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A cost-effectiveness threshold analysis of a multidisciplinary structured educational intervention in pediatric asthma

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ABSTRACT

Objective: Asthma educational interventions have been shown to improve several clinically and economically important outcomes. However, these interventions are costly in themselves and could lead to even higher disease costs. A cost-effectiveness threshold analysis would be helpful in determining the threshold value of the cost of educational interventions, leading to these interventions being cost-effective. The aim of the present study was to perform a cost-effectiveness threshold analysis to determine the level at which the cost of a pediatric asthma educational intervention would be cost-effective and cost-saving. **Methods:** A Markov-type model was developed in order to estimate costs and health outcomes of a simulated cohort of pediatric patients with persistent asthma treated over a 12-month period. Effectiveness parameters were obtained from a single uncontrolled before-and-after study performed with Colombian asthmatic children. Cost data were obtained from official databases provided by the Colombian Ministry of Health. The main outcome was the variable “quality-adjusted life-years” (QALYs). **Results:** A deterministic threshold sensitivity analysis showed that the asthma educational intervention will be cost-saving to the health system if its cost is under US\$513.20. Additionally, the analysis showed that the cost of the intervention would have to be below US\$967.40 in order to be cost-effective. **Conclusions:** This study identified the level at which the cost of a pediatric asthma educational intervention will be cost-effective and cost-saving for the health system in Colombia. Our findings could be a useful aid for decision makers in efficiently allocating limited resources when planning asthma educational interventions for pediatric patients.

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KEYWORDS

Adherence; asthma; asthma education; cost-effectiveness; quality-adjusted life-years

Introduction

Asthma is the most common chronic disease in children [1] and a major public health problem worldwide, particularly in low- and middle-income countries (LMICs) such as Colombia [2]. Despite important advances in the knowledge of the physiopathology and the clinical aspects of the treatment of asthma, particularly over the past 20 years, many pediatric patients still fail to achieve adequate control of their asthma [3], producing a significant economic burden for patients as well as for healthcare systems [4]. Although the persistent high morbidity and the rather poor long-term asthma control that have occurred may be the result of various factors, many of these factors are related to poor patients'/parents' knowledge of and skills in several aspects of the disease, and therefore they are potentially susceptible to be modified by educational interventions in order to decrease the high morbidity associated with this prevalent chronic disease [5].

Adequate and effective treatment of asthma requires a mastering of several self-care skills such as early recognition of exacerbations, proper identification and avoidance of asthma triggers, adequate inhalation technique, and proper use of maintenance and rescue medications by using an asthma action plan [6]. Asthma educational interventions, mainly those that incorporate behavioral components, have been shown to improve the knowledge, skills, and attitudes of asthmatic pediatric patients and their parents, positively impacting several clinically important outcomes such as days of school absence, days of restricted activity, emergency department visits, and hospital admissions [5–7]. However, effective educational interventions that improve adherence to long-term therapies are complex and multidimensional, generally comprising multiple individual and group sessions over short consecutive time periods of about a month to a month and a half (with a length of the interventions ranging

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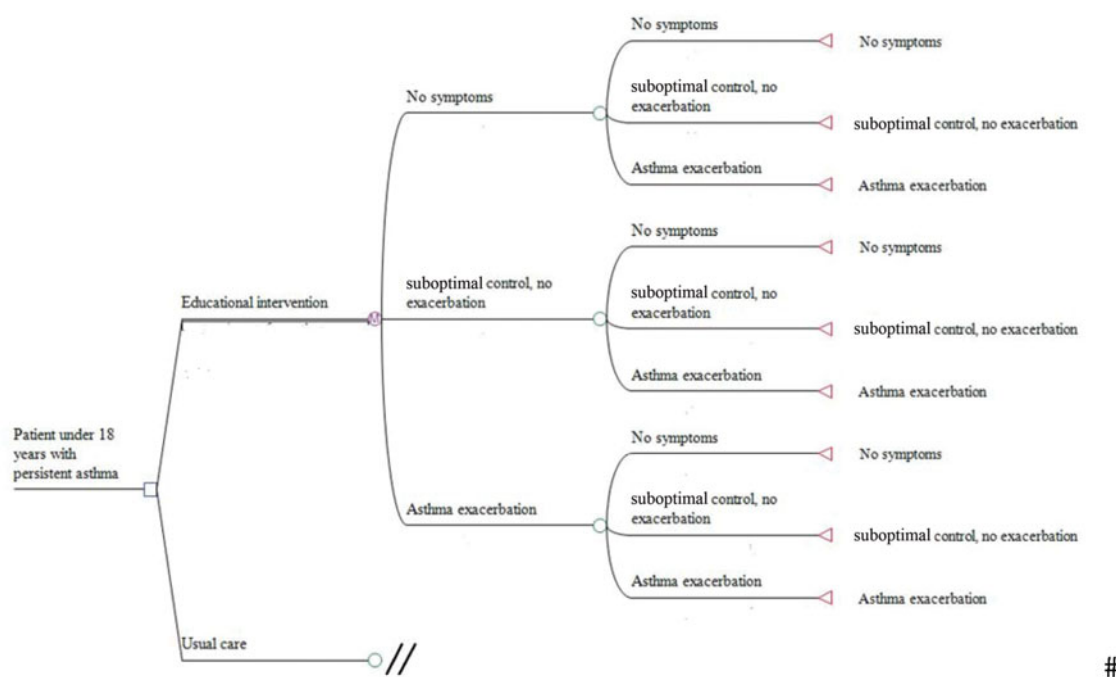


Figure 1. Diagram of the Markov model for each treatment option.

from one to twelve months), almost always incorporating asthma prevention measures, attack management plans, and sometimes also a social skills component [7]. The wide variability and complexity of the characteristics and the duration of asthma educational interventions in children make obtaining exact knowledge of the cost of implementing such interventions difficult. Although some educational interventions are more intensive because they are matched to the needs of the population (e.g., more intensive for more severe asthma), there is evidence showing that the most effective educational interventions are those with more intensive follow-ups, with multiple educational sessions using combinations of instructional modalities, and with reinforcement over time [8], which can become quite expensive. It is important to take into account the cost of implementing asthma educational interventions, because these interventions are costly in themselves and could lead to even higher disease costs [9].

Demonstrating not only effectiveness but also cost-effectiveness and cost-savings is important for advocating for a new intervention. Cost-effectiveness analysis provides a tool that can combine the cost and the effectiveness of alternative treatments. Specifically, due to the complexity and wide variability of the characteristics and the duration of asthma educational interventions in children, a cost-effectiveness threshold analysis could be helpful in determining the threshold value of the cost of the educational interventions, leading to these interventions being cost-saving and cost-effective [10]. However, studies reporting the cost-effectiveness of asthma educational interventions in children are scarce, and few of them have

been performed in any LMIC [11–13], where the economic burden of the disease is the greatest. Furthermore, to the best of our knowledge, none of these published studies have established the above-mentioned threshold values.

Accordingly, the aim of the present study was to perform a cost-effectiveness threshold analysis to determine the level at which the cost of the educational interventions would be cost-effective and cost-saving for the health system in Colombia, a South American LMIC.

Materials and methods

Model structure

In order to meet the objectives of the study, we used a Markov simulation model with three mutually exclusive nonabsorbent states (regular Markov chain) [14], labeled “no symptoms,” “suboptimal control, no exacerbation,” and “asthma exacerbation,” based on the economic implications of each of these three states (Figure 1). For each of the two comparators (usual care vs. educational intervention), the model followed pediatric asthma patients at 1-week intervals for 12 months. In the same manner as the model developed by Price and Briggs [15] and three models previously developed by our group [16–18], due to the chronic and episodic nature of asthma, a cycle length of 1 week was considered appropriate because it represents a meaningful period of time in the clinical status of a patient with asthma and was considered to be the minimum time that would allow the

succession of events of the disease to be reflected correctly. Likewise, in accordance with the above-mentioned models, we did not include costs for the treatment of adverse events derived from therapy in our cost-effectiveness model, because there is evidence to support that treatment of adverse events in asthma therapy accounts for <1% of the total costs of asthma treatment [19, 20].

The main outcome of the model was quality-adjusted life-years (QALYs), a measure of disease burden that includes both the quality and the duration of life.

Treatment adherence

In the real world, the effectiveness of asthma treatments can be diminished due to low therapeutic adherence. Inadequate adherence to asthma medications has been shown to be associated with a range of poor long-term outcomes, with clinical and economic implications such as emergency department (ED) visits and hospitalizations of asthmatic children [21, 22], although low therapeutic adherence can be positively impacted by asthma educational interventions (targeting both intentional and non-intentional barriers to adequate adherence) [23]. Therefore, we adjusted the effectiveness for each treatment by taking into account its respective rate of adherence. However, the impact of adherence on effectiveness was not incorporated into the model as an explicit parameter; instead, we used the adherence rates to inhaled corticosteroids (ICs) over time calculated in a previous study performed by our group [18] and assumed that the differences in effectiveness between the two strategies were largely due to their different adherence rates to ICs. In addition to an adjustment to the effectiveness, we also adjusted costs according to the rate of therapeutic adherence. Finally, the adherence-adjusted costs and effectiveness were incorporated into the model.

Sources of data

Disease outcomes and clinical parameters

The effectiveness data were obtained from a single uncontrolled before-and-after study carried out with asthmatic children living in Bogota, the capital city of Colombia, and nearby municipalities [24]. The study evaluated the impact on outcomes with clinical and economic implications (such as quality of life, lung function, school and work absenteeism, and ED visits and hospitalizations for asthma exacerbations) in asthmatic children aged 2–15 years (and their parents or caregivers), one year after their inclusion in a comprehensive and structured educational program (that included individual and group educational sessions, programmed and unscheduled pediatric pulmonologist visits, and multidisciplinary

respiratory care evaluation, in line with a national evidence-based asthma clinical practice guideline [25].)

Transition probabilities

Transition probabilities were calculated according to the following steps: First, following the methodology proposed by Briggs et al. [26], “baseline” transition probabilities were taken from those calculated in a previous model for pediatric patients with persistent asthma undergoing treatment with regular ICs, in which a complete level of adherence to therapy was assumed [16]. Second, transitional probabilities for both strategies were adjusted based on a modification to the “baseline” values according to the probabilities of the rate of adherence over time [18]. Third, adjustments were made for converting the effectiveness data reported in the above-mentioned study to 1-week probabilities. Since it is possible to convert an instantaneous rate to a probability over a particular time period if the rate is assumed to be constant over that period, we calculated 1-week probabilities of the events based on the instantaneous rates derived for these events [16, 26]. Finally, we adjusted the effectiveness for each strategy by modifying the “baseline” transitional probabilities according to the 1-week probabilities previously calculated.

Health outcomes

In the same manner as was done in our previous asthma models, utility values for the three health states included in the model were based on a utility valuation survey of 76 parents of children with asthma in Colombia using standard gamble methodology [17]. Parents were chosen as the most suitable patient-proxy respondents given that many children with asthma would be too young to provide reliable responses. The description of the health state comprised three domains, based on those reported in the Pediatric Asthma Health Outcome Measure: symptoms, emotions, and activity [27]. Descriptions of the three domains were largely derived from this study and were validated by clinical experts. Health states corresponding to “no symptoms,” “suboptimal control, no exacerbation,” and “asthma exacerbation” had utility values of 0.989, 0.705, and 0.275, respectively. The number of QALYs was calculated as the utility value given to a particular health state multiplied by the length of time spent in that state.

Resource utilization and costs

Each Markov model health state had an associated cost that was considered from the perspective of the national healthcare system in Colombia. Unit costs of all medications were taken from the Drug Price Information System (SISMED, 2011) [28], an official database provided by the Colombian Ministry of Health and Social Protection,

which is an important and representative primary source of drug prices in the country. The IC used in the model was budesonide. Calculation of the costs of daily therapy with budesonide was based on the estimated average daily dose appropriate for treating pediatric patients with mild-to-moderate persistent asthma according to current national and international evidence-based clinical practice guidelines for asthma [25, 29] and the relative use of available concentrations for the medication according to current market research.

In order to determine the utilization rates of health resources and the rate of events for each of the three health states of the model, we performed a review of the literature, used the results of a previous consensus of experts consisting of a panel of 10 local pediatric pulmonologists [25], and reviewed electronic medical records (EMRs) of pediatric patients hospitalized for asthma exacerbations. The data collected on healthcare utilization were: the number of planned consultations with a general practitioner, pediatrician, or pediatric pulmonologist; the number of unscheduled medical visits; the amount of asthma medication used (reliever medications, systemic corticosteroids); and the number of pulmonary function tests and other procedures (radiology procedures, laboratory tests, and ambulance). Healthcare resource use for the “no symptoms” and the “suboptimal control, no exacerbation” health states were based on a systematic review of the literature and the responses given by the above-mentioned panel of local pediatric pulmonologists using the Delphi technique [25, 30]. Healthcare resource use for the “asthma exacerbation” state was calculated based on a review of the EMRs of 512 patients discharged with a principal diagnosis of asthma (ICD-10 codes J450, J451, J458, J459, or J46X) from Clinica Infantil Colsubsidio, a pediatric clinic located in the city of Bogota that receives patients from one of the most representative medical insurance companies in the city. Hospital-managed exacerbations involved management of asthma either in an ED alone or with subsequent management as an inpatient (in an asthma inpatient ward and/or in a pediatric intensive care unit). To reflect this, the cost associated with this health state was calculated as a weighted average of the costs of exacerbations managed in the ED and of those managed during an inpatient stay, based on the frequency of hospital admission seen in our review of EMRs.

Per-unit prices of healthcare resources and cost of events were obtained from a previously published study carried out in Colombia [25] and previous reports based on a database provided by the Colombian Ministry of Health and Social Protection, in accordance with the Single Classification for Health Procedures (CUPS) and the International Disease Classification (ICD-10) that are

relevant for asthma (ICD-10 codes J450, J451, J458, J459, or J46X).

Costs were calculated in Colombian pesos (COPs) and converted to dollars (US\$) based on the average exchange rate for 2014 (1US\$ = 2000.68 COP) [31]. All the costs were adjusted to 2014 COPs before converting them to US\$. Given that the duration of the model was 1 year, costs and effects were not discounted. The study protocol was approved by the local ethics board.

Sensitivity analyses

A series of one-way, two-way, and multi-way deterministic sensitivity analyses and the effect of alternative model specifications were examined. Data ranges in the sensitivity analyses were derived from various sources: For unit costs of resources, data ranges were $\pm 25\%$ of the base value, because it was considered that this range represents a reasonable one for these unit costs (Table 1). For unit costs of all medications, data ranges in sensitivity analyses were established based on the lowest and highest values reported in SISMED. The cost of the educational intervention was determined by a deterministic threshold sensitivity analysis in order to ascertain the value required for these interventions to be cost-saving and cost-effective for the health system. The cost-saving threshold was defined as the value at which the educational intervention savings outweighed the intervention costs. The cost-effectiveness threshold was defined as the value

Table 1. Values of unit costs (US\$, 2014).

Cost items	Unit costs	Lower value	Higher value
General practitioner consultation	17.81	13.36	22.26
Pediatrician consultation	29.21	21.90	36.51
Treatment in the emergency department	39.74	29.81	49.68
Spirometry	13.25	9.93	16.57
Albuterol via pMDI ^{a,b}	2.78	2.01	3.48
Budesonide (cost per day) ^c	1.11	0.83	1.39
Prednisolone $\times 5$ mg ^e	0.03	0.02	0.04
Hospitalization for asthma exacerbation	290.18	102.24	16585.41
Others (radiology procedures, laboratory tests, ambulance)	27.26	20.44	34.01

Notes.

^apMDI – pressurized metered-dose inhaler.

^bUnit cost for albuterol pMDI 100 mcg, 200 doses/inhaler.

^cCalculation of the daily cost of budesonide was based on the estimated average daily dose appropriate for treating pediatric patients with mild-to-moderate persistent asthma according to current asthma guidelines and the relative use of available concentrations for each medication according to current market research.

^dUnit cost per tablet.

at which the educational intervention was below a predefined willingness-to-pay (WTP) threshold of US\$33,300 (threshold value based on the local gross domestic product (GDP) per capita, proposed by the World Health Organization, to be used in the developing countries). In addition, a probabilistic sensitivity analysis using a second-order Monte Carlo simulation was conducted in order to account for the uncertainties associated with the model parameters, using a cohort of 10,000 trial simulations for both strategies. A second-order Monte Carlo simulation involves specifying the distribution for input parameters in the model and sampling a random value from these distributions, allowing the joint effect of parameter uncertainty to be assessed. This probabilistic sensitivity analysis allowed us to generate 95% uncertainty intervals (UIs) for costs and effects. These were represented on a cost-effectiveness graph in order to show the estimated joint distribution of incremental costs versus incremental effects and were evaluated using a net benefit analysis [32]. All analyses were performed using TreeAge Pro 2016 software (TreeAge software, Williamstown, MA).

Results

Healthcare resource use and costs associated with the health states of the model

Of the total of 512 EMRs of asthma exacerbations reviewed, 17.8% of the exacerbations were managed in the ED, 81.2% in the asthma inpatient ward, and 1% in the pediatric intensive care unit. As expected, the weekly cost per patient associated with the “asthma exacerbation” health state was greater than that for the other two health states of the model (Table 2).

Transition probabilities

As expected, the resulting transition probabilities (point estimates) of the Markov model from any of the three health states to the “no symptoms” health state were greater for the educational intervention strategy when compared to the usual care strategy. In the same manner, the resulting transition probabilities from any of the three health states to the “asthma exacerbation” health state were greater for the usual care strategy when compared to the educational intervention strategy (Table 3).

Cost-saving and cost-effectiveness threshold analysis

A deterministic threshold sensitivity analysis suggested that asthma educational intervention would be cost-saving for the health system if its cost is under US\$513.20

Table 2. Healthcare resource use and costs associated with model health states (US\$, 2014).

Health state	Resources costed	Weekly cost per patient ^g
No symptoms	GP ^a consultation, pediatrician consultation, spirometry, BUD ^b via pMDI ^b	19.85
Suboptimal control, no exacerbation ^c	GP consultation, pediatrician consultation, unscheduled medical visit, spirometry, albuterol via pMDI, BUD via pMDI	32.83
Asthma exacerbation ^e	GP consultation, pediatrician consultation, spirometry, albuterol via pMDI, treatment in the ED ^f , hospitalization for asthma exacerbation, prednisolone × 5 mg, others (radiology procedures, laboratory tests, ambulance), BUD via pMDI	230.44

Notes.

^aGP consultation, consultation with general practitioners.

^bBUD, budesonide.

^cpMDI, pressurized metered-dose inhaler.

^dWe assumed that patients in the “suboptimal control, no exacerbation” health state needed albuterol via pMDI two puffs every six hours during the cycle length of 1 week and one unscheduled medical visit every two months.

^eWe assumed that patients in the “asthma exacerbation” health state needed albuterol via pMDI two puffs every 20 minutes for the first hour, two puffs every hour for the next 2 hours, two puffs every other two hours for the next 6 hours, 2 puffs every four hours for the next 48 hours, and finally two puffs every six hours for the remainder of the week. Additionally, we assumed that patients in this health state needed prednisolone 1 mg/kg/day for five days.

^fED, emergency department.

^gWhen assuming a complete level of adherence to controller therapy.

(Figure 2). Additionally, the analysis suggested that the cost of the asthma educational intervention would have to be below US\$967.40 in order to be cost-effective (Figure 3).

Probabilistic sensitivity analysis

A probabilistic sensitivity analysis using second-order Monte Carlo simulation was carried out in order to

Table 3. Baseline transition probabilities for asthma educational intervention and usual care strategies for treating pediatric patients with persistent asthma.

Transition from	Transition to		
	No symptoms	Suboptimal control, no exacerbation	Asthma exacerbation
No symptoms			
Asthma educational intervention	0.975	0.024	0.0003
Usual care	0.933	0.057	0.009
Suboptimal control, no exacerbation			
Asthma educational intervention	0.927	0.072	0.0005
Usual care	0.887	0.097	0.016
Asthma exacerbation			
Asthma educational intervention	0.266	0.733	0.0004
Usual care	0.255	0.733	0.012

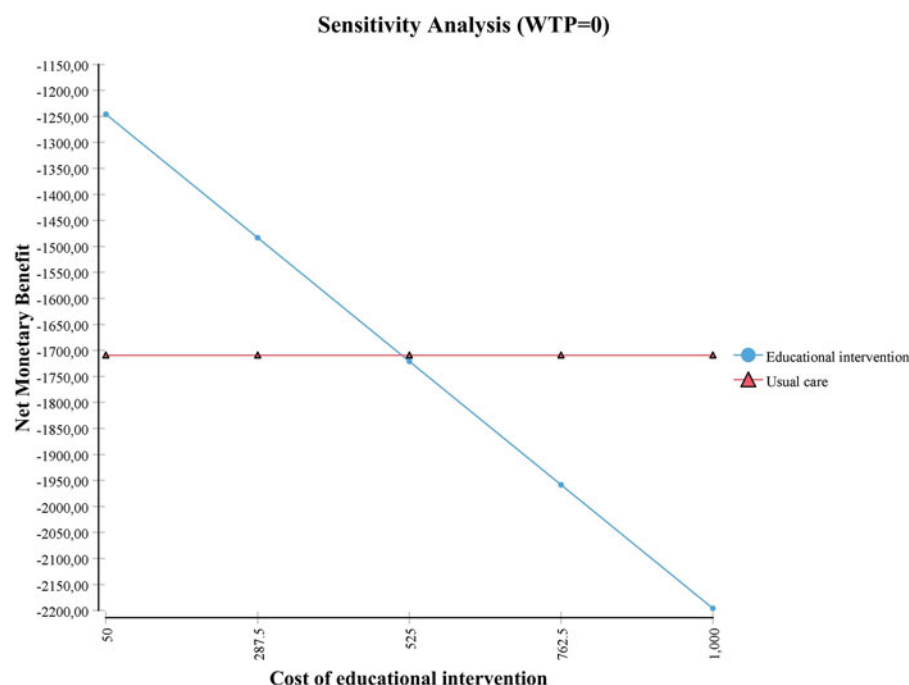


Figure 2. Cost-effectiveness threshold analysis to determine the level at which the cost of the educational intervention is cost-saving. *The deterministic threshold sensitivity analysis suggested that the asthma educational intervention would be cost-saving to the health system if its cost is under US\$513.2.

account for the uncertainties associated with the model's parameters, using the cost-saving and cost-effectiveness thresholds established in the deterministic threshold sensitivity analysis. Parameter distributions used in the probabilistic sensitivity analysis are shown in Table 4.

The results of the probabilistic sensitivity analysis using the cost-saving threshold of the cost of educational intervention are graphically represented as a scatter plot in Figure 4. This scatter plot shows that compared with the usual care strategy, educational intervention strategy

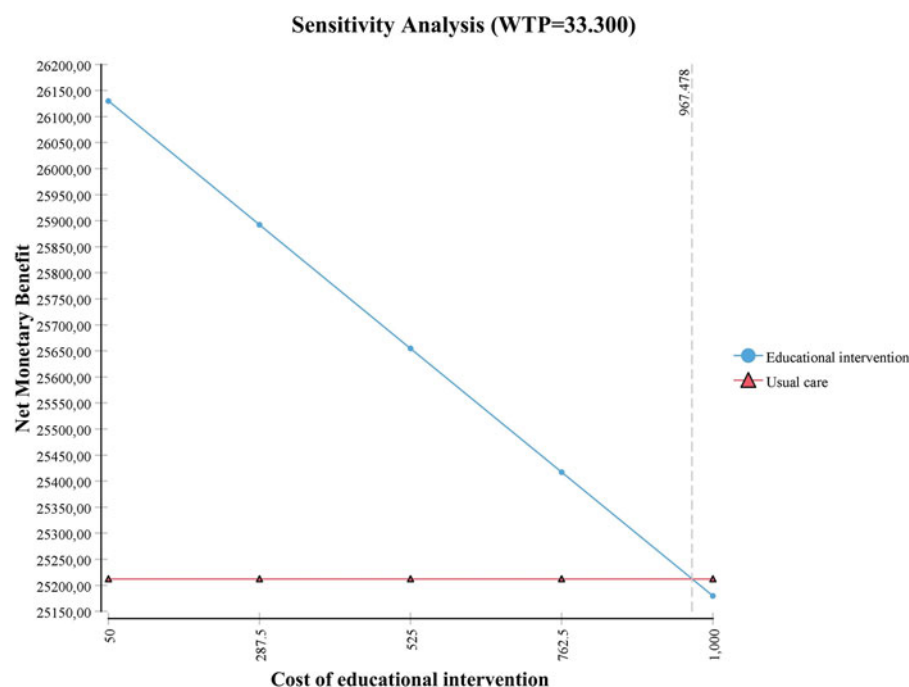


Figure 3. Cost-effectiveness threshold analysis to determine the level at which the cost of the educational intervention is cost-effective. *The deterministic threshold sensitivity analysis suggested that the cost of the asthma educational intervention would have to be below US\$967.4 in order to be cost-effective.

Table 4. Parameter distributions used in the probabilistic sensitivity analysis.^a

Probability distributions	Distribution parameters	Distribution parameters
Beta distribution	Alpha	Beta
Probability from no symptoms to no symptoms*	106.106	7.607
Probability from no symptoms to asthma exacerbation*	396.254	42029.30
Probability from suboptimal control, no exacerbation to no symptoms*	44.313	5.645
Probability from suboptimal control, no exacerbation to asthma exacerbation*	393.584	24205.42
Probability from asthma exacerbation to no symptoms*	297.745	869.882
Probability from asthma exacerbation to asthma exacerbation*	395.148	32261.70
Effectiveness of educational intervention	386.646	11224.37
Utilities		
- No symptoms state	3.411	0.038
- Suboptimal control, no exacerbation state	117.295	49.081
- Asthma exacerbation state	289.725	763.820
Gamma distribution	Alpha	Lambda
Cost of no symptoms state	44.444	21.063
Cost of suboptimal control, no exacerbation state	44.444	1.353
Cost of weekly use of daily ICS	64.00	12.877
Lognormal distribution	Mean for ln(x)	SD for ln(x)
Cost of asthma exacerbation	5.477	1.006

Notes. ^aBaseline transition probabilities were adjusted based on the calculated level of adherence at different points of time (47.6, 39.6, 35.9, 28.5, 29.7, and 28.5% at 2, 4, 6, 8, 10, and 12 months after beginning treatment with inhaled corticosteroids).

tends to be associated with similar costs and a greater gain in QALYs. Based on the results from this simulation, the 95% UIs for cost per patient treated with educational intervention and usual care strategies were US\$1,254.90 to \$2,201.40 and US\$1,035.70 to \$3,650.80, respectively. The 95% UIs for utilities were 0.767–0.864 and 0.755–0.849 QALYs, respectively. While in 33.1% of the iterations educational intervention strategy was associated with a lower cost compared with the usual care strategy, in 100% of the iterations the former strategy was associated with a greater gain in QALYs compared with the latter strategy.

The results of the probabilistic sensitivity analysis using the cost-effectiveness threshold of the cost of educational intervention showed that the 95% UIs for cost per patient treated with educational intervention and the usual care strategies were US\$1,645.50 to \$2,807.30 and US\$1,035.70 to \$3,650.80, respectively. The 95% UIs for utilities were 0.7676–0.8640 and 0.7551–0.8491 QALYs, respectively. While in 14.6% of the iterations the educational intervention strategy was associated with a lower cost compared with the usual care strategy, in 100% of the iterations the former strategy was associated with a greater gain in QALYs compared with the latter strategy.

Discussion

The present study shows that compared with the usual care, pediatric asthma educational interventions similar

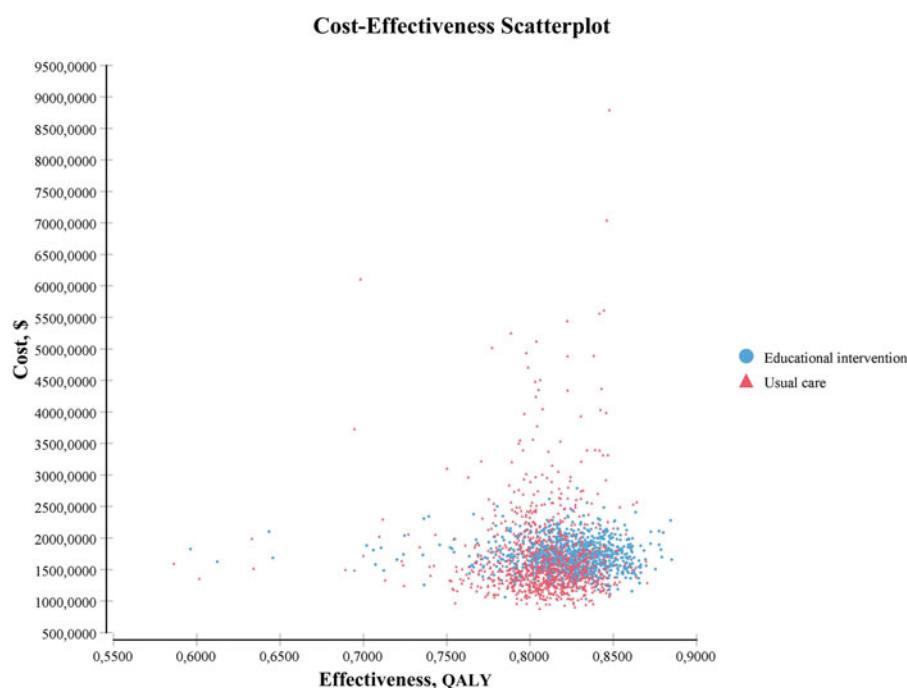


Figure 4. Scatter plot of each iteration's cost and effectiveness values for each strategy in asthmatic children *The X-axis shows the effectiveness measured as quality-adjusted life-years (QALYs); the Y-axis shows the costs measured in dollars (US\$, 2014). Each point represents one of the 10,000 trial runs, where each input was assigned a random value according to its probability density function.

to those evaluated in the present study can be cost-saving and cost-effective within a range of costs (cost-saving threshold under US\$513.20 and cost-effective threshold under US\$967.40) that seem reasonable and easily achievable for the Colombian healthcare system and probably for other similar LMIC's healthcare systems. Additionally, probabilistic sensitivity analyses indicated that these estimates were robust to simultaneous changes in model parameters.

The most notable result to emerge from the study is that the cost-saving and cost-effectiveness thresholds identified can be used to assist policy makers and clinicians in efficiently allocating limited resources when planning educational interventions aimed at reducing the huge clinical and economic burden of pediatric asthma.

Our study provides additional support for the recommendation that asthma education interventions should be incorporated into routine pediatric asthma care. This is because our results provide confidence in the cost-saving and cost-effective nature of low-cost and even moderate-cost asthma educational interventions (compared to the cost of ED visits and hospitalizations for asthma exacerbations that the intervention prevents) intended to improve the mastering of several self-care skills such as early recognition of exacerbations, proper identification and avoidance of asthma triggers, adequate inhalation technique, and proper use of maintenance and rescue medications.

Our recommendation in regard to the incorporation of asthma education interventions that incur costs below the cost-saving and cost-effectiveness thresholds identified into routine pediatric asthma care in Colombia is supported by a previous study carried out in two Colombian tertiary care institutions that evaluated the cost-benefit of an asthma educational program in a population of adult patients with moderate-to-severe asthma. The educational intervention comprised newly developed educational resources (a booklet and a video) and two group sessions, and had an average cost per patient of US\$39.50, and its implementation produced a total cost-savings of US\$1,390.60, mainly due to a significant reduction in ED visits and hospitalizations for asthma exacerbations [11].

Our results are in good agreement with those reported by Cruz, A. A., who evaluated the impact and the cost-effectiveness of a program for control of asthma in 2,385 patients living in a low-income setting in Salvador, Bahia, Brazil. The authors reported that the implementation of the program was associated with a reduction in healthcare resource utilization and in the rate of hospital admissions due to asthma in the entire city by 74%. Additionally, the program was shown to be cost-effective by reducing costs to the public health system (US\$387 patient/year) and the families (US\$789 patient/year) [13]. Our results also agree with those reported by Clark et al., who reported that they did not find significant differences in healthcare

use between a population of low-income urban children with asthma participating in an educational intervention intended to improve asthma management at home when compared with those assigned to the usual care without regard to previous hospitalization. However, when the comparison was restricted to children who had been hospitalized during the preceding year, the experimental group had a significant decrease in the number of ED visits and hospitalizations for asthma exacerbations during the year of follow-up when compared to the control group, saving US\$11.20 for every US\$1 spent on delivering health education [12]. Those results, as well as ours, support the contention that asthma educational interventions have a greater potential to be cost-effective in countries where asthma care is less developed or those with limited health insurance or social security, where hospital costs are relatively high and the impact on family income can be much greater [33], and in patients with moderate-to-severe asthma [34]. Due to the fact that all the educational interventions included group sessions, these results also draw attention to the important potential economic and clinical benefits of group sessions in asthma educational interventions. Group educational sessions are a highly cost-effective strategy for asthma education because the asthma educator can meet with multiple parents/caregivers (and patients) at the same time. Additionally, group educational sessions can have invaluable behavioral benefits, because hearing other parents/caregivers talk about problems, fears, and concerns that match their own can be educational. This is because when they hear testimonies from other parents/caregivers of asthmatic children, it is easier to realize that they are not alone and they can learn about strategies for coping with their problems, fears, and concerns [35].

We are aware that our study may have three limitations: The first is that we did not account for the severity of asthma in the analyses. This is an important issue, because asthma educational interventions have been considered to be more cost-effective in patients with moderate-to-severe asthma than in patients with mild disease [36]. However, although asthma severity was not specified in the study from which we extracted the effectiveness data, it can be inferred that the majority of participants had moderate-to-severe asthma, because in the year previous to the educational intervention 74% of the participants had been in the ED, 33% had required at least one hospitalization, and 4% had required at least one pediatric intensive care unit admission due to asthma exacerbations. Consequently, it is possible that the findings of this study could not be completely applicable to pediatric patients with mild asthma. The second is that input effectiveness parameters were derived from a single study instead of identifying and combining all available data sources. However, we derived the input

effectiveness parameters from a study evaluating the effectiveness of an educational intervention in a population of Colombian asthmatic children in order to achieve a more accurate modeling of the disease's natural history and to obtain more reliable data. Additionally, data on effectiveness of educational intervention were subject to wide sensitivity analyses. Nevertheless, we acknowledge that the results of our study need to be applied with caution, since it is possible that they are only applicable to educational interventions similar to those evaluated in this study. Finally, due to the fact that we only included direct costs and third-payer perspective in the analysis, the cost-savings and cost-effectiveness for the healthcare system could be underestimated. In fact, if indirect costs (e.g., loss in productivity due to asthma-related morbidity such as work loss for caregivers of school-age asthmatic children, loss due to traveling to and from healthcare appointments, and loss due to waiting in ED and physician's offices) had been included in the analyses, major cost-savings and QALY gains could be expected.

Conclusion/key findings

In conclusion, this study identified the level at which the cost of pediatric asthma educational interventions similar to those evaluated in the present study would be cost-effective and cost-saving for the health system in Colombia, a South American LMIC (cost-saving threshold under US\$513.20 and cost-effective threshold under US\$967.40). Our findings could be a useful aid for decision makers in efficiently allocating limited resources when planning asthma educational interventions for pediatric patients. A cost-effectiveness threshold analysis of different types of educational interventions (group, clinic, home, telephonic) tailored to children of different ages and varying degrees of asthma severity will need to be performed in the future. Additionally, future studies should identify target populations for which asthma educational interventions will be most cost-effective.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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