Cost-effectiveness of Metered-Dose Inhalers for Asthma Exacerbations in the Pediatric Emergency Department

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KEY WORDS
asthma, metered-dose inhalers, nebulizers, β agonist, cost-effectiveness

ABBREVIATIONS
ED—emergency department
MDI—metered-dose inhaler
CI—confidence interval
LOS—length(s) of stay
ICER—incremental cost-effectiveness ratio
Can$—Canadian dollars
NZ$—New Zealand dollars

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WHAT'S KNOWN ON THIS SUBJECT: Treatment of mild and moderate asthma exacerbations in emergency departments can be efficaciously delivered by using either metered-dose inhalers or wet nebulization. Cost is a frequently cited reason for not using metered-dose inhalers over nebulization in emergency departments.

WHAT THIS STUDY ADDS: Metered-dose inhalers are a cost-efficient mode of delivery for bronchodilators, and transitioning from nebulization to metered-dose inhaler in pediatric emergency departments may result in significant cost savings associated with each admission averted.

abstract

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OBJECTIVE: To compare the incremental cost and effects (averted admission) of using a metered-dose inhaler (MDI) against wet nebulization to deliver bronchodilators for the treatment of mild to moderately severe asthma in pediatric emergency departments (EDs).

METHODS: We measured the incremental cost-effectiveness from the perspective of the hospital, by creating a model using outcome characteristics from a Cochrane systematic review comparing the efficacy of using MDIs versus nebulizers for the delivery of albuterol to children presenting to the ED with asthma. Cost data were obtained from hospitals and regional authorities. We determined the incremental cost-effectiveness ratio and performed probabilistic sensitivity analyses using Monte Carlo simulations.

RESULTS: Using MDIs in the ED instead of wet nebulization may result in net savings of Can$154.95 per patient. Our model revealed that using MDIs in the ED is a dominant strategy, one that is more effective and less costly than wet nebulization. Probabilistic sensitivity analyses revealed that 98% of the 10 000 iterations resulted in a negative incremental cost-effectiveness ratio.
Sensitivity analyses around the costs revealed that MDI would remain a dominant strategy (90% of 10 000 iterations) even if the net cost of delivering bronchodilators by MDI was Can$70 more expensive than that of nebulized bronchodilators.

CONCLUSIONS: Use of MDIs with spacers in place of wet nebulizers to deliver albuterol to treat children with mild-to-moderate asthma exacerbations in the ED could yield significant cost savings for hospitals and, by extension, to both the health care system and families of children with asthma. *Pediatrics* 2011;127:e1105–e1111

Asthma is among the most common presentations to an emergency department (ED). As many as 1 in 8 children are thought to have asthma, and these children account for up to 8% of all pediatric ED visits.[1,2]

The mainstay of treatment for children with acute asthma exacerbations are inhaled selective β_2 agonists, which can be delivered via wet nebulization or metered-dose inhalers (MDIs) with age-appropriate holding chambers.[3,4] A systematic review comparing the 2 modes of delivery found that MDIs are at least equivalent, and most likely superior, to nebulizers when considering clinical outcomes and adverse effects.[5] Furthermore, the authors of the systematic review suggest that use of an MDI yields several practical benefits, such as decreased risks for cross infection and the ability of the patient to use his or her personal device.

Despite this evidence, as recently as 2007 only 2 of 10 Canadian pediatric EDs routinely used MDIs. One of the frequently cited barriers to routine use of MDIs are concerns regarding cost.[6] Although Leversha et al[7] reported that total health care costs should be lower when MDIs are used in the ED because of the anticipated lower rates of admission associated with their use, there are several reasons why their reported estimates may be inaccurate. Their report potentially overestimated cost savings, as a Cochrane systematic review comparing these 2 modes of delivery reported confidence intervals (CIs) for hospitalization rates that overlapped 1.0[5]. In addition, these authors likely underestimated potential economic savings as a result of not incorporating shorter lengths of stay (LOS) into their economic model that resulted from use of MDIs and spacers. Furthermore, their study did not determine the incremental costs of using MDIs and spacers in averting a hospital admission.

The objective of the present study was to determine the incremental cost and effects of using MDIs and spacers compared with wet nebulization in averting a hospital admission for the treatment of children with acute mild to moderately severe asthma exacerbations in a tertiary care pediatric ED.

METHODS

Design

We built a decision model to measure the incremental cost-effectiveness between the 2 modes of delivery of β-agonist bronchodilators in the treatment of pediatric asthma in the ED. Outcomes associated with either treatment strategy, such as probability of admission and ED LOS, were extracted from a published Cochrane systematic review[5] of MDIs versus nebulization for ED management of asthma exacerbations. Cost data were obtained from 2 tertiary academic pediatric health centers in western Canada: British Columbia Children's Hospital and Alberta Children's Hospital. These costs were then averaged. Costs and outcomes from these sources were used to build a model from which cost-effectiveness was calculated and sensitivity analyses were performed.

This cost-effectiveness study was performed from the perspective of a hospital, including ED and hospital admission costs. The focus of this study is on the differential cost and effect of varying ED treatments for acute exacerbations, rather than that of long-term treatment protocols on quality of life or longer-term clinical outcomes. The time horizon for this study is limited to the time of ED admission to 2 days post-ED admissions, accounting for an average admission duration of 48 hours.[5] Patient disposition from the ED was used as the effectiveness outcome; being discharged from the hospital was considered a success, and being admitted for ongoing treatment was considered a failure. Because human subjects and patient medical records were not used for this study, ethics approval was not required.

Model Patient Characteristics and Outcomes

Children enrolled in randomized controlled trials included in the Cochrane systematic review[5] served as our reference population, and we applied their characteristics to our decision model. These were children aged 2 to 18 years, with an acute asthma exacerbation coming to the ED for treatment, excluding children with severe respiratory distress requiring ICU admission or chronic cardiorespiratory illnesses (other than asthma). Specific symptom severity score tools varied between randomized controlled trials but overall were equivalent in representing children with mild-to-moderate asthma. The reference setting was a combination of the British Columbia Children's Hospital and Alberta Children's Hospital EDs, both of which are Canadian urban tertiary care pediatric EDs staffed with certified pediatric emergency specialists.

Treatment Protocol

We projected a range of costs based on 2 treatment protocols, one of which used only a β agonist and the other also incorporated ipratropium bromide. We assumed 3 to 6 inhalations of albuterol 500 to 1000 μg via MDI with a spacer at 20-minute intervals versus 3 to 6 treatments of albuterol 2500 or 5000 μg via wet nebulization at 20-minute intervals. We created the second model that included ipratropium bromide, as we thought it represents a more expensive treatment a patient may receive for treatment of asthma in the ED. We assumed nebulized ipratropium was administered at 3 treatments of 500 μg given at 20-minute intervals or 3 treatments of ipratropium

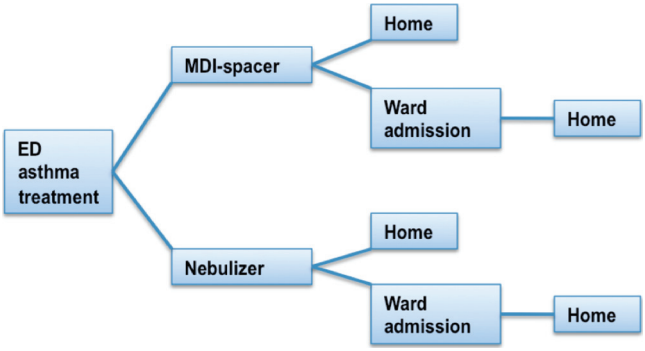

FIGURE 1
Decision model for ED treatment of acute pediatric asthma exacerbations.

bromide 60 to 100 μg via MDI at 20-minute intervals.

Decision Model

We calculated the costs associated with the treatment of a child in the pediatric ED with an acute asthma exacerbation beginning from treatment in the ED to discharge from the hospital (directly from the ED or after ward admission). The algorithm is displayed in Fig 1.

Model Parameters

Parameters included in this model were the probability of averting an admission (1-probability of admission) and costs associated with the treatment protocol using either of 2 modes for delivering albuterol. The costs associated with the treatment protocol included direct pharmacologic costs and nursing wages for their respective average ED LOS. These costs are displayed in Table 1.

Probability of Admission

The probability of averting a hospital admission was determined using the pooled probability of admission associated with either albuterol mode of delivery as reported by the Cochrane systematic review of holding chambers (spacers) versus nebulizer for β-agonist treatment of acute asthma[5].

Costs

All costs are expressed in Canadian dollars (Can$). Because the nature of treatment of acute asthma exacerbation is short in duration, neither the cost nor the effects were discounted.

ED Staffing Costs

Average nursing care costs per hour, per patient, were derived from the annual cost of nursing labor at the British Columbia Children's Hospital ED cost center divided by the cumulative number of patient hours serviced during that same year. This information was provided by the British Columbia Provincial Health Services Authority Decision Support Services department. The average nursing hourly cost was multiplied by the ED LOS associated with each of the treatment protocols in our model.

The physician costs associated with the treatment of asthma exacerbation in the ED were assumed to be similar between patients treated with MDIs and nebulizers. Therefore, we omitted physician fees from this cost comparison.

Drug and Delivery-Device Costs

All ED unit costs for drugs and delivery devices were obtained from the British Columbia Children's Hospital and the Alberta Children's Hospital pharmacy and purchasing departments.

The ED MDI albuterol cost per patient was calculated by using the cost of 1 MDI canister per patient regardless of dosage, as albuterol MDI canisters are not transferable or reusable between patients. During the 2009 pandemic H1N1 season, our institution's infection control department felt that current cleaning techniques were insufficient and therefore made this recommendation. The ED spacer cost

TABLE 1 Baseline Values for the Model Parameters

Variable	Value, Can$
Costs	
RN fees per h per patient[a]	33.05
MDI albuterol per patient (SD)[b]	2.96 (0.08)
MDI spacer per patient (including sterilization when applicable) (SD)[b]	11.98 (10.80)
Hospital admission stay, per d[a]	1043
Nebulization albuterol/patient (SD) (includes wall oxygen for delivery)[b]	2.67 (1.98)
Nebulization kit (SD) (mask and tubing)[b]	2.08 (0.13)
MDI ipratropium bromide[b]	18.34
Nebulization ipratropium bromide (SD)[b]	1.470 (0.042)
Utilization measures	
Average MDI LOS in the ED, h (SD)	0.83 (0.42)
Average nebulization LOS in the ED, h (SD)	1.41 (0.73)
Probability of admission	
MDI	0.094
Nebulization	0.16
Admission length LOS, d (SD)	
MDI	2.21 (0.98)
Nebulization	1.92 (0.98)

RN indicates registered nurse.
[a] British Columbia Children's Hospital ED cost center and British Columbia Provincial Health Services Authority Decision Support Services department.
[b] British Columbia Children's Hospital and Alberta Children's Hospital pharmacy and purchasing departments.

per patient was derived from the average cost of using a reusable spacer and its associated sterilization costs between uses (as directed by the manufacturer and using a single-use spacer, which is given to the patient on discharge).

The ED nebulized albuterol cost was derived from the average of the costs associated with each of the aforementioned possible combinations calculated by using the cost per dose (2500 or 5000 μg), including the cost of wall oxygen used for nebulization, multiplied by the number of treatments (3–6). In other words, we averaged the cost of 3 treatments of 2500 μg, 3 treatments of 5000 μg, 4 treatments of 2500 μg, 4 treatments of 5000 μg, and so forth to 6 treatment of 2500 μg and 5000 μg. The cost of nebulizer kits was obtained by calculating the average cost between the 2 mask sizes available.

Hospital Stay Costs

Because admission to the hospital for ongoing treatment is considered a failure of the ED treatment protocol, admission costs were added to treatment costs. The British Columbia Provincial Health Services Authority Decision Support Services department provided us with the average daily cost for inpatient asthmatic patients of $1043, which includes nursing and pharmacologic costs. This figure was multiplied by an average inpatient LOS for asthmatic exacerbation of 2 days, as suggested by findings from the Cochrane systematic review[5] and Alberta Children's Hospital (Dr Johnson, unpublished data, 2009). To this we added physician fees of $268.34 for the initial admission consultation and a hospital visit on the second day,[8] for a total of $2354.34 per admission.

Model Assumptions

We made several assumptions in building this model.

Steroid and Other Medications

We assumed that oxygen supplementation would be provided when required. As administration of steroids and other medication are often included in individual center protocol (both inpatient and on discharge), regardless of the mode of albuterol delivery, these costs were not included in this cost comparison. Moreover, outcome measures reported in the Cochrane systematic review were not specifically associated with steroid use.[5]

Human Resource Costs Associated With Treatment Delivery

Each ED's protocol varies, whether administered by a nurse, a respiratory therapist, or partially by the parents. It is also possible that within an adopted protocol, individual sets of patient and parents, based on previous experience, may need more or less providers' assistance. For the purpose of this study, we assumed that the mode of bronchodilator delivery is not associated with a differential labor cost.

Hospital Admission Duration

Although inpatient use of MDIs versus nebulization may affect the duration of admission, we have assumed that ED choice of treatment delivery modality bears no effect on the duration of admission LOS. Therefore, although the probability of hospital admission is an outcome affected by the choice of ED treatment delivery, costs associated with each of these hospital admissions did not vary between treatment modalities in our model.

Analyses

Incremental Cost-effectiveness Analysis

To determine the incremental cost-effectiveness (ICER) per hospital ward admission averted, the difference in cost associated with each of the albuterol modes of delivery was divided by the difference in probability of hospital admission for a child treated with either delivery mode, as calculated from our model.

One-Way Sensitivity Analyses

To identify variables most influential to our model, we performed 1-way sensitivity analyses.

Probabilistic Sensitivity Analyses

Probabilistic sensitivity analyses were performed by using Monte Carlo simulations to explore the uncertainty around our baseline ICER to address the combined variability of our model variables. Pooled results for ED LOS, the probability of hospital admission, and average costs were fit with theoretical distributions. We used β distributions to model the probability of admissions, as they are commonly used to describe uncertainty or variability in proportions or prevalence. For LOS, we used γ distributions, which are a family of nonzero continuous probability distributions often used to model waiting time or time to event; they are also used in financial services to model size of loans or claims. Although cost could be modeled using normal distributions, when the SD is sizable, they would allow for negative numbers; in these instances, we used γ distributions.

Each of these distributions was sampled 10 000 times simultaneously, generating an interval around the baseline ICER. A cost-effectiveness plane was also created to illustrate the distribution of the incremental costs and effectiveness (Fig 2).

In addition, we performed a sensitivity analysis around the cost assumptions of MDI delivery and nebulization to estimate the difference in cost of drugs and related devices (spacer, tubing, mask, and wall oxygen) for which the ICER would change in direction.

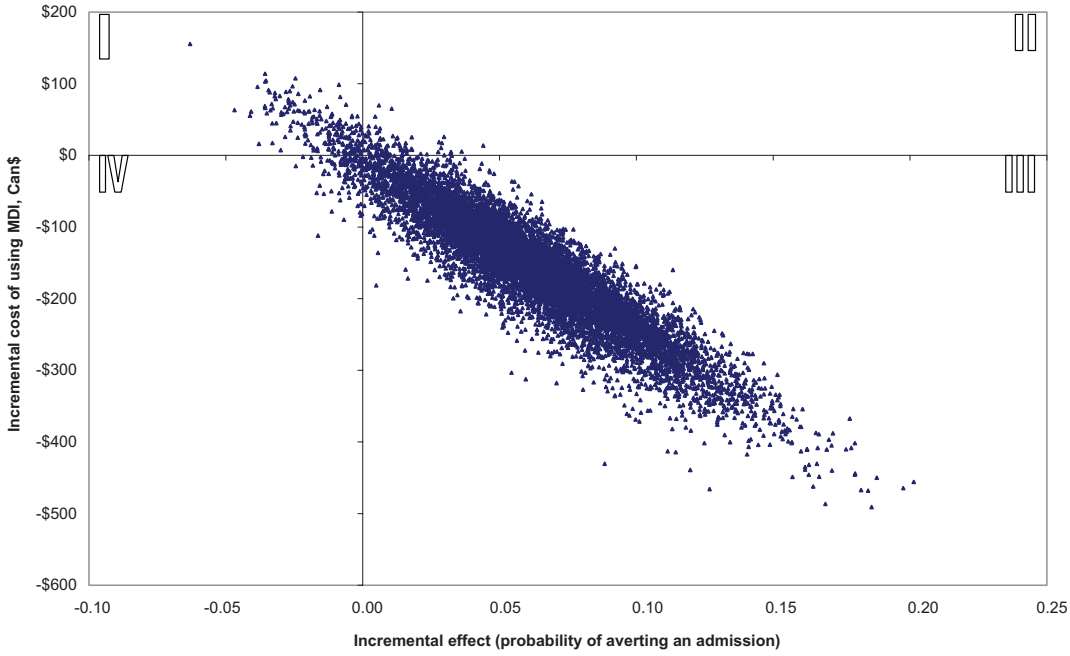

FIGURE 2
ICER of using MDIs instead of nebulization. Quadrant I: MDI is a dominated strategy; it is more costly and has a higher probability of admission than nebulization. Quadrant II: MDI is more costly but has a lower probability of admission than nebulization. Quadrant III: MDI is a dominant strategy; it is less costly and has a lower probability of admission than nebulization. Quadrant IV: MDI is less costly but has a higher probability of admission than nebulization.

TABLE 2 Baseline Model of Cost-effectiveness of an MDI Versus Nebulization in the Treatment of ED Pediatric Asthma Exacerbations

Treatment Protocol	Cost, Can$	Effect (Admission Averted)	Incremental Cost-effectiveness (Can$ per Admission Averted)
Overall MDI and space chamber with hospital admission costs	262.73	0.906	—
Averaged drug and delivery-device costs	14.94	—	—
Averaged nursing time for the LOS in ED costs	27.42	—	—
Probability of admission multiplied by hospital admission costs	220.37	—	—
Wet nebulization with hospital admission costs	417.68	0.844	—
Averaged drug and delivery-device costs	4.75	—	—
Averaged nursing time for the LOS in ED costs	46.60	—	—
Probability of admission multiplied by hospital admission costs	366.33	—	—
Incremental	−154.95	0.062	−2499.16

RESULTS

Incremental Effect

The pooled difference in probability of admission was 0.062 (95% CI: −0.0043 to 0.1304). Although not statistically significant, the CI favored the MDI protocol and is reflected in our probabilistic sensitivity analyses. Detailed cost comparisons are listed in Table 2.

Incremental Costs

The costs associated with using the MDI protocol to treat a patient in the ED with asthma in our model was Can$262.73 (without ipratropium bromide) compared with Can$417.68 when the nebulized protocol was chosen, which resulted in a net cost saving of Can$154.95 per patient treated when using the MDI protocol.

Incremental Cost-effectiveness Ratio

The MDI protocol resulted in a higher probability of preventing a hospital admission while being less expensive, which resulted in a negative ICER (−Can$2499 per admission averted) and indicates that the MDI strategy is dominant.

Probabilistic Sensitivity Analyses

More than 98% of the 10 000 points from the probabilistic sensitivity analysis resulted in a negative ICER. These results are illustrated by the cost-effectiveness plane (Fig 2), in which each of the 10 000 points represent a pair of values linking an incremental cost and a difference in probability of averting a hospital admission associated using the MDI treatment protocol over nebulization.

The Monte Carlo simulation also found that MDI would remain dominant in 90% of the 10 000 runs if the cost of MDI administration was as

much as Can$70 higher than that of nebulization.

The ICER was also calculated on the model including the costs of ipratropium bromide, resulting in a negative ICER (−Can$2226.98 per admission averted). Comparable to the baseline model, Monte Carlo simulations found that 97% of the 10 000 points resulted in a negative ICER.

One-Way Sensitivity Analyses

One-way sensitivity analyses revealed that the probability of admission had the greatest influence on the model's ICER and brought the ICER to as far as −Can$2107.66 per admission averted, favoring nebulization. Therefore, in the range of probability of admission favoring nebulization, the use of an MDI becomes a dominated strategy and thus a more costly and less effective means of averting an admission from an asthma exacerbation.

DISCUSSION

We found that using MDIs with spacers in place of nebulizers to deliver bronchodilators (either albuterol alone or both albuterol and ipratropium bromide) to children with mild-to-moderate asthma exacerbations would, in most cases, result in both cost savings and a reduction in hospitalizations, which in economic terms is known as a dominant strategy.

Breaking down the differential costs between the 2 treatment strategies revealed that the MDIs and spacers were more expensive than nebulized drugs and devices. Although the shorter ED LOS associated with MDI use contributed to lesser costs, it is the lower probability of admission and its associated costs that is the main factor in MDI being more cost-effective. Although the risk ratio for probability of admission between treatment strategies of 0.65 (95% CI: 0.4–1.06) was not statistically significant, the probabilistic sensitivity analysis yields greater benefit for MDIs with spacers because all but the high extreme for MDIs and low extremes for nebulization in probability of admission favor MDIs with spacers.[9]

We found only 1 other study, by Leversha et al,[7] reporting costs of treating children with acute asthma exacerbations in the ED. They also reported lower costs associated with MDI use. However, their study, a randomized controlled trial, included only a retrospective cost comparison, and their costs were not related to objective effectiveness outcomes. Their cost parameters were calculated by using a model with a fixed ED visit cost of 190 New Zealand dollars (NZ$) (including fixed overhead costs, human resources, investigations, and treatment costs), added to the cost of albuterol and its delivery devices (NZ$30.60 for the MDI versus NZ$3.52 for the nebulization) and the average hospital admission cost of NZ$1814 per patient. They concluded that the mean cost of treatment with MDIs was NZ$825 compared with NZ$1282 with nebulization and documented similar clinical efficacy.

The main differences between the study by Leversha et al[7] and our study is that we took into consideration the differential ED LOS associated with each treatment strategy and used pooled data (larger sample) outcomes.

In addition to conducting a probability sensitivity analyses, we compared the baseline model with 1 that included the costs associated with ipratropium bromide. Although there is little if any published evidence regarding the effectiveness of ipratropium via MDIs with spacers, some EDs include ipratropium bromide in the treatment of moderate and severe asthma exacerbations because results of studies adding nebulized ipratropium to albuterol suggest it reduces the number of hospitalizations, decreases clinical asthma scores, and improves lung function compared with nebulized β agonists alone.[10–13] The relative cost of ipratropium MDIs are substantially greater than nebulized ipratropium, so it adds an additional $17 per patient to the costs of an albuterol MDI and spacer. Nonetheless, even in the extreme scenario in which all patients were treated with ipratropium bromide as well as with albuterol, the outcome of our cost-effectiveness model was not altered.

Our study's main limitation, similar to that of Leversha et al,[7] is that we used a costing model with retrospectively reported averaged group outcomes (LOS, treatment doses, and physician fees) rather than prospectively collecting individual subjects' resource utilization data. Such a process would be labor- and cost-intensive and preclude the possibility of including as large a sample of subjects to determine outcomes as we did using pooled data from a systematic review. Because the treatment outcome parameters came exclusively from randomized controlled trials, whether the treatment efficacy reported would be translated to effectiveness and is generalizable to community ED settings is unknown.

In addition, our results are only generalizable to single-payer health care models similar to that used in Canada. In the United States, substantial cost variability may exist because of multiple different payers; consequently, our results may not be applicable to all US health care settings.

CONCLUSIONS

Use of MDIs with spacers in place of wet nebulizers to deliver albuterol to treat children with mild-to-moderate asthma exacerbations in the ED could yield significant cost savings for hospitals and, by extension, to both the health care system and families of children with asthma.

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