# A Randomized Trial of Single-Dose Oral Dexamethasone Versus Multidose Prednisolone for Acute Exacerbations of Asthma in Children Who Attend the Emergency Department

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**Study objective:** In acute exacerbations of asthma in children, corticosteroids reduce relapses, subsequent hospital admission, and the need for ß$_2$-agonist bronchodilators. Prednisolone is the most commonly used corticosteroid, but prolonged treatment course, vomiting, and a bitter taste may reduce patient compliance. Dexamethasone has a longer half-life and has been used safely in other acute pediatric conditions. We examine whether a single dose of oral dexamethasone is noninferior to prednisolone in the emergency department (ED) treatment of asthma exacerbations in children, as measured by the Pediatric Respiratory Assessment Measure (PRAM) at day 4.

**Methods:** We conducted a randomized, open-label, noninferiority trial comparing oral dexamethasone (single dose of 0.3 mg/kg) with prednisolone (1 mg/kg per day for 3 days) in patients aged 2 to 16 years and with a known diagnosis of asthma or at least 1 previous episode of ß$_2$-agonist–responsive wheeze who presented to a tertiary pediatric ED. The primary outcome measure was the mean PRAM score (range of 0 to 12 points) performed on day 4. Secondary outcome measures included requirement for further steroids, vomiting of study medication, hospital admission, and unscheduled return visits to a health care practitioner within 14 days.

**Results:** There were 245 enrollments involving 226 patients. There was no difference in mean PRAM scores at day 4 between the dexamethasone and prednisolone groups (0.91 versus 0.91; absolute difference 0.005; 95% CI −0.35 to 0.34). Fourteen patients vomited at least 1 dose of prednisolone compared with no patients in the dexamethasone group. Sixteen children (13.1%) in the dexamethasone group received further systemic steroids within 14 days after trial enrollment compared with 5 (4.2%) in the prednisolone group (absolute difference 8.9%; 95% CI 1.9% to 16.0%). There was no significant difference between the groups in hospital admission rates or the number of unscheduled return visits to a health care practitioner.

**Conclusion:** In children with acute exacerbations of asthma, a single dose of oral dexamethasone (0.3 mg/kg) is noninferior to a 3-day course of oral prednisolone (1 mg/kg per day) as measured by the mean PRAM score on day 4. [Ann Emerg Med. 2016;67:593-601.]

Please see page 594 for the Editor's Capsule Summary of this article.

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## INTRODUCTION

### Background

Asthma is a major cause of pediatric morbidity and mortality.[1,2] In acute exacerbations, corticosteroids reduce relapses, subsequent hospital admission, and the need for ß$_2$-agonist bronchodilator therapy.[3] The British Guideline on the Management of Asthma[4] recommends commencing oral prednisolone early for children presenting with exacerbations of asthma and, if they are discharged, continuing treatment for up to 3 days.

Prednisolone is a relatively short-acting corticosteroid with a half-life of 12 to 36 hours, thereby requiring a multiple-dose regimen.[5] A prolonged treatment course, unpleasant bitter taste, and vomiting may reduce patient compliance.[6] In one study, caregivers of children with asthma reported compliance to the prescribed course of oral corticosteroid therapy only 64% of the time.[7] In contrast, dexamethasone is a long-acting corticosteroid with a half-life of 36 to 72 hours[5] and is used safely in children with croup and bacterial meningitis.[5,8,9]

**Editor's Capsule Summary**

*What is already known on this topic*

Single-dose dexamethasone is an alternative to a short course of prednisone to treat an asthma exacerbation.

*What question this study addressed*

Is treatment of children with an acute asthma exacerbation with single-dose dexamethasone (0.3 mg/kg) inferior to prednisolone (1 mg/kg per day) as measured by the Pediatric Respiratory Assessment Measure score at day 4?

*What this study adds to our knowledge*

In this open-label trial of 245 children aged 2 to 16 years, a single dose of dexamethasone was not inferior to prednisolone.

*How this is relevant to clinical practice*

Given the potential for increased compliance, clinicians should consider a single dose of oral dexamethasone for the emergency treatment of a child with an asthma exacerbation.

There are currently 7 published randomized controlled trials and a meta-analysis comparing dexamethasone with prednisolone in the treatment of acute asthma exacerbations in children.[10-17] There are limitations to each of the trials in terms of study design, sample size, and dosing regimen, and the age of patients enrolled varied between studies. In addition, the lack of consistent and reliable outcome measures makes the results difficult to interpret.

### Importance

If effective, a single-dose corticosteroid regimen may overcome the challenges of poor compliance associated with a multiple-dose corticosteroid regimen for acute asthma exacerbation in children.

### Goals of This Investigation

We hypothesized that a single dose of oral dexamethasone was noninferior to prednisolone for 3 days in the treatment of acute exacerbations of asthma in children, as measured by the Pediatric Respiratory Assessment Measure (PRAM) at day 4.

## MATERIALS AND METHODS

### Study Design and Setting

From July 2011 to June 2012, a randomized controlled trial was conducted in the emergency department (ED) of Our Lady's Children's Hospital, Crumlin in Dublin, Ireland, a tertiary pediatric hospital with an annual ED census of 35,000.

### Selection of Participants

Eligible participants were children aged 2 to 16 years with a history of asthma who presented to the ED with an acute asthma exacerbation. A history of asthma was defined as either at least 1 previous episode of ß$_2$-agonist–responsive wheeze or a previous diagnosis of asthma, made by a pediatrician or clinician of comparable experience. An exacerbation of asthma was defined as acute asthma that prompts ED assessment, with any or all of the following clinical features: dyspnea, wheeze, acute cough, increased work of breathing, increased requirement for ß$_2$-agonist from baseline use, or $SaO_2$ less than 95%.

Children with a critical or life-threatening asthma exacerbation, active varicella or herpes simplex infection, documented concurrent infection with respiratory syncytial virus, temperature greater than 39.5°C, use of oral or intravenous corticosteroids in the previous 4 weeks, concurrent stridor, galactose intolerance, the Lapp-lactase deficiency or glucose-galactose malabsorption, a history of tuberculosis exposure, or significant comorbid disease were also excluded. A critical or life-threatening asthma exacerbation was defined (as per the Our Lady's Children's Hospital, Crumlin ED asthma guideline) as patients displaying 1 or more of the following clinical features: confused or drowsy, maximal accessory muscle use or recession, poor respiratory effort (including bradypnea), exhaustion, silent chest, cyanosis, $SaO_2$ less than 90% in air, marked tachycardia, unable to verbalize normally (ie, different from baseline verbal ability), and pneumothorax.

Before the study commenced, the research team conducted training sessions for all ED nurses and emergency physicians on good clinical practice guidelines and on all aspects of the study, including the use of the PRAM score.[18,19] After eligibility for inclusion in the study was confirmed, informed consent was obtained from the parent or legal guardian. In all cases where appropriate, informed assent was obtained from the patient.

We used a randomization design achieved by generating numeric codes in random permuted blocks of 12 subjects. The randomization process was designed by the study statistician (G.C.) and was kept in a locked storage cupboard in the hospital's pharmacy department. The recruiting clinician took the next available numbered envelope from the prerandomized pack of study envelopes contained in a locked storage cupboard in the ED. This envelope contained the subject identification number of each enrolled patient and stated to which treatment arm they were assigned.

### Interventions

This was an open-label study. Enrolled patients were randomized to receive a single dose of oral dexamethasone 0.3 mg/kg (maximum dose 12 mg) (DEX) or a 3-day

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