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Commercial valved spacers versus home-made spacers for delivering bronchodilator therapy in pediatric acute asthma: a cost-effectiveness analysis

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ABSTRACT

Objective: Although valved spacers are the preferred method for administering metered-dose inhaler bronchodilators such as albuterol in pediatric acute asthma, their high cost and their lack of availability have limited their use, especially in low- and middle-income countries (LMICs). Because of this, it is a common practice to use home-made spacers, although a formal analysis evaluating their cost-effectiveness is lacking. Therefore, the objective of this study was to analyze the cost-effectiveness of home-made spacers compared to commercial valved spacers for delivering bronchodilator therapy in pediatric acute asthma.

Methods: A decision-analysis model was used to estimate health outcomes and costs of a simulated cohort of pediatric patients treated for acute asthma. Effectiveness parameters were obtained from a systematic review of the literature. Cost data were obtained from hospital bills and from the national manual of drug prices in Colombia. The study was carried out from the perspective of the national healthcare system in Colombia, a middle-income country (MIC). The main outcome of the model was avoidance of hospital admission.

Results: Base-case analysis showed that compared to commercial valved spacers, administering bronchodilators with home-made spacers results in lower overall treatment costs (US\$126.75 vs. US\$128.59 average cost per patient) without a significant difference in the probability of hospitalization avoided (0.8500 vs. 0.8500).

Conclusions: The present study shows that in Colombia, an MIC, compared with commercial valved spacers, the use of home-made spacers for administering bronchodilator therapy is more cost-effective because it yields a similar probability of hospital admission at lower overall treatment costs.

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Introduction

Asthma exacerbations in pediatric patients are associated not only with a considerable medical burden but also with a heavy economic burden for both healthcare systems and society as a whole (1). Poor asthma control and acute exacerbations of the disease have been considered to be the cause of about one third of direct costs and almost all of the indirect costs of asthma, with a more than three-fold increase in the costs of asthma treatment when an exacerbation of the disease occurs (2).

The first-line treatment medications for treating pediatric asthma exacerbations are inhaled bronchodilators and systemic corticosteroids (3). Although

albuterol, the most frequently used bronchodilator, has been traditionally delivered via nebulization, the advantages of delivering albuterol via metered-dose inhalers with a valved spacer (MDI + S), which could be due to a variety of factors, have been increasingly reported. Specifically, when compared with nebulization, albuterol delivered via MDI + S has been associated with significant improvements in clinically important outcomes such as hospitalization rate (4,5) and length of stay (LOS) (6). Additionally, when compared to nebulization, albuterol delivered via MDI + S has been associated with significant advantages in other important outcomes such as clinical severity scores (4), extra-pulmonary sympathetic effects (anxiety, tachycardia, and tremor) (7), administration

time, use of personal resources, child and parent treatment satisfaction, and staff and caregiver risk during respiratory infection epidemics (8,9). Notably, when compared to nebulization, delivery via MDI + S has been shown to be more cost-effective, involving a lower probability of hospital admission at lower total treatment costs (10). However, despite all these advantages of albuterol delivered via MDI + S, the high cost and the lack of availability of commercially-produced valved spacers have limited their use in low- and middle-income countries (LMICs) (11). Because of this limitation, for treating pediatric asthma exacerbations, in LMICs it is a common practice to administer albuterol via an MDI attached to home-made spacers, including plastic cold-drink bottles, plastic mineral water bottles (12), polystyrene cups (12–14), and even plastic zip-up and paper spacers, (15) with differences in efficacy between them. Although it is to be expected that the acquisition cost of home-made spacers will be negligible compared to commercial valved spacers, a lower aerosol particle deposition in the airways and the consequently diminished bronchodilator response with their use could result in reduced clinical efficacy of albuterol and increased overall treatment costs (13,14). Cost-effectiveness analysis (CEA) is a tool that can combine and compare the cost and the effectiveness of alternative treatments. Specifically, a CEA could be helpful in determining if the savings obtained by using home-made spacers instead of commercial valved spacers outweigh the increased cost associated with the reduced clinical efficacy of albuterol. However, to the best of our knowledge, there are no CEAs aimed at evaluating home-made spacers for delivering bronchodilator therapy in pediatric acute asthma. Therefore, the objective of this study was to analyze the cost effectiveness of home-made spacers compared to commercial valved spacers for delivering bronchodilator therapy in children with acute asthma exacerbations presenting to an emergency department (ED) or equivalent care setting in a middle-income country (MIC).

Material and methods

Model structure

To analyze the cost-effectiveness of home-made spacers compared to commercial valved spacers for delivering bronchodilator therapy in pediatric patients with asthma exacerbations, we modified a decision-analysis model previously utilized by our group (16). We defined an asthma exacerbation as a deterioration in asthma resulting in an ED visit. The model

illustrates how a typical pediatric patient navigates the healthcare system to receive treatment for an asthma exacerbation. When the patient presents to the ED, there is a probability (probability node) of an inadequate response to initial treatment and a requirement for additional treatment. After treatment in the ED, the model incorporates the probability of hospital admission or discharge from the hospital directly from the ED (Figure 1).

The primary outcome of the cost-effectiveness model was avoidance of hospital admission for asthma, considering an avoidance of hospital admission as a success and hospital admission for treating an asthma exacerbation episode as a failure. The time horizon of the CEA analysis was limited to the period of time required for treating an acute asthma episode; therefore, the discounting of effects and costs was not relevant in the present model, given the fact that the time horizon was less than 12 months. The present model evaluated direct medical costs and disease health outcomes from the Colombian third-payer perspective.

Study population of reference

Patient characteristics and details of interventions administered in the randomized controlled trials (RCTs) included in a Cochrane systematic review with a meta-analysis aimed at comparing the response to inhaled beta-2 agonists delivered through MDI using home-made spacers with that using commercially-produced spacers in children with acute exacerbations of wheezing or asthma (17) defined our reference population. Specifically, we analyzed patients aged 2 months to 18 years with mild to moderate asthma exacerbations requiring ED management. Children were excluded if they had a history of cardiac, hepatic, skeletal, neuromuscular, or pulmonary diseases other than asthma; if they had already received beta-2 agonists, xanthines, or oral corticosteroids before going to the hospital, if they were unable to use an MDI and spacer, or if they experienced a severe or life-threatening asthma exacerbation. The beta-2 agonists used were albuterol, terbutaline, and fenoterol hydrobromide. The doses of beta-2 agonists administered ranged from 1000 µg to 2400 µg of albuterol and from 400 µg to 600 µg of fenoterol hydrobromide. The dose of terbutaline was not stated.

The home-made spacers used were plastic cold-drink bottles (sealed and unsealed), plastic mineral water bottles, polystyrene cups, and cardboard cones, with volumes ranging from 200 ml (for polystyrene

cups) to 500 up to 750 ml (for plastic bottles). The commercial valved spacers used were Aerochamber[®], Cipla[®], and NebuChamber[®], with volumes ranging from 145 to 700 ml.

Source of data

Disease outcomes and probabilities

Outcomes associated with the use of either of the two spacers, namely probability of requirement for additional treatment and probability hospitalization after initial care in the ED, were extracted from the above-mentioned systematic review (17).

Resource utilization and costs

Because the CEA was conducted from the Colombian third-payer perspective, only direct costs were included in the CEA analysis. Specifically, the costs of the two spacers evaluated, as well as other consumables (fluids, supplies, and oxygen treatment), medical and therapy services (including respiratory therapy), diagnostics tests and procedures (white count blood, C-reactive protein, and chest X-ray studies), and hotel services (hospital stay) were included (18).

For cost calculations of the home-made spacers, we used the current market price of a plastic mineral water bottle, because it was the most commonly-used home-spacer in the primary RCTs included in the above-mentioned systematic review (17). For calculating the cost of commercial valved spacers, we used a 510 ml spacer of transparent polystyrene made in Colombia that meets all technical specifications and requirements, including a one way inspiratory valve of low resistance, with a soft plastic face mask or nozzle (Inhalocamara Pediátrica[®], Medioplast, Bucaramanga, Colombia).

For calculating the cost of additional bronchodilator treatment, we included all costs associated with administering albuterol via nebulization with compressed air/oxygen, including albuterol nebules and disposable nebulizer equipment (comprising nebulizer bowls and masks), because nebulization was the mode of delivery for additional bronchodilator treatments in the primary RCTs included in the systematic review (17).

The cost of MDI delivery of albuterol was calculated using the cost of one MDI canister per patient. Likewise, the cost of albuterol nebules was calculated using the cost of one albuterol nebule per patient.

Unit costs of all medications were obtained from the Drug Price Information System (SISMED, 2018) (19), 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 Colombia. Direct costs of asthma exacerbations requiring hospital attendance were primarily obtained from hospital accounting reports from the Fundación Hospital de La Misericordia (18). This hospital is a pediatric clinic located in Bogotá, the capital city 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 were considered to be reasonably well representative of the asthma costs of the whole country.

All costs collected were as close to reimbursement or true costs as possible. Costs were calculated in Colombian pesos (COP) and converted to U.S. dollars (USD) based on the average exchange rate for 2018 (US\$1 = COP2,956.55) (20). All the costs were adjusted to 2018 U.S. dollars.

The study protocol was approved by the local research ethics committee.

Sensitivity analyses

To assess the robustness of the model, one-, two-, and multi-way deterministic sensitivity analyses were performed using plausible variations in key model parameters. Values used in the deterministic sensitivity analyses were based on plausible ranges, including 95% confidence intervals (95% CIs) when available. Additionally, a probabilistic sensitivity analysis (PSA) using second-order Monte Carlo simulation with 10 000 iterations (assigning uncertainty distributions to input parameters in the model and sampling a random value from each distribution simultaneously), was used to deal with parameter uncertainty. Based on the PSA results, we calculated 95% uncertainty intervals (UI) for costs and effects and generated a cost-effectiveness plane (to show the estimated joint distribution of incremental costs versus incremental effects) (21). All analyses were performed using TreeAgePro 2016 software (TreeAge Software, Williamstown, MA, USA).

Results

Baseline and range values of parameters included in the model

The base-case values and ranges used in the deterministic sensitivity analyses, including unit costs of resources, costs of both spacers, probability of requirement for additional treatment, and probability of hospital admission after initial care in the ED, along with their respective sources, are presented in Table 1.

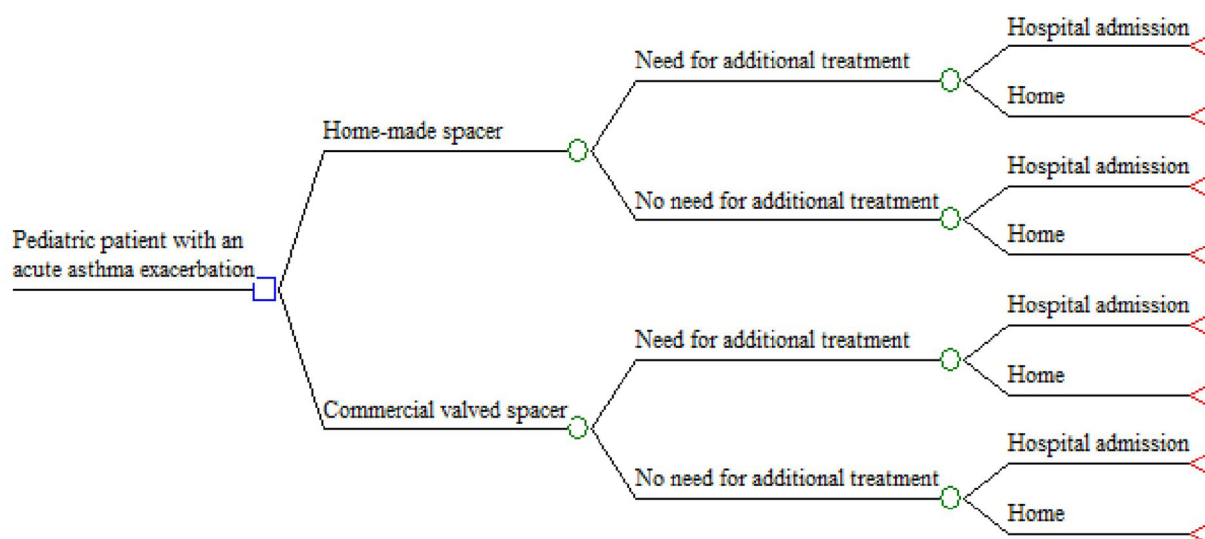


Figure 1. Diagram of cost-effectiveness model for each spacer.

Table 1. Baseline and range values of parameters included in the model*.

Items	Base-case value	Lower value	Higher value
Probability of hospitalization with commercial valved spacer (17)	0.15	0.1125	0.1875
Probability of hospitalization with home-made spacer adjustment factor (17)	1.00	0.63	1.59
Probability of requirement for additional treatment with commercial valved spacer (17)	0.18	0.135	0.225
Probability of requirement for additional treatment with home-made spacer adjustment factor (17)	1.18	0.84	1.65
Cost of commercial valved spacer	4.8	3.6	6.0
Cost of home-made spacer	0.66	0.495	0.825
Cost of disposable nebulizer equipment (18)	8.8	6.5	11.1
Cost of albuterol nebules (18)	5.9	4.4	7.4
Cost of MDI of albuterol (18)	9.9	7.4	12.4
Cost of inpatient asthma exacerbation (18)	581.9	436.5	727.5
Cost of ED asthma exacerbation (18)	38.8	21.1	64.1

*MDI: metered dose inhaler, ED: emergency department Costs are expressed in American dollars (US\$).

Base-case analysis

Under the base-case assumptions, the model showed that compared to commercial valved spacers, the use of home-made spacers for delivering bronchodilator therapy in pediatric asthma exacerbations was associated with lower total costs (US\$126.75 vs. US\$128.59 average cost per patient) without a significant difference in the probability of hospitalization avoided (0.8500 vs. 0.8500). Therefore, a cost-minimization analysis was applied in order to compare costs when effects do not differ between groups. A cost-minimization approach eliminates the need to calculate an incremental cost-effectiveness ratio (Table 2).

Sensitivity analyses

In the deterministic sensitivity analyses, our base-case analyses were robust to variations of all key model parameters. Parameter distributions used in the PSA are shown in Table 3. 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 to commercial valved spacers, using home-made spacers for delivering bronchodilator therapy in pediatric asthma exacerbations tends to be associated with lower overall treatment costs and a similar probability of hospital admission. Based on the PSA results, the 95% UI for cost per patient treated with home-made spacers and with commercial valved spacers was US\$90.67 to \$171.39 and US\$97.45 to \$165.88, respectively. The 95% UI for avoidance of hospitalization was 0.7924 to 0.8985 and 0.8107 to 0.8848, respectively. In 49.5% of the iterations, home-made spacer use was associated with a lower probability of hospital admission and lower costs compared with commercial valved spacers.

Discussion

The present study shows that in Colombia, an MIC, when compared to commercial valved spacers, using home-made spacers for delivering bronchodilator therapy in children with acute asthma exacerbations

Table 2. Base-case cost-effectiveness analysis of commercial valved spacers versus home-made spacers for delivering bronchodilator therapy in pediatric asthma exacerbations.

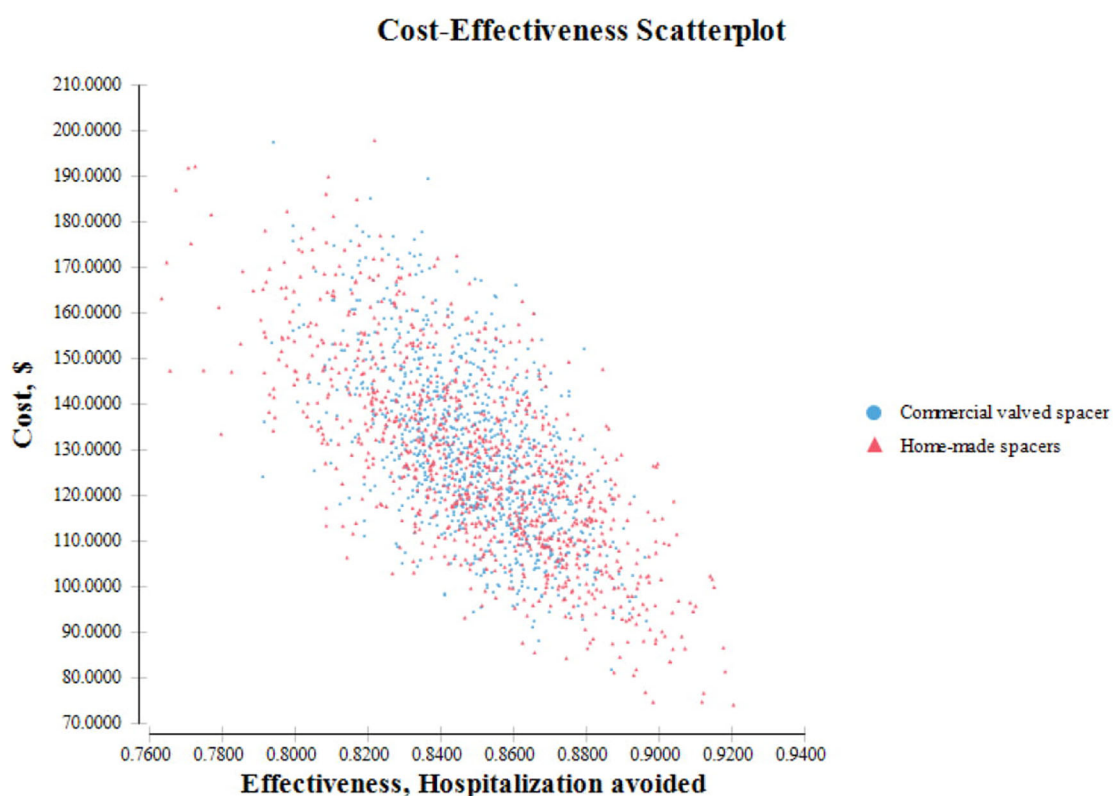
All patients						
Category	Strategy	Cost (US\$)	Incremental cost (US\$)	Effectiveness (avoidance of hospital admission)*	Incremental effectiveness (avoidance of hospital admission)	Cost/effectiveness
Absolutely dominated	HMS	126.75	–	0.8500	–	149.11
	CVS	128.59	1.84	0.8500	0.00	151.29

*HMS: home-made spacer, CVS: commercial valved spacer.

Table 3. Parameter distributions used in the probabilistic sensitivity analysis*.

Probability distribution	Distribution parameters	
Beta distribution	Alpha	Beta
Probability of hospitalization with commercial valved spacer	54.25	307.41
Probability of requirement for additional treatment with commercial valved spacer	52.3	238.25
Gamma distribution	Alpha	Lambda
Cost of treatment with commercial valved spacer	64.00	13.33
Cost of treatment with home-made spacer	64.00	96.96
Cost of disposable nebulizer equipment	384.16	78.40
Cost of albuterol nebules	64.00	10.85
Cost of MDI of albuterol	64.00	6.46
Cost of inpatient asthma exacerbation	64.00	0.11
Cost of ED asthma exacerbation	13.03	0.34

*MDI: metered dose inhaler, ED: emergency department.

**Figure 2.** Scatter plot of each iteration's cost and effectiveness values for each spacer in pediatric 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.

presenting to an ED or equivalent care setting is a more cost-effective strategy, because it involves a similar probability of hospital admission at lower overall treatment costs. Our base-case results were robust to variations of

all key model parameters and assumptions, and the PSA results were consistent with the base-case analyses.

The most remarkable result to emerge from the present study is that it provides evidence of the cost-

effectiveness of home-made spacers, a common and widely-used device for delivering albuterol and other bronchodilators for treating pediatric asthma exacerbations in LMIC.

The use of home-made spacers instead of commercial valved spacers could help to ensure a more efficient management of asthma exacerbations, which are responsible for a significant amount of the clinical and economic burden of the disease in pediatric patients. A device that is useful not only for lowering the probability of hospital admission but also for lowering overall treatment costs of such a highly prevalent and costly disease is greatly desirable in countries such as Colombia and other MICs, where health resources are always scarce and finite. Notably, our results support the recommendation that the use of a bottle spacer should be incorporated into guidelines for asthma management in LMICs (12).

There are several theoretical advantages of using valved spacers over non-valved devices (e.g. home-made spacers), such as improvement in coordination with inspiratory flow, prevention of the ingress of moisture and dilution of the aerosol inside the spacer after the exhalation, elimination of the cold-Freon effect, avoidance of leaking of the aerosol from the spacer, and reduction of the size of the aerosol particles (22,23). However, there are also theoretical advantages of using non-valved spacers over valved devices, such as an increase in pulmonary aerosol deposition, especially in young children or those with moderate to severe airway obstruction (because the resistance of the valves on inspiration may be difficult to overcome for such patients), and minimization of the amount of dead space in the spacer (24). It is worth mentioning that a recent study evaluating two types of spacers (although neither one was a home-made spacer) in asthmatic children reported a lack of agreement between the amount of in-vitro albuterol delivery and the clinical bronchodilator responsiveness observed between the two types of spacers (25). Although in our study it is probable that the final clinical response to bronchodilator therapy is a balance between the benefits of the two types of spacers, several considerations must be taken into account when interpreting and putting into practice the results of the present analysis. First, it is important not only to make an appropriate selection of the home-spacer device but also to ensure its correct use and administration. Zar et al. investigated the relative efficacy of three spacers, including two home-made spacers (a modified 500-ml cold drink bottle and a polystyrene cup), and the effect of leaks in the delivery system by comparing delivery using a sealed and an unsealed cold

drink bottle. After evaluating lung deposition using Tc-99m DTPA, it was determined that while the median aerosol deposition for the commercial spacer and the sealed bottle were equivalent (40.5% vs 44%), the median aerosol deposition was significantly greater with the sealed bottle than with the unsealed one (43.5% vs 24%), and in turn, the median aerosol deposition was significantly greater with the unsealed bottle than with the polystyrene cup (24.0% vs 9.5%) (14). Additionally, Zar et al., with the aim of investigating the clinical applicability of the above-mentioned study, evaluated changes in clinical score and pulmonary function in 88 children aged 5 to 13 years with acute asthma after using the same three spacers for administering fenoterol hydrobromide. Along the same line, although for children with mild exacerbations there were no significant differences by spacer type in any of the outcomes, for those with moderate to severe exacerbations, the sealed bottle performed better than the unsealed bottle, and in turn the unsealed bottle performed better than the polystyrene cup (12,13). Taken together, these studies suggest that a sealed 500-ml cold-drink bottle seems to be the most effective home-made spacer for children with asthma exacerbations, even for those with moderate to severe exacerbations. Second, the lack of differences in clinical response could be due, at least in part, to the fact that high doses of beta-2 agonists given in the primary RCTs included in the meta-analysis are close to the plateau of the dose-response curve, making home-made spacers perhaps less efficient when lower doses of bronchodilators are given (26). Third, we adopted a conservative approach with respect to the commercial valved spacer used and priced in our analyses. Other more commonly used commercial valved spacers, such as those reported in the primary RCTs included in the meta-analysis (Aerochamber[®], Cipla[®], and NebuChamber[®]), are much more costly than the commercial spacers included in our study, which would make it easier to demonstrate the cost-effectiveness of home-made spacers. Finally, although a recent study found a similar level of asthma control among adult asthmatic patients treated with beclomethasone-dipropionate IDM attached to a commercial valved spacer or a home-made spacer (27), the results of the present CEA should not be extrapolated to the use of inhaled corticosteroids in asthmatic children.

We acknowledge that at least four limitations could have influenced the results obtained in the present analysis: first, the primary outcome of the CEA model was derived from only one RCT. However, this was a high-quality, well-conducted RCT that was powered enough to demonstrate equivalence between the two

types of spacers. Second, resource utilization and cost data were obtained from a single clinical center and therefore 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 city. Moreover, the costs were subject to wide sensitivity analyses. Third, our results are restricted to patients attended in the ED or equivalent care setting and do not consider other potential benefits beyond the acute asthma episode, which may have been treated using either of the two types of spacers. Finally, the differences in costs associated with the two types of spacers could be due to imprecision of their estimates, because their 95% UIs overlap. Therefore, we cannot be 95% confident or more about which is the better spacer with regards to their economic value.

Conclusion/key findings

In conclusion, the present analysis shows that in Colombia, an MIC, compared to commercial valved spacers, the use of a sealed 500-ml cold-drink bottle as home-made spacer for delivering bronchodilator therapy in children with acute asthma exacerbations presenting to an ED or equivalent care setting is a more cost-effective strategy, because it involves a similar probability of hospital admission at lower overall treatment costs. Our findings may help to assist the clinical decision-making process when planning the optimal spacer for treating pediatric asthma exacerbations in LMICs.

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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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