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Cost-effectiveness of budesonide-formoterol in maintenance therapy of asthma patients

Costo-efectividad de budesonida-formoterol en el tratamiento de mantenimiento en pacientes con asma

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Abstract

Objective: to perform a cost-effectiveness analysis of asthma treatment with budesonide/formoterol against other treatment options used at Mexico's National Institute for Respiratory Diseases.

Methods: A complete economic evaluation of cost-effectiveness from a public health perspective, comparing the use of budesonide/formoterol as maintenance therapy with fluticasone/vilanterol in 103 female asthma patients managed at INER between 2015 and 2021.

Results: Average cost per patient was $743.23 USD, $733.36 USD for budesonide/formoterol and $767.24 USD for fluticasone/vilanterol. Pharmacological treatment represented over 70% of management costs for both groups, followed by follow-up visits and exacerbation management costs. LABA-ICS represented the highest proportion of pharmacologic management costs with a statistically significant difference amongst groups with an incremental cost of $80.17 USD for the fluticasone/vilanterol group. The budesonide/formoterol group showed an ICER of $613.31 USD for reducing the proportion of patients experiencing exacerbations during follow-up. Considering the willingness to pay threshold based on one GDP per capita ($10,902.98 USD in 2022), budesonide/formoterol represented a very cost-effective option.

Conclusions: The ICER favored budesonide/formoterol over fluticasone/vilanterol in terms of cost-effectiveness. A 5.5% reduction in patient exacerbations indicated decreased disease burden. While not statistically significant, fewer exacerbations per patient might still cut costs by lowering emergency visits and hospitalizations.

Keywords: Cost-effectiveness analysis; Asthma; Budesonide; Formoterol fumarate.

Resumen

Objetivo: Estimar el costo-efectividad del tratamiento del asma con budesonida-formoterol *vs* otros protocolos prescritos en el Instituto Nacional de Enfermedades Respiratorias de México.

Métodos: Se llevó a cabo la evaluación económica completa desde una perspectiva de salud pública, comparando budesonida-formoterol con fluticasona-vilanterol como terapias de mantenimiento en 103 pacientes asmáticos entre 2015 y 2021.

Resultados: El costo promedio por paciente fue de $743.23 dólares; $733.36 dólares para budesonida-formoterol y $767.24 para fluticasona-vilanterol. En ambos grupos, más del 70% de los costos se destinaron al tratamiento farmacológico, seguido de las visitas de seguimiento y los costos de tratamiento por exacerbaciones. La mayor parte de los costos farmacológicos se debió a LABA-ICS, con una diferencia significativa de $80.17 dólares más en el grupo de fluticasona-vilanterol. Para reducir la proporción de pacientes con exacerbaciones durante el seguimiento, budesonida-formoterol mostró un ICER de $613.31 dólares. Considerando el umbral de disposición a pagar, según el PIB per cápita ($10,902.98 USD en 2022), budesonida-formoterol resultó ser una opción altamente rentable.

Conclusiones: El tratamiento con budesonida-formoterol tuvo mayor costo-beneficio que fluticasona-vilanterol en pacientes con asma, con una reducción del 5.5% en exacerbaciones y, esto a su vez, puede disminuir los costos de atención en el servicio de Urgencias y las hospitalizaciones.

Palabras clave: Análisis de costo-efectividad; Asma; Budesonida; Fumarato de formoterol.

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INTRODUCTION

The estimated prevalence of asthma in the Mexican population is 17% and the direct annual costs of treatment range between 32 and 35 million dollars.[1] This disease represents one of the main causes for hospital visits, with a high rate of hospitalizations. Additionally, 70% of the costs of asthma management is due to uncontrolled asthma, which contributes to hospitalization costs, emergency room visits and deaths.[2,3]

International guidelines establish that asthma treatment includes the use of drugs that bring symptoms relief, such as beta androgenic agonists, systemic corticosteroids, and ipratropium bromide. Another aspect of treatment includes drugs that prevent the onset of symptoms, such as cromoglycate and nedocromil, inhaled corticoids, long acting β2 agonist (LABA), theophylline, and leukotriene modifiers.[2]

In accordance with the Global Initiative for Asthma (GINA) guidelines, asthma treatment can be divided in five steps based on disease severity: mild asthma for steps 1 and 2, where inhaled corticosteroids (ICS) such as budesonide, fluticasone, beclomethasone, mometasone, and ciclesonide are prescribed for teenagers and adults based on the needs and characteristics of each patient.[4] For moderate to severe asthma, steps 3 to 5 include the combination of ICS with LABA agents such as formoterol, vilanterol, indacaterol or salmeterol at the highest maintenance doses.[4]

Additionally, the National Asthma Education and Prevention Program (NAEPP) recommends the use of short-acting β2 agonists (SABA) as needed for intermittent asthma in step 1. For persistent asthma, they recommend low daily doses of ICS and SABAs as required in step 2; daily ICS/formoterol and as needed in step 3 (low dose) and step 4 (high dose); a daily dose of ICS/LABA + LAMA and SABA as needed in step 5; and daily doses of ICS/LABA + oral systemic corticosteroids + SABA as required for Step 6.[5]

Specifically, budesonide has been used as an effective method of controlling asthma in a large range of patients, including children, and the use of formoterol has proven a capacity to rapidly control asthma symptoms and sustained control during the day or night. The combination of both products retains the individual benefits of each while improving treatment adherence.[6-8]

According to GINA, treatment results in exacerbations define management in primary care as:

Mild or moderate: patient speaks with full sentences, prefers to be seated or lying down, is not agitated, increase in respiratory frequency, 100 to 120 beats per minute (BPM), 90-95% O2 saturation, PEF>50% or better.

Severe: speaks with isolated words, stays seated in a forward-leaning position, respiratory frequency, >30/min, use of accessory muscles, >120 bpm, O2 saturation <90%, PEF ≤50% or better. High-risk symptoms: confusion or somnolence.[4]

Some published evidence exists on the profitability of maintenance and symptom relief treatment with budesonide-formoterol in comparison with other asthma treatments.[7,8] However, there are no studies comparing profitability against other available treatment options in Mexico.

The aim of this study was to conduct a cost-effectiveness analysis of the treatment of asthma with budesonide-formoterol against other treatment options used at Mexico's National Institute for Respiratory Diseases (INER).

METHODS

Model

A decision tree was used to conduct an economic evaluation of cost-effectiveness on the use of budesonide-formoterol as maintenance therapy in comparison with fluticasone-vilanterol, where the model mapped proportion of patients with presence of exacerbations during a follow-up of one year, as shown in **Figure 1**.

Study Population

The sample consisted of 103 female patients 18 year or older diagnosed with asthma and managed at INER during the period from 2015 to 2021, being this a subset from a larger cohort of patients attended as part of a specific institutional program focused on the analysis of women's health. We included subjects who attended at least five consecutive visits during a year, meaning that the sum of time between them amounts between 335 and 395 days, during which patients received the same treatment. Such criteria had the objective to homogenizing the study population and completing the necessary follow-up period to identify health results variation in relation to the number of visits and follow-up time.

Comparators

Patients had different treatment options during follow-up, including Budesonide-formoterol (n = 73), Fluticasone-vilanterol (n = 30) and Fluticasone-Salmeterol (n = 2). However, due to the low number of patients with Fluticasone-Salmeterol, we decided to include only patients treated with budesonide-formoterol and fluticasone-vilanterol for our cost-effectiveness analysis and descriptive analysis.

Costs

Direct medical costs were quantified through a bottom-up micro-costing approach, considering follow-up visits, laboratory testing, pharmacological treatment and crisis or exacerbation management.

Follow-up visits included costs of first time and subsequent visits at INER, laboratory studies included those directly related to the disease, such as spirometry and determination of fractional exhaled nitric oxide (FeNO). Pharmacologic treatment included ICS-LABA medication, antileukotrienes, theophylline and biologic treatment. We calculated total medication for each patient by determining the number of days elapsed between visits, multiplied it by the prescribed daily dose of the allocated treatment, adding them up to obtain the total number of doses during follow-up time. Exacerbations or crisis management included ambulatory visits, emergency room admissions and hospitalizations.

The total cost for each concept was estimated by multiplying unitary costs provided by INER and IMSS (Mexican Social Security Institute) by the quantity of resources utilized and then annualized to consider variation of follow-up time for

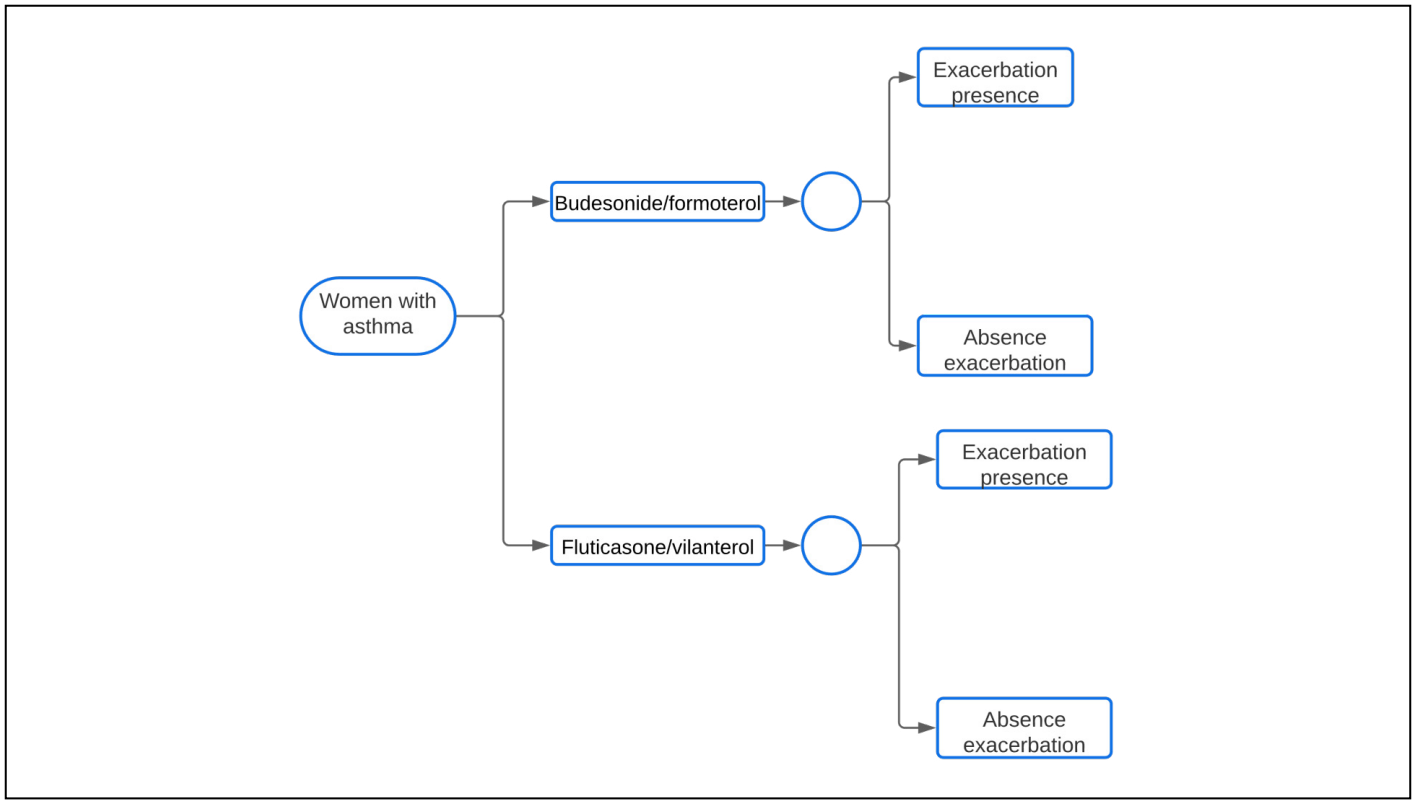


Figure 1. Decision tree model for asthma exacerbation during follow-up

each patient. All costs are presented in US dollars (1 USD = 0.04971633 MXN) and based on unitary costs of 2023.

Perspective, time horizon and discount rate

As established in the Mexican Guideline for Economic Evaluation Conduction for the Basic Drug List and Product Catalog, the perspective adopted was from a health service provider, in this case the National Institute for Respiratory Diseases (INER), which is part of Mexico's Public Health Sector.

The chosen time horizon of one year contributed to reducing the confusion factor derived from climatic conditions variation across the year. However, a longer time horizon was not appropriate due to heterogeneity of data. We did not apply discount rates due to the one-year time frame.

Efficacy and evaluation of results

We used the presence of exacerbations during follow-up period for effectiveness evaluation, as well as the average number of exacerbations for each group. We estimated the incremental cost-effectiveness rate (ICER) between budesonide-formoterol and fluticasone-vilanterol, comparing the ICER with the value of one gross domestic product (GDP) per capita. Such a comparison is in accordance with the World Health Organization's statement that classifies interventions by ICERs lower as a GPD per capita as very cost-effective, those between one and three GDP per capita as cost-effective, and finally, those above three GDP per capita are not cost-effective. The ruling for final decision was the ICER that reflects the cost per unit of efficacy gained between the comparators. The cut-off values to evaluate the ICER align to the guideline for economic evaluations by Mexico's General Health Council, considering as GDP per capita for Mexico the amount of $10,902.98 USD during the third trimester of 2022. This is the reference value utilized for the inclusion criteria for sanitary technologies into Mexico's public health system.[9] **Table 1**

Sensibility analysis

Variations in efficacy outcomes and costs were explored through univariate deterministic and probabilistic sensitivity analysis.

RESULTS

Patient characteristics, exacerbations, cost per patient and ICER

Based on the established criteria, we found 103 patients whose treatment during the follow-up period was as follows: 73 received budesonide-formoterol and 30 were treated with

Table 1. Cost effectiveness based on estimated ICER and GPD per capita.

IF	THEN
0 < ICER ≤ 1 GPD per capita ($ 10,902.98 USD)	Very Cost Effective
1 < ICER ≤ 3 GPD per capita ($ 32,708.93 USD)	Cost Effective
ICER> 3 GPD per capita ($32,708.93 USD)	Not Cost Effective

fluticasone-vilanterol, another intervention (Fluticasone-salmeterol) represented less than 1% of patients and was excluded from the analysis.

Baseline characteristics (Table II) showed an age average of 57 years; 56 for the budesonide-formoterol (B/F) and 60 for the fluticasone-vilanterol (F/V) group, with no significant difference among the groups. The average weight was 66 kgs., with a 6 kgs difference among treatment groups (IC95% 2-11, p = 0.01), while the sample's average BMI was 29, being larger for the F/V group with no statistical significance.

Socioeconomic status analysis showed that 83% of the sample belonged to the low and medium levels and highlighting that 50% of the patients in the F/V group was in the low level. Main occupation was homemaking (82.5%) followed up by employee (16.5%) and finally students, with no significant difference among groups. When asked about pets with hair or feathers, 54.4% of patients mentioned owning one.

Regarding comorbidities, we observed that 1 in 3 patients had allergic rhinitis, 19% had hypertension, and 16% had diabetes. One patient mentioned being diagnosed with Samter's Triad, and no patients reported a diagnosis of atopic dermatitis. No statistically significant differences were found on this subject. **Table 2**

Use of resources

Regarding resource allocation (**Table 3**), we found both groups presented with exacerbation episodes or required crisis management. Ambulatory management was provided in 20% of the F/V group and 14% of the B/F group. Close to 7% of both groups required an emergency ward visit. None of the patients of either group required hospitalization due to exacerbations during the follow-up period.

Laboratory findings showed that spirometry tests were performed in all these events, while FeNO was only required during follow-up of 10% of patients in the B/F group and

Table 2. Baseline characteristics by treatment group.

Characteristics	Total (n = 103)	Budesonide-formoterol (n = 73)	Fluticasone-vilanterol (n = 30)	p
Age (mean (SD))	56.99 (13.22)	55.76 (13.16)	60.47 (13.02)	0.134
Weight (median [IQR])	66.00 [59.00, 74.50]	64.00 [58.00, 73.00]	69.00 [64.00, 79.25]	0.011
Height (mean (SD))	151.17 (6.41)	150.49 (6.17)	152.80 (6.81)	0.097
BMI (median [IQR])	28.83 [25.74, 32.59]	27.97 [25.30, 32.31]	30.45 [28.00, 33.31]	0.065
Socioeconomic Level n (%)				0.743
Low	44 (42.7)	29 (39.7)	15 (50.0)	
Medium	42 (40.8)	31 (42.5)	11 (36.7)	
High	16 (15.5)	12 (16.4)	4 (13.3)	
No data	1 (1.0)	1 (1.4)	0 (0.0)	
Occupation n (%)				0.41
Student	1 (1.0)	1 (1.4)	0 (0.0)	
Homemaker	85 (82.5)	58 (79.5)	27 (90.0)	
Employee	17 (16.5)	14 (19.2)	3 (10.0)	
Pets with fur or feathers n (%)	56 (54.4)	43 (58.9)	13 (43.3)	0.221

...continuation table 2.

Characteristics	Total (n = 103)	Budesonide-formoterol (n = 73)	Fluticasone-vilanterol (n = 30)	p
Comorbidities				
Allergic rhinitis n (%)	34 (33.0)	22 (30.1)	12 (40.0)	0.461
Hypertension n (%)	20 (19.4)	15 (20.5)	5 (16.7)	0.858
Diabetes Mellitus 2 n (%)	16 (15.5)	15 (20.5)	1 (3.3)	0.058
SAMTER n (%)	1 (1.0)	1 (1.4)	0 (0.0)	1
Atopic dermatitis n (%)	0 (0.0)	0 (0.0)	0 (0.0)	NA

7% of the F/V group. Regarding pharmacological treatment, there was no statistically significant difference, but 67% of patients in the F/V required the addition of antileukotriene treatment (montelukast) versus 59% in the B/F group, where all other treatment additions were more predominant. **Table 3**

Cost analysis showed an average cost per patient was $743.23 USD (SD $279.31 USD), slightly lower for the B/F group with $733.36 USD (D.E. $318.72 USD) vs F/V ($767.24 USD), with no statistical significance (IC95% 11.45-145.25, p = 0.026). Pharmacological treatment represents most of the estimated management costs (71% and 74% for B/V and F/V respectively) followed by the cost of follow-up visits (B/F:12%, F/V:11%) and finally the costs associated to exacerbation or crisis management, with 3% for B/F and 2% for F/V. For the case of pharmacological treatment, LABA-ICS represented the highest proportion of the costs,

Table 3. Treatment resources utilization.

Intervention	Total (n = 103)	Budesonide-formoterol (n = 73)	Fluticasone-vilanterol (n = 30)	p
Follow-up visits n (%)	103 (100.0)	73 (100.0)	30 (100.0)	NA
(mean (SD))	3.75 (0.57)	3.75 (0.60)	3.73 (0.52)	0.872
Crisis management				
Ambulatory n (%)	16 (15.5)	10 (13.7)	6 (20.0)	0.615
(mean (SD))	0.16 (0.36)	0.14 (0.35)	0.20 (0.41)	0.427
Emergency visit n (%)	7 (6.8)	5 (6.8)	2 (6.7)	1
(mean (SD))	0.10 (0.41)	0.11 (0.46)	0.07 (0.25)	0.63
Hospitalization n (%)	103 (100.0)	73 (100.0)	30 (100.0)	-
(mean (SD))	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	-

...continuation table 3.

Intervention	Total (n = 103)	Budesonide-formoterol (n = 73)	Fluticasone-vilanterol (n = 30)	p
Laboratory testing				
Spirometry n (%)	103 (100.0)	73 (100.0)	30 (100.0)	-
(mean (SD))	4.00 (0.00)	4.00 (0.00)	4.00 (0.00)	-
FeNO n (%)	9 (8.7)	7 (9.6)	2 (6.7)	0.926
(mean (SD))	0.09 (0.28)	0.10 (0.30)	0.07 (0.25)	0.637
Pharmacologic treatment				
ICS-LABA n (%)	103 (100.0)	73 (100.0)	30 (100.0)	NA
Antileukotrienes n (%)	63 (61.2)	43 (58.9)	20 (66.7)	0.609
Theophylline n (%)	8 (7.8)	5 (6.8)	3 (10.0)	0.891
Acetylcysteine n (%)	1 (1.0)	1 (1.4)	0 (0.0)	1
Systemic steroids n (%)	2 (1.9)	2 (2.7)	0 (0.0)	0.897
Biologics n (%)	1 (1.0)	1 (1.4)	0 (0.0)	1
LAMA n (%)	12 (11.7)	9 (12.3)	3 (10.0)	1

and we found a statistically significant difference among the groups with an incremental cost of $80.17 for the F/V group in comparison to the B/F group. **Table 4**

The proportion of patients who presented with exacerbation episodes during follow-up, was 18% for the B/F group and 23% for F/V, with the average number of exacerbations per year was 0.25 and 0.27 for the B/F and F/V groups respectively. Neither of these differences was statistically significant (p = 0.71 and p = 0.87).

ICER

For the effectiveness assessment of reduction of the proportion of patients who present exacerbations during follow-up, the ICER for the B/F group vs F/V was $613.31

Table 4. Annual costs by treatment group (average (SD) in USD

Intervention	Total (n = 103)	Budesonide-formoterol (n = 73)	Fluticasone-vilanterol (n = 30)	p
Follow-up visit	87.44 (13.77)	87.61 (14.31)	87.03 (12.59)	0.849
Crisis management	19.75 (69.15)	21.33 (76.92)	15.88 (45.94)	0.718
Ambulatory	3.61 (8.48)	3.19 (8.07)	4.65 (9.47)	0.429

...continuation table 4.

Intervention	Total (n = 103)	Budesonide-formoterol (n = 73)	Fluticasone-vilanterol (n = 30)	p
Emergency visit	16.13 (67.78)	18.15 (75.88)	11.23 (42.76)	0.64
Hospitalization	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	NaN
Laboratory studies	98.98 (18.80)	99.53 (19.25)	97.64 (17.88)	0.645
Spirometry	93.19 (4.16)	93.23 (4.25)	93.11 (4.01)	0.903
FeNO	5.79 (18.81)	6.31 (19.51)	4.53 (17.23)	0.665
Pharmacologic treatment	532.76 (253.54)	518.87 (285.07)	566.57 (150.59)	0.388
ICS-LABA	407.18 (94.35)	383.83 (87.85)	464.00 (86.23)	<0.001
Antileukotrienes	91.05 (90.73)	91.39 (94.93)	90.21 (81.12)	0.953
Theophylline	2.55 (9.27)	2.47 (9.51)	2.73 (8.82)	0.896
Acetylcysteine	0.24 (2.47)	0.34 (2.93)	0.00 (0.00)	0.524
Systemic steroids	0.36 (2.76)	0.51 (3.27)	0.00 (0.00)	0.398
Biologics	17.63 (178.89)	24.87 (212.49)	0.00 (0.00)	0.524
LAMA	13.76 (42.46)	15.46 (46.33)	9.62 (31.44)	0.529
Total	743.23 (279.31)	733.36 (318.72)	767.24 (146.08)	0.578

USD, which, considering the willingness to pay threshold based on one GDP per capita ($10,902.98 USD in 2022) the B/F combination represents a very cost-effective option. **Table 5**

Sensibility analysis for proportions of patient with exacerbation showed that a decreased effectiveness (5%) and cost (10%) values for B/F showed big impact in the ICER results, as well as an increase of 5% and 10% effectiveness and cost values for F/V. For the number of exacerbations, a 10% increased B/F effectiveness value and 10% decreased effectiveness value for F/V had the biggest impact on ICER (**Figure 2**). Probabilistic analysis resulted in a uniform distribution around the origin, with ICERs being very cost-effective in about 24% and 25% of the cases for the proportion of patients with no exacerbation and the mean number of exacerbations, respectively. **Figure 3**

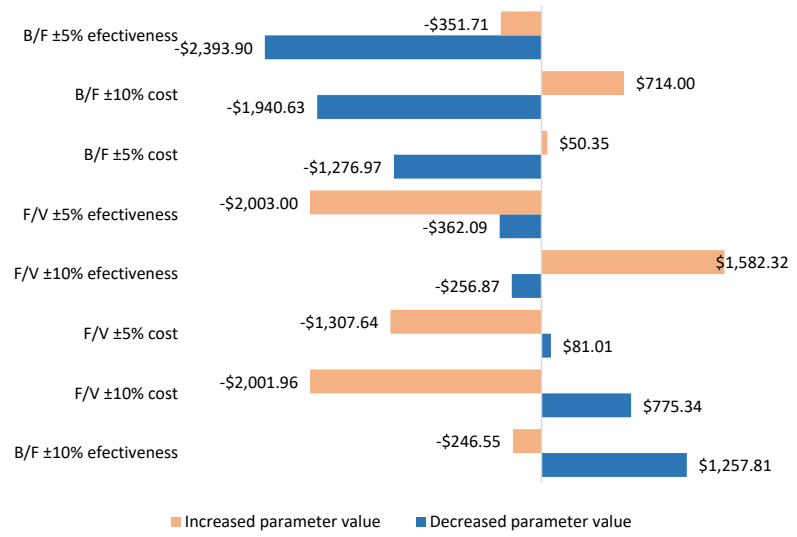
DISCUSSION

Asthma is a widespread chronic airway disease with a variable evolution, where exacerbation prevention is one of the main goals of long-term treatment established in different guidelines.

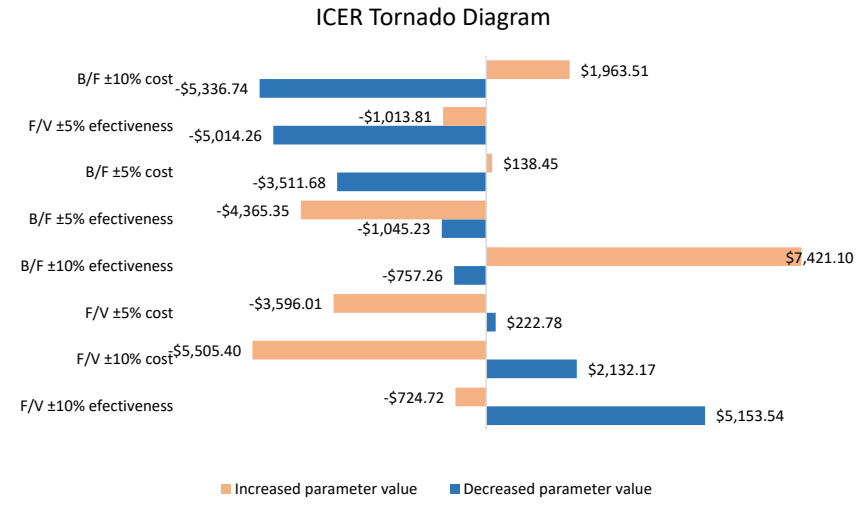
Exacerbation episodes are characterized by a worsening of symptoms and the associated breathing difficulties result in a burden that affects quality of life and signify an increase in medical resources' expenditure, affecting both the patient and the health system, where studies have estimated that expenditure in patients who present exacerbation episodes doubles the necessary resources in patients without exacerbations.[10-12]

Table 5. Incremental Cost-Effectiveness analysis evaluating effectiveness as the reduction in patient proportion that present exacerbation episodes (USD costs)

Effectiveness assessment	Treatment	Cost	Incremental cost	Effectiveness	Incremental effectiveness	RCEI
Patients with exacerbations	Budesonide formoterol	$ 733.36		0.18		
	Fluticasone vilanterol	$ 767.24	$ 33.89	0.23	0.06	$ 613.31
Number of exacerbations	Budesonide formoterol	$ 733.36		0.25		
	Fluticasone vilanterol	$ 767.24	$ 33.89	0.27	0.02	**$1,686.61**



a) Proportion of patients with no exacerbations



b) Mean number of exacerbations

Figure 2. Univariate deterministic sensibility analysis; a) proportion of patients with no exacerbation and b) mean number of exacerbations.

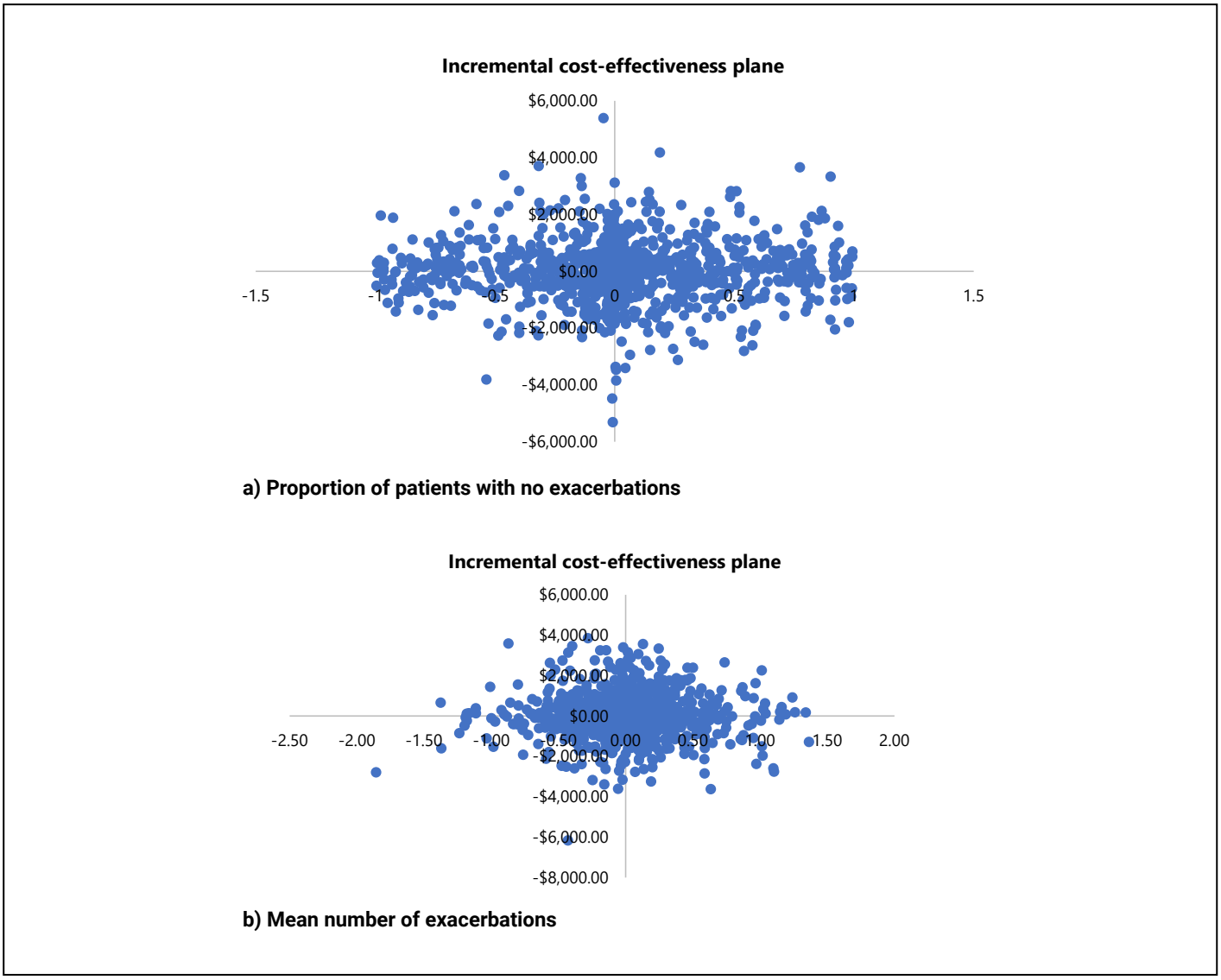


Figure 3. Cost-effectiveness plane: a) proportion of patients with no exacerbation and b) mean number of exacerbations.

There are currently different ICS-LABA combinations available for asthma management with different property profiles, but the combination treatment strategies were found to be the most effective intervention for the prevention of asthma exacerbations in a systematic review and network meta-analysis.[10]

The two combinations here studied have had their clinical efficacy compared in different studies, including a mixed treatment comparison where both treatments were comparable in terms of lung function and quality of life, but exacerbation results were inconclusive.[13]

Another comparison of early effects of budesonide/formoterol maintenance and reliever therapy with fluticasone furoate/vilanterol for asthma patients requiring step-up from inhaled corticosteroid monotherapy found that both groups showed improvement in airway inflammation, pulmonary function and symptoms from baseline to 2 weeks. From 2 to 4 weeks, the budesonide/formoterol group exhibited continuous improvement in most measured parameters, while the fluticasone/vilanterol patients reached a plateau in their improvement. Additionally, the budesonide formoterol patients showed significant FeNO improvement as well as in IOS parameters (resonance frequency and integrated area of low frequency reactance) and in the Asthma Control Questionnaire score versus the FF/VI group by week 4.[14]

On the subject of cost-effectiveness, there are no similar comparisons between these two treatments, but an analysis of budesonide/formoterol against fluticasone monotherapy in moderate-persistent asthma with data from Germany, Greece, Israel, The Netherlands, Portugal, and South Africa found that the single inhaler combination of budesonide/formoterol was both most effective than fluticasone alone, and cost-neutral, with a possibility of it being cost-effective in some countries.[15]

Other economic analysis has found the combination of budesonide/formoterol in separate inhales as cost-effective when compared with budesonide monotherapy and the single inhaler combination was also found to be cost-saving against the same regimen in separate inhalers.[16-18]

Our findings show that the combination treatment of budesonide and formoterol was a very cost-effective option

when compared with the combination of fluticasone with vilanterol in adult female patients with asthma over a 1-year time horizon from a Mexican public health perspective. Probabilistic sensibility analysis showed this happened in 25% of the simulated cases.

Amongst the limitations of the present study, we must mention the retrospective nature of our analysis, the heterogeneity of the assigned treatments during visits that made it necessary to apply strict criteria to homogenize our study sample, which may have resulted in similar probabilities of presenting an exacerbation for both groups. The database did not include patients with hospitalizations, which may prove an underestimation of the resources utilized.

Another point we must bring forward is that the present analysis did not include indirect costs into consideration, precluding us from estimating the economic impact of these costs, or adopting a social perspective as required by the guidelines for economic evaluation provided by Mexico's General Health Council.

Still, the present study results provide helpful information on the decision process for asthma management, where the cost-effectiveness of a combination within a strategy that has been found the most effective in exacerbation management, might be decisive element during treatment selection from a public health perspective.

Highlights

- Asthma is a widespread chronic airway disease with a variable evolution where exacerbations represent an important burden that affects quality of life and increases medical resources' expenditure, placing exacerbation prevention as one of the main goals of long-term treatment where ICS-LABA combinations are very effective interventions.
- The ICER by effectiveness unit for budesonide/formoterol was very cost-effective in comparison with fluticasone/vilanterol. The 5.5% difference of patients that presented exacerbation during the follow-up period represents a decrease in the burden of the disease. Likewise, there was a reduction in the number of exacerbations per patient, which was not statistically significant but may represent a source for cost saving by reducing emergency visits and hospitalizations.
- Our study results provide helpful information on the decision process for asthma management where the cost-effectiveness of a combination within a strategy that has been found the most effective in exacerbation management, might be decisive element during treatment selection from a public health perspective.

CONCLUSIONS

The ICER by effectiveness unit for B/F is very cost-effective in comparison with F/V. The clinical difference lies in the percentage of patients that presented with exacerbation episodes during the follow/up period of one year of 5.5%, which represents a decrease in the burden of the disease. Likewise, there was a reduction in the average number of exacerbations per patient. Both outcomes were not statistically significant in the present analysis, but may represent a substantial source of cost saving by a reduction in emergency ward admissions or hospitalizations.

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Conflicts of interest

María C. Cano Salas, Erika C. López Estrada, Jorge Salas-Hernández, Monserrat E. Arroyo-Rojas, Mauricio Castañeda-Valdivia and Monserrat Escobar-Preciado declare no conflict of interest for the present study. Silvia Guzmán Vázquez, Sergio Ricardo García-García, Herman Soto Molina and Homero Garcés-Flores declare a paid work relationship with HS Pharmacoeconomic Studies.

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REFERENCES

1. Ocampo J, Gaviria R, Sánchez J. Prevalencia del asma en América Latina. Mirada crítica a partir del ISAAC y otros estudios. Rev Alerg Mex. 2017; 64: 188-197.
2. Rely K, McQuire SE, Alexandre PK, Escudero GS. Costo-efectividad del tratamiento de salmeterol/fluticasona en comparación con leucotrieno montelukast para el control del asma infantil Value Health. 2011; 14: S43-S47.
3. Domínguez-Ortega J, Phillips-Anglés E, Barranco P, Quirce S. Cost-effectiveness of asthma therapy: a comprehensive review. J Asthma. 2015; 52: 529-537.
4. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention; 2022. www.ginasthma.org
5. Expert Panel Working Group of the National Heart, Lung, and Blood Institute (NHLBI) administered and coordinated National Asthma Education and Prevention Program Coordinating Committee (NAEPPCC), Cloutier MM, Baptist AP, Blake KV, Brooks EG, Bryant-Stephens T, DiMango E, et al. 2020 Focused Updates to the Asthma Management Guidelines: A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group [published correction appears in J Allergy Clin Immunol. 2021 Apr; 147:1528-1530]. J Allergy Clin Immunol. 2020; 146: 1217-1270.
6. Zetterström O, Buhl R, Mellem H, Perpiñá M, et al. Improved asthma control with budesonide/formoterol in a single inhaler, compared with budesonide alone. Eur Respir J. 2001; 18: 262-268.
7. Tamminen K, Laine J, Soini E, Martikainen J, et al. Cost-effectiveness analysis of budesonide/formoterol maintenance and reliever therapy versus fixed combination treatments for asthma in Finland. Curr Med Res Opin. 2008; 24: 3453-3461.
8. Cisneros C, Quiralte J, Capel M, Casado MA, et al. Análisis coste-efectividad de budesonida/formoterol en el tratamiento de mantenimiento y a demanda (Symbicort SMART®) frente a salmeterol/fluticasona más terbutalina, en el tratamiento del asma persistente en España. Pharmacoecon. Span. Res. Artic. 2010; 7: 163-175.
9. Consejo de Salubridad General. Guía de Evaluación de Insumos para la Salud [Internet]. México; 2023. http://www.csg.gob.mx/descargas/pdf/priorizacion/cuadro-basico/guias/insumos_salud/GEI_Enero_2023.pdf
10. Loymans RJ, Gemperli A, Cohen J, Rubinstein SM, et al. Comparative effectiveness of long term drug treatment strategies to prevent asthma exacerbations: network meta-analysis. BMJ. 2014; 348: g3009.

11. Jackson DJ, Sykes A, Mallia P, Johnston SL. Asthma exacerbations: origin, effect, and prevention. J Allergy Clin Immunol 2011; 128: 1165-74.
12. Ivanova JI, Bergman R, Birnbaum HG, Colice GL, et al. Effect of asthma exacerbations on health care costs among asthmatic patients with moderate and severe persistent asthma. J Allergy Clin Immunol 2012; 12: 1229-35
13. Svedsater H, Stynes G, Wex J, Frith L, et al. Once-daily fluticasone furoate/vilanterol versus twice daily combination therapies in asthma-mixed treatment comparisons of clinical efficacy. Asthma Res Pract. 2016; 2: 4.
14. Hozawa S, Terada M, Haruta Y, Hozawa M. Comparison of early effects of budesonide/formoterol maintenance and reliever therapy with fluticasone furoate/vilanterol for asthma patients requiring step-up from inhaled corticosteroid monotherapy. Pulm Pharmacol Ther. 2016; 37: 15-23.
15. Ericsson K, Bantje TA, Huber RM, Borg S, et al. Cost-effectiveness analysis of budesonide/formoterol compared with fluticasone in moderate-persistent asthma. Respir Med. 2006; 100: 586-594.
16. Andersson F, Stahl E, Barnes PJ, Löfdahl CG, et al. Adding formoterol to budesonide in moderate asthma--health economic results from the FACET study. Respir Med. 2001; 95: 505-512.
17. Jönsson BG, Berggren FE, Svensson K, O'Byrne PM. Budesonide and formoterol in mild persistent asthma compared with doubling the dose of budesonide - a cost-effectiveness analysis. Eur Respir J 2001; 16 (Suppl 31): 3487.
18. Rosenhall L, Borg S, Andersson F, Ericsson K. Budesonide/formoterol in a single inhaler (Symbicort) reduces healthcare costs compared with separate inhalers in the treatment of asthma over 12 months. Int J Clin Pract. 2003; 57: 662-667.