December 1, 2018

Management of Acute Exacerbation of Asthma Presenting to the Emergency Department or Urgent Care

Introduction / Background

Discharge data for pediatric patients who had presented to the emergency department had shown that patients were returning to the ED with subsequent visits without having filled the prescriptions given to them at time of discharge from the ED. Other finding showed that many who may have filled the prescriptions were not taking the full course of prednisone (5 days). There was variation in whether patients were prescribed prednisone or dexamethasone. A review of evidence was conducted to determine which corticosteroid medication was most effective and which regimen was most preferred by patients and parents and to standardize care of pediatric patients presenting to the ED and urgent cares (UCs) with acute asthma exacerbation.

Definitions for terms marked with * and Abbreviations may be found in an Abbreviations and Definitions section below.

Clinical Question

P	*(Population/Problem)*	Among pediatric outpatients (2 to 18 years old) with acute asthma exacerbation,
I	*(Intervention)*	does administering initial dose dexamethasone in the ED and dispensing the second dose at the time of ED discharge to take home for the next day
C	*(Comparison)*	compared to discharge home with a prescription for a total of 5 days of the steroid prednisone
O	*(Outcome)*	improve safety, effectiveness, and compliance?

Target Population for the Recommendation

Inclusion Criteria

Pediatric patients, ages 2 to 18 years old, presenting to the ED or UCs with acute asthma exacerbation

Exclusion Criteria

Any patient not meeting the inclusion criteria

Target Users for the Recommendations

Target users include, but are not limited to: Physicians, Advanced Practice Registered Nurses (APRNs), and other providers who care for children with acute asthma exacerbations in an ED or UC.

Evidence-Based Care Recommendations

It is strongly recommended the care provider administer the initial dose of dexamethasone in the ED or UC and provide the caregiver the second dose at time of discharge to take home with them to administer at home the following day to improve safety, effectiveness, and compliance *(Meyer, 2014 [1a]; Pardue Jones, 2016 [1b]; Redman, 2013 [1b])*.

Recommendation Strength
Strong

Note 1: Dexamethasone was equally effective and pharmacologically equivalent to prednisone/prednisolone, regarding patient outcomes (i.e. relapse rates, return ED visits, hospitalizations) *(Normansell, 2016 [1a]; Keeney, 2014 [1a]; Meyer, 2014 [1a]; Pardue Jones, 2016 [1b]; Redman, 2013 [1b]; Paniagua, 2017a [2a]; Andrews, 2012 [5a])*.

Note 2: Dexamethasone 0.6mg/kg twice was the most frequently oral dose reviewed in the literature *(Normansell, 2016 [1a]; Keeney, 2014 [1a]; Meyer, 2014 [1a]; Redman, 2013 [1b]; Paniagua, 2017b [2a])*.

Note 3: Study findings were not able to determine superiority of dosage, formulation or route of administration of dexamethasone or prednisone/prednisolone *(Normansell, 2016 [1a]; Meyer, 2014 [1a]; Pardue Jones, 2016 [1b]; Redman, 2013 [1b]; Paniagua, 2017b [2a])*.

Note 4: Dexamethasone was associated with better tolerance, compliance *(Keeney, 2014 [1a]; Meyer, 2014 [1a]; Pardue Jones, 2016 [1b]; Redman, 2013 [1b]; Paniagua, 2017b [2a]; Aljebab, 2018 [3a]; Williams, 2013 [4b])* and cost savings *(Williams, 2013 [4b]; Andrews, 2012 [5a])* by patients and caregivers.

Note 5: Study results have shown that the majority of parents preferred the use of 1 to 2 doses of oral or IM dexamethasone, compared to a 5-day course prednisone/prednisolone, for the management of acute asthma exacerbations for their child in the ED *(Meyer, 2014 [1a]; Pardue Jones, 2016 [1b]; Paniagua, 2017b [2a]; Szlam, 2015 [4a]; Williams, 2013 [4b])* and to have all medications when discharged from the ED *(Pardue Jones, 2016 [1b]; Szlam, 2015 [4a])*.

Dimensions of Judging the Recommendation Strength for Improved Safety, Effectiveness, and Compliance

1. Safety / Harm *(Side Effects and Risks)*	☒ Minimal		☐ Moderate / Neutral		☐ Serious
2. Health benefit to patient	☒ Significant		☐ Moderate / Neutral		☐ Minimal
3. Burden on population to adhere to recommendation	☒ Low		☐ Unable to determine		☐ High
4. Cost-effectiveness to healthcare system	☒ Cost-effective		☐ Inconclusive		☐ Not cost-effective
5. Directness of the evidence for this target population	☒ Directly relates		☐ Some concern of directness		☐ Indirectly relates
6. Impact on quality of life, morbidity, or mortality	☒ Positive		☐ Moderate / Neutral		☐ Negative
7. Grade of the Body of Evidence *(See Evidence Table below; *GNA – Grade Not Assignable)*	☒ High ⊕⊕⊕⊕	☐ Moderate ⊕⊕⊕◯	☐ Low ⊕⊕◯◯	☐ Very Low ⊕◯◯◯	☐ GNA*
Overall Strength of the Recommendation:	**☒ Strong**	**☐ Moderate**	**☐ Weak**	**☐ Consensus Only**	

Given the dimensions above for each recommendation and that more answers to the left of the scales indicate support for a stronger recommendation, the recommendation statements reflect the strength of each recommendation as judged by the development group.
(Note that for negative recommendations, the left/right logic may be reversed for one or more dimensions.)

Discussion/Synthesis of the Evidence and Dimensions for the Recommendation

There was a high quality body of evidence, including several systematic reviews *(Normansell, 2016 [1a]; Keeney, 2014 [1a]; Meyer, 2014 [1a]; Pardue Jones, 2016 [1b]; Redman, 2013 [1b])*, informing this clinical question. The authors of the systematic reviews reviewed many of the same studies and came to similar conclusions. Consistent findings supported dexamethasone to be just as effective and pharmacologically equivalent to prednisone/prednisolone *(Normansell, 2016 [1a]; Keeney, 2014 [1a]; Meyer, 2014 [1a]; Pardue Jones, 2016 [1b]; Redman, 2013 [1b]; Paniagua, 2017b [2a]; Andrews, 2012 [5a])*. Pooled results failed to demonstrate a statistically significant difference between the dexamethasone and the prednisone/prednisolone therapies for the outcomes of relapse rates or revisit rates to the clinic or ED, symptom improvement or rate of hospitalization. Although there were limitations in the evidence, it suggests dexamethasone and prednisolone are of equal efficacy *(Normansell, 2016 [1a]; Keeney, 2014 [1a]; Meyer, 2014 [1a]; Pardue Jones, 2016 [1b]; Redman, 2013 [1b]; Paniagua, 2017b [2a])*.

None of the studies in the systematic reviews were true equivalence studies *(Normansell, 2016 [1a]; Keeney, 2014 [1a]; Meyer, 2014 [1a]; Pardue Jones, 2016 [1b]; Redman, 2013 [1b])*. However, findings suggest dexamethasone and prednisone/prednisolone are equally effective therapies *(Normansell, 2016 [1a]; Keeney, 2014 [1a]; Meyer, 2014 [1a]; Pardue Jones, 2016 [1b]; Redman, 2013 [1b]; Paniagua, 2017b [2a])*. Numerous factors such as palatability, treatment length, volume to be taken, adverse effects, and cost contribute to the potential benefits of dexamethasone *(Normansell, 2016 [1a]; Keeney, 2014 [1a]; Meyer, 2014 [1a]; Redman, 2013 [1b]; Aljebab, 2018 [3a]; Williams, 2013 [4b]; Andrews, 2012 [5a])*. Both PO and IM dexamethasone were associated with less vomiting in the ED and at home *(Keeney, 2014 [1a]; Meyer, 2014 [1a]; Redman, 2013 [1b]; Paniagua, 2017b [2a]; Aljebab, 2018 [3a])*. Given the equal effectiveness of the medications, dexamethasone may be preferred because of similar outcomes, simple dosing strategy, better tolerance, reduced vomiting, fewer missed work/school days, convenience for patients, improved compliance and likelihood of being taken in its' entirety and cost savings *(Normansell, 2016 [1a]; Keeney, 2014 [1a]; Meyer, 2014 [1a]; Pardue Jones, 2016 [1b]; Redman, 2013 [1b]; Paniagua, 2017b [2a]; Aljebab, 2018 [3a]; Szlam, 2015 [4a]; Williams, 2013 [4b]; Andrews, 2012 [5a])*.

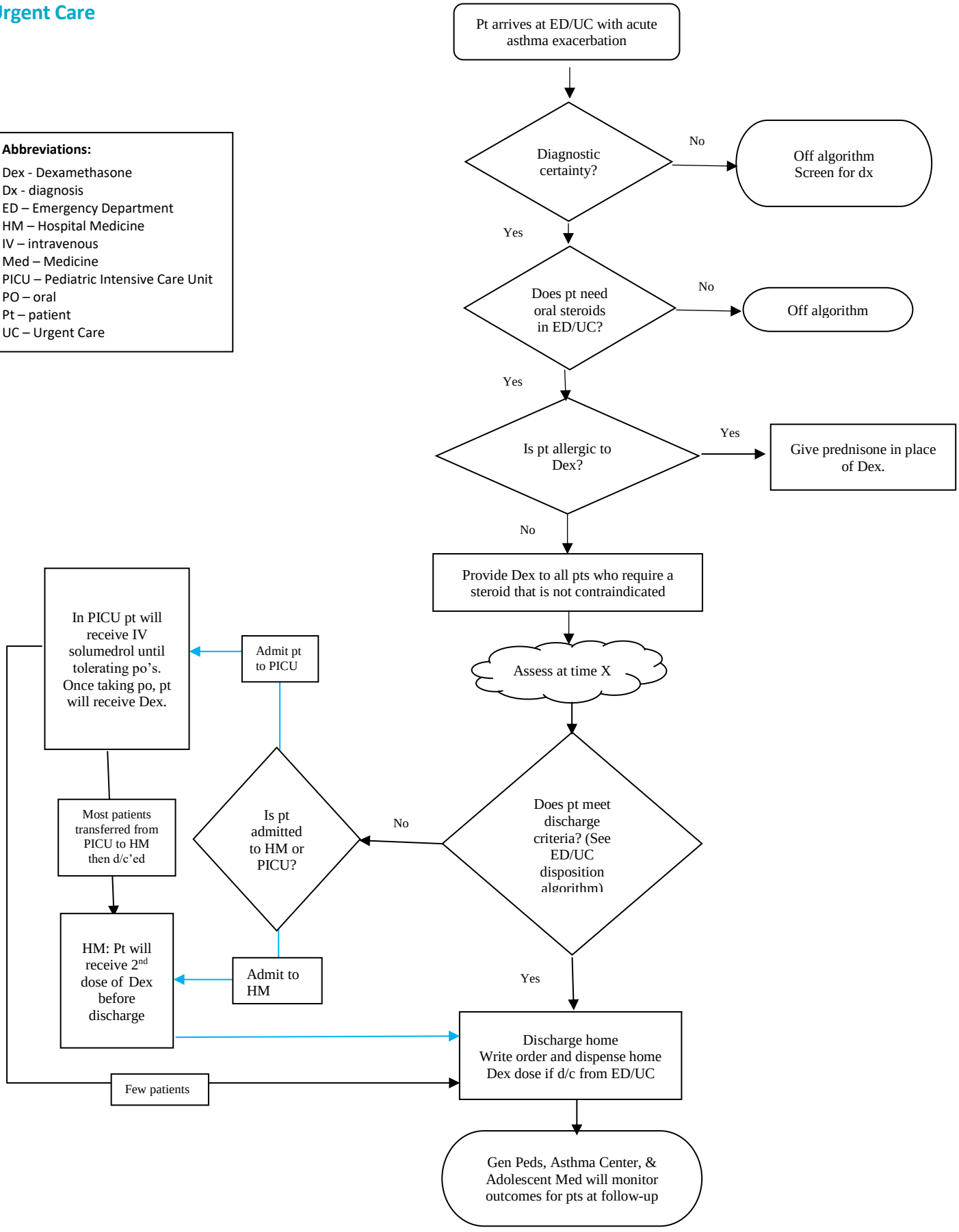
The hospitalist can dispense a second dose in the ED before discharge; thereby ensuring a high degree of compliance and obviating the need for a prescription, which studies have shown parents may fail to fill *(Meyer, 2014 [1a]; Pardue Jones, 2016 [1b]; Redman, 2013 [1b])*. Studies have found the majority of parents and caregivers preferred the use of 1 to 2 doses of an oral corticosteroid (dexamethasone) to a 5-day course (prednisone/prednisolone) for the management of

acute asthma exacerbations for their child in the ED *(Meyer, 2014 [1a]; Redman, 2013 [1b]; Paniagua, 2017b [2a]; Szlam, 2015 [4a]; Williams, 2013 [4b])*. It was reported the majority of caregivers preferred all medications when discharged from the ED even if filling the prescription(s) was made easy *(Redman, 2013 [1b]; Szlam, 2015 [4a]; Williams, 2013 [4b])*. Increased compliance was attributed to parents having received the second dose to give to the patient after discharge from the ED *(Meyer, 2014 [1a]; Pardue Jones, 2016 [1b]; Redman, 2013 [1b])*.

Algorithm for Management of Acute Exacerbation of Asthma Presenting to the Emergency Department or Urgent Care

Abbreviations:

Dex - Dexamethasone
Dx - diagnosis
ED – Emergency Department
HM – Hospital Medicine
IV – intravenous
Med – Medicine
PICU – Pediatric Intensive Care Unit
PO – oral
Pt – patient
UC – Urgent Care



Abbreviations and Definitions

Abbreviations

Emergency Department (ED)

Hospital Medicine (HM)

Advanced Practice Registered Nurses (APRNs)

General Pediatrics (Gen Peds)

Pediatric Intensive Care Unit (PICU)

Intramuscular (IM)

Intravenous (IV)

Implementation

Applicability & Feasibility Issues

Due to state law, the APRNs were not permitted to dispense and dose the medication from the ED and UCs and the hospital was unable to charge for the second dose of dexamethasone which was given in-hand. APRNs were required to work with a physician to get the medication dispensed to the patient/family and charge submitted. For prepackaging of medication supplied by pharmacy and administered at home, a standardized grouping of doses needed to be agreed upon.

Staff education needed to be developed and completed for all involved including educating community providers of the evidence and need for practice change. ED/UCs patient and family educational materials needed to be updated to ensure accurate and consistent discharge information.

Relevant CCHMC Tools

Emergency Department (ED) Acute Asthma Exacerbation Epic Order Set

Urgent Care (UC) Acute Asthma Exacerbation Order Epic Set

Knowing Notes – Growing Through Knowing – Dexamethasone for Asthma (KN-0996, 01/16)

Outcome Measures

- Process measures:
  - Number of visits for an acute asthma exacerbation where patient (≥ 2 years old) was prescribed dexamethasone in ED/UC out of all ED/UC visits seen and given any steroid.
  - Number of ED/UC visits of patients (≥ 2 years old) with acute asthma exacerbation where second dose of dexamethasone was provided to patient in hand prior to discharges out of all visits where an initial dose of dexamethasone was given in the ED/UC
- Outcome Measure:
  - Proportion of patients given dexamethasone at an initial visit for acute asthma exacerbation who returned to any CCHMC location (ED, UC, inpatient unit, outpatient clinic) and required any additional corticosteroid within 7 days of the index visit.

Consensus Process and Conclusion

Given the strength of evidence for the clinical practice change to dexamethasone, a formal consensus gathering process was not conducted for development of the care algorithm. The planned change was presented to all groups within the ED and UCs (Pediatric Emergency Medicine faculty, Clinical Staff and APRNs) at a staff meeting. Following presentation of the algorithm and evidence, questions, objections and concerns were addressed, through discussion, staff consented to the practice change. A standardized grouping of doses was agreed upon for home use, so prepackaging could be arranged.

CRITERIA FOR INCLUSION, EVIDENCE SEARCH STRATEGIES, AND SEARCH RESULTS

Criteria for considering studies for this review

Types of Studies	All study designs were considered for inclusion in this systematic review
Types of Participants	Pediatric outpatients (2 to 18 years old) with acute asthma exacerbation was the applicable patient population considered for inclusion in this systematic review
Types of Interventions	Administration of the initial dose dexamethasone in the ED and dispensing the second dose at the time of ED discharge to take home for the next day compared to administering prednisone in the ED and providing a prescription for a total of 5 days of the steroid prednisone were the intervention and comparisons considered for inclusion in this systematic review
Types of Outcomes	Improved safety, effectiveness and compliance were the outcomes considered for inclusion in this systematic review
Exclusion Criteria, *if any*	Studies addressing adult patients with asthma exacerbation were excluded from this systematic review

Search Strategy

Search Methods

To select evidence for critical appraisal by the group for this BESt, the databases below were searched using search terms, limits, filters, and date parameters to generate an unrefined, "combined evidence" database. This search strategy focused on answering the clinical questions addressed in this document and employing a combination of Boolean searching on human-indexed thesaurus terms (e.g., MeSH) as well as "natural language" searching on words in the title, abstract, and indexing terms.

Search Databases	Search Terms	Limits, Filters, & Search Date Parameters	Date of Most Recent Search
☒ MedLine via PubMed or Ovid ☒ CINAHL ☒ Cochrane Database for Systematic Reviews ☒ Embase ☒ Scopus	All combinations of the following key terms: • Dexamethasone, decadron, Dexamethasone/ or dexamethasone.mp. • Prednisone, prednisolone, prednisone.mp. or Prednisone/ corticosteroid, steroid • Peds, pediatric • Patient safety, medication safety • asthma, asthma exacerbation, asthma.mp. or Asthma/ • dosage • cost • parent perspective	Publication Dates or Search Dates: • 01/2000 to 05/2018 ☒ English Language ☒ Pediatric Evidence Only: • 2-18 years • Child [MeSH] OR Adolescent [MeSH] • "preschool child (2 to 5 years)" or "child (6 to 12 years)" or "adolescent (13 to 18 years)") ☒ Other Limits or Filters: • Humans	05/17/2018

Search Results

The citations were reduced by eliminating duplicates, review articles, non-English articles, and adult articles (e.g., limits/filters above). The resulting abstracts and full text articles were reviewed by a methodologist to eliminate low quality and irrelevant citations or articles. During the course of the BESt development, additional articles were identified from subsequent refining searches for evidence, clinical questions added to the guideline and subjected to the search process, and hand searching of reference lists. The dates of the most recent searches are provided above.

Electronic and manual searches for evidence identified a total of 496 articles.
Four hundred forty-six articles were discarded, as they were duplicates or not related to the clinical question of interest based on title and/or abstract review. Fifty articles were reviewed in full texts with thirty-nine excluded/discarded due to poor quality or not addressing the clinical question. Eleven articles met the inclusion criteria above and are included in the BESt and evidence table.

TEAM MEMBERS & CONFLICTS OF INTEREST

Group / Team Members

Multidisciplinary Team

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Conflicts of Interest were declared for each team member and:

☒ No financial or intellectual conflicts of interest were found.
☒ No external funding was received for development of this recommendation.

☐ The following conflicts of interest were disclosed:

Conflict of interest declarations information is maintained in Cincinnati Children's ePAS *(electronic Protocol Administration System)*.

FUTURE RESEARCH AGENDA

1. In children evaluated in the ED/UC for an acute asthma exacerbation that is classified as mild can the child be treated with a single dose of dexamethasone with increasing need for return to care?
2. In children evaluated in the ED/UC for an acute asthma exacerbation and treated with dexamethasone is there an optimal timing for the second dose to be given (current range 24-48 hours)?

LEGEND Evidence Evaluation System *(Let Evidence Guide Every New Decision)*

Full tables of the LEGEND evidence evaluation system are available in separate documents:

- Table of Evidence Levels of Individual Studies by Domain, Study Design, & Quality *(abbreviated table below)*
- Grading a Body of Evidence to Answer a Clinical Question
- Judging the Strength of a Recommendation

Table of Evidence Levels *(see link above for full table)*:

Quality Level	Definition
1a† or 1b†	Systematic review, meta-analysis, or meta-synthesis of multiple studies
2a or 2b	Best study design for domain
3a or 3b	Fair study design for domain
4a or 4b	Weak study design for domain
5a or 5b	General review, expert opinion, case report, consensus report, or guideline
5	Local Consensus

†a = good quality study; b = lesser quality study

Table of Grade for the Body of Evidence *(see link above for full table)*:

Grade	Definition
High	Good quality, High-level studies with consistent results
Moderate	Good quality, Lower-level OR Lesser quality, Higher-level studies with consistent* results
Low	Good or lesser quality, Lower-level with results that may be inconsistent
Very Low	Few Good or Lesser quality, Low-level studies that may have inconsistent results
Grade Not Assignable	Local Consensus

Table of Language and Definitions for Recommendation Strength *(see link above for full table)*:

Language for Strength	Definition
It is strongly recommended that… It is strongly recommended that… not…	When the dimensions for judging the strength of the evidence are applied, there is high support that benefits clearly outweigh risks and burdens. (or visa-versa for negative recommendations)
It is recommended that… It is recommended that… not…	When the dimensions for judging the strength of the evidence are applied, there is moderate support that benefits are closely balanced with risks and burdens.
It is suggested that… It is suggested that… not…	When the dimensions for judging the strength of the evidence are applied, there is weak support that benefits are closely balanced with risks and burdens.
There is insufficient evidence to make a recommendation…	

Evidence-Based Clinical Care Recommendation Development Process

The process by which these recommendation statements were developed is documented in the BESt Development Process Manual; relevant development materials are kept electronically. The recommendations contained in this BESt were formulated by a multidisciplinary working group, which performed a systematic search and critical appraisal of the literature using LEGEND *(see section above)*. The BESt has been reviewed and approved by clinical experts not involved in the development process.

Recommendations have been formulated by a consensus process directed by best evidence, patient and family preference, and clinical expertise. During formulation of these recommendations, the team members have remained cognizant of controversies and disagreements over the management of these patients. They have tried to resolve controversial issues by consensus where possible and, when not possible, to offer optional approaches to care in the form of information that includes best supporting evidence of efficacy for alternative choices.

Revision Process

The BESt will be removed from the Cincinnati Children's website, if content has not been revised within five years from the most recent publication date. A revision of the BESt may be initiated at any point within a five year period that evidence indicates a critical change is needed. Team members reconvene to explore the continued validity and need of the BESt.

Review History

Date	Event	Outcome
12/1/18	**Original Publication**	New BESt/Care Algorithm developed and published

Permission to Use the BESt

This Best Evidence Statement *(BESt)* and any related implementation tools *(if applicable, e.g., screening tools, algorithms, etc.)* are available online and may be distributed by any organization for the global purpose of improving child health outcomes. Website address: http://www.cincinnatichildrens.org/service/j/anderson-center/evidence-based-care/recommendations/default/

Examples of approved uses of the BESt include the following:

- copies may be provided to anyone involved in the organization's *(outside of Cincinnati Children's)* process for developing and implementing evidence-based care guidelines;
- hyperlinks to the Cincinnati Children's website may be placed on the organization's website;
- the BESt may be adopted or adapted for use within the organization, provided that Cincinnati Children's receives appropriate attribution on all written or electronic documents; and
- copies may be provided to patients and the clinicians who manage their care.

Notification to Cincinnati Children's (EBDMInfo@cchmc.org) is appreciated for all uses of any BESt or its companion documents which are adopted, adapted, implemented, or hyperlinked.

Please cite as

Murtagh-Kurowski, E. et al, (2018). Cincinnati Children's Hospital Medical Center: Best Evidence Statement: Management of Acute Exacerbation of Asthma Presenting to the Emergency Department or Urgent Care http://www.cincinnatichildrens.org/service/j/anderson-center/evidence-based-care/recommendations/default/, BESt 213, pages 1-15, 12/1/18.

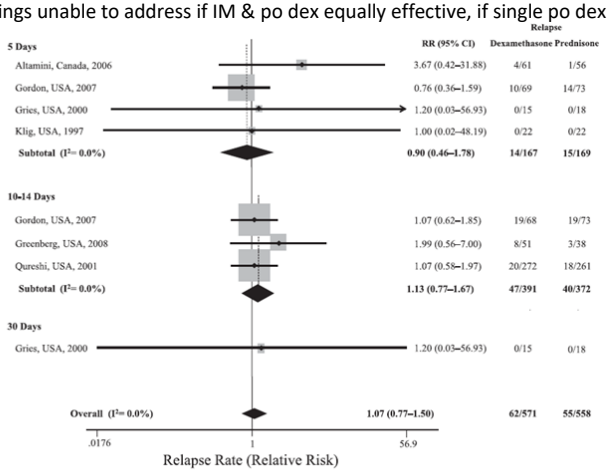
For more information

About this BESt, its companion documents, or the Cincinnati Children's Evidence-Based Care Recommendation Development process, contact The James M. Anderson Center for Health Systems Excellence at Cincinnati Children's Hospital Medical Center at EBDMinfo@cchmc.org.

Note / Disclaimer

This Best Evidence Statement addresses only key points of care for the target population; it is not intended to be a comprehensive practice guideline. These recommendations result from review of literature and practices current at the time of their formulations. This BESt does not preclude using care modalities proven efficacious in studies published subsequent to the current revision of this document. This document is not intended to impose standards of care preventing selective variances from the recommendations to meet the specific and unique requirements of individual patients. Adherence to this BESt is voluntary. The clinician in light of the individual circumstances presented by the patient must make the ultimate judgment regarding any specific care recommendation.

Evidence Table for Included Articles *(i.e., articles meeting inclusion criteria; Dimension 1 for each outcome)*

ED Dexamethasone for Asthma Exacerbation						
Study Citation	**Study Type**	**N** Sample Size	**Population** (Setting, Patients)	**Intervention / Comparison Groups**	**Outcomes**	**Evidence Level**
	Significant Results and Conclusions Including estimates with associated precision *(e.g., Odds Ratios or NNT with Confidence Intervals) as well as* Limitations / Risk of Bias, Gaps, Applicability, Consistency, or other Notes					
Normansell, 2016	Systematic Review	18 studies 2438 total participants (both adults & children)	Parallel RCTs, irrespective of blinding or duration, that evaluated dose or duration of oral steroid vs any other dose or duration, for management of asthma exacerbations in adults & children. Evidence is current to April 2016	To assess the efficacy & safety of any dose or duration of oral steroids vs any other dose or duration of oral steroids for adults and children with an asthma exacerbation, investigators analyzed adults & children data separately	• hospital admission • serious adverse events	**1a**
	• Evidence is not strong enough to reveal whether shorter or lower-dose regimens are generally less effective than longer or higher-dose regimens, or if the latter are associated with more adverse events. Events were too infrequent to permit conclusions about the superiority of one treatment over the other, or their equivalence • Any changes recommended for current practice should be supported by data from larger, well-designed trials. • Varied study design and outcome measures limited the number of meta-analyses that we could perform. • Greater emphasis on palatability and on whether some regimens might be easier to adhere to than others could better inform clinical decisions for individual patients • No convincing evidence of differences in outcomes between a higher dose or longer course and a lower dose or shorter course of prednisolone or dexamethasone, or between prednisolone and dexamethasone					
Keeney, 2014	Systematic Review/Meta-analysis	6 studies	RCTs regarding acute asthma exacerbation treatment in either an ambulatory or ED setting comparing dexamethasone with prednisone or prednisolone in pts ≤18 yrs old; databases searched thru Oct. 19, 2013	Systematic review & meta-analysis of RCTs to determine if PO or IM dexamethasone is equivalent or superior to 5-day course of oral prednisone/prednisolone; Dex. given as single IM dose in 3 studies, single po dose in 1 study, & multiple oral doses in 2 studies	• unscheduled return visits (clinic visit, ED visit, hospital admission) for acute exacerbation • vomiting in the ED • vomiting at home	**1a**
	• Pooled results did not demonstrate statistically significant difference between therapies for relapse rate to clinic, ED, or hospitalization, suggesting the 2 therapies are equivalent. • Dex patients experienced less ED and home vomiting • Findings unable to address if IM & po dex equally effective, if single po dex dose equivalent to multiple doses, or differences in efficacy & palatability between po predinsones forms.  FIGURE 2 Relapse rates.					

Meyer, 2014	Systematic Review Meta-analysis	6 studies	Studies comparing efficacy of PO or IM dexamethasone vs prednisone/ prednisolone in pediatric asthma exacerbations treatment	Evaluate evidence comparing efficacy of dexamethasone with prednisone in the treatment of pediatric asthma exacerbations	• Return to baseline activity • Asthma scores • Relapse	**1a**

- None of the pediatric clinical trials found any differences comparing dexamethasone & prednisone in treating mild - moderate asthma exacerbations
- Meta-analysis demonstrated no difference in unscheduled physician revisits & symptomatic return to baseline after ED discharge
- Factors such as palatability, dosage frequency, length treatment course, adverse effects, & cost contribute to potential dex benefit with dex being equally effective
- Hospitalist can dispense 2nd dose at d/c from hospital thereby ensuring high degree of compliance, obviating need for prescription that 33- 65% of ped pts fail to have filled
- Qureshi, 2001 – more pts in prednisone group were noncompliant compared to dexamethasone group (4% vs 0.4%; *P* =.004); dexamethasone group received a dispensed 2nd dose whereas prednisone group had to fill a prescription
- Greenburg, 2008 – all patients given medications in prepared blister packs before discharge from the ED –no significant difference in relapse rates between dexamethasone & prednisone groups (16% vs 8%, respectively; *P* = 0.27); dexamethasone group had a slightly higher mean pediatric asthma score at presentation compared to prednisone group (8 vs ; *P* =.003), potentially explaining higher relapse rate, not statistically significant, in dexamethasone group
- Growing evidence suggests shorter course of dexamethasone is as efficacious as prednisone in treatment of mild to moderate asthma exacerbations in children presenting to the ED
- Studies have shown parents prefer a shorter course of corticosteroids13 even if it requires IM injections, this option is usually reserved for children who cannot take po formulations or for whom IV access cannot be acquired
- Each study of po dexamethasone used 0.6 mg/kg per dose, and all but 1 study investigated 2 daily doses; None of the studies were true equivalence studies

Author	Follow-up (days)	Dexamethasone Revisits (%)	Prednisone Revisits (%)	Risk Difference (95% CI)	Weight (%)
Altamimi et al[32]	5	4/61 (6.6)	1/56 (1.8)	0.05 (–0.02 to 0.12)	19
Gordon et al[25]	14	15/68 (22.1)	16/73 (21.9)	0.00 (–0.14 to 0.14)	5.1
Greenberg et al[33]	10	8/51 (15.7)	3/38 (7.9)	0.08 (–0.05 to 0.21)	5.6
Gries et al[27]	28	0/15 (0)	0/17 (0)	0.00 (–0.11 to 0.11)	7.4
Klig et al[26]	5	0/21 (0)	0/21 (0)	0.00 (–0.09 to 0.09)	12.4
Qureshi et al[31]	10	20/272 (7.4)	18/261 (6.9)	0.00 (–0.04 to 0.05)	50.5
Overall effect (P = 0.32)				***0.02 (–0.02 to 0.05)***	

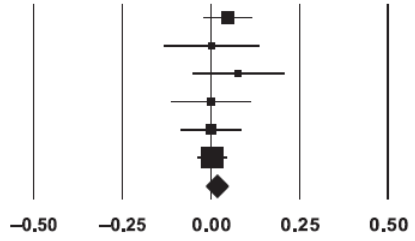


FIGURE 1 Comparison of studies reporting unscheduled physician visits between the dexamethasone and prednisone groups.

Author	Follow-up (days)	Dexamethasone Improved (%)	Prednisone Improved (%)	Risk Difference (95% CI)	Weight (%)
Altamimi et al[32]	5	40/56 (71.4)	41/54 (75.9)	0.79 (0.34 to 1.86)	14
Gordon et al[25]	4	40/66 (60.6)	39/68 (57.4)	1.14 (0.57 to 2.28)	21.5
Gries et al[27]	5	11/15 (73.3)	11/17 (64.7)	1.50 (0.33 to 6.83)	4.5
Qureshi et al[31]	10	212/272 (77.9)	206/261 (78.9)	0.94 (0.62 to 1.43)	60
Overall effect (P = .90)				***0.98 (0.71 to 1.35)***	

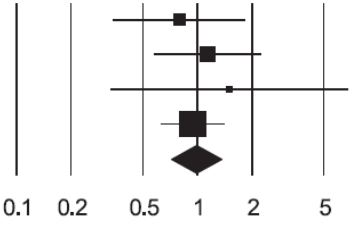


FIGURE 2 Comparison of studies reporting symptomatic return to baseline between the dexamethasone and prednisone groups.

Pardue Jones, 2016	Systematic Review	NA	pediatric patients presenting with mild moderate-severity or severe exacerbation	Review available modalities to assess & manage exacerbations by clinicians caring for pedi pts, including some treatments beyond NAEPP guidelines; review NAEPP-recommended txts to provide full range of treatments available	• Improved symptoms	**1b**
	• Current guidelines recommend treatment of moderate to severe asthma exacerbations with oral prednisone or dexamethasone. Oral prednisone/prednisolone (1–2 mg/kg/day) taken for a 3–5 day course or dexamethasone (0.3–0.6 mg/kg) given in either a one or two-dose regimen. • Evidence supports the use of dexamethasone in preference to prednisone or prednisolone in the treatment of acute asthma exacerbations • No increased risk of relapse for children receiving dexamethasone compared to prednisone/prednisolone; Other studies suggest use of 2-day dexamethasone therapy to be superior to 5-day prednisone/prednisolone in cost-effectiveness, patient compliance & palatability; • Caregiver preference of dexamethasone administration over prednisolone because it eliminates the need for filling a prescription to simplify the home treatment regimen					
Redman, 2013	Systematic Review	6 studies	RCTs comparing efficacy of prednisolone & dexamethasone for pediatric asthma exacerbations	Answer question: in children with acute asthma exacerbation requiring steroids, does dexamethasone have similar efficacy to prednisolone in achieving decreased airway inflammation, decreased admission rates & LOS	• Admission • LOS • Airway inflammation	**1b**
	• All six studies supported dexamethasone to be just as effective as prednisolone; Limited evidence suggests dexamethasone and prednisolone are of equal efficacy (Grade B). • Research supports the use of corticosteroids in the management of acute asthma exacerbations (Grade A). • Dexamethasone is a long-acting corticosteroid and can be used as an oral or intramuscular alternative to prednisolone (Grade B). • Most important factors in selecting a steroid for a young child is whether the drug will be easily swallowed and retained – High non-compliance with prednisolone (4% vs 0.4% for dex) (41% of prednisolone takers refused more than 30% of the doses) – In terms of retaining steroids, vomiting is noted as a common side effect of prednisolone; dexamethasone can be used as an antiemetic & better retained Qureshi, 2001 – 2nd dex dose dispensed directly to parents, prednisone grp parents had to fill prescription for remaining pred doses (prednisolone pts/parents were non-compliant (4% vs 0.4%; p=0.004); no significant difference between: relapse rates (7.4% vs 6.9%) hospitalization rates (11% vs 12%), symptom persistence at 10 days (22% vs 21%) Greenburg, 2008 – all patients given medications in prepared blister packs before discharge from the ED –no significant difference in relapse rates between dexamethasone & prednisone groups (16% vs 8%, respectively; P = 0.27);					
Paniagua, 2017	RCT	557 294 vs 296	Patients aged 1-14 years who presented to the ED with acute asthma	Determine if 2 doses of dexamethasone are as effective as 5 days of prednisolone/prednisone to improve symptoms & QoL in children with asthma exacerbations admitted to the ED Measured at 7 & 14 days via phone interviews	• Improved symptoms • Quality of Life • Unscheduled returns • Admissions, • Adherence, • Vomiting	**2a**
	• At day 7, experimental & conventional groups did not show differences related to persistence of symptoms (56.6%, 95% CI 50.6-62.6 vs 58.3%, 95% CI 52.3-64.2, respectively), QoL (80.0 vs 77.7, not significant [ns]), Admission rate (23.9% vs 21.7%, ns), Unscheduled ED return visits (4.6% vs 3.3%, ns), Vomiting (2.1% vs 4.4%, ns). • Adherence was greater in the dexamethasone group (99.3% vs 96.0%, *P* < .05) • A high percentage of parents in the 2 groups expressed a preference for the 2-day treatment (93.8% vs 94.7%) • 2 doses of dex may be effective alternative to 5-day course prednisone/prednisolone for asthma exacerbation, as measured by persistence of symptoms & quality of life at day 7					
Aljebab, 2018	Prospective Cohort Observational	255	Children (2–16 years) suffering from asthma or croup treated in the children's emergency department (ED) of 2 hospitals Gurayat General Hospital (GGH) in Saudi Arabia (SA) & Derbyshire Children's Hospital in the UK (2–18 years). Conducted for 3 months, February to April 2015 in GGH. Only children ≤12 yrs old in SA because ped admits are limited to these. In the UK in the children's accident & emergency (A&E) dept & hospital wards for 3 months September to December, 2015	Short-course oral corticosteroids routinely used to treat acute asthma & croup were evaluated & compared for tolerability & palatability in Saudi Arabian (SA) & UK children In SA, prednisolone base 5 mg tablets, prednisolone sodium phosphate 15 mg/5 mL syrup & dexamethasone 0.5 mg/5 mL elixir. In UK, pts treated with prednisolone base 5 mg tablets, prednisolone sodium phosphate 5 mg soluble tablets & dexamethasone sodium phosphate 2 mg/5 mL solution	• Palatability • Tolerability	**3a**

	• In SA, 122 pts (2–10 yrs), 52 prednisolone base tablets, 37 prednisolone sodium phosphate syrup & 33 dexamethasone elixir. • In the UK, 133 pts (2–16 yrs), 38 prednisolone base tablets (mainly crushed/dispersed), 42 prednisolone sodium phosphate soluble tablets & 53 dex sodium phosphate oral solution. • In both countries, dex had the highest palatability scores (SA mean: 1.97; UK mean: 3) & prednisolone base tablets had the lowest (SA mean: 1.12; UK mean: 1.39). Prednisolone base tablets were rated least palatable & least well tolerated, but palatability scores improved for all formulations of pred with each subsequent dose. • In SA prednisolone base tablets were associated with more nausea (24vs7 pts, p=0.008) & vomiting (5vs0 pts, p=0.073) than sodium phosphate syrup. • In the UK, vomiting occurred more frequently with prednisolone base (8 pts) than sodium phosphate soluble tablets (2 pts) (p=0.041). • In both centers, Dex sodium phosphate solution was the most palatable preparation & associated with less side effects: vomiting (1vs0 pts), nausea (7vs3 pts); abdominal pain (10vs8 pts) occurred more with dex sodium phosphate solution than dexamethasone elixir.					
Szlam, 2015	Cross-sectional	100	Caretakers of pedi pts between ages 2 yrs & 18 yrs with an acute asthma exacerbation treated in a tertiary pedi hospital ED (PED) with oral steroids & inhaled β-agonists	Evaluate parental, provider, caregiver preferences in use of single dose oral DEX vs prednisolone Pts treated with either single dose DEX or prednisolone 5-day course	• Parental Preference	**4a**
	• 79 (79%) caretakers reported preferential use of dex vs course of prednisolone • No adjusted association of dex preference to age, race, ethnicity, insurance, care giver education level, hx of asthma exacerbation, hx asthma in sibling or parent, or reported ease of filling the prescription • There was an association of dex preference in caregivers whose pts had a prior PICU admission - caregivers had a lower preference (not statistically significant) for dex vs prednisolone (odds ratio = 0.27; 95% confidence interval = 0.07-0.98) • Study findings indicate the majority of caregivers prefer: – use of single-dose dex in tx of an acute asthma exacerbation – to have all medications at d/c from PED despite reporting ease of filling a prescription (45%)					
Williams, 2013	Cross-sectional Survey study	100	Parents of ED asthmatic pts, 1 - 17 yrs old, with previous use of systemic steroids for an asthma exacerbation at Medical University of South Carolina's Pediatric ED from August 2011 to April 2012.	Determine if parents have a preference between short & long courses of oral corticosteroids for management of acute asthma exacerbations Survey questions aimed to characterize each pt's asthma severity, assess parental preference in steroid dosing (i.e. 1-2 days vs 5 days), determine parental preference for inhaled medication delivery options, evaluate controller compliance & medication costs	• Parental preference	**4b**
	• No statistically significant association between: – child's age & parental preference for duration of systemic steroid use during next asthma exacerbation (P = .22) – hospital admission & parental preference for duration of systemic steroid for child's next asthma exacerbation (P = .43) – whether parents pay for their child's asthma medications & cost of each medication (P = .27 and .38, respectively) • 95% of parents surveyed were interested in trying a short course of oral corticosteroids for a further asthma exacerbation • 88% preferred 1 to 2 doses to a 5-day regimen steroid course for their child's next asthma exacerbation • The majority of our parents prefer for their child use of 1-2 days of an oral corticosteroid to 5-day course in management of acute asthma exacerbations in the ED • Given comparable efficacy, potential cost savings, & parental preference for shorter course of steroids, dexamethasone may be attractive alternative to oral prednisone/prednisolone, with fewer barriers. • ED physicians may want to consider asking parents about their preference regarding systemic steroid to be used in their child's treatment plan in order to best improve compliance					
Andrews, 2012	Decision Analysis	100	Pediatric asthma patients: 5 days of oral prednisone and 2 days of oral dexamethasone	Evaluate cost-effectiveness of dexamethasone vs prednisone for pediatric asthma exacerbations in ED, either prescription for 2nd dose or 2nd dose dispensed at ED discharge, using estimates from published studies rates of prescription filling, compliance, steroid efficacy, comparing 2 arms	Projected rates of ED relapse visits, hospitalizations within 7 to 10 days of the sentinel ED visit, direct costs, and indirect costs	**5a**

Decision/Cost-effectiveness Analysis Results* for Both Systemic Steroid Delivery Systems Applied to Cohort of Pediatric Asthma Patients Treated in the ED for Acute Exacerbation

	ED Relapse Visits/100 Patients	Hospital Admissions/ 100 Patients	Direct Cost/ 100 Patients	Direct + Indirect Cost/ 100 Patients
Dexamethasone × 2 doses (prescription given for 2nd dose)	10	2.4	$17,200	$18,500
Dexamethasone × 2 doses (second dose dispensed in ED)	8	1.9	$13,900	$15,000
Prednisone/prednisolone × 5 doses	12	2.8	$20,500	$22,000

*Data assume 7- to 10-day follow-up period and do not include sentinel ED visit cost. Medication costs represent the average across children ages 2, 8, and 18 years. Results are presented in 2010 dollars.

- Decision analysis model illustrates use of 2 days of dexamethasone instead of 5 days of prednisone at the time of ED visit for asthma may lead to a decreased number of ED visits and hospital admissions within 7 to 10 days of the sentinel ED visit and provides cost savings.

REFERENCES

Evidence Level in [ ], Table of Evidence Levels above

Keeney, GE; Gray, MP; Morrison, AK et al.: Dexamethasone for acute asthma exacerbations in children: a meta-analysis. Pediatrics, 133(3): 493-9, 2014, [1a].

Meyer, JS; Riese, J; and Biondi, E: Is dexamethasone an effective alternative to oral prednisone in the treatment of pediatric asthma exacerbations? Hospital Pediatrics, 4(3): 172-80, 2014, [1a].

Normansell, R; Kew, KM; and Mansour, G: Different oral corticosteroid regimens for acute asthma. Cochrane Database of Systematic Reviews, (5): Cd011801, 2016, [1a].

Redman, E, and Powell, C: Question 1: Prednisolone or dexamethasone for acute exacerbations of asthma: do they have similar efficacy in the management of exacerbations of childhood asthma? Archives of Disease in Childhood, 98(11): 916-9, 2013, [1b].

Pardue Jones, B; Fleming, GM; Otillio, JK; Asokan, I; and Arnold, DH: Pediatric acute asthma exacerbations: Evaluation and management from emergency department to intensive care unit. Journal of Asthma, 53(6): 607-17, 2016, [1b].

Paniagua, N; Lopez, R; Munoz, N et al.: Randomized Trial of Dexamethasone Versus Prednisone for Children with Acute Asthma Exacerbations. Journal of Pediatrics, 191: 190-196.e1, 2017a, [2a].

Paniagua, N; Lopez, R; Muñoz, N et al.: Randomized Trial of Dexamethasone Versus Prednisone for Children with Acute Asthma Exacerbations. Journal of Pediatrics, 191: 190-190, 2017b, [2a].

Aljebab, F; Alanazi, M; Choonara, I; and Conroy, S: Observational study on the palatability and tolerability of oral prednisolone and oral dexamethasone in children in Saudi Arabia and the UK. Archives of Disease in Childhood, 103(1): 83-88, 2018, [3a].

Szlam, S, and Arnold, DH: Identifying parental preferences for corticosteroid and inhaled beta-agonist delivery mode in children with acute asthma exacerbations. Clinical Pediatrics, 54(1): 15-8, 2015, [4a].

Williams, KW; Andrews, AL; Heine, D; Russell, WS; and Titus, MO: Parental preference for short- versus long-course corticosteroid therapy in children with asthma presenting to the pediatric emergency department. Clinical Pediatrics, 52(1): 30-34, 2013, [4b].

Andrews, AL; Wong, KA; Heine, D; and Scott Russell, W: A cost-effectiveness analysis of dexamethasone versus prednisone in pediatric acute asthma exacerbations. Academic Emergency Medicine, 19(8): 943-8, 2012, [5a].