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Efficacy of Metered-Dose Inhalers for Children With Acute Asthma Exacerbations

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Summary. Objective: To compare the effectiveness of the administration of inhaled beta-agonists delivered via a metered-dose inhaler (MDI) with spacers—as part of an evidence-based asthma pathway developed to manage acute asthma exacerbations in children at the emergency room level and in inpatient management—against administration via nebulization. Design: Case with historical control. Setting: KK Women's and Children's Hospital (Singapore). Participants: A total of 19,951 children (infants to older children) aged 18 years and younger who attended the emergency room for asthma exacerbations. Main Outcome Measures: Average length of stay, proportion admitted to high dependency or intensive care, proportion readmitted for unresolved symptoms within 72 hr, cost per patient and overall. Results: There was no increase in the mean proportion of emergency room attendances admitted to inpatient care with use of an MDI (mean difference 0.97%, 95% CI: −1.6–3.5%, $P = 0.447$), nor of children admitted to intensive care (0.21 vs. 0.20 pre- and post-pathway, $P = 0.827$) or to high dependency units (2.21 vs. 1.37 pre- and post-pathway, $P = 0.200$) but a significant reduction in the within 72 hr re-attendance rate (mean difference 1.4%, 95% CI: 0.78–2.0%, $P < 0.001$) with use of an MDI. The average length and cost per patient for an inpatient stay for acute asthma exacerbations was reduced with use of an MDI. Conclusions: The use of an MDI with spacer as part of an evidence-based asthma pathway was effective in the management of acute asthma exacerbations in the emergency room setting and for inpatient management. **Pediatr Pulmonol. 2011; 46:421–427.** © 2010 Wiley-Liss, Inc.

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INTRODUCTION

Nebulizers have long been the standard of care in emergency rooms for the administration of beta-agonists to patients with acute asthma. In recent years, studies have shown that metered-dose inhalers (MDIs) with a spacer are effective in the treatment of acute asthma, even in young children[1] in an emergency room setting.[2,3] In fact, there is increasing evidence that the use of MDIs with spacer is as effective as nebulization for managing acute asthma.[4–7]

In a study of 61 children admitted for acute asthma, Dewar et al.[7] found that the use of MDI with spacer showed a trend toward a shorter hospital stay than the use of a nebulizer (36.5 hr vs. 40.0 hr). Two studies have found that the use of MDI with spacer has a cost advantage over the use of a nebulizer. A study conducted at a center in the United States found that switching to MDI with spacer would save the center US $83,000 annually, and charges to patients could be lowered by approximately US $300,000 per year.[8] A second study at a center in Auckland, New Zealand found that switching to MDI with spacer in the

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emergency room setting would be as effective as a nebulizer with a lower mean cost per emergency room presentation of NZ $457.[9] Despite these findings, there is still resistance to the use of MDI with spacer in the medical community as a whole.

Another strategy that has been shown to have positive results in the treatment of asthma is the implementation of a clinical asthma pathway. In a study of 267 emergency room patients with asthma, Norton et al.[10] found that the implementation of a clinical pathway for the emergency room treatment of patients with acute exacerbations of asthma resulted in a significant reduction of patient admissions for further management of acute exacerbations (13.5% vs. 27.5% in the pre-implementation group, $P = 0.02$).

In 2003, when SARS hit Asia and spread to various parts of Europe and Canada, there was a great fear that the use of nebulizers had contributed to the rapid spread of the disease, especially among inpatients.[11] This prompted us to develop an asthma pathway that included the use of MDIs with spacers instead of nebulizers for both emergency room visits and inpatient management to reduce the spread of infections to other patients and to health staff. Our purpose was to develop an evidence-based pathway using an MDI with spacer for the treatment of acute asthma in children, and to successfully implement this change into current medical practice. This pathway was implemented in mid-2003.

The purpose of this study was to review the efficacy of our evidence-based asthma pathway, which uses MDI with spacer instead of a nebulizer to administer beta-agonists, in the management of acute asthma exacerbations in children in both the emergency room and inpatient settings.

METHODS

This study was carried out at the largest Children's Hospital in Singapore, the KK Women's and Children's Hospital. It is a tertiary referral hospital, but it also provides primary- and secondary-level care to children. The facility's emergency room receives about 100,000 attendances per year. About 3,000–3,600 of these are for acute asthma exacerbations, of which about 30% are admitted with a mean length of stay of about 2.68 days. Prior to the study, the emergency room had no clear protocols for the management of asthma exacerbations. Most patients received beta-agonists administered by nebulizer, and the need for additional bronchodilators was based on individual practice.

In preparation for the study, a multidisciplinary group was convened to review the literature regarding the use of MDIs for the administration of medication for acute asthma exacerbations in hospital settings, as well as the literature regarding comparisons between the use of an MDI and a nebulizer. This information was used to draw up an effective clinical pathway that used MDI with spacer for the treatment of acute asthma exacerbations in the emergency room setting and during inpatient treatment.

In the new asthma pathway, the severity of the exacerbation was clearly defined and the management protocol was standardized based on this severity. All patients with mild, moderate, or severe exacerbations were administered the beta-agonist salbutamol via MDI with spacer. The anticholinergic ipratropium bromide was also routinely administered via MDI with spacer to reduce the need for admissions.[12,13] The ipratropium bromide puffs were administered following the salbutamol puffs. In the Children's Emergency, the number of salbutamol puffs was standardized to 10 puffs for children >10 kg and 5 puffs for children <10 kg, whilst 4 puffs of ipratropium bromide were given to children >10 kg and 2 puffs to children <10 kg. Patients for whom respiratory arrest was imminent received salbutamol and/or ipratropium bromide via nebulizer. Oxygen or additional medications, including steroids, were administered if warranted based on severity (Fig. 1). All patients with moderate or severe exacerbations were given oral steroids, or intravenous steroids if unable to take orally. At the end of the treatment cycle, the patient was reassessed and a decision was made as to whether the patient would be admitted, and if so, whether the patient would be admitted to the general ward, the high dependency unit, or the intensive care unit. Patients with severe exacerbations were admitted to the high dependency unit and those with impending respiratory collapse requiring intubation and ventilation were admitted to the intensive care unit (Fig. 1).

If the patient was admitted, emergency room doctors would order a continuation of treatment with bronchodilators, treatment to be initiated by the ward nurses upon the patient's arrival to ensure there would be no delay in the continuation of treatment while the patient was being seen by the junior doctor (Fig. 2).

Prior to initiation of the new clinical pathway, the frequency of nebulization treatment during inpatient treatment was decided by the most junior staff who reviewed the patients. Per the new pathway, the frequency of the inhaled beta-agonist during inpatient treatment was pre-determined to be at 15-min intervals in the first hour, then the patient was reviewed to determine whether the frequency could be reduced. Ipratropium bromide was not routinely administered during inpatient management except in the case of severe exacerbation as the literature does not suggest any additional benefits with ipratropium bromide[12,13] (Fig. 3). The number of puffs of salbutamol was calculated based on the child's body weight at 0.2–0.3 puffs/kg up to a maximum of 30 kg body weight or up to a maximum of 10 puffs at each administration. The administration of the puffs were given as single actuations

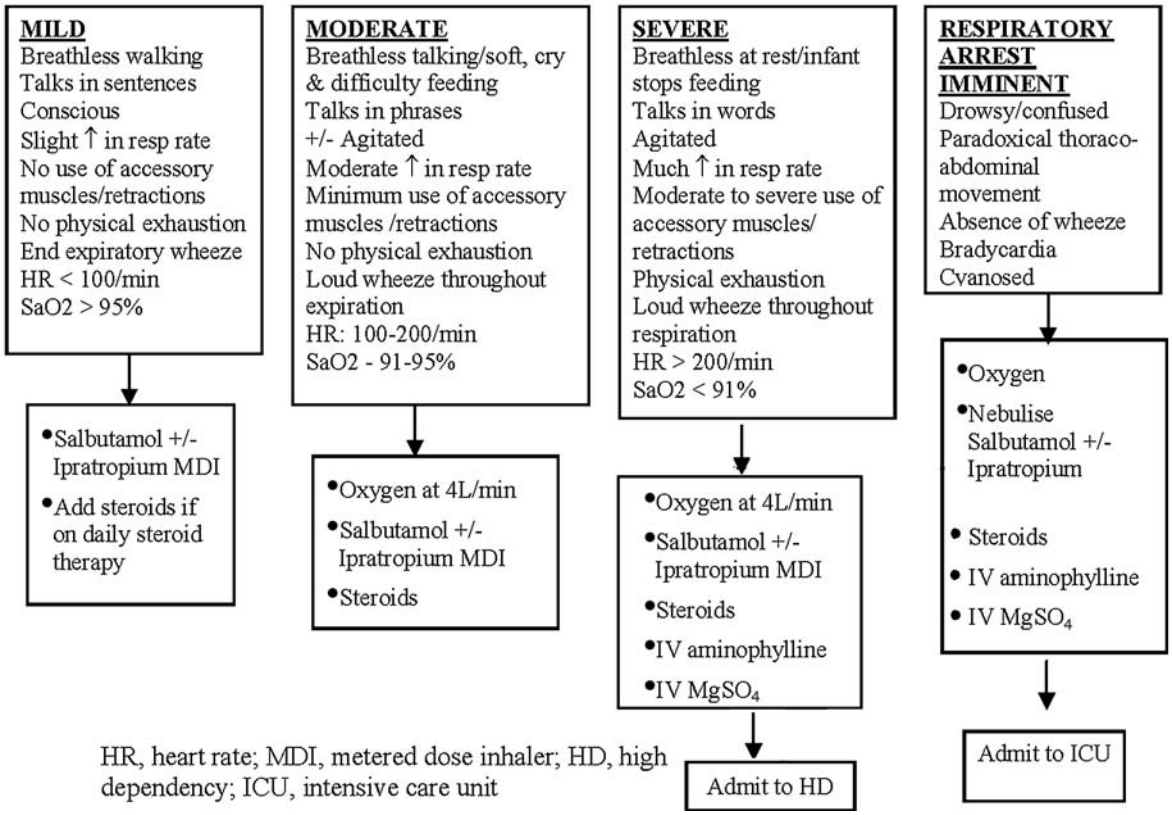

Fig. 1. Management of asthma in the Children's Emergency.

followed by tidal breathing either with a face mask in younger children <6 years old or through the mouth piece in the older children.

For the purposes of infection control, the pathway required that MDI spacers be designated for individual use only, and the spacers were to be sterilized after each use. As such, the spacer that we used was called the Space Chamber, a registered trademark of Medical Developments International Limited from Australia, which could be autoclaved after each patient use. The spacers we used

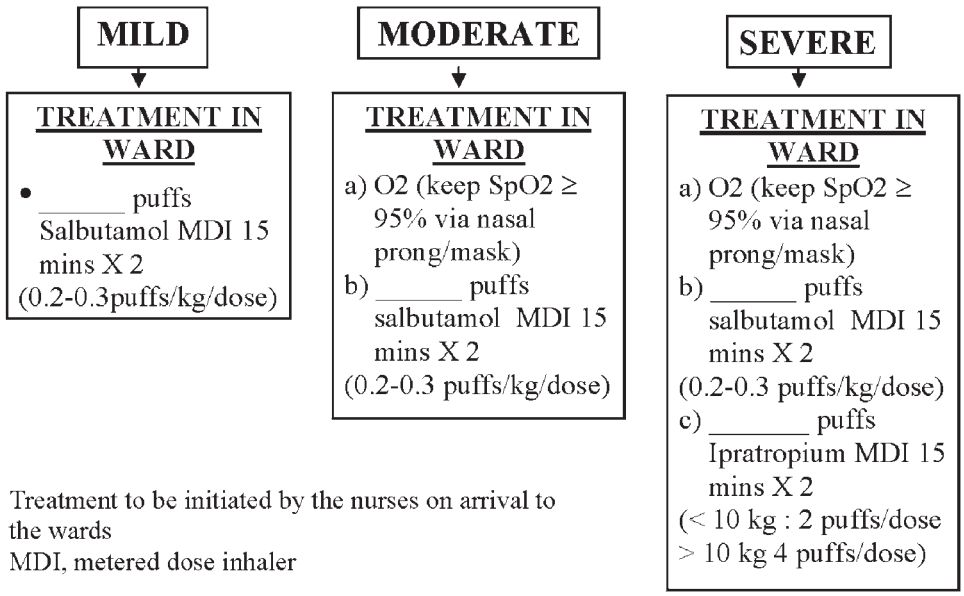

Fig. 2. Continuation of treatment from the Children's Emergency to the inpatient ward.

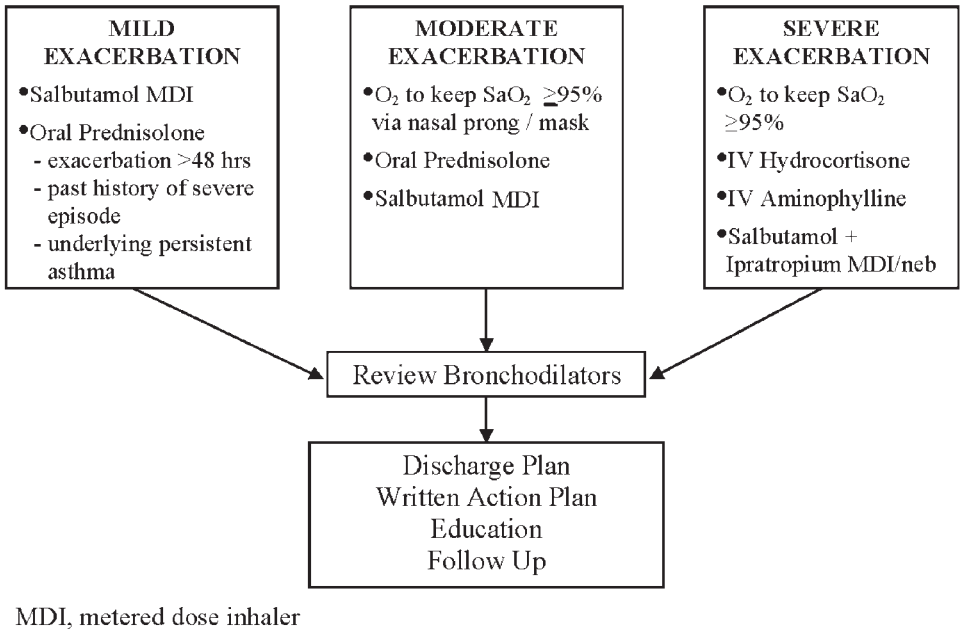

Fig. 3. Inpatient management of acute asthma.

also allowed the delivery of oxygen during administration of the beta-agonist, which was ideal.

As part of discharge planning, doctors needed to decide on the chronic management of the asthma. In addition to deciding on the long-term pharmacotherapy, a strong emphasis was placed on patient education and the use of written asthma action plans. Education encompassed educating parents on etiology, trigger factors, allergen avoidance, drug therapy, recognition of an asthma exacerbation and home management of such exacerbations, and when to consult a doctor. Education was aimed at addressing parental and/or patient knowledge of—and attitudes toward—asthma to improve compliance with treatment,[14–18] as compliance to therapy is a crucial component of management for any chronic illness. For patients deemed to have more severe asthma, patient education was delivered by specially trained asthma nurses. Patients with milder asthma received education in group training, which was conducted by the pharmacists. Trigger factors were identified and allergen avoidance was advised to reduce exacerbations[19–22] with particular emphasis on house dust mite avoidance and cigarette smoking in the community.

Upon discharge, all patients were also given a written asthma action plan. We have found this to be very useful because once patients get home, they may forget which medication to use and how much of it to administer. The action plan serves to remind patients to use their daily controller medications and empowers them to manage mild exacerbations at home. It also prompts the patients to seek urgent hospital treatment in cases of severe exacerbations and/or failure of self-medication.[23] The use of asthma management plans has been shown to reduce hospital admissions, emergency room visits, unscheduled visits to the doctor for asthma, days off of work, nocturnal awakening and the risk of death.[24–28]

The study is a retrospective study. All patients who presented with an asthma exacerbation to the hospital were included. All patients presenting to the hospital will be registered into the hospital's database and the diagnosis captured. These data can be retrieved for each year. All patients that were admitted for an asthma exacerbation will be put on the asthma pathway. An outcome and variance form for all asthma admissions will be filled up and this is used to track compliance to the pathway. A co-ordinator was employed to monitor compliance to the pathway. The new asthma pathway was initiated in mid-2003. In order to compare data from full-year sets of data, we compared yearly data from 2000 to 2002 (pre-pathway years) to yearly data from 2004 to 2006 (pathway years). We made comparisons with regard to the proportion of emergency room attendances admitted for further management, the proportion admitted to high dependency and intensive care, the average length of inpatient stay, and cost for inpatient care. This study was approved by the Institutional Review Board of KK Women's and Children's Hospital.

Statistics

All analyses were performed using SPSS 17.0 and statistical significance was set at $P < 0.05$. The differences

between the two cohorts (2000–2002 vs. 2004–2006) on the mean proportions of emergency room attendances admitted to inpatient care, children admitted to intensive care, to high dependency units, within 72 hr re-attendance rate, the average length of an inpatient stay for acute asthma exacerbations and the cost per patient for those managed as an inpatient were assessed using two Sample *t*-tests when normality and homogeneity assumptions were satisfied otherwise the nonparametric Mann–Whitney *U*-test was applied.

RESULTS

From year 2000 to 2006, the KK Women's and Children's Hospital emergency room saw from 3,000 to 3,600 attendances per year by children with asthma exacerbations aged 18 years and below. Prior to implementation of the asthma pathway using MDI with spacer (years 2000–2002 with a total of 10,258 episodes), a mean (standard deviation) % per year of 30.3 (4.6)% of these emergency room attendances for acute asthma exacerbation were admitted for further management of their asthma exacerbations. Of patients who were seen for asthma and discharged, 5.2 (1.4)% re-attended within 72 hr for unresolved symptoms of asthma. After implementation of the asthma pathway (years 2004–2006 with a total of 9,693 episodes), 31.2 (6.1)% of emergency room attendances for acute asthma exacerbations were admitted for further management of their asthma exacerbations. However, only 3.8 (1.2)% of those who were seen for asthma and discharged re-attended within 72 hr for unresolved asthma symptoms. Thus, after implementation of the MDI with spacer as part of the asthma pathway, there was a slight but insignificant increase in the proportion of children in the acute emergency setting who were admitted ($P = 0.447$, mean difference 0.97%, 95% CI: −1.6–3.5%) but there was a significant decrease in the number of re-attendances for unresolved symptoms within 72 hr ($P < 0.001$, mean difference 1.4%, (95% CI: 0.78–2.0%).

Overall, patient compliance with the use of MDI and spacer was good at 98%. The main use of nebulizers was in the emergency room and in high dependency. Prior to implementation of the asthma pathway (years 2001–2002), the average length of inpatient stay was 2.68 days. After implementation of the asthma pathway (years 2004 to 2006), the average length of inpatient stay was 2.27 days (Fig. 4). For patients admitted to high dependency, the average length of stay decreased from 3.09 days in 2004 to 2.78 days in 2006. The number of patients admitted to high dependency decreased whilst the number admitted to the intensive care unit remained stable (Fig. 5). We also compared the proportion of patients admitted to high dependency and to intensive care pre- and post-pathway. The proportion of patients admitted to intensive care remained stable (0.21 vs. 0.20 pre- and post-pathway, $P = 0.827$). The proportion of patients admitted to high dependency decreased, but not to a significant degree (2.21 vs. 1.37 pre- and post-pathway, $P = 0.200$).

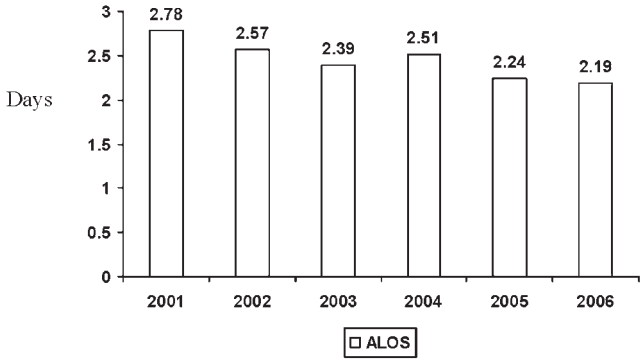

Fig. 4. Average length of stay (ALOS) before and after implementation of asthma pathway.

With the implementation of an MDI with spacer as part of the asthma pathway, the cost per patient for those managed as an inpatient was reduced from $1136.85 to $992.50. This translated to a savings of $142,906.50 per year for inpatient management.

DISCUSSION

Our results show that implementation of the standardized asthma pathway in the emergency room, using MDIs with spacer for the administration of beta-agonists instead of nebulizers, did not lead to a significant increase in the number of asthma admissions. It did, however, lead to a decrease in re-attendances for unresolved asthma. The number of admissions remained stable at about 30% of cases, a figure that includes all age groups from infants to older children. These findings support those of earlier studies, which were based on smaller cohorts, regarding the efficacy of MDI with spacer for even infants and young

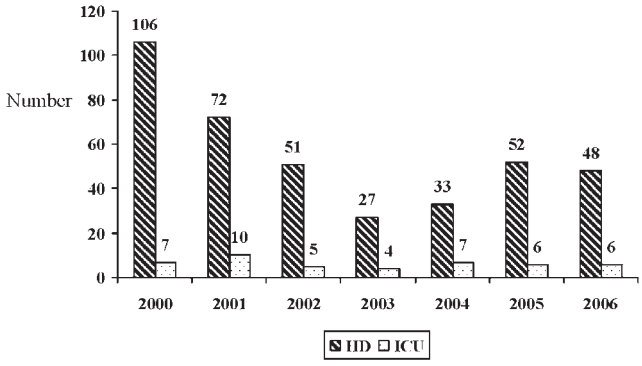

Fig. 5. Admissions to high dependency (HD) and intensive care (ICU) before and after implementation of asthma pathway.

children.[1–3] However, our results did not demonstrate a reduction in admissions as was shown by Norton et al.[10]

Patients who were admitted post-implementation had a shorter mean length of stay, 2.27 days compared to 2.68 days pre-implementation, a finding that is in agreement with the report by Dewar et al.[7] There was no increase in the proportion of severe exacerbations that required admission to the intensive care unit or to high dependency. For patients admitted to the intensive care unit, the pathway did not stipulate which mode of delivery was to be used for the administration of the beta-agonist. However, in many instances, the intensivist delivered the beta-agonist via an MDI with spacer even in intubated patients. In addition, the use of MDI with spacer necessitated educating parents on its use, which simplified the continuity of its use at home.

With regard to financial considerations, our conversion to the asthma pathway using MDIs with spacer instead of nebulizers led to a substantial cost savings to the hospital and to the patient. This finding is in agreement with those of earlier studies conducted in the United States[8] and New Zealand.[9] Such savings should be of considerable interest given the current state of rising health-care costs.

It should be mentioned that during the initial implementation of the pathway, we did note reservations by the medical staff regarding the efficacy of using MDIs with spacer compared to nebulizers. Over the first few months, a number of staff would resort to the use of nebulizers. We also had patients who requested nebulizers because they were accustomed to using the device. A good deal of perseverance was required for successful implementation. Making the change in practice required the support of the hospital administration and senior doctors to strongly affirm and be advocates for evidence-based practice. Over time, staff could see that patients who used an MDI with spacer did no worse than patients who used nebulizers, and the mindset of the staff changed. Patients also learnt over time to accept this change in practice when they came to the hospital to be treated. In fact, after completion of the study, patient compliance was found to be 100% in year 2007. These findings are in agreement with those of an earlier study in an Australian population,[29] which also found that it takes time, clinical evidence and specific strategies to successfully implement a new treatment guideline.

In conclusion, the current study demonstrated that using an MDI with spacer as part of an evidence-based asthma pathway can be used for the management of acute asthma in children in both the emergency room and inpatient settings. It is a safer and more cost-effective method for delivering inhaled beta-agonist to children with acute asthma exacerbations. The use of a holistic approach to manage this chronic illness, encompassing education and written asthma action plans, allows for the improved management of this condition in children.

What Is Already Known on This Topic

- Inhaled beta-agonists have traditionally been administered via nebulization for the treatment of acute asthma exacerbations.
- Nebulization remains the main mode of delivery for acute asthma in many countries.
- Many reviews have suggested that MDI with a spacer device may be equally effective.

What This Study Adds

- Use of a MDI in the emergency room for asthma exacerbations does not increase the proportion of children admitted to inpatient care.
- Use of a MDI does not increase the proportion of children admitted to intensive care or high dependency units for asthma exacerbations.
- Use of a MDI reduces length of inpatient stay for acute asthma exacerbations and cost per patient for those managed as an inpatient.

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