Official Title:	Single Dose Dexamethasone is Not Inferior to Two Doses in Mild to Moderate Pediatric Asthma Exacerbations in the Emergency Department
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Methods

We performed a single-site, prospective, parallel group, un-blinded randomized clinical trial which enrolled a convenience sample of patients aged 2-20 years with previously diagnosed asthma presenting to a single emergency department with a mild to moderate exacerbation of asthma. The hospital's institutional review board approved the study and informed consent was obtained from eligible patients' legal guardians or adult patients (18-20 years age). In addition, patients 7 to 17 years of age provided written ascent.

Study Setting and Participants:

Children aged 2 to 20 years with a known history of asthma who presented to the Emergency Department at Women and Children's Hospital of Buffalo/Oishei Children's Hospital between April 2015 and March 2018 with an acute exacerbation of mild or moderate asthma were eligible for the study. Asthma severity was defined by Pediatric Asthma Scores[2, 12] (PAS). Mild asthma is defined as: PAS of 5 to 7; Moderate asthma is defined as: PAS of 8 to 11; Severe asthma is defined as: PAS of 12 or more. History of asthma is defined by physician diagnosis of at least one prior episode of wheezing which responded to beta agonists. Patients were excluded from the study if they had signs of severe asthma exacerbation (PAS of 12 or more), had used oral steroids in the last 2 weeks, had chronic lung disease (e.g., cystic fibrosis), had been given parenteral steroids, or if they vomited two doses of oral steroids in emergency department.

Research assistants screened asthma patients through the electronic medical record between the hours of 8 a.m. and 11 p.m. 7 days a week. Patients were approached sequentially based on registration time. If a patient appeared to meet study criteria, his/her ED treating physician was approached by the research assistant for identifying patient's eligibility. If a patient was fully eligible, the legal guardian and/or patient were approached for consent.

Study Protocol:

Block randomization was used to generate a list to be used for subject assignment with a 1:1 ratio of allocation to the single dose group and the two dose group. Demographic information such as age, gender, race, duration of asthma symptoms, number of previous hospitalizations, and current medication was collected. Pertinent exam findings such as patient's vital signs, pulse oximetry, and PAS were also collected along with medications given in the ED.

Group 1 was given 0.6mg/kg (max 16mg) of dexamethasone orally in the emergency department. Group 2 was given the same dose in the emergency department, and then a prescription for a second dose was sent to their pharmacy to be filled and administered at home 24 hours later. We worked with a nearby 24-hour pharmacy to ensure medication availability; however, pharmacy preference was left up to the family. Both groups received asthma treatment following a standardized asthma care path.

All patients were contacted by phone by a research assistant on the 6th day following the emergency department visit. Research assistants were not completely blinded during the study. They were initially blinded to the study group at the start of the phone interviews; however, during the course of the

interview they did ask if the prescription for the second dose of dexamethasone was filled and if the medication was given to the patient. Information collected during the phone interview included additional visits to medical providers (ED, primary care or urgent care) for continued asthma symptoms, information was collected on the reason for visit, whether symptoms continued or worsened, and if additional treatment was needed (scheduled visits and unrelated visits were excluded). School days missed due to asthma exacerbation; length of time symptoms persisted; compliance with the recommended steroid regimen; and any vomiting, side effects or medication administration problems caused by the steroids was also collected.

Analytic Plan:

Descriptive characteristics were computed for all patients combined and separately by dexamethasone group assignment. Categorical variables were reported as proportions in percentage, and continuous level variables as means and standard deviations. Separate independent t-tests were used to assess differences by group for post-discharge outcomes of interest including days for symptoms to resolve. Separate binary logistic regression adjusting for age, gender and severity of exacerbation were conducted to assess group differences in post-discharge outcomes including patients who had a return visit for unresolved asthma symptoms (ED, primary care or urgent care), days to symptom resolution, any missed school days between discharge and follow-up, rates of vomiting, and side-effects (changes in appetite, insomnia, mood swings); odds ratios with 95% confidence intervals were reported. Similar analyses were conducted to compare events and side effects between Groups 1 and 2 by asthma severity, using an intention-to-treat approach. Based on our clinical experience, we based our a-priori sample size calculation on an estimated non-inferiority limit of 11% and a rate of 12% return for asthma for each group. With a power of 80% and alpha of 0.05, a minimum sample size of 216 (108 subjects per group) was determined. All statistical tests were two-tailed, and analyses conducted with SYSTAT 13 (SYSAT Software, 2004).