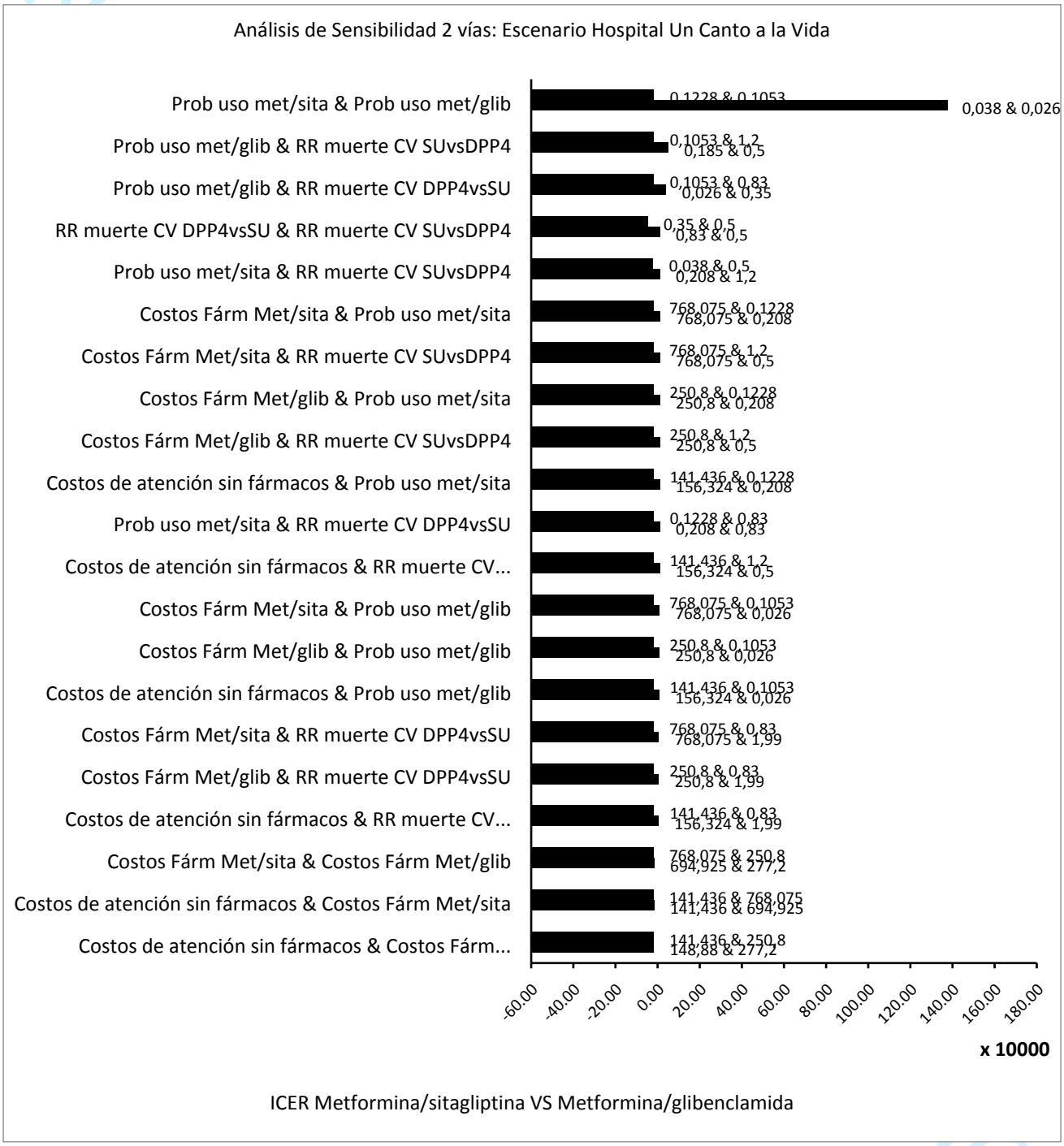


Figura suplementaria 2 - Análisis de sensibilidad dos vías: Diagrama de tornado, escenario Sistema Público de Salud.