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## Cost-Effectiveness of Dulaglutide Compared with Liraglutide and Glargine in Type 2 Diabetes Mellitus Patients in Colombia

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### ABSTRACT

**Background:** Diabetes treatment includes very diverse drugs. It is essential to identify which drugs offer the best value for their costs. **Objectives:** To estimate comparative cost-effectiveness for treating diabetes mellitus with dulaglutide, liraglutide, or glargine in Colombia. **Methods:** A Markov model including diabetic microvascular and macrovascular complications was used to estimate cost-effectiveness. We used annual cycles, a 5-year time horizon, 5% discount rate, and third-party payer's perspective. Main outcomes were quality-adjusted life-years (QALYs) and incremental cost-effectiveness ratios (ICERs). Transition probabilities were obtained from primary studies and costs from local databases and studies. We used a threshold of 3 times the Colombian per capita gross domestic product (US \$17,270 for 2015; US \$1 = 2,743 Colombian pesos) to assess cost-effectiveness. **Results:** Total costs related to dulaglutide, liraglutide, and glargine were US \$8,633, US \$10,756, and US \$5,783, yielding 3.311 QALYs, 3.229 QALYs, and 3.156 QALYs, respectively. Dulaglutide dominated liraglutide given lower total

costs and higher QALYs. The estimated ICER for dulaglutide compared with glargine was US \$18,385, greater than the accepted threshold. Sensibility analysis shows that decreased dulaglutide cost, increased consumption of glargine, nondaily injection, and number and cost of glucometry could result in ICERs lower than the threshold. Probabilistic sensitivity analysis showed consistent results. **Conclusions:** This estimation indicates that dulaglutide dominates liraglutide. Its ICER is, however, greater than the accepted threshold for Colombia in base case compared with glargine. By increasing population weight or glargine consumption, dulaglutide becomes cost-effective compared with glargine, which could identify a niche where dulaglutide is the best option. **Keywords:** Colombia, cost-effectiveness analysis, diabetes, dulaglutide, insulin glargine, liraglutide, quality-adjusted life-years.

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### Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disease associated with high morbidity and mortality [1]. Its incidence and prevalence will rise in the near future, especially in developing countries [2]. International treatment guidelines suggest several therapeutic options with diverse adverse effects and ways of administration [3]. Insulin directly lowers glycemic levels and is the mainstay of treatment for many patients. Glargine is a widely used basal insulin that requires daily administration [3]. Glucagon-like peptide 1 (GLP-1) analogues affect insulin homeostasis through endogenous pathways [4]. Dulaglutide is a GLP-1 analogue with prolonged action and half-life because of its resistance to degradation and its low renal clearance, allowing once-weekly administration. Liraglutide is another GLP-1 analogue similar to dulaglutide but it requires daily injection. Available studies show some benefits in terms of glycemic control, hypoglycemia events, and weight change when

compared with glargine [5–7] and similar results when compared with liraglutide [8,9]. The cost of dulaglutide is, however, an issue, especially when compared with glargine.

The purpose of this study was to estimate the cost-effectiveness of dulaglutide compared with glargine and liraglutide in Colombian patients with T2DM, considering differences in health benefits and costs.

### Methods

We performed a cost-effectiveness estimation of treating Colombian patients with T2DM with no microvascular complications with dulaglutide compared with liraglutide or with glargine. Liraglutide was selected as the most representative GLP-1 analogue in the Colombian market. We created a Markov model using TreeAge Pro 2009 (TreeAge Software, Inc., Williamstown, MA) and following official Colombian health technology

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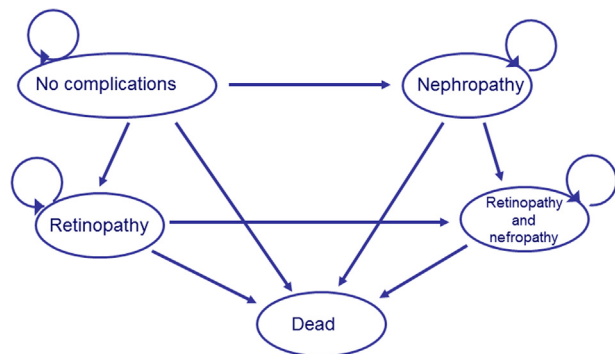
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assessment recommendations [10]. A countable state space for the Markov chain was considered.

We estimated direct medical costs from a third-party payer's perspective (Colombian health care system) with a 5-year time horizon, with sensitivity analysis at 3 and 10 years. We deemed these time horizons to be long enough to show differences between interventions. A 5% annual discount rate was used in the base case, with sensitivity analysis ranging from 0% to 12%. Main effectiveness outcomes were quality-adjusted life-years (QALY) and incremental cost-effectiveness ratio (ICER) of dulaglutide compared with liraglutide and glargine. We also estimated the number of patients developing nephropathy, retinopathy, acute myocardial infarction, stroke, hypoglycemia, or experiencing death in a hypothetical cohort of 10,000 patients with T2DM with no previous microvascular complication and an average age of 55 years. All costs refer to 2015 and are expressed in US dollars with a mean conversion rate for 2015 of US \$1 = 2743 Colombian pesos. The ICER threshold was defined as US \$17,270 (3 times the Colombian per capita gross domestic product). This is the upper limit of the cost-effectiveness threshold accepted by local agencies.

Patients are assumed to start using dulaglutide, liraglutide, or glargine and continue with the same treatment until the end of the simulation. No restriction on previous diabetes treatment is assumed. The model (Fig. 1) uses 6-month cycles. We assumed this time to be sufficient to show differences in glycemic control and appearance of microvascular complication. For this model, we contemplated only those health states that are relevant to the clinical management of T2DM and could be directly impacted by glycemic control, and assumed that all patients start without any microvascular or macrovascular complications. Patients can then transition to having nephropathy, retinopathy, both, or die. Mortality was dependent on age, on the basis of official Colombian data, adjusted by a relative risk (RR) for diabetic patients [11].

Table 1 presents the main variables introduced in the model. Patients on each treatment differ in the probability of achieving the goal of less than 7% of glycated hemoglobin ( $HbA_{1c}$ ), as well as in hypoglycemia rate and in weight change. These data were obtained from clinical trials comparing dulaglutide with liraglutide or with glargine [5–9]. We started by either reporting data contained in or calculating them from available information from primary studies for the comparison between glargine and dulaglutide. Because no statistically significant differences between dulaglutide and liraglutide were found in  $HbA_{1c}$  and hypoglycemia [8,9], we assumed their values to be equal in the model. Differences in glycemic control influence transition probabilities to microvascular complications. The presence of one microvascular complication also increases the risk of having another [12].



**Fig. 1 – Markov model used in the estimation. All patients are assumed to start in the “No complications” state.**

Acute myocardial infarction (AMI) and stroke can occur in all patients. Risks for these events were extracted from literature and are influenced by glycemic status [13]. Hypoglycemia can also occur in all patients, and probabilities were based on clinical trials [5–9]. Weight change obtained from primary studies was also integrated [5–9].

Another important transition probability is mortality. Baseline mortality was obtained by multiplying the Colombian general population mortality rate for 55-year-old adults obtained from life tables [14] by the RR of death in patients with T2DM [11]. This mortality was then multiplied by additional death RRs associated with microvascular complications of T2DM.

We considered only direct medical costs. Costs of glargine and liraglutide for 2015 were obtained from SISMED (*Sistema de información de precios de medicamentos*), the official database for drug sale volumes and prices. Dulaglutide was not available in the Colombian market and so the producer provided the expected launch price. We assumed a daily 1.8 mg dose of liraglutide and a weekly 1.5 mg dose of dulaglutide. We assumed a 0.2 international unit/kg dose of glargine and 70 kg mean body weight. This weight implies a body mass index (BMI) of 25 in a population with an average height of 1.65 m. Glargine users were also charged daily with the cost of a needle [15] and one glucometry. Patients affected by microvascular complications had an additional cost associated with follow-up. Resources were identified by creating a base case with experts and their cost was estimated from the national tariff manual established in 2001, with a 30% increase [16]. Patients with retinopathy were charged for outpatient visits (two per year) and, in advanced cases (estimated to be 30%), for optical coherent tomography (one per patient), fluorescein angiography (one per patient), photocoagulation (one per patient), and antivascular endothelial growth factor injections (three per year). Patients with nephropathy were charged for outpatient visits (three per year), renal and cardiac sonograms (one per year), 24-hour proteinuria (two per year), creatinuria (two per year), complete blood cell count (three per year), renal function (three per year), parathyroid hormone test (four per year), vitamin D level (four per year), uric acid (four per year), lipid profile (four per year), and daily intake of losartan and atorvastatin. This was meant to represent average patients with nephropathy and retinopathy considering the great degree of variability in clinical severity and resource consumption they may have. AMI and stroke costs were estimated for the acute event and the subsequent necessary follow-up by using data from a local economic evaluation [15]. Because hypoglycemia cost can vary from being null to being extremely high, we assumed a conservative episode cost comprised by a single visit and basic laboratory examinations once a year.

Utilities were obtained from electronic registries and other diabetes evaluations. T2DM with no complications was attributed a 0.79 utility, on the basis of an analysis on 3867 British patients from the UK Prospective Diabetes Study [17]. Patients with a single microvascular complication were attributed lower utilities obtained from literature (retinopathy, 0.61; nephropathy, 0.551) [18]. We assumed a lower utility (0.5) for those having both complications. Each 1 point reduction in BMI was attributed a 0.006 utility [19]. Patients experiencing hypoglycemia, AMI, and stroke presented a reduction in utility of 0.0142, 0.26, and 0.06, respectively [20,21]. Patients on dulaglutide were attributed a nondaily injection utility of 0.022 per year, considering the alternative treatment in which all patients had daily injections [22]. These values were introduced with beta distributions.

### Sensitivity Analysis

We assessed the effect of modifying the time horizon (from 3 years to 10 years) and the discount rate (from 0% to 12%). We

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