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To cite this article: Carlos E. Rodriguez-Martinez, Monica P. Sossa-Briceño & Jose A. Castro-Rodriguez (2019): Advantage of inhaled corticosteroids as additional therapy to systemic corticosteroids for pediatric acute asthma exacerbations: a cost-effectiveness analysis, Journal of Asthma, DOI: [10.1080/02770903.2019.1628254](https://doi.org/10.1080/02770903.2019.1628254)

To link to this article: <https://doi.org/10.1080/02770903.2019.1628254>



Accepted author version posted online: 05 Jun 2019.
Published online: 17 Jun 2019.



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Advantage of inhaled corticosteroids as additional therapy to systemic corticosteroids for pediatric acute asthma exacerbations: a cost-effectiveness analysis

Carlos E. Rodriguez-Martinez, MD, MSc^{a,b} , Monica P. Sossa-Briceño, MD, MSc^c, and Jose A. Castro-Rodriguez, MD, PhD^d 

^aDepartment of Pediatrics, School of Medicine, Universidad Nacional de Colombia, Bogota, Colombia; ^bDepartment of Pediatric Pulmonology and Pediatric Critical Care Medicine, School of Medicine, Universidad El Bosque, Bogota, Colombia; ^cDepartment of Internal Medicine, School of Medicine, Universidad Nacional de Colombia, Bogota, Colombia; ^dDivision of Pediatrics, School of Medicine, Pontificia Universidad Catolica de Chile, Santiago, Chile

ABSTRACT

Objective: Although the efficacy of systemic corticosteroids (SCs) in acute asthma exacerbations is well established, the fact that many children still require admission to hospital and that SCs have a slow onset of action are cause of concern. For this reason, the use of inhaled corticosteroids (ICS) as a therapy added to SCs has been explored, with no clarity about its cost-effectiveness. The aim of the present study was to evaluate the cost-effectiveness of ICS in addition to SCs (ICS + SCs) compared to standard therapy with SCs for treating pediatric asthma exacerbations.

Methods: A decision-analysis model was developed to estimate the cost-effectiveness of SCs compared to ICS + SCs for treating pediatric patients with acute asthma exacerbations. Effectiveness parameters were obtained from a systematic review of the literature. Cost data obtained from hospital bills and from the national manual of drug prices. The study was carried out from the perspective of the national healthcare system in Colombia. The main outcome of the model was avoidance of hospital admission.

Results: For the base-case analysis, the model showed that compared to SCs, therapy with ICS + SCs was associated with lower total costs (US\$88.76 vs. US\$97.71 average cost per patient) and a lower probability of hospital admission (0.9060 vs. 0.9000), thus showing dominance.

Conclusions: This study shows that compared with standard therapy with SCs, ICS + SCs for treating pediatric patients with acute asthma exacerbations is the preferred strategy because it was associated with a lower probability of hospital admission, at lower total treatment costs.

ARTICLE HISTORY

Received 2 March 2019
Accepted 1 June 2019

KEYWORDS

Asthma exacerbation; health economics; inhaled corticosteroid; systemic corticosteroid

Introduction

Childhood asthma is the most common chronic disease in childhood and a major public health problem in the US as well as in many other countries, such as Colombia (1,2). Despite relatively recent advances in our understanding of the inflammatory nature of the disease and the availability of highly effective medications to control their symptoms, many pediatric patients continue to have poor asthma control with frequent disease exacerbations (3). Acute asthma exacerbations not only have a significant impact on the utilization of health care and the quality of life of children and their families, but also account for a large part of disease costs (4). National and international evidence-based asthma clinical practice

guidelines recommend the use of inhaled beta 2 agonists and systemic corticosteroids (SCs) as the first-line agents for acute asthma exacerbations (5,6).

The efficacy of SCs in acute asthma exacerbations is well established, with a positive impact on several clinically important outcomes such as reduction in hospital admission rate, symptom scores, and the number of relapses after discharge from the emergency department (ED) (7). However, despite SCs use, many children still require hospital admission, and one reason may be that SCs have a slow onset of action (3–4 h after their administration) (8).

For this reason, the use of other anti-inflammatory therapies for acute asthma exacerbations, such as

inhaled corticosteroids (ICS) (7), has been explored. Potential advantages of ICS might be a faster onset of action and a greater efficacy in diminishing airway reactivity and edema, because of their direct delivery to the airways due to their non-genomic effect (9). Thus in addition to the well-known anti-inflammatory effects of corticosteroids effected through three genomically independent mechanisms by binding to a cytoplasmic glucocorticoid receptor, ICS, but not SCs, cause immediate local bronchial mucosal vasoconstriction and inhibition of edema formation mediated by non-genomic mechanisms (10). The main non-genomic mechanisms involve the activation of endothelial nitric oxide (NO) synthase and NO synthesis, which produces an increase in noradrenergic neurotransmission in the airway vasculature, with a consequent reduction in airway blood flow (11). The reduction in airway blood flow is a desirable effect in asthmatic patients, given that they have a significantly increased blood flow in the airway mucosa (12).

Therefore, various studies have shown the benefit of ICS as an additional therapy for acute asthma exacerbation in a number of outcomes such as peak expiratory flow rate (PEFR) (13), release/discharge time from the ED/hospital (14), hospital length of stay (LOS) (15), and hospital admission rate (16). However, due to the additional cost incurred when using ICS in addition to SCs, it is necessary to investigate whether the clinical benefits of their addition outweigh their cost. In this context, a cost-effectiveness analysis (CEA) provides a tool that allows comparing the cost and the effectiveness of alternative treatments. Although it has been reported that the addition of ICS for treating pediatric asthma exacerbations could reduce the overall cost (15), to the best of our knowledge, a formal evaluation of the cost-effectiveness of this strategy has not been previously performed or published.

The aim of the present study was to evaluate the cost-effectiveness of (ICS + SCs) compared to standard therapy with SCs for treating pediatric patients with acute asthma exacerbations in the ED.

Methods

Model structure

To evaluate the cost-effectiveness of ICS + SCs compared to standard therapy with SCs for treating pediatric patients with acute asthma exacerbations in the ED, we modified a previous decision-analysis model developed by Doan, Q. et al. for estimating the cost-effectiveness of metered-dose inhalers for asthma

exacerbations in the ED (17). For each of the two comparators, the model depicts a pediatric patient who presents to the ED with an acute asthma exacerbation and there is a probability (probability node) of improvement and discharge from the hospital (directly from the ED or after admission). After patients are discharged from the hospital, the model incorporates the probability of unscheduled hospital visits in the next 4 weeks following the intervention (Figure 1). The main outcome of the model was avoidance of hospital admission (unplanned overnight stay in the ED alone or with subsequent management as an inpatient in an asthma inpatient ward and/or in a pediatric intensive care unit). The time horizon for the measurement and valuation of costs and health outcomes within the CEA covered the period between randomization and discharge from the hospital if the child was admitted for unscheduled visits to the hospital in the next 4 weeks following the randomization. Because of the short-term horizon of the study (less than 12 months), neither the cost nor the effects were discounted. The model compared direct medical costs (for diagnosis or treating patients with acute asthma exacerbations) and disease outcomes from the perspective of the national healthcare system in Colombia.

Source of data

Disease outcomes and probabilities

The probability of hospital admission was determined using the pooled probability of admission associated with each of the two strategies as reported in the relevant randomized clinical trials (RCTs). Likewise, the rate of readmission after discharge from hospital with each of the two strategies was derived from relevant RCTs. With this objective, we performed a systematic review and meta-analysis of RCTs published up to July, 2018. In order to identify potentially relevant studies, we performed searches of computerized databases (MEDLINE, CENTRAL, LILACS, and CINAHL) with the following search strategy: (budesonide OR ciclesonide OR mometasone OR beclomethasone OR flunisolide OR fluticasone OR triamcinolone) AND (prednisone OR prednisolone OR hydrocortisone OR methylprednisolone OR dexamethasone OR betamethasone), limited with the terms children OR child OR pediatric OR adolescents OR infants OR pre-schoolers). No language restrictions were applied.

To be included in the model, the studies had to be RCTs of parallel-group or cross-over design, include children between 2 and 18 years of age who consulted

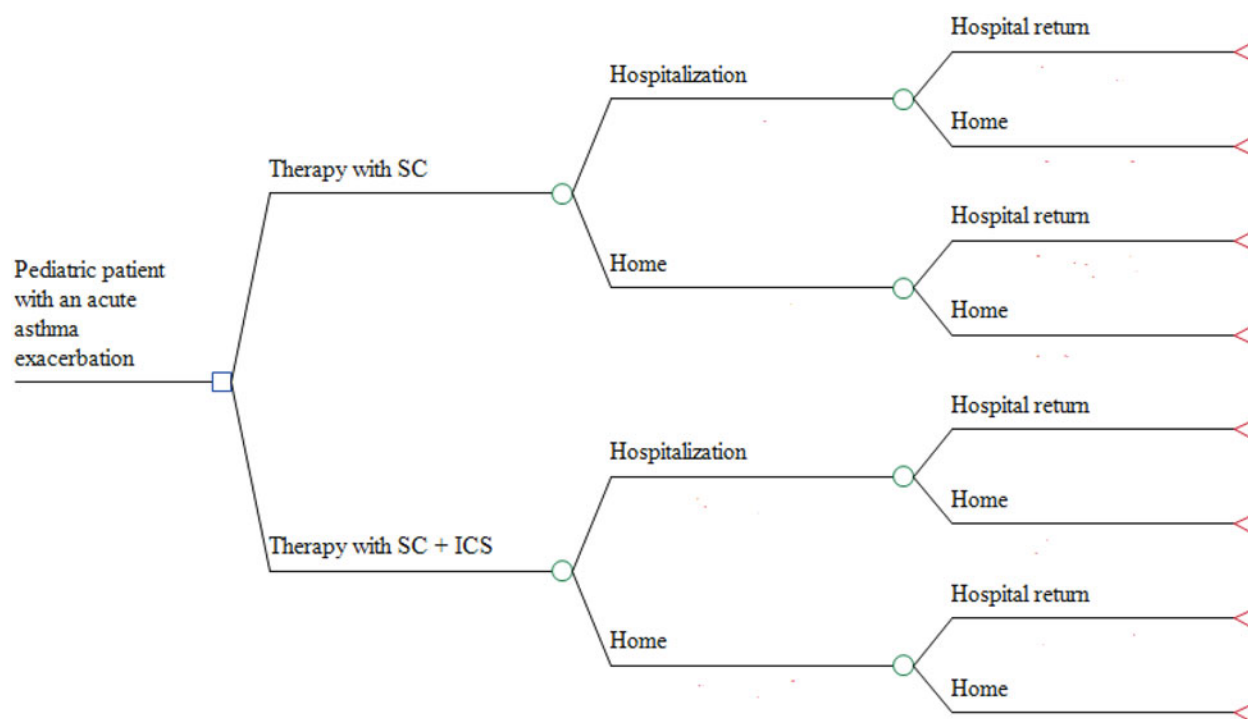


Figure 1. Diagram of cost-effectiveness model for each treatment option.

in the ED or equivalent due to an acute asthma exacerbation, compare the use of any ICS as additional therapy with any SC administered by any route, and report at least one of the outcomes of interest (probability of hospital admission and rate of readmission after discharge from hospital). We did not include studies that involved children with prior use of SCs 2 weeks before the enrollment, nor letters or abstracts. Two authors of the present review (CERM, JACR) independently determined whether the studies met eligibility criteria. Disagreement was resolved by consensus. To evaluate the cost-effectiveness of ICS + SCs compared to standard therapy with SCs for treating pediatric patients with severe acute asthma exacerbations, a second analysis was performed, including only patients with severe acute asthma exacerbations in the model.

After applying the above-mentioned eligibility criteria, data from 6 articles were evaluated and included in the model (14,16,18–21). There was total agreement between the two independent reviewers on inclusion of studies. The outcome hospital admission from the ED was calculated using a random-effects model with pooled estimate of five studies (1395 participants) (14,16,18,20,21), and the outcome hospital readmission was also calculated using a random-effects model with pooled estimate of four studies (1201 participants) (14,16,19,20).

Data inputs: resource utilization and costs

As mentioned, the CEA was conducted from the perspective of the national healthcare system in Colombia, and hence only direct costs were included in the analysis. Specifically, the costs of medications (including SCs and ICS), equipment (spacer, masks, and nebulizer bowl), chest X-rays, and additional diagnostic and therapeutic procedures performed during the asthma-related ED visit and/or the asthma-related hospitalization (either primary or relapse event, when appropriate) were taken into account. All costs gathered were as close to reimbursement or true costs as possible (Table 1).

Costs associated with asthma exacerbations were derived from the review of the electronic medical records (EMRs) and hospital accounting reports for all pediatric patients who were admitted with a principal discharge diagnosis of asthma exacerbation (ICD-10 codes J45.901, J45.21, J45.31, J45.41, J45.51, J45.902, J45.22, J45.32, J45.42, J45.52) over a 24-month period from January 2016 to December 2017 at the Fundación Hospital de La Misericordia. This hospital is a pediatric clinic located in the city of Bogotá, the city capital of Colombia, that receives patients from the majority of and the most representative medical insurance companies in the country, and consequently the cost data gathered was considered to be reasonably well representative of the asthma costs

Table 1. Total median costs associated with asthma exacerbations categorized by the hospital service to which the patient was admitted *.

Category	ED	PW	PIMC	PICU
Medical and therapy services				
Medical	11.5 (8.9–14.4)/ 36.8%	46.2 (24.6–73.0)/ 17.6%	72.9 (45.0–87.9)/ 5.9%	57.9 (39.3–146.6)/ 4.5%
Respiratory therapy	0.0 (0.0–0.0)/ 0.0%	0.0 (0.0–6.9)/ 1.3%	18.5 (7.1–32.1)/ 2.5%	16.9 (3.6–25.8)/ 0.9%
Diagnostic tests and procedures				
Laboratory	0.0 (0.0–31.5)/ 17.4%	0.0 (0.0–20.2)/ 3.8%	49.4 (8.4–152.8)/ 6.8%	204.7 (87.8–391.3)/ 10.0%
Imagenologic studies	12.1 (0.0–15.1)/ 17.6%	12.4 (0.0–16.5)/ 4.3%	30.3 (17.5–121.5)/ 4.6%	128.6 (63.6–187.2)/ 4.9%
Consumables				
Medications	6.7 (3.9–6.8)/ 18.4%	21.9 (13.1–35.3)/ 10.0%	67.2 (49.5–132.9)/ 8.1%	216.1 (45.6–341.4)/ 7.7%
Fluids and supplies	0.9 (0.1–4.0)/ 6.1%	11.0 (4.3–22.8)/ 4.5%	46.0 (29.2–63.1)/ 4.3%	128.5 (39.9–165.9)/ 5.2%
Nebulization and oxygen treatment	0.0 (0.0–4.2)/ 3.7%	21.7 (6.8–52.1)/ 9.5%	90.7 (54.2–168.0)/ 8.9%	67.2 (32.5–175.5)/ 3.6%
Hotel services				
Hospital stay	0.0 (0.0–0.0)/ 0.0%	97.3 (56.4–317.8)/ 49.0%	800.4 (398.9–860.1)/ 58.8%	1241.4 (909.9–2096.3)/ 63.4%
Total	38.8 (21.1–64.1)	260.5 (113.7–567.4)	1212.4 (717.6–1609.6)	2501.8 (1771.6–3405.0)

* Costs expressed in American dollars (US\$) and presented as median (interquartile range) and percentage of the total cost.

of the whole country. Additionally, unit costs of all medications were taken from the Drug Price Information System (SISMED, 2018) (22), an official database provided by the Colombian Ministry of Health and Social Protection, which constitutes an important and representative primary source of medication prices in the country. Direct medical costs of pediatric asthma exacerbations were retrospectively collected by dividing the patients into 4 groups: those admitted to the ED only, those admitted to the pediatric ward (PW), those admitted to the pediatric intermediate care unit (PIMC), and those admitted to the pediatric intensive care unit (PICU). However, because the percentage of admissions for asthma to hospital services in a referral hospital may not be generalizable to a broader and general asthma population, the average cost per exacerbation included in the model was calculated by means of a weighted average of the probability of requiring admission to different hospital services for asthma exacerbations as reported in the literature (23).

The recommended dosage of prednisolone for treatment of pediatric asthma exacerbations in patients age 13 years or older is 60 mg once or twice daily for five days. The recommended dosage of prednisolone for treatment of pediatric asthma exacerbations in children age 2 year or older is based on weight and given once or twice daily for five days. The average cost of treating a child with prednisolone for one episode of asthma exacerbation was computed as a weighted average based on the distribution of children age 1–12 years, by weight, in the EMR cohort of patients. Calculation of the cost of ICS was based on the estimated average dose reported in the relevant RCTs and the relative use of available concentrations for each medication according to current market research.

Costs were calculated in Colombian pesos (COP) and converted to dollars (US\$) based on the average exchange rate for 2018 (1 US\$ = 2000.68 COP) (24). All the costs were adjusted to 2018 COPs before converting them to US\$. The study protocol was approved by the local ethics board.

Sensitivity analyses

A series of one-way, two-way, and multi-way sensitivity analyses (using a tornado diagram) was carried out, and the effect of alternative model specifications were examined. Data ranges in sensitivity analyses were derived from various sources: For unit costs of resources, data ranges were $\pm 25\%$ of the base values, because it was considered that this range represents a reasonable one for these unit costs (Table 1). For probability of improvement and discharge from the hospital (directly from the ED or afterward admission) and probability of readmission to the hospital for treatment of asthma symptoms in the next 4 weeks following the intervention, 95% confidence intervals (95% CI) obtained from meta-analysis were considered a plausible range for variation. In addition, a probabilistic sensitivity analysis (PSA) using 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. Distributions were chosen according the methodology suggested by Briggs et al (25). They suggest the beta distribution for binomial outcomes, where parameters can vary between zero and one, for example probabilities, and the gamma distribution for costs where parameters are non-negative. This PSA allowed us to

Table 2. Baseline and range values of parameters included in the model*.

Cost items	Base-case value	Lower value	Higher value
Probability of hospitalization with SCs [14,16,19,20]	0.10	0.075	0.125
Probability of hospitalization with ICS + SCs adjustment factor [14,16,19,20]	0.94	0.79	1.13
Probability of readmission after hospitalization with SCs [14,18,19]	0.029	0.022	0.036
Probability of readmission after treatment in the ED with SCs [16]	0.044	0.033	0.055
Probability of readmission after hospitalization with ICS + SCs [14,18,19]	0.045	0.034	0.056
Probability of readmission after treatment in the ED ICS + SCs [16]	0.05	0.038	0.063
Probability of hospitalization with ICS + SCs adjustment factor (severe exacerbations) [16]	0.71	0.46	0.96
Cost of hospitalization for asthma exacerbation with SCs [15,18]	581.9	436.5	727.5
Cost of hospitalization for asthma exacerbation with ICS + SCs [15,18]	448.4	336.3	560.5
Cost of hospitalization for readmission with SCs [14,16]	108.0	81.0	135.0
Cost of hospitalization for readmission with ICS + SCs [14,16]	73.8	55.4	92.3

*SCs, systemic corticosteroids; ICS, inhaled corticosteroids; ED, emergency department.

generate 95% uncertainty intervals (UIs) for costs and effects. These were shown graphically on a cost-effectiveness plane in order to show the estimated joint distribution of incremental costs versus incremental effects and were evaluated using net benefit analysis (26). Subsequently, a cost-effectiveness acceptability curve (CEAC) was derived from these data (27) in order to identify which alternative would be the most cost-effective at various thresholds of willingness-to-pay (WTP) for hospital admission avoided. All analyses were performed using TreeAgePro 2016 software (TreeAge Software, Williamstown, MA, USA).

Results

Clinical and demographic characteristics of patients admitted for asthma exacerbation

The median (IQR) age of the 252 pediatric patients admitted for asthma exacerbation was 5.0 (3.0–7.0) years. The age group distribution was: 112 (44.4%) <5 years, 136 (53.9%) between 5 and 12 years, and the remaining 4 (1.7%) between 13 and 18 years. Of the study participants, 120 (47.6%) were male and 132 (52.4%) were female. The median (IQR) LOS was 4.0 (2.0–7.0) days.

Healthcare resource use and costs associated with the hospital setting to which the patients were admitted

Of the total of 252 EMR of asthma exacerbations reviewed, 20 (7.9%) were exacerbations requiring ED consultation only, 128 (50.8%) requiring admission to the PW, 76 (30.2%) requiring admission to the PIMC, and the remaining 28 (11.1%) requiring admission to the PICU. As expected, the total direct cost per attack was significantly higher in patients with severe asthma

attacks (patients admitted to PICU or PIMC) when compared to moderate and mild attacks (patients admitted to PW or those requiring ED consultation only). Additionally, regarding the proportion of resources and services billed according to the hospital setting to which the patients were admitted, in general the more severe the asthma exacerbation, the greater the percentage of the bill attributable to hotel services (hospital stay) (Table 1).

Baseline and range values of parameters included in the model

Baseline and high and low values of each key variable included in the model, including unit costs of resources, costs of medications, probability of hospitalization, and probability of unscheduled visits to the hospital in the next 4 weeks following the intervention, along with their respective sources, are presented in Table 2.

Base-case analysis

Using the base-case assumptions, the model showed that compared to standard therapy with a SCs, therapy with ICS + SCs for treating pediatric patients with acute asthma exacerbations was associated with lower total costs (US\$88.76 vs. US\$97.71 average cost per patient) and a lower probability of hospital admission (0.9060 vs. 0.9000), thus showing dominance. A position of dominance negates the need to calculate an incremental cost-effectiveness ratio (Table 3).

When the analysis was restricted to patients with severe acute asthma exacerbations, the model showed that compared to standard therapy with SCs, therapy with ICS + SCs for treating pediatric patients with acute asthma exacerbations was associated with lower total costs (US\$77.30 vs. US\$97.71 average cost

Table 3. Base-case cost-effectiveness analysis of systemic corticosteroids vs. systemic corticosteroids + inhaled corticosteroids for treating pediatric asthma exacerbations.

Category	Strategy	Cost (US\$)	Incremental cost (US\$)	Effectiveness (avoidance of hospital admission) *	Incremental effectiveness (avoidance of hospital admission)	Cost/effectiveness
All patients						
Absolutely dominated	ICS + SCs	88.76	–	0.9060	–	97.97
	SCs	97.71	8.95	0.9000	–0.0060	108.56
Patients with severe asthma exacerbations						
Absolutely dominated	ICS + SCs	77.30	–	0.9340	–	82.76
	SCs	97.71	20.41	0.9000	–0.0340	108.56

Table 4. Parameter distributions used in the probabilistic sensitivity analysis*.

Probability distribution	Distribution parameters	Distribution parameters
Beta distribution	Alpha	Beta
Probability of hospitalization with SCs	57.50	517.50
Probability of hospitalization with ICS + SCs adjustment factor	6.40	0.41
Probability of readmission after hospitalization with SCs	62.12	2087.41
Probability of readmission after treatment in the ED with SCs	61.14	1328.41
Probability of readmission after hospitalization with ICS + SCs	61.08	1296.15
Probability of readmission after treatment in the ED ICS + SCs	60.75	1154.25
Probability of hospitalization with ICS + SCs adjustment factor (severe exacerbations)	8.82	4.54
Gamma distribution	Alpha	Lambda
Cost of hospitalization for asthma exacerbation with SCs	64.00	0.11
Cost of hospitalization for asthma exacerbation with ICS + SCs	64.00	0.14
Cost of hospitalization for readmission with SCs	64.00	0.59
Cost of hospitalization for readmission with ICS + SCs	64.01	0.87

*SCs, systemic corticosteroids; ICS, inhaled corticosteroids; ED, emergency department.

per patient) and a lower probability of hospital admission (0.9340 vs. 0.9000), thus showing dominance. Again, a position of dominance negates the need to calculate an incremental cost-effectiveness ratio (Table 3).

Sensitivity analyses

One-way, two-way, and multi-way deterministic sensitivity analyses (using a tornado diagram) showed that the cost of care in the ED has the highest impact on the model outcome. However, although as the cost of care in the ED increases the standard therapy with SCs tends to be more cost-effective, therapy with ICS + SCs was the dominant strategy over all the ranges of the cost of care in the ED analyzed.

Parameter distributions used in the PSA are shown in Table 4. As mentioned above, beta distribution was used to model probabilities and gamma distribution was used to model costs. The results of the PSA are graphically represented as a scatter plot in Figure 2. This scatter plot shows that compared with the standard therapy with the SCs strategy, therapy with

ICS + SCs tends to be associated with lower costs and lower probability of hospital admission. Based on the results from this simulation, the 95% UI for cost per patient treated with SCs and with ICS + SCs were US\$80.74 to \$119.30 and US\$73.55 to \$105.06, respectively. The 95% UI for avoidance of hospitalization was 0.8750 to 0.9231 and 0.8792 to 0.9362, respectively. In 82.5% of the iterations, the therapy with ICS + SC was associated with a lower probability of hospital admission and lower costs compared with the standard therapy with SCs. The CEAC shows that the probability that therapy with ICS + SC provides a more cost-effective use of resources compared with standard therapy with SCs exceeds 99% for all WTP thresholds (Figure 3).

When the analysis was restricted to patients with severe acute asthma exacerbations, the cost of care in the ED was shown to have the highest impact on the model outcome, but again the therapy with ICS + SCs was the dominant strategy over all the ranges of the cost of care in the ED analyzed. Based on the simulations of the PSA, the 95% UI for cost per patient treated with SCs and with ICS + SCs were US\$79.87 to \$118.22 and US\$64.25 to \$92.77, respectively. The

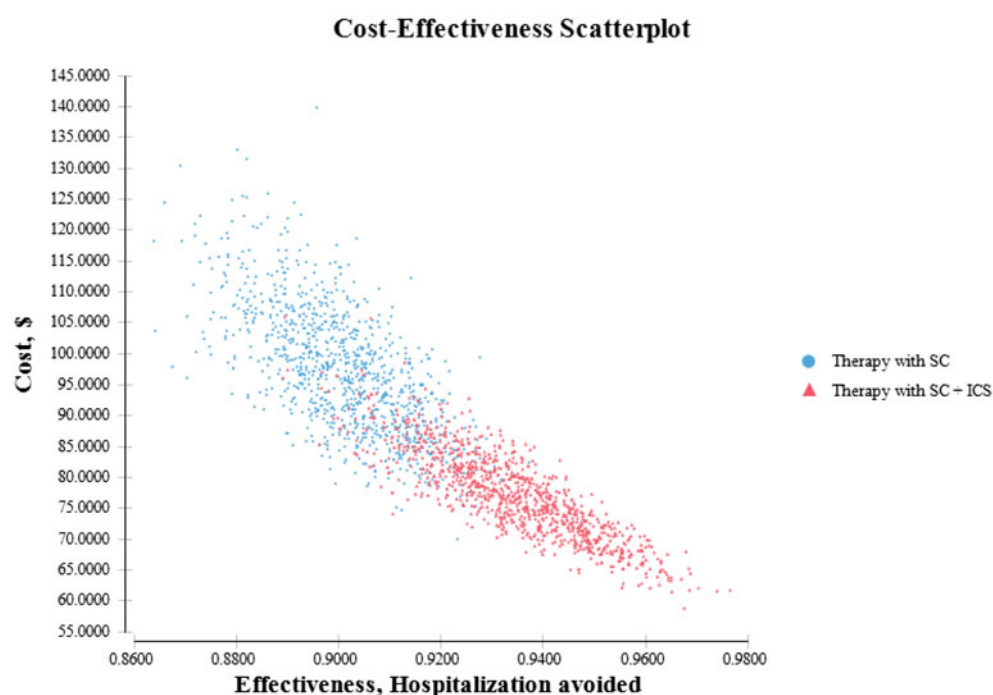


Figure 2. Scatter plot of each iteration's cost and effectiveness values for each strategy in pediatric acute asthma exacerbations. * The X-axis shows the effectiveness measured as hospitalizations avoided; the Y-axis shows the costs measured in dollars (US\$, 2018). Each point represents one of the 10,000 trial runs, where each input was assigned a random value according to its probability density function.

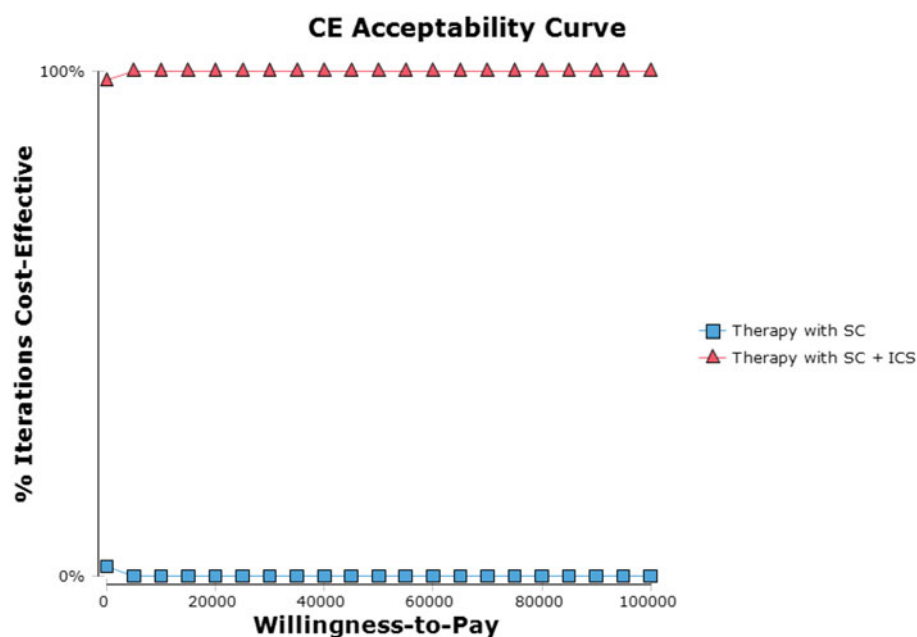


Figure 3. Cost-effectiveness acceptability curve with standard therapy with SC versus therapy with ICS as additional therapy to SC for treating pediatric patients with acute asthma exacerbations. * The cost-effectiveness acceptability curve shows the probability that therapy with ICS as additional therapy to SC provides a more cost-effective use of resources compared with standard therapy with SC exceeds 99% for all WTP thresholds.

95% UI for hospitalization avoided was 0.8762 to 0.9234 and 0.9039 to 0.9629, respectively. In 98.2% of the iterations, the therapy with ICS + SCs was associated with a lower probability of hospital admission and lower costs compared with the standard therapy

with SC strategy. Again, the CEAC shows that the probability that therapy with ICS + SCs provides a more cost-effective use of resources compared with standard therapy with SCs exceeds 99% for all WTP thresholds.

Discussion

The present study shows that compared to standard therapy with SCs, therapy with ICS + SCs for treating pediatric patients with acute asthma exacerbations is a dominant strategy, because it involved a lower probability of hospital admission at lower total treatment costs. Although the variable that exhibited a significant effect on these results was the cost of care in the ED, therapy with ICS + SCs was the dominant strategy over all the ranges of the cost of care in the ED analyzed. It is worth mentioning that the cost-effectiveness of the above-mentioned strategy is even greater when the analysis was restricted to patients with severe acute asthma exacerbations.

The findings of the present study support the concept that in addition to SCs, a well-established, traditional, and recommended therapy in all high-quality clinical practice guidelines in pediatric asthma for treating acute pediatric asthma exacerbations, the use of ICS + SCs could help to ensure a more efficient management of the disease, especially in patients with severe acute asthma exacerbations. These findings are important because of the huge clinical and economic burden of pediatric asthma exacerbations, especially in Colombia and other middle-income countries (MICs). A strategy that is useful not only for decreasing the probability of hospitalization due to acute asthma exacerbations but also for decreasing total treatment costs is highly desirable in countries or settings where health resources are always scarce, such as Colombia and other countries with a similar economic profile. However, cost-effectiveness results from different countries are not easily comparable, mainly because of inter-country differences in prices of labor, services and goods (including pharmaceuticals), volume of resources, administrative costs, use of high-tech interventions, access to and provision of specialized care instead of primary care, and payment schemes (28,29).

The latest version of the Global Initiative for Asthma (GINA) report does not recommend the use of ICS as a therapy in addition to SCs, arguing that the evidence is conflicting, and that potential side effects in children under 5 years of age and their costs are factors that should be taken into account. Additionally, the agent, dose, and duration of treatment with ICS in the management of acute asthma remain unclear (6). Our study provides evidence supporting the concept that the beneficial clinical effects of ICS when added to the standard acute asthma treatment of children outweigh the costs, especially in patients with severe asthma exacerbations.

Our results are in good agreement with those reported by Sung et al. (14), who in a RCT including 44 children with moderate to severe asthma exacerbations showed that those on nebulized budesonide (BUD) in addition to prednisone and nebulized salbutamol were released from the ED or discharged from the hospital significantly more rapidly than those who received a placebo and also had a lower (although non-significant) probability of admission to the inpatient ward (14). Likewise, Alangari et al. showed that in children with acute asthma exacerbation treated with BUD nebulization added to the standard treatment during the first hour in the ED, although the addition of BUD nebulization did not decrease the admission rate, it significantly decreased the admission rate of children with severe acute asthma (16). This significant clinical effect in patients with severe acute asthma exacerbations concurs well with our findings regarding a greater cost-effectiveness of the BUD as added therapy in patients with severe exacerbations and with previous studies showing that nebulized high-dose BUD was associated with better clinical healing and lower rates of admission in children experiencing moderate to severe asthma exacerbations when compared with children with less-severe exacerbations (8,20). Razi et al., in an RCT comparing the addition of high-dose inhaled BUD to standard therapy in children admitted for asthma exacerbations, found that patients assigned to the BUD group had a significantly shorter total hospital LOS and significantly fewer hospital admissions, and consequently a lower overall cost of treatment. This is because, given the fact that the median hospital LOS for patients in the BUD group was 36 h shorter than the placebo group, the cost of treatment for a patient treated with BUD was US\$130 less than for a patient in the placebo group (15). With respect to the post-discharge follow-up, with follow-up periods varying between 72 h and 4 weeks, four studies comparing BUD nebulization added to the standard acute asthma treatment reported non-significant differences in the rate of readmission to the hospital for treatment of asthma symptoms when compared with a placebo (14,16,19,20).

A number of potential limitations need to be considered. First, resource utilization and cost data were obtained from a single clinical center and may not be representative of the whole country. However, these data were obtained from a pediatric clinic that receives patients from one of the most important and representative medical insurance companies in the country. Additionally, costs were subject to wide

sensitivity analyses. Second, differences in both costs and health benefits between standard therapy with SCs and therapy with ICS+SCs could be due to imprecision of their estimates, because their 95% UI overlap. Therefore, we cannot be at least 95% confident about which is the better strategy with regards to their economic value. Third, although observational studies are increasingly used in cost-effectiveness studies, mainly because of their presumed superior external validity and for providing useful data to generalize from RCTs (such as natural history or local rates for key events in the model), we only included RCTs in the model. This is because we considered that in light of the objectives of the study, RCTs are the best source of unbiased efficacy data, therefore improving the internal validity of the model.

Conclusion/key findings

In conclusion, the present analysis shows that in Colombia, an MIC, compared with standard therapy with SCs, therapy with ICS as a therapy in addition to SC for treating pediatric patients with acute asthma exacerbations is a dominant strategy, because it shows a lower probability of hospital admission at lower treatment costs. This dominance was more marked for children experiencing severe asthma exacerbations than for those experiencing less-severe exacerbations. Our findings may help to support clinical decision-making when planning pharmacological therapy for pediatric patients with acute asthma exacerbations.

Declaration of interest

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

ORCID

Carlos E. Rodriguez-Martinez  <http://orcid.org/0000-0003-2560-6693>

Jose A. Castro-Rodriguez  <http://orcid.org/0000-0002-0708-4281>

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