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ORIGINAL RESEARCH ARTICLE

A Relative Cost of Control Analysis of IDegLira versus Other Forms of Basal Insulin Intensification in Mexico

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Abstract

Objectives Achieving glycemic control in patients with type 2 diabetes is important as it reduces the risk of complications and their related clinical and economic burden. Yet therapeutic inertia due to the fear of hypoglycemia, complex treatment regimens, weight gain, and therapy costs, among others, limits achieving glycemic control. This analysis aims to assess the short-term cost of control (cost per patient achieving treatment goals) with insulin degludec/liraglutide (IDegLira) versus other forms of basal insulin intensification (insulin glargine titration, basal-bolus therapy, and the combination of insulin glargine and lixisenatide: IGlarLixi) in type 2 diabetes patients not controlled with basal insulin in the Mexican private setting.

Methods The proportion of patients achieving treatment goals was obtained from DUAL V and DUAL VII studies (full trial population) and a indirect treatment comparison analyzing IDegLira versus IGlarLixi. Annual cost of treatment was estimated using unitary costs from IQVIA's Pharmaceutical Market Mexico (PMM) audit and wholesale acquisition costs (both from December 2021). The cost of control was estimated by dividing the annual cost of treatment by the proportion of patients achieving the corresponding treatment goal: glycated hemoglobin (HbA1C) < 7.0%, HbA1C < 7.0% without weight gain, HbA1C < 7.0% without hypoglycemia, and HbA1C < 7.0% without hypoglycemia and weight gain. One-way sensitivity analyses were conducted to assess how variations in the model inputs impacted cost-effectiveness outcomes.

Results The proportion of patients achieving treatment goals was higher for IDegLira versus other forms of basal insulin intensification in all endpoints assessed. The annual cost of treatment with IDegLira was similar to the cost of treatment versus IGlarLixi or versus basal-bolus therapy ($54,659 versus $55,831 MXN and $51,008 versus $52,987 MXN, respectively), and higher in comparison with insulin glargine titration ($52,186 versus $40,194 MXN). The cost of controlling one patient with IDegLira was lower than any other form of basal insulin intensification, for all treatment goals.

Conclusion When integrating the greater clinical efficacy of IDegLira with its annual cost, it can be shown that within 1 year, IDegLira is the best option in terms of value for money for payers in a private healthcare setting in Mexico in comparison with other forms of basal insulin intensification. Thus, investing in IDegLira not only represents a greater clinical benefit, but also an economical one for payers.

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1 Introduction

Type 2 diabetes (T2D) is a multifactorial progressive disease associated with a pancreatic β-cell dysfunction, insulin resistance, and an inability to suppress glucagon secretion [1]. In Mexico, the prevalence of T2D has grown 78% in the last 18 years, affecting one in ten adults, most of them above 60 years old [2, 3].

Key Points for Decision Makers

The percentage of patients achieving treatment goals with IDegLira is greater compared with the percentage of patients reaching treatment goals with other forms of basal insulin intensification.

IDegLira is the best option in terms of value for money due to a lower cost of control compared with other forms of basal insulin intensification.

Despite innovations in treatment options, T2D is causing a high morbidity and mortality due to microvascular and macrovascular complications, which according to large epidemiological studies[1], are closely related to the degree and duration of hyperglycemia, estimated by glycated hemoglobin (HbA1C) [4–6].

In Mexico, 68% of T2D patients are not in glycemic control, making T2D and its complications the second leading cause of mortality among adults aged between 45 and 64 years old and one of the leading causes of disability [7–9].

Complications also pose a significant economic burden on patients, health systems, and society. At the patient level, the annual cost of T2D and multiple complications is estimated at $169,559 Mexican pesos (MXN), which is equivalent to Mexico's 2020 gross domestic product (GDP) per capita[2] [10–13]. At the country level, the cost of T2D was estimated at $506 billion MXN in 2018, and 85% of this cost was related to complications [14].

Nowadays, clinical practice guidelines focus primarily on the detection and treatment of modifiable risk factors for cardiovascular disease (CVD) and the achievement of glycemic control goals of HbA1C < 7.0% with minimal hypoglycemia or other adverse effects of treatment [15]. Due to the progressive nature of T2D, most patients with T2D will eventually require insulin to maintain adequate HbA1C levels. Many patients will need to intensify their insulin regimen over time [15]. When basal insulin has been titrated to an acceptable fasting glucose, but HbA1C remains above target, guidelines currently recommend proceeding to combination injectable therapy to cover postprandial glucose excursions. Options include the addition of a glucagon-like peptide-1 receptor agonist (GLP-1 RA) or one to three injections of a rapid-acting mealtime insulin, or switching from basal insulin to a premixed insulin regimen [16]. IDegLira is a combination of insulin degludec and GLP-1 RA liraglutide, and is indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2D inadequately controlled on basal insulin or liraglutide [17]. According to the results of the DUAL program, a clinical study that included nine clinical trials comparing the safety and efficacy of IDegLira versus placebo and other active medications [e.g., GLP-1 RA, sulfonylurea, degludec, glargine U100, Basal-Bolus, and glargine U100 as add ons to sodium-glucose cotransporter-2 (SGLT2i) therapy], benefits from IDegLira include significant reductions in HbA1C, low risk of hypoglycemic events, and reductions in body weight in comparison with other forms of basal insulin intensification [18, 19]. With the participation of 270 patients enrolled in four out of the nine clinical trials, Mexico was part of the DUAL program, and all the evidence on safety and efficacy showed strong, positive results of IDegLira compared with its comparators.

The aim of this analysis was to evaluate the short-term cost effectiveness of IDegLira versus other forms of basal insulin intensification (insulin glargine titration, basal-bolus therapy, and IGlarLixi) in T2D patients in Mexico who were not controlled with basal insulin.

2 Methods

The analysis assessed the cost per patient achieving treatment targets (cost of control) for the following endpoints: (a) HbA1C < 7.0%, (b) HbA1C < 7.0% without weight gain, (c) HbA1C < 7.0% without hypoglycemia, and (d) HbA1C < 7.0% without hypoglycemia and weight gain.

2.1 Clinical Data

Clinical inputs used in the analysis were obtained from the DUAL clinical study program, including DUAL V (IDegLira versus IGlar 100), DUAL VII (IDegLira versus IGlar U100 + IAsp), and an indirect treatment comparison (ITC) comparing IDegLira versus IGlarLixi (the combination of insulin glargine and lixisenatide) [18, 19, 22]. Based on the existence of these published head-to-head evidence and a robust ITC insulin glargine titration, basal-bolus therapy, and IGlarLixi were chosen as IDegLira's comparators in the present analysis.

DUAL V was a 26 week, open-label study comparing the safety and efficacy of IDegLira and continued up-titration of insulin glargine U100 in patients with T2D not achieving glycemic targets on insulin glargine [18]. DUAL VII was a 26 week, open-label study comparing the safety and efficacy of IDegLira and basal-bolus therapy in patients with T2D not achieving glycemic targets on insulin glargine [19].

In the absence of head-to-head trial data to provide comparative evidence for IDegLira versus IGlarLixi, an indirect treatment comparison based on published data was conducted [22]. The following phase 3 trials were used as

[1] Such as the UK Prospective Diabetes Study (UKPDS), the Diabetes Control and Complications Trial (DCCT), and the Diabetes Intervention Study (DIS).

[2] GDP per capita estimated using an exchange rate of $20.06 MXN = 1 USD, results in $167,085 MXN.

Table 1 Proportion of patients achieving treatment goals

	IDegLira (%)	Comparator (%)	*P*-value
Full DUAL V trial population (IDegLira $n = 278$, insulin glargine U100 $n = 279$) [18]			
HbA1C < 7.0%	71.6%	47.0%	< 0.001
HbA1C < 7.0% without weight gain	50.0%	19.7%	< 0.001
HbA1C < 7.0% without hypoglycemia	54.3%	29.4%	< 0.001
HbA1C < 7.0% without weight gain and hypoglycemia	38.8%	12.2%	< 0.001
Full DUAL VII trial population (IDegLira $n = 252$, basal-bolus scheme $n = 254$) [19]			
HbA1C < 7.0%	66.0%	67.0%	NS
HbA1C < 7.0% without weight gain	43.3%	15.5%	< 0.0001
HbA1C < 7.0% without hypoglycemia	57.6%	33.5%	< 0.0001
HbA1C < 7.0% without weight gain and hypoglycemia	38.2%	6.4%	< 0.0001
ITC (IDegLira versus IGlarLixi) [22]			
HbA1C < 7.0%	70%	54.9%	< 0.0001
HbA1C < 7.0% without weight gain	54%	34.2%	< 0.0001
HbA1C < 7.0% without hypoglycemia	56%	31.7%	< 0.0001
HbA1C < 7.0% without weight gain and hypoglycemia	42%	19.9%	< 0.0001

Statistical significance was assessed at the 95% confidence level. *HbA1C* glycated hemoglobin, *IDegLira* insulin degludec/liraglutide, *IGlarLixi* insulin glargine/lixisenatide, *ITC* indirect treatment comparison

sources for the ITC: IDegLira trials—DUAL II [23] and DUAL V [18]; IGlarLixi trials—LixiLan-L [24]. Data from SWITCH 2 [25], the only phase 3 study comparing IDeg with IGlar U100 in a population solely comprised of insulin-experienced patients with T2D, was also used to strengthen the comparison. Outcomes of interest at 6 months of follow-up were as follows: change from baseline in HbA1c levels, change from baseline in body weight, insulin dose at end of trial, rate of American Diabetes Association (ADA)-documented symptomatic hypoglycemic events, rate of severe or blood glucose (BG)-confirmed hypoglycemic events, and the proportion of patients achieving HbA1c < 7%, HbA1c < 7% without weight gain, HbA1c < 7% without hypoglycemic events (severe or BG-confirmed in the DUAL trials, ADA-documented symptomatic in LixiLan-L), HbA1c < 7% without weight gain or hypoglycemic events (severe or BG-confirmed in the DUAL trials, ADA-documented symptomatic in LixiLan-L). Estimation of the treatment effects of IDegLira relative to IGlarLixi used in the present analysis were performed according to Bucher et al. [26].

All three analyses using the clinical inputs from the DUAL V trial, DUAL VII trial, and the ITC, included the full trial population; thus, no subanalyses were made. This decision was made so that all patients with T2D were represented in the analysis. The proportion of patients achieving all endpoints in all three comparisons is presented in Table 1.

2.2 Cost Data

Costs were estimated from the private healthcare perspective in Mexico and were expressed in MXN. Costs that were included in the analysis comprised the study drugs (IDegLira, insulin glargine, rapid insulin, and IGlarLixi). These unitary costs were obtained in December 2021 from IQVIA's Pharmaceutical Market Mexico (PMM) audit. Costs of needles and supplies for self-monitoring of blood glucose (SMBG) testing were extracted from published wholesale acquisition costs in December 2021 [27].

To estimate the daily cost of treatment, doses (at the end of the trial, from DUAL V and DUAL VII studies and the ITC) were multiplied by the unitary cost of each intervention. Annual costs of treatment per patient were obtained by multiplying the daily costs by 365 (Table 2).

As the analysis is intended to assist decision-makers in the short-term, a 1 year time horizon was chosen to reflect the outcomes in this period. Thus, no discounting was applied, and no other costs (such as diabetes-related complications) were included. This time horizon is aligned with other short-term cost-effectiveness analyses evaluating the use of IDegLira [20, 21].

2.3 Evaluation of Cost of Control

An economic model developed in Microsoft Excel was used to estimate the cost of control per patient. The cost of control for each comparator was calculated by dividing the annual cost of treatment (as of December 2021, obtained from IQVIA's PMM audit and wholesale acquisition costs) by the proportion of patients achieving the desired goal (Fig. 1).

The cost of control was assessed for the following endpoints: HbA1C < 7.0%, HbA1C < 7.0% without weight gain, HbA1C < 7.0% without hypoglycemia, and HbA1C < 7.0% without hypoglycemia and weight gain. These endpoints are

Table 2 Annual cost of treatment per patient (MXN)

	IDegLira (MXN)	Comparator (MXN)
Full DUAL V trial population (IDegLira $n = 278$, insulin glargine U100 $n = 279$) [18]		
Insulin	$48,287	$36,296
Needles	$430	$430
SMBG	$3469	$3469
Total	$52,186	$40,194
Full DUAL VII trial population (IDegLira $n = 252$, basal-bolus scheme $n = 254$) [19]		
Insulin	$47,109	$40,861
Needles	$430	$1720
SMBG	$3469	$10,406
Total	$51,008	$52,987
ITC (IDegLira versus IGlarLixi) [22]		
Insulin	$50,760	$51,932
Needles	$430	$430
SMBG	$3469	$3469
Total	$54,659	$55,831

IDegLira insulin degludec/liraglutide, *IGlarLixi* insulin glargine/lixisenatide, *ITC* indirect treatment comparison, *MXN* Mexican pesos, *SMBG* self-monitoring of blood glucose

Fig. 1 Cost of control calculation

$$\textit{Cost of achieving target A with comparator X} = \frac{\textit{Annual cost of Comparator X}}{\textit{\% of patients in comparator X achieving target A}}$$

considered relevant in the treatment of T2D patients who are not controlled with basal insulin, as well as being aligned with the endpoints reported in the clinical evidence used in the present analysis [18, 19, 22].

2.4 Sensitivity Analysis

To assess the robustness of the base case findings, a one-way sensitivity analysis was performed by carrying out a +10% variation in turn on the IDegLira cost of medication, a ±10% variation on the needles cost and SMBG testing cost, and finally a −10% variation on the proportion of patients treated with IDegLira achieving targets.

3 Results

3.1 Annual Cost of Interventions

Annual treatment cost with IDegLira was higher versus insulin glargine titration due to higher acquisition costs of IDegLira. In comparison with basal-bolus therapy or IGlarLixi, the annual cost of treatment was similar (Table 2). Needles and SMBG testing costs were higher for the basal-bolus therapy due to the frequency of applications and monitoring per day (Table 2).

3.2 Number Needed to Treat

IDegLira resulted in the lowest number needed to treat (NNT) to bring one patient to goal for all endpoints in all comparisons (Fig. 2). For HbA1C < 7.0%, the NNT with IDegLira varied between 1.4 and 1.5 patients (meaning 66–72 out of every 100 patients will achieve the goal), whereas for the comparators it varied between 1.5 and 2.1 patients (that is, 55–67 out of every 100 patients will achieve the goal, Fig. 2).

Differences were greater in all comparisons for composite treatment goals, which included avoidance of confirmed hypoglycemia and/or weight gain (Fig. 2). Specifically, for HbA1C < 7.0% without hypoglycemia and weight gain the NNT with IDegLira varied between 2.4 and 2.6 patients. In contrast, the NNT with IGlarLixi, basal-bolus therapy, or IGlar titration was 5.0, 15.6, and 8.2 patients, respectively (Fig. 2).

3.3 Cost of Control

IDegLira resulted in the lowest cost of control per patient for all endpoints in all comparisons (Fig. 3). For HbA1C < 7.0%, the cost of controlling a patient with IDegLira varied between $72,885 and $78,543 MXN, whereas for the comparators it ranged between $79,085 and $101,695 MXN.

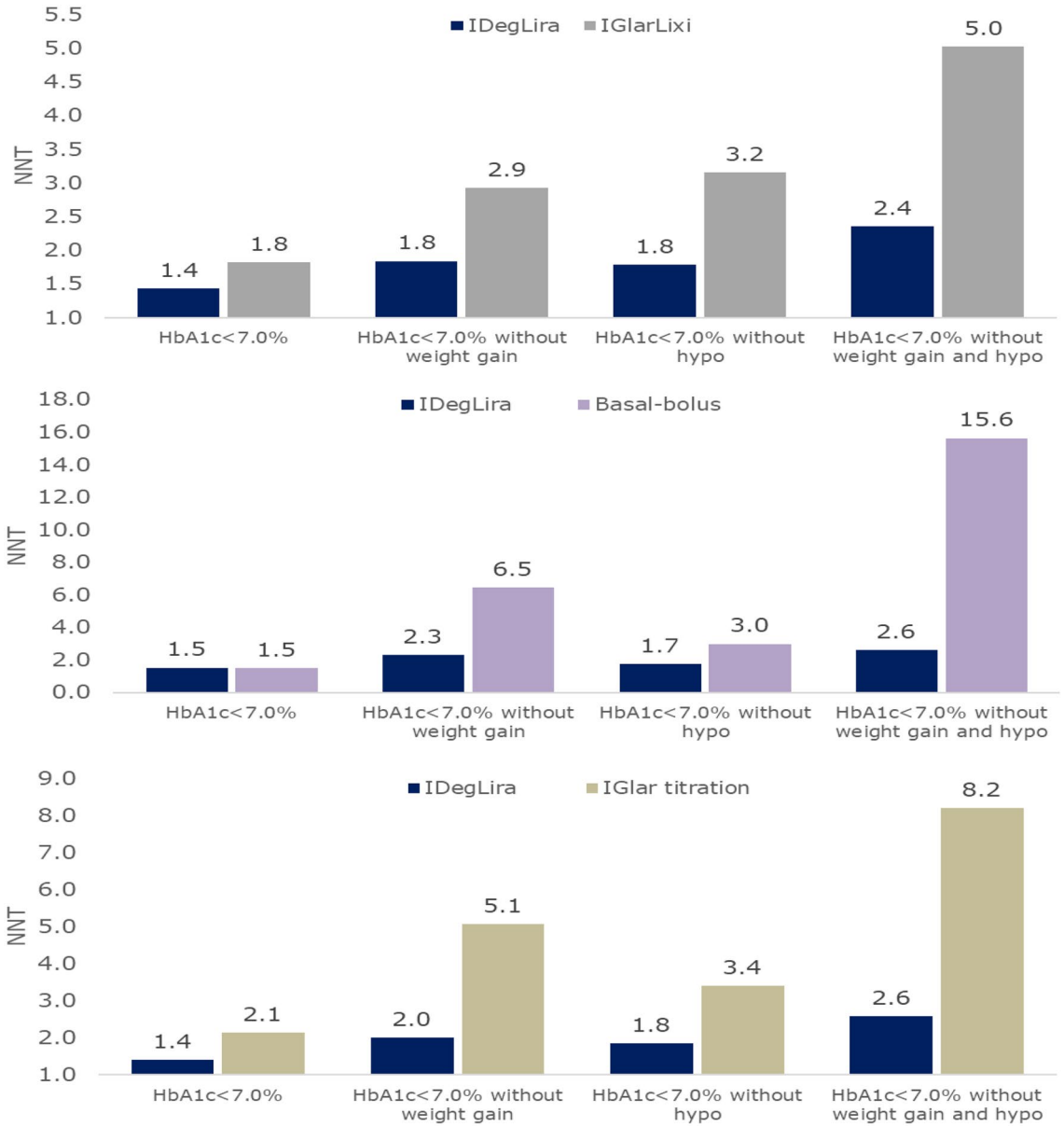

Fig. 2 Number needed to treat, IDegLira versus comparator. *HbA1C* glycated hemoglobin, *IDegLira* insulin degludec/liraglutide, *IGlar* insulin glargine, *IGlarLixi* insulin glargine/lixisenatide, *NNT* number needed to treat

Differences were greater for composite treatment goals in all comparisons. Specifically, the greatest difference in cost on control was seen in the composite endpoint of HbA1C < 7.0% without hypoglycemia and weight gain, where the cost of controlling a patient with IDegLira varied between $128,737 and $134,500 MXN, whereas for the comparators it varied between $280,557 and $827,924 MXN.

In terms of the relative spending to bring patients into control, the analysis showed that for every $100 MXN spent on IDegLira, $117, $102, and $129 MXN were required to achieve HbA1C < 7.0% with insulin glargine titration, basal-bolus therapy, and IGlarLixi, respectively (Table 3). To achieve HbA1C < 7.0% without hypoglycemia and weight gain, for every $100 MXN spent on IDegLira, $245, $620, and $218 MXN were required with insulin glargine titration, basal-bolus therapy, and IGlarLixi, respectively (Table 3).

3.4 Sensitivity Analysis

The cost of control was lower with IDegLira versus comparators in most of the sensitivity analyses that were conducted (data not shown; results in supplementary

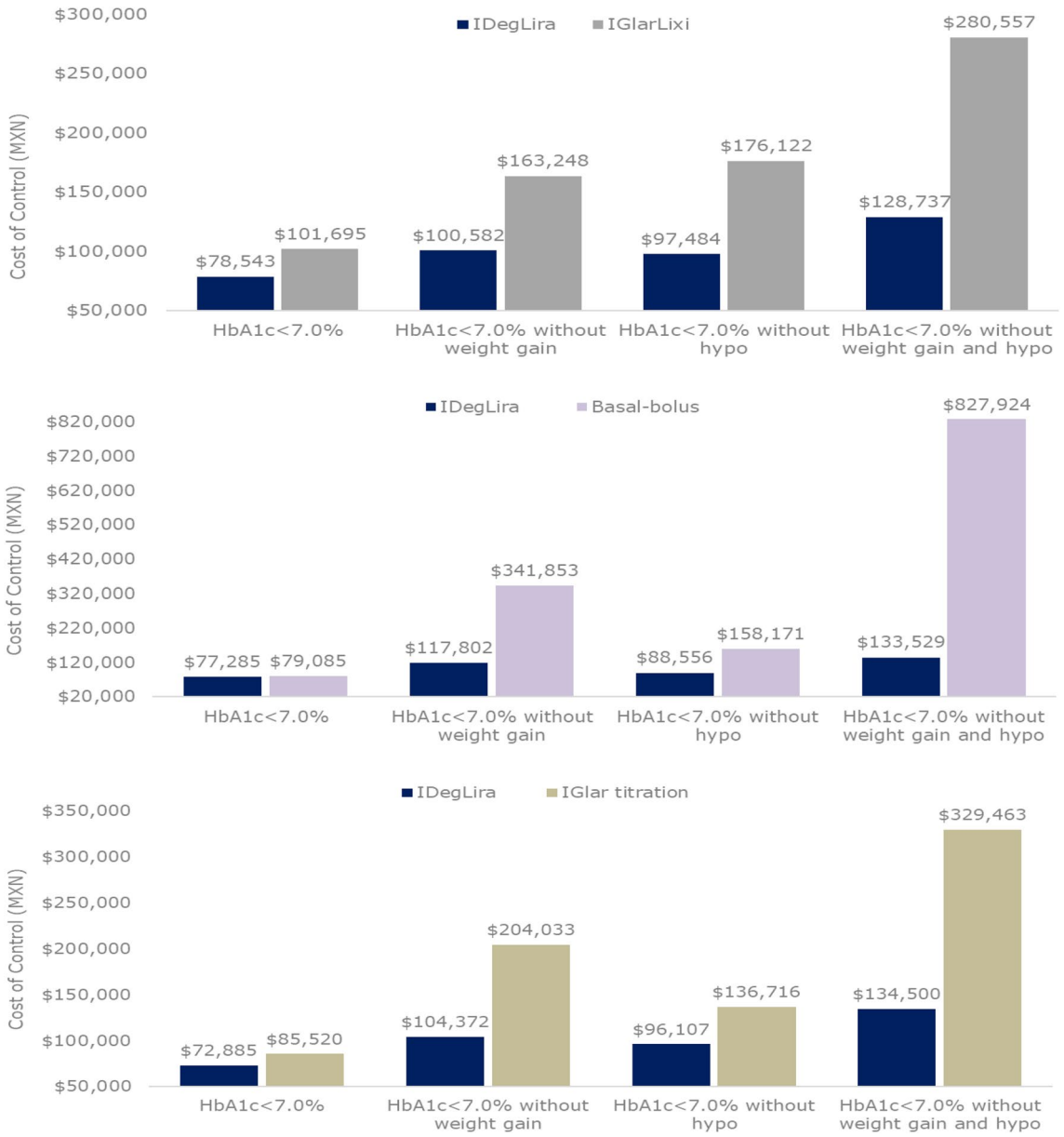

Fig. 3 Cost of control per patient, IDegLira versus comparators. *HbA1C* glycated hemoglobin, *IDegLira* insulin degludec/liraglutide, *IGlar* insulin glargine, *IGlarLixi* insulin glargine/lixisenatide, *MXN* Mexican pesos

materials). Findings were not impacted by variations (± 10%) in the needles and SMBG costs. The only endpoints in which the cost of control was higher with IDegLira versus comparators were as follows: (1) In the comparison against basal-bolus when the IDegLira medications cost was increased by 10%, where the cost of control for the HbA1c < 7.0% endpoint with IDegLira was $5338 MXN higher than the comparators, and (2) in the comparison against basal-bolus when the proportion of patients treated with IDegLira achieving HbA1c < 7.0% was 10% lower, where the cost of control observed was $6787 MXN higher than the comparators.

4 Discussion

T2D complications pose a significant clinical and economic burden to patients, health systems, and society in Mexico [14, 28, 29]. Therefore, it is crucial to effectively treat the patients, targeting both glycemic control and risk factors to reduce the clinical and economic burden of T2D complications [6, 30–33].

When the annual cost and efficacy of every intervention is considered, it can be seen that controlling a patient with IDegLira is less costly compared with other interventions.

Table 3 Relative cost of control (IDegLira = $100)

	IGlar titration (MXN)	Basal bolus (MXN)	IGlar-Lixi (MXN)
HbA1C < 7.0%	$117	$102	$129
HbA1C < 7.0% without weight gain	$195	$290	$162
HbA1C < 7.0% without hypoglycemia	$142	$179	$181
HbA1C < 7.0% without weight gain and hypoglycemia	$245	$620	$218

HbA1C glycated hemoglobin, *IDegLira* insulin degludec/liraglutide, *IGlar* insulin glargine, *IGlarLixi* insulin glargine/lixisenatide, *MXN* Mexican pesos

Thus, IDegLira represents a good option in terms of value for money for both patients and payers in comparison with other forms of basal insulin intensification in Mexico.

Therefore, optimizing access to an effective and comprehensive treatment in patients who require intensification of basal insulin could allow health institutions to better allocate the resources they have in the short and long term due to the prevention of hypoglycemia, reduced resource use (e.g., less injections), and control of risk factors for cardiovascular events. In addition, adopting the DUAL program's titration scheme (titration twice weekly), could reduce the spending on strips.

A strength of this analysis is that, within 1 year, it assesses the clinical and economic benefits of IDegLira versus insulin glargine titration, basal-bolus therapy, and IGlarLixi in a simple way, making it easy to be replicated and updated when clinical or cost inputs change. However, the temporal horizon can be a limitation when trying to project longer-term clinical and cost outcomes. Yet, it could be assumed that superior glycemic control in the short term would have a clinical and economical benefit in the long term given the association between glycemic control and the incidence of micro- and macroangiopathy.

An additional limitation is that adverse events, especially hypoglycemia, were not captured in the analysis; therefore, its cost and consequences were not taken into account. Although hypoglycemia was considered in the analysis as part of the endpoint, the cost of hypoglycemia management was not included. Including hypoglycemia when assessing interventions for basal insulin intensification is important as its cost may impact the results of the model. This is because, according to the Instituto Mexicano del Seguro Social (IMSS, the largest public healthcare institution in Mexico), the cost of treating one event of hypoglycemia varies between $7189 and $130,676 MXN[3], depending on whether it is ambulatory or if it requires hospitalization [10, 11, 34]. Therefore, a cost minimization analysis using data from DUAL VII could be further conducted to assess the extent to which hypoglycemia drives the results of this analysis.

Finally, the model outcomes assumed a consistent treatment effect over the whole 1 year time horizon; however, in real-world settings, this consistent effect might not hold due to persistence and adherence issues [35, 36]. This limitation was assessed on the sensitivity analysis by varying the proportion of patients treated with IDegLira achieving clinical endpoints. The overall outcomes did not vary from those observed in the base case, with the exception in the comparison against basal-bolus where the cost of control with IDegLira was higher. However, it is plausible that this limitation applies to all the comparators evaluated equally and not just the proportion of patients achieving clinical endpoints with IDegLira.

Regarding the existing evidence, short-term and long-term economic evaluations of IDegLira in comparison with up-tritation of IGlar and basal-bolus therapy on T2D patients who are not controlled with basal insulin have been conducted in the UK, Sweden, and US settings. In general, the results of these evaluations are consistent with the results of this study in concluding that IDegLira is a dominant or cost-effective intervention to intensify the treatment of patients with basal insulin. Furthermore, these analyses demonstrated that IDegLira also improves quality-adjusted life expectancy and could reduce the total cost of T2D patients who are not controlled with basal insulin [20, 21, 37–39].

5 Conclusions

The greater clinical efficacy of IDegLira in terms of bringing patients to treatment goals resulted in lower cost of control values per patient versus insulin glargine titration, basal-bolus therapy, or IGlarLixi from a healthcare payer perspective in Mexico.

Differences in cost of control per patient were greater when composite treatment goals were considered, especially for the goal of HbA1C < 7.0% without hypoglycemia and weight gain. These findings suggest that IDegLira is the most desirable option when seeking to comprehensively treat the patients by achieving goals beyond the HbA1C < 7.0% threshold.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s41669-023-00421-2.

Declarations

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[3] Costs published by IMSS in 2017, updated to prices of 2022 (22.27% inflation).

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Conflicts of interest Juan Carlos Garnica-Cuellara and Enrique Morales-Villegas, speakers on behalf of Novo Nordisk Mexico, have received consulting fees from Novo Nordisk Mexico in activities unrelated to this manuscript. However, they have not received any remuneration regarding the development of this manuscript. Enrique Morales-Villegas collaborated as principal investigator on DUAL VII, is speaker for Novo Nordisk Mexico and also received consulting fees from Novo Nordisk Mexico. Carmen Alicia Lopez-Forero and Bárbara Monroy-Cruz are employees of Novo Nordisk Mexico. Bhrugu Pariti, Swati Deshwal, and Manisha Sekharan are employees of Novo Nordisk A/S. Mariana Osorio-Hernández and Ida Caterina García-Appendini are employees of IQVIA Mexico, which received consulting fees from Novo Nordisk Mexico to support preparation of the analysis.

Compliance with ethics guidelines As this study used data from secondary sources and did not involve direct interaction with human or animal subjects, it was exempt from review by Novo Nordisk's ethics committee.

Consent to participate This study involves information coming from published literature and contain no patient personal information. Therefore, patients' consent is not needed.

Consent for publication Not applicable

Availability of data and materials The input data for this cost-effectiveness analysis was obtained by extracting relevant information directly from other clinical trials. Further details on the specific trials and data extracted can be found in the methods section of this publication.

Author contributions BM-C and CAL-F, conducted substantially to the design of this article. BM-C, BP, and SD conducted the economic analysis. BM-C and CAL-F conducted the collection data for the analysis tool, all authors participated in the writing sections of all the manuscript. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval for the version to be published.

Code availability (software application or custom code) The model was performed in MS Excel®; however, this is not available for its consultation.

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