The Cost-Effectiveness and Budget Impact of Introducing Indacaterol into the Colombian Health System

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ABSTRACT

Objectives: The main objectives were to estimate the cost-effectiveness and budget impact of indacaterol (a once-daily, long-acting-beta$_2$-agonist) compared with 1) salmeterol/fluticasone, 2) formoterol/budesonide, and 3) tiotropium for the treatment of chronic obstructive pulmonary disease in Colombia. **Methods:** A Markov model was utilized to simulate the progressive course of chronic obstructive pulmonary disease, distinguished by forced expiratory volume in 1 second predicted according to the four Global Initiative for Chronic Obstructive Lung Disease severity stages by using prebronchodilation values. Efficacy was based on the initial improvement in forced expiratory volume in 1 second, taken from either a network meta-analysis (salmeterol/fluticasone and formoterol/budesonide) or a randomized controlled trial (tiotropium). Colombian direct costs and life tables were incorporated in the adaptation, and analysis was performed from a health care payer perspective, discounting future costs (presented as US dollars) and benefits at 5%. A budget impact model was built to estimate the cost impact of indacaterol in Colombia over 3 and 5 years. **Results:** Indacaterol was found to be dominant (i.e., less costly and more effective) against both salmeterol/fluticasone and formoterol/budesonide per life year and quality-adjusted life-year gained after a 5-year time horizon. The average cost saving against salmeterol/fluticasone and formoterol/budesonide was US $411 and US $909 per patient, respectively. All probabilistic sensitivity analysis simulations indicated indacaterol to be less costly than salmeterol/fluticasone and formoterol/budesonide. Indacaterol was more effective and more costly than tiotropium, corresponding to an incremental cost-utility ratio of US $2584 per quality-adjusted life-year. **Conclusions:** The results indicate that by replacing salmeterol/fluticasone or formoterol/budesonide with indacaterol, there are possible cost savings for the Colombian health care system. This was demonstrated by both cost-effectiveness and budget impact models.

Keywords: Colombia, COPD, cost-effectiveness, indacaterol.

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Background

Chronic obstructive pulmonary disease (COPD) is a chronic disease affecting 8.9% [1] of the 14,958,285 [2] Colombians aged 40 years or older. Of these, 31% [1] belong to Global Initiative for Chronic Obstructive Lung Disease (GOLD) spirometric classification 2 to 4, as defined by GOLD [3]. In 2005, COPD was ranked as Colombia's seventh most disabling disease, with 9.8 disability-adjusted life-years per patient, and second or third when considering people older than 80 years and between 60 and 79 years old, respectively [4]. This proves that COPD is a major burden to the Colombian health care system. It has been estimated that the weighted average cost of COPD could be US $848.10 per patient per year in Colombia [5]. By using this average per-patient cost, the burden of COPD was found to be US $916 million in 2004, based on a COPD prevalence figure of 1,080,000 patients, and US $1129 million, based on 2012 projections of COPD prevalence, which estimate 1,331,000 patients [2]. This is approximately 0.7% to 0.9% of the Colombian gross domestic product (GDP). About 35% of these costs are related to hospitalizations to treat acute exacerbations [6]. It is unclear whether this estimate includes the cost of long-acting inhaled therapies used as maintenance therapy in COPD. An alternative source indicates that the annual spending on inhaled therapies—long-acting beta$_2$-agonist (LABA), long-acting muscarinic antagonist, and LABA with inhaled corticosteroids (ICSs)—for COPD in Colombia is estimated to be US $5.5 million (0.6% of the total cost of COPD), using data validated by Dr. Luis F. Giraldo [7], with LABA/ICS products being the market leaders (60% market share in COPD).

There are currently four long-acting inhaled products used in the treatment of COPD in Colombia: indacaterol 150 μg; a once-daily LABA, tiotropium 18 μg; a long-acting muscarinic antagonist; and two fixed-dose combinations (FDCs) of LABA and ICS: salmeterol/fluticasone 50/500 μg and formoterol/budesonide 9/320 μg. For the purposes of the current analysis, FDCs were

selected as the main comparators because these are most frequently used in GOLD stages 2 to 4. It should be noted, however, that ICSs are not recommended for patients at low risk of COPD exacerbations, such as those with % predicted forced expiratory volume in 1 second (FEV_1) of more than 50% and with zero or one exacerbation in the previous year by the current GOLD strategy [3]. Currently, no long-acting therapies have been included in the Colombian health benefit plan, despite the recommendation in the GOLD strategy. Currently, patients with COPD in Colombia must have their prescriptions approved by the health service on a case-by-case basis.

The decision of whether to include long-acting inhaled products in the national health plan, and if so which products might offer the best value for money, would pose a challenging question to Colombian decision makers. Different tools exist to facilitate the decision-making process on resource allocation, and one such tool is the cost-effectiveness (CE) analysis; it is highly suitable as it considers both the difference in effects gained (i.e., life years [LYs] or quality-adjusted life-years [QALYs]) and costs incurred between two interventions. Another commonly used tool is the budget impact model, which considers the changes in the health care budget when introducing a new therapy. Both tools have therefore been utilized numerous times to evaluate the CE and budget impact of therapies in COPD such as long-acting muscarinic antagonist or LABA alone, or the latter in combination with ICS. To the authors' knowledge, however, this is the first COPD CE study in a Latin American setting and the first CE evaluation of indacaterol compared with a combination of LABA and ICS. A CE analysis will help decision makers who are considering individual patient applications for long-acting inhaled products to treat COPD; it may also help to reconsider the case decision to include certain long-acting inhaled products in the Colombian Health Benefit Plan, thereby eliminating the need to assess patients on a case-by-case basis.

Methods

The CE analysis was performed by using a Markov model constructed in Microsoft Excel 2007, with 3-month cycles. The structure was identical to the model previously published by Price et al. [5] (Fig. 1). Health states were categorized by the ratio of prebronchodilator FEV_1 compared with that of the general population. The states were separated according to the GOLD spirometric classification [8]: mild (GOLD 1: 80%–100%), moderate (GOLD 2: 50%–80%), severe (GOLD 3: 30%–50%), and very severe COPD (GOLD 4: <30%) airflow limitation. The initial distribution

Fig. 1 – Model structure. GOLD, Global Initiative for Chronic Obstructive Lung Disease.

of disease severity in the model corresponded to the baseline characteristics observed in the Novartis Indacaterol phase III trial (INHANCE) (1.4%, 42.2%, 45.4%, and 11.0% from stage 1 to 4, respectively) [9]. To ensure that the model results were representative of the Colombian population, a disease severity distribution based on Colombian data was investigated as a scenario analysis based on the Colombian COPD cohort PREPOCOL [1]. Prediction of FEV_1 for the general population was done by utilizing a regression model published by Falaschetti et al. [10]; this was used as no Colombian-specific regression model was available. Each GOLD state in the model could be further subdivided into no exacerbation, nonsevere exacerbation (not requiring hospitalization), severe exacerbation (requiring hospitalization), and those having discontinued therapy. A 7% annual discontinuation rate of therapy was assumed, equal for all treatments.

The annual decline in lung function was 54 ml obtained from the OLIN study [11], which gives the rate of decline in prebronchodilator FEV_1. Normal lung function was compared against the lung function predicted by the annual rate of decline for patients with COPD to yield a percentage of predicted lung function for each year. The number of years it took for the percentage predicted value to cross the threshold of a GOLD class was taken as the median time for patients to progress one GOLD class. The median time was then converted into a probability of progressing by using the following equation: $1 - 0.5^{\wedge}(1/(\text{median time}))$.

Two different CE analyses were performed, the first against formoterol/budesonide 9/320 μg and the second against salmeterol/fluticasone 50/500 μg. Because there were no head-to-head trials between indacaterol and LABA/ICS, efficacy was instead based on a published network meta-analysis (NMA) [12]. This NMA used Bayesian statistics to compare all therapies linked in the network at once, considering both direct (i.e., head-to-head trials) and indirect evidence (i.e., via a common comparator) [13]. The NMA included 15 placebo-controlled randomized clinical trials of which 13 contained active treatments of interest: indacaterol 150 μg (n = 5 studies), formoterol/budesonide 9/320 μg (n = 3), salmeterol/fluticasone 50/500 μg (n = 5), excluding those with only an Asian study population. The present analysis uses FEV_1 results reported in the NMA publication: indacaterol 150 μg increased FEV_1 with 180 ml (95% credible interval [CrI] 110–250 ml) after 12 weeks; the corresponding number for formoterol/budesonide 9/320 μg was 90 ml (95% CrI 10–160 ml) and 150 ml (95% CrI 100–230 ml) for salmeterol/fluticasone 50/500 μg (Table 1). The outcome presented above was adjusted for two covariates: the proportion of current smokers and the proportion with severe or very severe COPD. This set of results from the NMA was selected to ensure that the model could properly account for the patient characteristics that would have an impact on the results.

A second analysis was based on the clinical study INHANCE [9], a head-to-head trial of indacaterol versus open-label tiotropium 18 μg, applying the transition matrix published by Price et al. [5].

No exacerbation data were available from the NMA; thus, only FEV_1 was considered in this analysis; however, exacerbation rates were included in the analysis versus tiotropium. These were taken from the INHANCE study. The baseline rate of exacerbations from the placebo arm of the trial was 0.72 per patient-year [9]. Rate ratios were applied to the baseline rate of exacerbation: 0.67 (95% CI 0.46–0.99) and 0.70 (95% CI 0.48–1.03) for indacaterol and tiotropium, respectively. As the exacerbation rates by disease severity (i.e., GOLD stage) were not available, the same rate of exacerbations per year was applied to all four disease severity groups. The impact of such an assumption was tested in a scenario by applying values from a systematic review [14]. Exacerbations were further classified as severe or nonsevere. Exacerbations requiring hospitalizations were considered severe. The distribution of severe to nonsevere exacerbations was derived for each disease severity group on the basis of INHANCE [9].
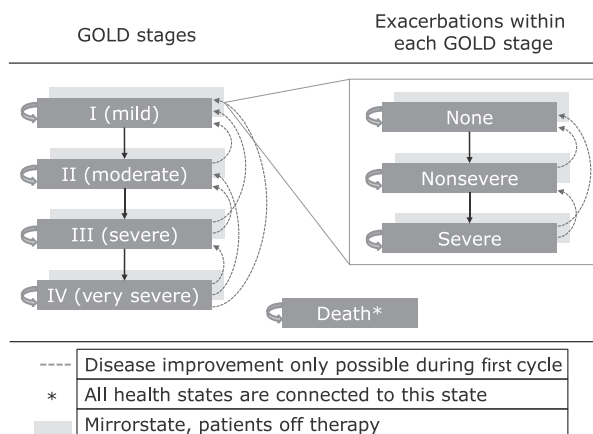
Table 1 – Model efficacy inputs.					
	Difference vs. placebo				
	(Based on NMA) [15]			**(Based on trial)** [9]	
	Ind 150 μg	**Sal/Flu**	**For/Bud**	**Ind 150 μg**	**Tio 18 μg**
FEV_1 change from baseline to 12 wk (95% CrI)					
No adjustment	180 ml (160–210)	140 ml (120–160)	90 ml (70–110)	180 ml (148–215)	140 ml (105–180)
Adjusting for covariates*	180 ml (110–250)	150 ml (100–230)	90 ml (10–160)		
Exacerbations†	0.67	0.67	0.67	0.67	0.70

COPD, chronic obstructive pulmonary disease; Crl, credible interval; FEV_1, forced expiratory volume in 1 s; For/Bud, formoterol/budesonide; Ind, indacaterol; NMA, network meta-analysis; Sal/Flu, salmeterol/fluticasone; Tio, tiotropium.
* Adjusting for proportion of smokers and proportion of patients with severe and very severe COPD.
† Risk ratio compared with placebo.

The risk of mortality associated with each severity (GOLD) stage was based on data used in a previously published model by Rutten-van Molken [15]. These rates described all-cause mortality for patients with COPD. In the current analysis, it was assumed that the majority of recorded deaths would be due to respiratory disease–related causes. However, age-specific mortality was considered by the inclusion of all-cause mortality. This was based on Colombian interim life tables published by the *Departamento Administrativo Nacional de Estadistica* [16].

The indacaterol clinical trial program collected health utilities by using the EuroQoL five-dimensional (EQ-5D) questionnaire. EQ-5D questionnaire index scores were prepared by using the UK "York Tariff" [17]. Mean values from these studies were analyzed to provide model inputs, and the variation around the mean was used to inform sensitivity analyses. EQ-5D questionnaire results were summarized by disease severity status to yield a mean utility weight for each disease severity class as shown in Table 2 [5]. Utility values from the literature were tested as a scenario analysis. These came from a utility study in patients with COPD conducted by Stahl et al. [18], who valued health state utilities for each of the disease severity classes as defined by prebronchodilator FEV_1 values. In addition, utility decrements associated with exacerbations were taken from a publication by Rutten-van Molken et al. [19]. Exacerbation decrements were applied only in the exacerbation states, and the decrement takes place within that cycle only.

Three types of direct costs were considered in the model analysis: 1) drug acquisition cost, 2) cost of maintenance therapy,

and 3) cost of exacerbation. The acquisition cost (Table 3) for tiotropium was obtained from *Ministerio de protección social de la republica de Colombia* 2011 [20] and that for LABA/ICS from *Ministerio de protección social de la republica de Colombia* 2008 [21] and corrected to 2011 [22]. Costs of COPD maintenance (Table 4) were based on 30 clinical records from Teleton University Hospital's pulmonary rehabilitation program in 2010 and consisted of other medications, cost of visits, cost of radiologic tests, and cost of laboratory tests. The cost of exacerbation was dependent on severity. Nonsevere exacerbations consisted of ambulatory and emergency events, but no hospitalizations. Cost of ambulatory events was based on medication costs [21], and the costs of visits were derived from the Teleton University Hospital's pulmonary rehabilitation program, whereas the frequencies were based on the GOLD strategy and expert opinion. The cost of emergency visits was based on 144 billing records. Cost of severe exacerbations consisted of ambulatory emergency events and hospitalizations. The costs of ambulatory events and emergency visits were estimated in the same way as for nonsevere exacerbations. The cost of hospitalization was based on 29 billing records in 2010. Costs were converted to US dollars with the following exchange rate: 1 USD = COP 1771.13, as on April 20, 2012 [23].

The base-case CE analysis was performed with a 5-year time horizon, and both cost and effect outcomes were discounted with a 5% rate. The model predicted the potential gains in LYs and QALYs, as well as costs incurred. Both one-way sensitivity analysis (OWSA) and probabilistic sensitivity analyses (PSAs) were conducted. In the one-way sensitivity analysis, each variable in the model was set to the outer limits of the confidence interval. The PSA is a stochastic analysis, where all parameter uncertainty in the model is evaluated at once. One thousand model iterations were performed, varying all model parameters each time carrying second order uncertainty, within logical ranges. Costs were varied according to a gamma distribution, utilities by a beta distribution, rate ratios by a log-normal distribution, and patient transitions by a Dirichlet distribution.

A budget impact analysis with a 3- and 5-year horizon was performed, considering only the cost of the four long-acting inhaled products used in the treatment of COPD in Colombia. The size of the eligible population was estimated in the following way. The adult population 40 years or older in Colombia was 14,958,285 in 2012 [2], with a COPD prevalence of 8.9% [1]. Only 12.6% [1] of those suffering from COPD, however, have been diagnosed; further, this analysis only considers those who have a severity of GOLD 2 or worse, which is only 31.1% of all diagnosed patients with COPD [1]. Based on observations in a Swiss study [24] on the compliance to GOLD strategy, it is estimated that 60.0% of the patients with a severity of 2 to 4 will

Table 2 – Utility values applied per GOLD stage and disutility for exacerbation.		
	Ind trials (CI) [5]	**Literature, mean ± SD** [18]
Utility per health state		
Mild COPD	0.82 (0.80–0.84)	0.84 ± 0.15
Moderate COPD	0.80 (0.79–0.81)	0.73 ± 0.23
Severe COPD	0.77 (0.77–0.78)	0.74 ± 0.25
Very severe COPD	0.74 (0.74–0.76)	0.52 ± 0.26
Exacerbations [15]		
Nonsevere		−0.01
Severe		−0.08

CI, confidence interval; COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; Ind, indacaterol.

Table 3 – Cost of interventions.

	Ind	Tio	For/Bud	Sal/Flu
Brand name	Onbrez Breezhaler	Spiriva	Symbicort	Seretide
Dosage (µg)	150	18	9/320	50/500
Price (COP) [28,29]	115,500	103,285	158,490	135,084
Package size	30	30	60	60
Number of dosages per day	1	1	2	2
Price per day (COP)	3850	3443	5283	4503
Price per day (US $)	2.17	1.94	2.98	2.54

Note. 1 USD = COP 1771.13 [23].
COP, Colombian pesos; For/Bud, formoterol/budesonide; Ind, indacaterol; Sal/Flu, salmeterol/fluticasone; Tio, tiotropium; USD, US dollar.

be treated with tiotropium, FDC, or indacaterol. This results in a patient population of 31,301 in 2012, with an annual increase of 1.156% (Table 5).

Results

Base-Case Analysis Versus FDC

Within a 5-year time horizon, indacaterol 150 µg was found to be dominant (i.e., less costly and more effective) against both salmeterol/fluticasone and formoterol/budesonide per LY and QALY gained. The cost savings against both salmeterol/fluticasone and formoterol/budesonide corresponded to US $411 and US $908, respectively. The estimated gains in LYs were 0.003 and 0.007 compared with salmeterol/fluticasone and formoterol/budesonide, respectively. The corresponding QALY gains were 0.004 and 0.010. The greater increase in incremental QALYs compared with LYs was a consequence of the patient composition at baseline, influencing the amount of time patients spent in the different GOLD stages. Additional sensitivity analysis demonstrated that the gain in incremental QALYs was higher than LYs for a patient population with moderate or severe COPD at baseline, in contrast to a patient population with a very severe COPD at baseline.

Sensitivity Analysis Versus FDC

The PSA was run for the comparisons versus salmeterol/fluticasone and formoterol/budesonide. The results of the 1000 iterations were plotted in Figure 2, with 65.7% of the simulations indicating indacaterol to be less costly and more effective compared with salmeterol/ fluticasone and 94.2% of the simulations indicating the same with indacaterol compared with formoterol/budesonide. For 100% of the simulations, indacaterol was less costly than comparators.

Scenario Analyses

One scenario tested the baseline composition of the starting cohort (i.e., disease severity and mean) based on the PREPOCOL cohort. This cohort consists of less severe patients than the indacaterol trial and therefore has less capacity to benefit as compared with a more severe population. Consequently, as expected, this scenario resulted in an increase in cost savings whereas the incremental QALYs gained decreased.

A second analysis was carried out versus tiotropium. The incremental cost-utility ratio was US $2584 per QALY after 5 years, well below a threshold of US $5274 (COP 9,340,940, equal to the per-capita GDP). The cost per LY gained was similar with US $2899. Indacaterol was found to be dominant against tiotropium if the US $2.17 per-day price was lowered by 1.4% to US $2.14. Over a 5-year time horizon, 47.2% of the combined simulations against tiotropium fell within the northeast quadrant of the CE plot, meaning that it requires evaluation of its CE to see whether it meets willingness-to-pay threshold requirements (US $5274). Another 0.7% fell in the northwest quadrant, suggesting that indacaterol was dominated; 0.4% fell in the southwest quadrant, indicating the proportion of iterations that were inferior (i.e., less cost and fewer QALYs); while the remaining 51.4% fell within the southeast quadrant, where the scenario was dominant. A CE acceptability curve was created on the basis of PSA simulation, found in Figure 3. There was a 78% probability that the ICUR would fall below US

Table 4 – Costs of maintenance and exacerbations per GOLD stage in US $.

	GOLD stage			
	Mild	Moderate	Severe	Very severe
Annual maintenance cost*				
Other medications	179	179	205	2810
Cost of visits	175	175	222	315
Cost of radiologic	128	128	328	477
Cost of laboratory	115	115	127	109
Exacerbations*		Nonsevere		Severe
Ambulatory visit (per event)		18		18
Emergency visit (per event)		397		368
Hospitalization (per event)		–		1963

For/Bud, formoterol/budesonide; GOLD, Global Initiative for Chronic Obstructive Lung Disease; Ind, indacaterol; Sal/Flu, salmeterol/fluticasone; Tio, tiotropium.
* Based on 144 Clinical records from Teletón University Hospital pulmonary rehabilitation program. 2010.

Table 5 – Budget impact analysis over 3 y.						
	Year 1		Year 2		Year 3	
	Wo*	W[†]	Wo*	W[†]	Wo*	W[†]
Patient population	31,301[‡]		31,663[§]		32,029[§]	
GOLD 2 (87.1%)						
Ind	0	7,360	0	7,445	0	7,531
Tio	11,449	6,815	11,581	6,893	11,715	6,793
For/bud	7,905	6,542	7,996	6,618	8,089	6,694
Sal/flu	7,905	6,542	7,996	6,618	8,089	6,694
GOLD 3 (11.3%)						
Ind	0	670	0	677	0	685
Tio	1,339	881	1,355	891	1,370	901
For/bud	889	987	909	998	919	1,010
Sal/flu	889	987	909	998	919	1,010
Tio + FDC[‖]	194	0	196	0	198	0
Tio + FDC[¶]	194	0	196	0	198	0
GOLD 4 (1.7%)						
Ind	0	47	0	47	0	48
Tio	145	130	147	131	148	133
For/bud	122	106	123	107	125	109
Sal/flu	122	106	123	107	125	109
Tio + FDC[‖]	65	65	66	66	66	66
Tio + FDC[¶]	65	65	66	66	66	66
Difference in cost in US $ (W − Wo)						
GOLD 2	−197,016		−199,293		−201,597	
GOLD 3	−282,031		−285,291		−288,589	
GOLD 4	−5,378		−5,440		−5,503	
Total	−484,424		−490,024		−495,689	

FDC, fixed-dose combination; For/Bud, formoterol/budesonide; GOLD, Global Initiative for Chronic Obstructive Lung Disease; Ind, indacaterol; Sal/Flu, salmeterol/fluticasone; Tio, tiotropium; W, with; Wo, without.

* Analysis without Ind on the market.
[†] Analysis with Ind on the market.
[‡] Population is estimated by 14,958,285 × 8.9% × 12.6% × 31.1% × 60% = 31,301.
[§] Increased with 1.156% from previous year.
[‖] For/Bud.
[¶] Sal/Flu.

$5,274 (equivalent to the per-capita GDP) and 94.5% that it would fall below US $15,821 (three times the per-capita GDP).

Budget Impact Analysis

The budget impact model forecasted that the introduction of indacaterol in Colombia would result in a cost saving of US $1.47 million after 3 years and US $2.48 million after 5 years. The amount, however, of cost savings was very much dependent on whether indacaterol replaced the more expensive salmeterol/fluticasone, formoterol/budesonide, and triple therapy or the less expensive tiotropium. In Table 5, the cost savings are presented by GOLD stage for the first 3 years. Indacaterol was forecasted to mainly replace tiotropium and to a lesser extent salmeterol/fluticasone and formoterol/budesonide in patients with stage 2 severity on the GOLD scale. In GOLD 3, indacaterol was predicted to replace triple therapy, leading to substantial cost savings.

Results were affected by the assumed proportion of salmeterol/fluticasone and formoterol/budesonide usage. In the base case, formoterol/budesonide was assumed to have 50% market share, leading to cost savings of US $2.48 million. A 100% market share for formoterol/budesonide would result in US $3.54 million savings, while a 100% market share for salmeterol/fluticasone would result in a US $1.42 million cost saving after 5 years.

Discussion

Our analyses demonstrated that indacaterol was an effective and cost-saving treatment option for patients with COPD in Colombia compared with both salmeterol/fluticasone and formoterol/budesonide. The PSA [2], however, showed that there is substantial uncertainty around the incremental gain in QALYs for both analyses. In contrast, there was much less uncertainty around the cost savings. Part of the uncertainty in the results is explained by the use of the mixed treatment comparison results, which were adjusted for the presence of two covariates; these results, while allowing the consideration of smoking status and disease severity, resulted in an increased CrI when computing the PSA results. In an alternative scenario using mixed treatment comparison results unadjusted for any covariates, the point estimate results were similar but the PSA results showed a slightly narrower range of QALY estimates, and were contained entirely in the southeast quadrant. There was a trade-off between selecting the analysis with less uncertainty but no covariate adjustment for patient characteristics and the analysis with more uncertainty but consideration of patient characteristics; the base case chose the latter, which is also a more conservative estimation of indacaterol's potential clinical benefit. These results were sensitive to changes
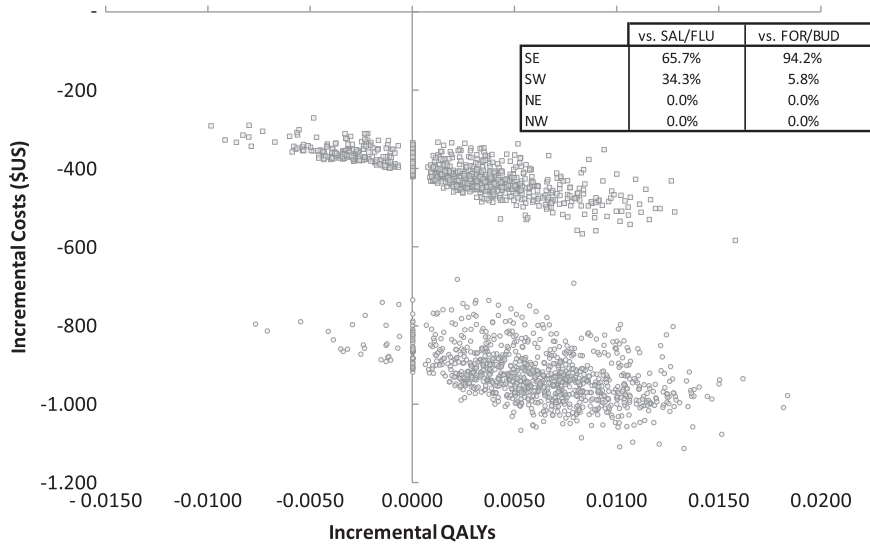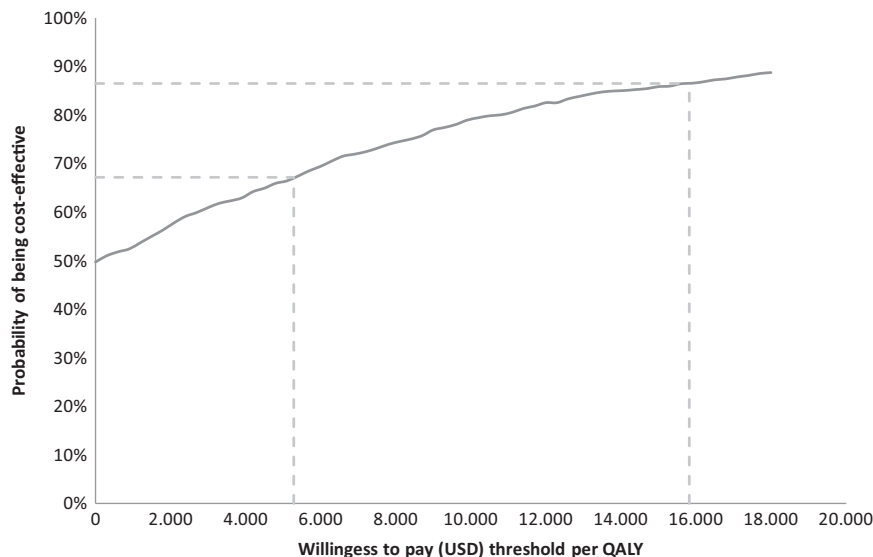
Fig. 2 – Cost-effectiveness plane, indacaterol versus salmeterol/fluticasone (boxes) and indacaterol versus formoterol/budesonide (circles) based on the base-case analysis. For/Bud, formoterol/budesonide; NE, northeast; NW, northwest; QALY, quality-adjusted life-year; Sal/Flu, salmeterol/fluticasone; SE, southeast; SW, southwest.

in discontinuation rate, mortality rates, and FEV_1 improvement. Furthermore, the analysis against tiotropium showed that indacaterol would have a 78% probability of having an ICUR of less than or equal to a willingness to pay of US $5274 (three times the Colombian per-capita GDP). These results were found to be most sensitive to changes in baseline composition, thus COPD severity.

A number of limitations were identified in this model. First, this analysis did not consider a difference in exacerbations between indacaterol and LABA/ICS. Exacerbations were not the primary end point of the trials included in the NMA and therefore were not reported [12]. Exacerbations, however, have a small impact on the total result in comparison to changes in FEV_1. As an example, if one assumed no difference in exacerbation between indacaterol and tiotropium, the incremental costs increased by US $6 and the number of QALYs gained was reduced by 0.0002. The inclusion of exacerbation rates in the comparison of indacaterol versus LABA/ICS would therefore have only minor impact.

Second, QALYs have been used as the outcome for the main analysis; it is a limitation that all values, that is, both value set and decrements, were based on a European population. Incremental QALY results in this model showed that the differences among comparators were small. The impact in quality of life of symptoms such as cough, breathlessness, and dyspnea, however, was difficult to capture as a change in utility by using a nondisease-specific measure such as the EQ-5D questionnaire. However, it should be remembered that this study was based on direct clinical trial data and for this reason external applicability is unknown in the absence of real-world evidence. Maintenance and exacerbation costs included in the analysis were obtained from a single institutional source, and as such further actualization of the model results with additional sources of costs will improve its external validity.

Comorbidities commonly associated with COPD were not analyzed in terms of additional costs and risks because these patients were excluded from the clinical trials. It was not likely

Fig. 3 – Cost-effectiveness acceptability curve for indacaterol versus tiotropium (dotted lines indicated 1×GDP and 3×GDP). GDP, gross domestic product; QALY, quality-adjusted life-year.

that these assumptions would affect the CE results as they applied to all treatment arms. Real-life adherence and compliance were not included, as we do not have a reason to believe that there would be a difference between the treatment arms. In addition, the efficacy results from the intention-to-treat population would account for these parameters.

Another assumption that introduced uncertainty in the model was the 5-year projection from 6-month duration clinical trials. However, considering the limitations in conducting long-term clinical trials, not just for COPD, projections to 5-year time horizons are a common practice in pharmacoeconomic modeling studies for chronic diseases.

Finally, this analysis excluded any impact of the use of ICS in patients for whom it is not indicated. There is some evidence to suggest that long-term usage of high-dose LABA/ICS results in loss of bone mineral density at the femoral neck and lumbar spine [25]. In fact, each 500-mcg increase in beclomethasone dose or equivalent has been associated with a 9% increased risk of fractures in patients with COPD [26]. An increased risk of diabetes onset and progression in patients receiving high doses of ICS has also been found [27]. In addition, there is an increased risk of pulmonary infections such as pneumonia [28] and tuberculosis [29,30]. This latter risk is particularly important in Colombia, a country with a high prevalence of tuberculosis. Consideration of these adverse effects may lead to a more accurate assessment of the value of introducing indacaterol to replace FDC products.

In conclusion, the results indicate that by replacing salmeterol/fluticasone or formoterol/budesonide with indacaterol, there are probable cost savings for the Colombian health care system. This is an important finding as the prevalence of COPD (as assessed by spirometry) in Colombia is estimated to be 8.9% of those aged 40 years or older. Incremental CE results versus tiotropium showed that indacaterol had a high probability of demonstrating CE considering the current Colombian willingness-to-pay threshold (US \$5274). If the Colombian health system is considering newer inhaled treatments for COPD, the inclusion of indacaterol in the health benefit plan appears justified not only on the basis of clinical results but also economically on the basis of the analysis presented.

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