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Asthma Exacerbation CPG - Dexamethasone vs. prednisolone dosing for acute asthma exacerbation in children

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Office of Evidence Based Practice (EBP) – Critically Appraised Topic (CAT): Dexamethasone vs. prednisolone dosing for acute asthma exacerbation in children

Specific Care Question

In a child greater than 2 years old with an acute asthma exacerbation, are 1-2 doses of dexamethasone (intervention) as effective as a 5-day course of prednisolone (comparator) in prevention of symptom recurrence?

Recommendations from the Asthma CPG Committee and Based on Current Literature

While the Asthma Clinical Practice Guideline (CPG) Committee recommends use of systemic steroid in non-intensive care settings at Children's Mercy, the committee is unable to recommend for or against the use of a one-to-two-day course of dexamethasone (intervention) in comparison to prednisolone (comparator), based on the GRADE Evidence to Decision instrument[a] found in the Summary of Findings Table (see Table 1)[a]. The overall certainty in the evidence is low to very low[a]. Two systematic reviews and five single studies support use of dexamethasone and prednisolone in treatment of acute asthma exacerbations and both systemic steroids are effective in prevention of symptom recurrence.

The Asthma CPG Committee discussed additional considerations using the GRADE Evidence to Decision instrument[a] found in the Appendix. The CPG Committee through consensus agreed on a conditional recommendation for dexamethasone as the systemic steroid of choice in non-intensive care settings at Children's Mercy based on feasibility, value, and compliance for all stakeholders (see Appendix).

Literature Summary

Background

Acute asthma exacerbations are a leading cause for patients seeking emergent medical care at acute care centers and, although most patients are discharged within the same day, relapse of symptoms is still common requiring additional medical care and return to an acute care center (Elkharwili et al., 2020; Hemani et al., 2021; Kirkland et al., 2018). Systemic corticosteroids are a primary part of the treatment regimen for moderate to severe asthma exacerbations with dexamethasone and prednisolone most often prescribed (Fuhlbrigge et al., 2012; Normansell et al., 2016; Paniaqua et al., 2017). In spite of the proven efficacy of dexamethasone and prednisolone, these steroids, along with others, require the balance of benefits against the potential adverse events such as nausea, vomiting, or gastrointestinal distress (Normansell et al., 2016; Watnick et al., 2016). Evidence is limited to which medications and dosing provide maximum recovery from acute exacerbations in children, specifically to decrease relapse in symptoms. This review will summarize identified literature to answer the specific care question.

Study Characteristics

The search for suitable studies was completed on September 8, 2021. Amanda Nedved, MD, Erin Scott, DO, and Claire Seguin, MD reviewed the 42 titles and/or abstracts found in the search and identified[b] five systematic reviews and six single studies believed to answer the question. After an in-depth review of the identified systematic reviews[a] and single studies[a], two systematic reviews and five single studies answered the question.

Race/Ethnicity Race and ethnicity as defined by the individual authors were reviewed in the literature. Of the three studies that reported on race and ethnicity, 50-70% of participants were either black or Hispanic.

Are one to two doses of dexamethasone as effective as a five-day course of prednisolone in prevention of symptom recurrence?

Elkhharwili et al. (2020) recruited 60 patients aged 2-11 years and randomized into three groups. For purposes of this review, only group 1: single dose of 0.3 mg/kg dexamethasone and group 3: five days of 1.5 mg/kg/day prednisolone were compared for relapse rate of symptoms over five days.

Hermani et al. (2021) completed a retrospective review of 1,410 patients aged 3-21 years of age. The authors measured relapse of symptoms based on two interventions: receipt of dexamethasone or prednisolone prior to presentation to the emergency department (ED) and receipt of dexamethasone or prednisolone after ED presentation. All four groups received oral dexamethasone (0.5 mg/kg/day for a median of 1 day) or prednisolone (average dose of 1.8 mg/kg/day for median of 2 days) after arrival to the hospital.

Kirkland et al. (2018), a systematic review, reported on both adult and pediatric studies to analyze the optimal delivery method (oral or intramuscular) of dexamethasone compared to oral prednisolone. Only the pediatric studies are included in this review (Al-Wahadneh et al., 2006; Gordon et al., 2007; Gries et al., 2000; Klig et al., 1997). The primary outcome of relapse of symptoms was defined by the authors as any unscheduled visit to a health practitioner for worsening asthma symptoms or requiring subsequent treatment with corticosteroids. Reported relapse data within 10 days of discharge from the ED were reported.

Normansell et al. (2016), a systematic review, reviewed both adult and pediatric studies to analyze higher dose/longer course versus lower dose/shorter course for the outcome of re-admission during the follow-up period. Only the pediatric studies are included in this review (Altamimi et al., 2006; Cronin et al., 2015; Greenberg et al., 2008; Qureshi et al., 2001). The pediatric studies compared a single dose (0.6 mg/kg) of dexamethasone to a five-day dosing of prednisolone (2mg/kg). Relapse of symptoms, up to 15 days post discharge from the ED, was used as the parameters for follow up.

Paniagua et al. (2017) analyzed data on 557 randomized patients aged 1-14 years comparing the impact of two doses of dexamethasone to five days of prednisolone for relapse of symptoms defined as a return visit to the ED.

Volk et al. (2019) completed a retrospective review of a two-day course of dexamethasone to a five-day course of prednisolone on symptom recurrence within one week of initial visit to a hospital emergency department.

Watnick et al. (2016) analyzed the impact of a single dose of dexamethasone to a three-to-five-day course of prednisolone on relapse of symptoms in patients presenting to an area emergency room aged 3-17 years. Those that returned within 72 hours of discharge from the emergency room were counted as having a relapse but were only counted for their initial return.

Summary by Outcome

Relapse of Symptoms with 1 Day of Dexamethasone vs. 3-5 Days of Prednisolone.
Four studies (Elkharwili et al., 2020; Kirkland et al., 2018; Normansell et al., 2016; Watnick et al., 2016 measured the relapse in symptoms of an asthma exacerbation within 14 days following initial presentation, (n = 9,424). Based on the pediatric studies (n = 615) identified in the two systematic reviews (Kirkland et al, 2018; Normansell et al., 2016), the *OR* = 0.74, 95% CI [0.32, 1.69], p = .47 indicated the intervention of one day dosing of dexamethasone was not different to the comparator of three to five days dosing of prednisolone (see Figure 2 & *Table 1*). For the RCT study (Elkharwili et al., 2020), (n = 8,769), the *OR* = 0.63, 95% CI [.40, 1.01], p = .05 indicated the intervention of one day dosing of dexamethasone was not different to the three to five days dosing of prednisolone (see Figure 3 & *Table 1*). The cohort study (Watnick et al., 2016), (n = 40), *MD* = 3.00, 95% CI [-14.67, 20.67], p = .74 indicated the intervention of one day dosing of dexamethasone was not different to the comparator of three to five days dosing of prednisolone (see Figure 4 & *Table 1*).

Certainty Of The Evidence For Relapse of Symptoms with 1 Day of Dexamethasone vs. 3-5 Days of Prednisolone. The certainty of the body of evidence was low to very low. The body of evidence for the two systematic reviews (Kirkland et al., 2018; Normansell et al., 2016) was assessed to have serious risk of bias as demonstrated by lack of blinding of study participants and study personnel and serious imprecision due to low number of events (n = 35). The body of evidence for the RCT (Elkharwili et al., 2020) was found to have serious risk of bias as demonstrated by data analysis completed per protocol and very serious imprecision as demonstrated by a low number of subjects (n = 40). The one retrospective cohort study (Watnick et al, 2016) was assessed to have very serious imprecision as demonstrated by low number of events (n = 164).

Relapse of Symptoms with 2 Days of Dexamethasone vs. 5-6 Days of Prednisolone.
Three studies (Normansell et al., 2016; Paniagua et al., 2017; Volk et al., 2019) measured the relapse in symptoms of an asthma exacerbation within 14 days of the initial exacerbation, (*n* = 1,342). For the one systematic review (Normansell et al., 2016), using two of the pediatric studies (Greenberg et al., 2008; Qureshi et al., 2001) and the single RCT (Paniagua et al., 2017) met the criteria for review, (*n* = 1,279), the *OR* = 1.65, 95% CI [.85, 3.19], *p* = .14, indicated the intervention of two day dosing of dexamethasone was not different to the comparator of five to six day dosing of prednisolone (see Figure 5 & *Table 2*). The one cohort study (Volk et al., 2019), (*n* = 63), the *OR* = .33, 95% CI [.02, 7.13], *p* = .48, indicated the intervention of two-day dosing of dexamethasone was not different to five-to-six-day dosing of prednisolone (see Figure 6 & *Table 2*).

Certainty Of The Evidence For Relapse of Symptoms with *2 Days of Dexamethasone vs. 5-6 Days of Prednisolone.* The certainty of the body of evidence was low for the one systematic review and one RCT but very low for the observational study. The body of evidence for the systematic review (Normansell et al., 2016) and the RCT (Paniagua et al., 2017), was assessed to have serious risk of bias due to study participants and study personnel not blinded causing concern for performance bias. The observational study (Volk et al., 2019) was assessed to have very serious imprecision due to small number of events and subjects.

Relapse of Symptoms with 2 Doses of Dexamethasone vs. 5 Days of Prednisolone initiated after hospital arrival.
One study (Hermani et al., 2021) measured the relapse in symptoms of an asthma exacerbation within 10 days of the initial exacerbation, (*n*= 961). For the outcome of relapse of symptoms, the *OR* = 6.20, 95% CI [0.37, 103.50], *p* = .20 indicated the intervention of two days of dexamethasone was not different compared to five days of prednisolone initiated after hospital arrival (see *Table 3*).

Certainty Of The Evidence For Relapse of Symptoms with 2 Doses of Dexamethasone vs. 5 days of Prednisolone initiated after hospital arrival. The certainty of the body of evidence was very low. The body of evidence for the one observational study (Hermani et al., 2021) was assessed to have serious imprecision due to a low number of events and subjects. As only one study (Hermani et al., 2021) was identified to answer this question inconsistency could not be assessed.

Relapse of Symptoms with 1-3 doses of Dexamethasone vs. 1-3 doses of Prednisolone before hospital arrival.
One study (Hermani et al., 2021) measured the relapse in symptoms of an asthma exacerbation within 10 days of the initial exacerbation, (*n* = 449). For the outcome of relapse of symptoms, the *OR* = .76 95% CI [.14, 3.94], *p* = .74 indicated the intervention of one to three doses of dexamethasone was not different than one to three doses of prednisolone provided prior to hospital arrival in decreasing relapse of asthma symptoms (see *Table 4*).

Certainty Of The Evidence For Relapse of Symptoms with 1-3 doses of Dexamethasone vs. 1-3 doses of Prednisolone before hospital arrival. The certainty of the body of evidence was very low. The body of evidence for the one observational study (Hermani et al., 2021) was assessed to imprecision due to low number of events. As only one study (Hermani et al. 2021) was identified to answer this question, inconsistency could not be assessed.

Identification of Studies
Search Strategy and Results (see Figure 1)

"Status Asthmaticus"[Mesh] OR "Asthma/drug therapy"[Mesh] OR "asthma exacerbation*") AND ("Dexamethasone/administration and dosage"[Mesh] OR "Prednisolone/administration and dosage"[Mesh] OR "Prednisone/administration and dosage"[Mesh]) AND (child OR children OR pediatr* OR paediatr* OR infant OR adolescence
Records identified through database searching *n* = 41
Additional records identified through other sources *n* = 1

Studies Included in this Review

Citation	Study Type
*Elkharwili et al., 2020	RCT
Hermani et al., 2021	Cohort
*Kirkland et al., 2018	SR
* Normansell et al., 2016	SR
*Paniagua et al., 2017	RCT
Volk et al., 2019	Cohort
Watnick et al., 2016	Cohort

References marked with an asterisk indicate studies included in the meta-analysis

Studies Not Included in this Review with Exclusion Rationale

Citation	Reason for exclusion
SR Bravo-Soto et al., 2017	In Spanish language
SR Kirkland et al., 2019	Articles of interest are included in two of the included SR
SR Meyer et al., 2014	Articles of interest are included in in Kirkland et al. (2018) SR

Methods Used for Appraisal and Synthesis

[a]The GRADEpro Guideline Development Tool (GDT) is the tool used to create the Summary of Findings table(s) for this analysis.

[b]Rayyan is a web-based software used for the initial screening of titles and / or abstracts for this analysis (Ouzzani, Hammady, Fedorowicz & Elmagarmid, 2017).

[c]Review Manager (Higgins & Green, 2011) is a Cochrane Collaborative computer program used to assess the study characteristics as well as the risk of bias and create the forest plots found in this analysis.

[d]The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram depicts the process in which literature is searched, screened, and eligibility criteria is applied (Moher, Liberati, Tetzlaff, & Altman, 2009).

References to Appraisal and Synthesis Methods

[a]GRADEpro GDT: GRADEpro Guideline Development Tool (2015). McMaster University, (developed by Evidence Prime, Inc.). [Software]. Available from gradepro.org.

[b]Ouzzani, M., Hammady, H., Fedorowicz, Z., & Elmagarmid, A. (2016). Rayyan-a web and mobile app for systematic reviews. *Systematic Reviews, 5*(1), 210. doi:10.1186/s13643-016-0384-4

[a]Higgins, J. P. T., & Green, S. e. (2011). *Cochrane Handbook for Systematic Reviews of Interventions [updated March 2011]* (Version 5.1.0 ed.): The Cochrane Collaboration, 2011.

[d]Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097 **For more information, visit www.prisma-statement.org.**

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Acronyms Used in this Document

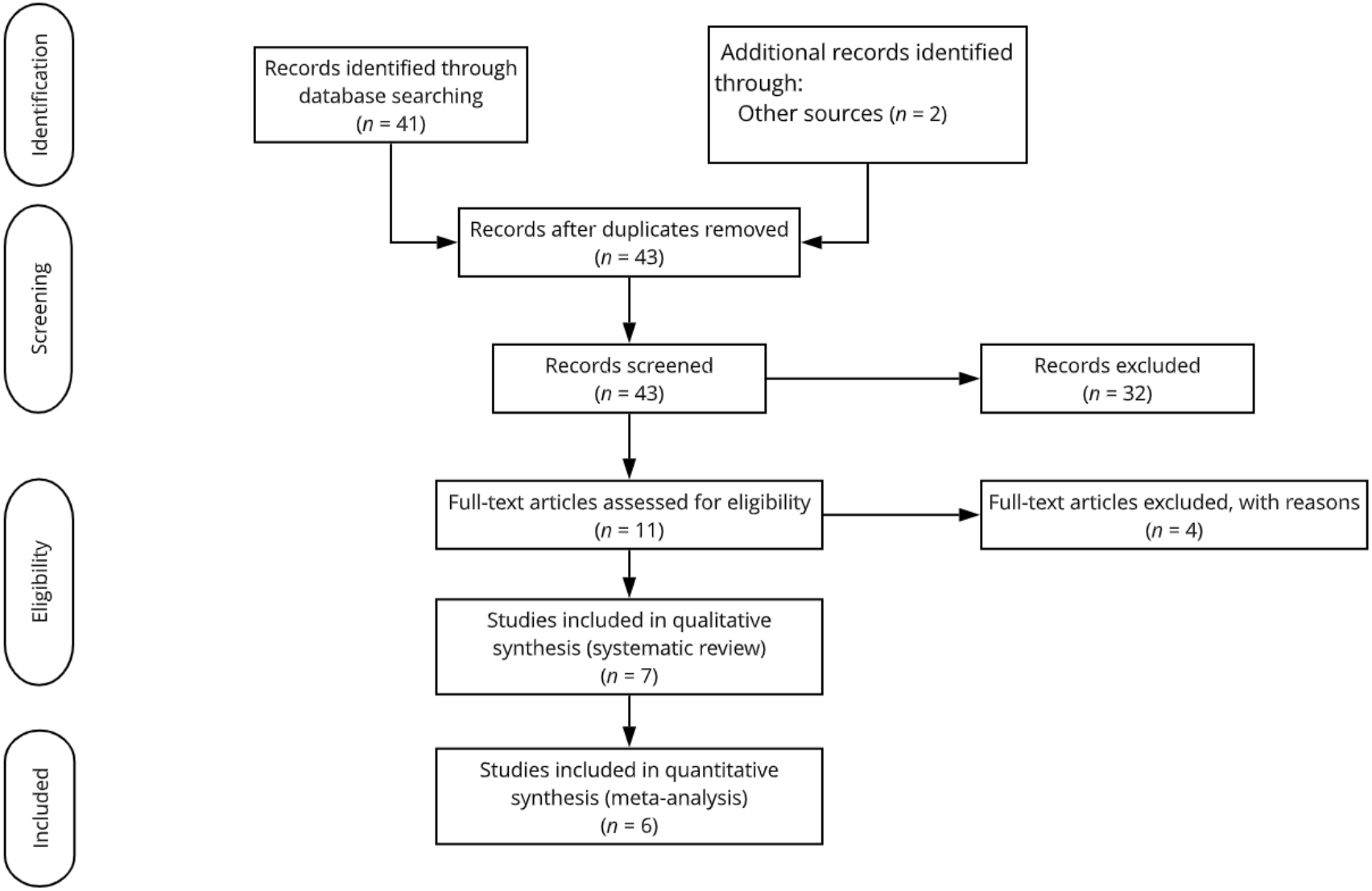
Acronym	Explanation
AGREE II	Appraisal of Guidelines Research and Evaluation II
CAT	Critically Appraised Topic
EBP	Evidence Based Practice
ED	Emergency Department
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Statistical Acronyms Used in this Document

Statistical Acronym	Explanation
CI	Confidence Interval
I^2	Heterogeneity test
M or $\bar{X}$	Mean
n	Number of cases in a subsample
N	Total number in sample
OR	Odds Ratio
P or p	Probability of success in a binary trial
RCT	Randomized controlled trial
RR	Relative risk
SD	Standard deviation
SE	Standard error
SR	Systematic Review

Figure 1

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRIMSA)[d]



Summary of Findings Table
Table 1

Summary of Findings Table[a]: Relapse of Symptoms 1 Day Dexamethasone vs. 3-5 Days Prednisolone

Certainty assessment							Summary of findings				
							Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With 5-day course of prednisolone	With 1-2 doses of dexamethasone		Risk with 5-day course of prednisolone	Risk difference with 1-2 doses of dexamethasone
Relapse of symptoms (1 day Dexamethasone vs. 3-5 days Prednisolone)											
615 (6 RCTs)	serious[a]	not serious	not serious	serious[b]	none	⨁⨁◯◯ Low	19/299 (6.4%)	16/316 (5.1%)	**OR 0.74** (0.32 to 1.69)	64 per 1,000	**16 fewer per 1,000** (from 42 fewer to 39 more)
Relapse of symptoms (1 day Dexamethasone vs. 3-5 days Prednisolone)											
40 (1 RCT)	serious[d]	not serious	not serious	very serious[c]	none	⨁◯◯◯ Very low	20	20	***MD* = 3.00** (-14.67, 20.67)	The mean relapse of symptoms (1 day Dexamethasone vs. 3-5 days Prednisolone) was **0**	MD **3 higher** (14.67 lower to 20.67 higher)
Relapse of symptoms (1 day Dexamethasone vs. 3-5 days Prednisolone)											
8769 (1 observational study)	not serious	not serious	not serious	serious[b]	none	⨁⨁◯◯ Low	143/7130 (2.0%)	21/1639 (1.3%)	**OR 0.63** (0.40 to 1.01)	20 per 1,000	**7 fewer per 1,000** (from 12 fewer to 0 fewer)

Notes:
a. both study participants and study personnel not blinded, concerns for performance bias
b. low number of events
c. low number of subjects
d. randomization not completed as stated and data analysis followed per protocol analysis

Table 2

Summary of Findings Table[a]: Relapse of symptoms 2 days Dexamethasone vs. 5-6 days Prednisolone

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With 5-day course of prednisolone	With 1-2 doses of dexamethasone	Relative effect (95% CI)	Risk with 5-day course of prednisolone	Risk difference with 1-2 doses of dexamethasone
Relapse of symptoms (2 days Dexamethasone vs. 5-6 days Prednisolone)											
1279 (3 RCTs)	serious[a]	not serious	not serious	serious[b]	none	⨁⨁◯◯ Low	15/675 (2.2%)	25/604 (4.1%)	**OR 1.65** (0.85 to 3.19)	22 per 1,000	**14 more per 1,000** (from 3 fewer to 45 more)
Relapse of symptoms (2 days Dexamethasone vs. 5-6 days Prednisolone)											
63 (1 observational study)	not serious	not serious	not serious	serious[c]	none	⨁◯◯◯ Very low	2/40 (5.0%)	0/23 (0.0%)	**OR 0.33** (0.02 to 7.13)	50 per 1,000	**33 fewer per 1,000** (from 49 fewer to 223 more)

Notes:

a. both study participants and study personnel not blinded, concerns for performance bias
b. low number of events
c. Low number of events and subjects

Table 3

Summary of Findings Table[a]: Relapse of symptoms 2 days Dexamethasone vs. 5 days Prednisolone initiated after hospital arrival hospitalized

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With 5-day course of prednisolone	With 1-2 doses of dexamethasone	Relative effect (95% CI)	Risk with 5-day course of prednisolone	Risk difference with 1-2 doses of dexamethasone
Relapse of symptoms (2 doses Dexamethasone vs. 5 doses Prednisolone during hospitalization)											
961 (1 observational study)	not serious	not serious	not serious	serious[a]	none	⨁◯◯◯ Very low	0/135 (0.0%)	18/826 (2.2%)	**OR 6.20** (0.37 to 103.50)	0 per 1,000	**0 fewer per 1,000** (from 0 fewer to 0 fewer)

Notes:

a. Low number of events and subjects

Table 4

Summary of Findings Table[a]: Relapse of symptoms 1-3 doses Dexamethasone vs. 1-3 doses Prednisolone before hospital arrival

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With 5-day course of prednisolone	With 1-2 doses of dexamethasone	Relative effect (95% CI)	Risk with 5-day course of prednisolone	Risk difference with 1-2 doses of dexamethasone
Relapse of symptoms (1-3 doses Dexamethasone vs. 1-3 doses Prednisolone before hospital arrival)											
449 (1 observational study)	not serious	not serious	not serious	serious[a]	none	⨁◯◯◯ Very low	5/294 (1.7%)	2/155 (1.3%)	**OR 0.76** (0.14 to 3.94)	17 per 1,000	**4 fewer per 1,000** (from 15 fewer to 47 more)

Notes:
a. Low number of events and subjects

Meta-analysis(es)
Figure *2*

Comparison: 1 day Dexamethasone versus 3-5 days Prednisolone, Outcome: Relapse of symptoms

	Dexamethasone		Prednisolone			Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Al-Wahadneh2006	1	16	3	14	11.3%	0.24 [0.02, 2.68]
Altamimi2006	3	56	1	54	12.2%	3.00 [0.30, 29.77]
Cronin2015	3	122	1	120	12.4%	3.00 [0.31, 29.25]
Gordon2007	8	86	11	73	52.9%	0.58 [0.22, 1.52]
Gries2000	1	15	3	17	11.4%	0.33 [0.03, 3.61]
Klig1997	0	21	0	21		Not estimable
Total (95% CI)		**316**		**299**	**100.0%**	**0.74 [0.32, 1.69]**
Total events	16		19			

Heterogeneity: Tau² = 0.09; Chi² = 4.39, df = 4 (P = 0.36); I² = 9%
Test for overall effect: Z = 0.72 (P = 0.47)

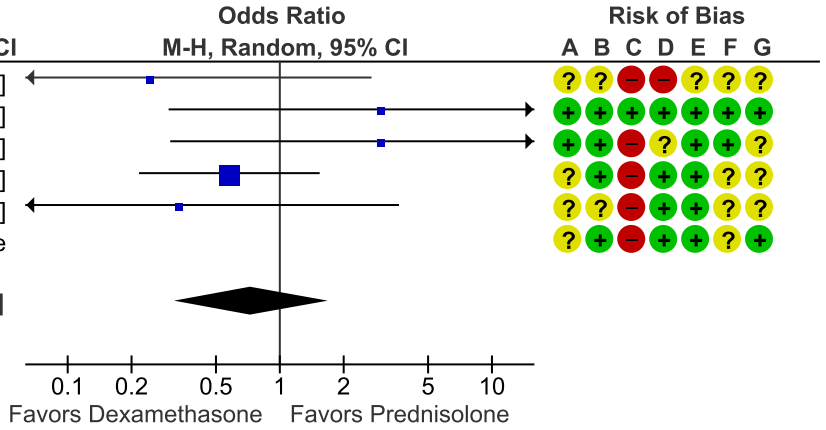
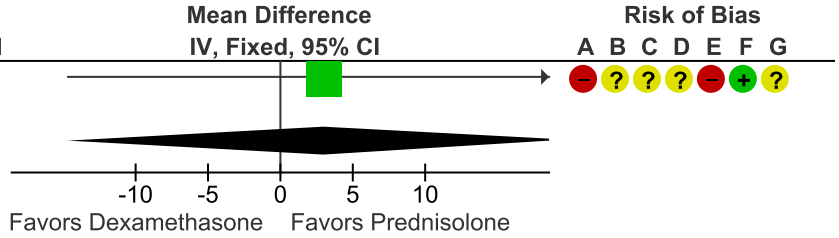


Figure *3*

Comparison: 1 day Dexamethasone versus 3-5 days Prednisolone, Outcome: Relapse of symptoms

	Dexamethasone			Prednisolone				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Elkharwili2020	7	35	20	4	20	20	100.0%	3.00 [-14.67, 20.67]
Total (95% CI)			**20**			**20**	**100.0%**	**3.00 [-14.67, 20.67]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.33 (P = 0.74)



Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

Figure *4*

Comparison: 1 day Dexamethasone versus 3-5 days Prednisolone, Outcome: Relapse of symptoms

Study or Subgroup	Dexamethasone Events	Total	Prednisolone Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Watnick2016	21	1639	143	7130	100.0%	0.63 [0.40, 1.01]
Total (95% CI)		**1639**		**7130**	**100.0%**	**0.63 [0.40, 1.01]**
Total events	21		143			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.94 (P = 0.05)

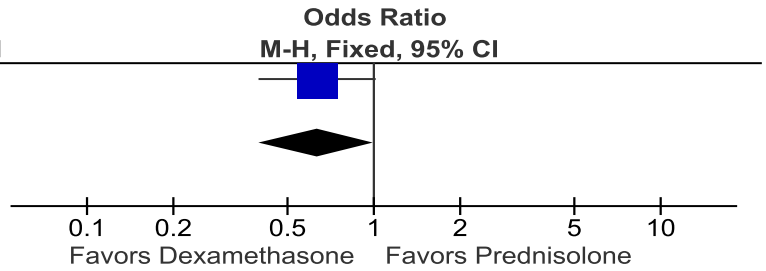


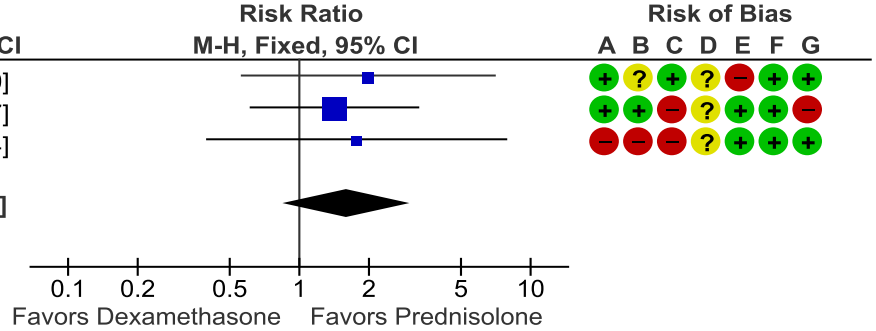
Figure *5*

Comparison: 2-day Dexamethasone versus 5-6 days Prednisolone, Outcome: Relapse of symptoms

Study or Subgroup	Dexamethasone Events	Total	Prednisolone Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Greenberg2008	8	51	3	38	22.8%	1.99 [0.56, 7.00]
Paniaqua2017	13	281	9	276	60.1%	1.42 [0.62, 3.27]
Qureshi2001	4	272	3	361	17.1%	1.77 [0.40, 7.84]
Total (95% CI)		**604**		**675**	**100.0%**	**1.61 [0.86, 3.01]**
Total events	25		15			

Heterogeneity: Chi² = 0.21, df = 2 (P = 0.90); I² = 0%

Test for overall effect: Z = 1.48 (P = 0.14)



Risk of bias legend

(**A**) Random sequence generation (selection bias)

(**B**) Allocation concealment (selection bias)

(**C**) Blinding of participants and personnel (performance bias)

(**D**) Blinding of outcome assessment (detection bias)

(**E**) Incomplete outcome data (attrition bias)

(**F**) Selective reporting (reporting bias)

(**G**) Other bias

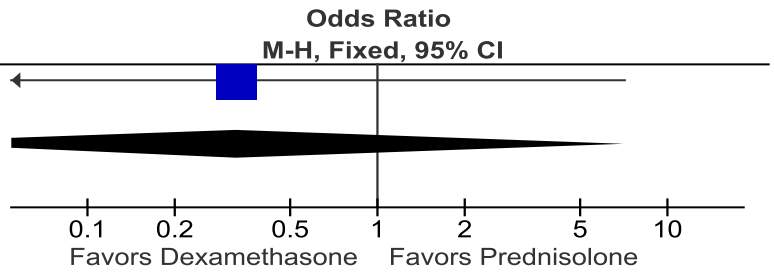
Figure *6*

Comparison: 2-day Dexamethasone versus 5-6 days Prednisolone, Outcome: Relapse of symptoms

	Dexamethasone		Prednisolone			Odds Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Fixed, 95% CI**
Volk2019	0	23	2	40	100.0%	0.33 [0.02, 7.13]
Total (95% CI)		**23**		**40**	**100.0%**	**0.33 [0.02, 7.13]**
Total events	0		2			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.71 (P = 0.48)



Characteristics of Intervention Studies

Elkharwili, 2020

Methods	**Randomized Control Trial**
Participants	**Participants:** Children with acute exacerbation of asthma **Setting:** Hospital (Tanta University Hospital, Egypt, March 2016 - October 2017) **Randomized into study:** *N* = 94 • **Group 1, 0.3 mg/kg oral dexamethasone for one day:** *n* = 35 • **Group 2, 0.6 mg/kg of oral dexamethasone for two days:** *n* = 32 • **Group 3, 1.5 mg/kg oral prednisolone***: n = 27* **Completed Study Treatment:** *N* = 81 • **Group 1:** *n* = 29 • **Group 2:** *n* = 29 • **Group 3:** *n* = 23 **Completed Follow-up Phase of Study:** *N* = 60 • **Group 1:** *n* = 20 • **Group 2:** *n* = 20 • **Group 3:** *n* = 20 **Gender, males (as defined by researchers):** • **Group 1:** *n* = 40% • **Group 2:** *n* = 50% • **Group 3:** *n* = 55% **Race / ethnicity or nationality:** • The authors did not identify race or ethnicity of the participants. **Age, mean in years (SD):** • **Group 1:** 5.93 (2.37) • **Group 2:** 6.52 (2.64) • **Group 3:** 6.15 (2.75)

	Inclusion Criteria: • children with a history of bronchial asthma, • those that presented with an asthma exacerbation, which was defined as a decrease in expiratory airflow • that could be documented and quantified by simple measurement of lung function (spirometry or peak expiratory flow (PEF)) • age 2 - 11 years • male or female **Exclusion Criteria:** • children aged 11 years • children with intubation history for previous asthma exacerbations • children with active varicella or herpes simplex infection in the past 3 weeks • children with documented concurrent infection with respiratory syncytial virus • use of oral or intravenous corticosteroids in the previous 4 weeks • concurrent stridor • known patients with tuberculosis • presence of other significant comorbidities such as: cardiac, immune, liver, endocrine, neurological and psychiatric disorders **Power Analysis:** Analysis at a p value of 0.05 and a power of 80% showed that a total sample size of 78 patients distributed as 1:1:1 in the three groups was necessary. The level of significance was set at a p value < 0.05, while p values of 0.01 and 0.001 were considered highly significant**.**
Interventions	**Group 1:** single dose of 0.3 mg/kg oral dexamethasone, with a maximum dose of 12mg/day for 1 day and continued with a placebo for the other 4 days **Group 2:** 0.6 mg/kg of oral dexamethasone, with a maximum dose of 16 mg/day in three divided doses for two consecutive days and continued with a placebo for the other 3 days **Group 3:** 1.5 mg/kg oral prednisolone per day for 5 days with a maximum dose of 60 mg in three divided doses
Outcomes	**Primary outcome(s):** • Change in physical examination, Pediatric Respiratory Assessment Measure (PRAM) score*, the Modified Pulmonary Index Score (MPIS)*, pulmonary function tests*, saturated oxygen, blood eosinophilic count and serum immunoglobulin E after 5 days of taking the corticosteroids **Secondary outcome:** • Vomiting, gastrointestinal tract (GIT) cramps and relapse rate were recorded as secondary outcomes of the study **Safety Outcome:** • Relapse Rate* *Outcomes of interest for the CPG Team

Notes	• Due to protocol deviations and participants lost to follow-up, the authors did not meet the sample size calculated to determine significance • There was no statistically significant difference in weight gain and blood sugar before and after 5 days of treatment within the same group • After 5 days of treatment, pairwise comparison showed a significant difference in blood sugar level only between group II and group III (p=0.004) • After 5 days of treatment, comparison of the participants showed that there was a highly statistical difference in MPIS, oxygen need, duration of hospital admission and PRAM within the three groups (p<0.001). • After 30 days, ATAZ Asthma Therapy Assessment Questionnaire (ATAQ) showed no significant differences among the three studied groups for missed days of school

Risk of bias table

Bias	Judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Article states that 94 eligible patients were assigned and randomized in a 1:1:1 ratio into three groups. It does not specify as to how the randomization was generated. Although this is stated, it shows that the following were the initial group allocations: Group I: 35 patients, Group II: 32 patients and Group III: 27 patients which does not prove that a 1:1:1 ratio was used.
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgment of low or high risk
Blinding of participants and personnel (performance bias)	Unclear risk	Article states that it was a double-blind clinical trial but doesn't describe any further information regarding blinding methods
Blinding of outcome assessment (detection bias)	Unclear risk	Insufficient information to permit judgment of low risk or high risk
Incomplete outcome data (attrition bias)	High risk	The authors identify in Table 1 that patients with protocol deviations (Group I: 6, Group II: 3, Group III: 4) were not counted as completing study. In Table 5 the authors only include in the final analysis the data from only the participants completing the follow-up phase therefore data is missing from 21 additional participants (Group i: 9, Group II: 9 and Group III: 3). With the removal of this data the authors did not meet the sample size needed to detect significance between the different groups.
Selective reporting (reporting bias)	Low risk	The only thing not noted in the outcomes table was the saturation oxygen, but there were other parameters captured such as PEF (%) and FEV1/FVC (%) so noted as low risk
Other bias	Unclear risk	There may be a risk of bias, but there is insufficient information to assess whether an important risk of bias exists.

Hemani, 2021

Methods	**Multisite Retrospective Cohort**
Participants	**Participants:** Patients 3 to 21 years admitted between January 1, 2013, and December 31, 2017, with primary discharge diagnosis, IDC 9 and ICD 10, of asthma exacerbation or status asthmaticus **Setting:** Atlanta, USA, Tertiary Children's Hospital System **Number enrolled into study:** *N* = 1410 • **Group 1, Dexamethasone (DEX) Initiated After Hospital Arrival:** *n* = 826 • **Group 2, Prednisone/prednisolone (PRED) Initiated After Hospital Arrival:** *n* = 135 • **Group 3, Dexamethasone (DEX) Before Hospital Arrival***: n* = 155 • **Group 4, Prednisone/prednisolone (PRED) Before Hospital Arrival:** *n* = 294 **Gender, males:** • **Group 1:** *n* = 531 (64.3%) • **Group 2:** *n* = 77 (57%) • **Group 3:** *n* = 96 (62%) • **Group 4:** *n* = 192 (65.3%) **Race** (reported numbers do not reach total enrolled, but reported percentages equal 100)**:** • Black ○ **Group 1:** *n* = 562 (72.3%) ○ **Group 2:** *n* = 76 (58%) ○ **Group 3:** *n* = 83 (55%) ○ **Group 4:** *n* = 152 (53.3%) • White ○ **Group 1:** *n* = 126 (16.2%) ○ **Group 2:** *n* = 33 (35%) ○ **Group 3:** *n* = 43 (29%) ○ **Group 4:** *n* = 76 (26.7%) • Asian ○ **Group 1:** *n* = 17 (2.2%) ○ **Group 2:** *n* = 1 (1%) ○ **Group 3:** *n* = 6 (4%) ○ **Group 4:** *n* = 8 (2.8%) • Other ○ **Group 1:** *n* = 72 (9.3%) ○ **Group 2:** *n* = 20 (15%) ○ **Group 3:** *n* = 18 (12%) ○ **Group 4:** *n* = 49 (17.2%)

Ethnicity:

- Hispanic or Latino
  - **Group 1:** *n* = 111 (13.5%)
  - **Group 2:** *n* = 26 (19%)
  - **Group 3:** *n* = 19 (12%)
  - **Group 4:** *n* = 31 (10.6%)
- Non- Hispanic or Latino
  - **Group 1:** *n* = 714 (86.6%)
  - **Group 2:** *n* = 109 (81%)
  - **Group 3:** *n* = 136 (88%)
  - **Group 4:** *n* = 262 (89.4%)

Age, mean in years, (SD):

- **Group 1:** 6.79 (3.3)
- **Group 2:** 6.54 (3.1)
- **Group 3:** 6.49 (3.3)
- **Group 4:** 6.87 (3.1)

Inclusion Criteria:

- Age of 3 to 21 years
- Receiving monotherapy with DEX or PRED
- Multiple asthma-related hospital visits within a 10-day period only the first encounter was captured

Exclusion Criteria:

- Less than 3 years of age
- Receiving an unspecified oral steroid or combination of DEX and PRED during acute illness
- Missing information about steroid administration prior to admission
- Methyl prednisone administration during acute illness
- Steroid administration in prior 2 weeks or receiving a prolonged steroid course
- Initial PICU admission
- Concurrent diagnosis of bronchiolitis, pneumonia, or croup
- Use of Bi-level positive airway pressure
- Supplemental therapies in the Emergency Department (e.g., antibiotics, oseltamivir, heliox, terbutaline, racemic epinephrine, hypertonic saline, chest physiotherapy, and budesonide)
- Pulmonary or cardiac comorbidities, sickle cell disease, down syndrome, or immunosuppression
- Hospital admissions with paper chart documentation
- Left against medical advice or readmission

Covariates Identified:

- Albuterol administration prior to hospital arrival

Interventions	**Both:** Received a clinical respiratory score; received albuterol; may receive ipratropium, magnesium, and supplemental oxygen • **Group 1:** Received an average dose of DEX 0.5 mg/kg per day for a median of 2 days while hospitalized • **Group 2:** Received an average dose of PRED 1.8 mg/kg per day for a median of 2 days while hospitalized • **Group 3:** Received an average dose of DEX 0.5 mg/kg per day for a median of 1 day while hospitalized • **Group 4:** Received an average dose of PRED 1.8 mg/kg per day for a median of 2 days while hospitalized
Outcomes	**Primary outcome:** • Length of stay (LOS)* **Secondary outcomes:** • PICU transfer during initial hospitalization* • Readmission within 10 days after hospital discharge* **Safety outcome:** • Not reported *Outcomes of interest to the CMH CPG /CAT development team
Notes	**Limitations:** • Retrospective study, susceptible to adjustment items • Majority of patients classified as mild intermittent or mild persistent asthma • Exclusion criteria prevented severe asthma exacerbation patient inclusion in study • Previous inhaled corticosteroid uses not included • Steroid adherence after discharge not tracked

Kirkland, 2018

Methods	Systematic Review (meta-analysis)
Objective	To examine the effectiveness and safety of a single dose of intramuscular (IM) corticosteroids provided prior to discharge compared to a short course of oral corticosteroids in the treatment of acute asthma patients discharged from an ED or equivalent acute care setting.
Methods	**Criteria for considering studies for this review** • **Types of studies:** RCTs or controlled clinical trials • **Participants:** Adults and pediatric patients presenting with acute asthma to an ED or acute care setting. • **Target Condition(s):** Acute asthma exacerbation **Search methods for identification of studies** • **Electronic databases searched:** Cochrane Airways Group Register of Trials and databases including Medline, Embase, EBM ALL, Global Health, International Pharmaceutical Abstracts, CINAHL, SCOPUS, ProQuest Dissertations and Theses Global, and LILACS. • **Search strategy employed:** ○ *Secondary Prevention; Acute Disease; Administration, Oral; Adrenal Cortex Hormones [*administration & dosage]; Anti-Asthmatic Agents [*administration & dosage]; Asthma [drug therapy] [*prevention & control]; Betamethasone [administration & dosage]; Dexamethasone [administration & dosage]; Emergency Service, Hospital; Injections, Intramuscular; Methylprednisolone [administration & dosage]; Patient Discharge; Prednisolone [administration & dosage]; Prednisone [administration & dosage]; Randomized Controlled Trials as Topic; Recurrence; Triamcinolone [administration & dosage] ○ Included full text, abstracts and unpublished data in search criteria. • **Searching other resources (such as reference list):** Reference lists of all primary studies and review articles were checked for additional references. Relevant manufacturers' web sites were also searched for additional study information. **Data collection and analysis** • **Inclusion criteria:** ○ RCTs and controlled clinical trials ○ Studies with acute exacerbation of asthma as primary reason for presentation to ED with no other co-existing complications ○ Asthma diagnosis had to be made either using international/national clinical guidelines or spirometric criteria or both • **Exclusion criteria:** ○ Studies that focused on corticosteroid treatment in hospitalized patients • **Population:** Adult and pediatric patients with uncomplicated exacerbation of asthma • **Setting:** Hospital ED or equivalent acute care setting • **Study Design:** Systematic review and meta-analysis • **Data collection process:** Two independent reviewers assessed study eligibility and study quality. Disagreements were resolved by a third party and assessed risk of bias using the Cochrane Risk of Bias toll. • **Assessment of the certainty of the evidence:** Quality of the evidence was measured/assessed using GRADE.

	• **Data Synthesis (what statistical plan do the authors establish a priori):** ○ **Random effects model** used and performed a sensitivity analysis with a fixed-effect model. ○ **Heterogeneity:** I^2 statistic used to measure heterogeneity. If substantial heterogeneity was identified, it was reported, and possible causes were explored using a prespecified subgroup analysis (see subgroup analysis below): ▪ Children (zero to 18 years of age) versus adults (18 years of age and older) to examine any potential age-specific treatment effects of IM or oral corticosteroids. ▪ Relapse occurring within 10 days and over 10 days post-discharge. ▪ Low versus moderate versus high exacerbation severity based on the pulmonary function taken at the time of the participant's presentation to the ED, prior to treatment with a bronchodilator. ▪ Co-interventions received (ICS versus ICS corticosteroids/long-acting $beta_2$-agonists (LABA). ○ **Sensitivity analysis carried out by removing the following types of studies from primary outcome analyses:** ▪ Studies that we consider to be at high risk of bias based on the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). ▪ Studies in which the duration of oral corticosteroid treatment was less than five days. ▪ The results from fixed-effect models were compared with the random-effects models for the main outcome. ▪ Studies in which supplemental corticosteroids were provided to the patients in the ED as a co-intervention
Results	**Study Selection (actual results/data)** **Number of articles identified:** *N* = 912 **Full-text articles assessed for eligibility:** *n* = 20 ○ **Studies included in qualitative synthesis:** *n* = 9 **Synthesis of quality of evidence** (strength of evidence): Using GRADE, the overall certainty of the evidence was assessed per outcome ranging from low to moderate with the following results per outcome: • Primary outcomes of relapse as well as relapse after 10 days was rated as low quality due to overall unclear to high risk of bias of the studies and imprecision due to wide confidence intervals including both benefit, harm and no effect. The subgroup analysis for relapse was rated at low quality due to the low number of available patients and wide confidence intervals. • Outcome for adverse events also ranked at low quality due to overall unclear to high risk of bias of the included studies and imprecision due to few events. • Outcome of symptom persistence and 24-hour $beta_2$-agonists use ranked as low quality due to the overall unclear to high risk of bias of the included studies as well as few events. • Outcome of peak expiratory flow ranked as moderate quality due ot imprecision of the results. **Synthesis of quantitative evidence: (pediatric patients only)** • **Overall Effect Size:** Intramuscular versus oral corticosteroids, Outcome: Relapse ▪ **Odd Ratio:** .78 ▪ **CI:** 95% CI [.38, 1.57], *p* = .49 ▪ **Heterogeneity** • I^2=0% • **Overall Effect Size:** Intramuscular versus oral corticosteroids, Outcome: Relapse intention to treat

	▪ **Odds Ratio:** .78 ▪ **CI:** 95% CI [0.38, 1.57], *p* = .48 ▪ **Heterogeneity** • I^2=0% • **Overall Effect Size:** Intramuscular versus oral corticosteroids, Outcome: Relapse within 10 days ▪ **Odds Ratio:** .75 ▪ **CI:** 95% CI [0.28, 2.0], *p* = .57 • **Overall Effect Size:** Intramuscular versus oral corticosteroids, Outcome: Relapse over 10 days ▪ **Odds Ratio: .**78 ▪ **CI:** 95% CI [0.38, 1.57, *p* = .48 ▪ **Heterogeneity** • I^2=0%
Discussion	**Summary of evidence** • Systemic corticosteroids were found to be an effective treatment in decreasing relapse of symptoms for acute asthma exacerbation for ED or equivalent acute care settings and assists with prevention of admission however, the optimal route of dosing and administration is unclear. **Limitations** • Lack of reporting out of data on secondary outcomes significantly limited the number of studies that could be used for the meta-analysis and impacted the authors' ability to draw meaningful conclusions or recommendations towards the overall effectiveness of IM corticosteroids. • Only four pediatric studies met the inclusion criteria. • The effectiveness of the corticosteroids results may have been impacted by the age of the children enrolled in the study meaning, younger children may not respond to the corticosteroids due to fewer airway eosinophils. • Co-interventions were poorly reported in studies reviewed and it is likely that some of the agents used may no longer be used. • Lack of reporting on the use of the ICS and ICS/LABA agents limited the review on its ability to estimate the impact of these agents on the efficacy of IM or oral corticosteroids. • Dosing of corticosteroids was not a criterion used for inclusion and thus, no conclusion drawn on the impact of dosing completed.
Funding	The National Institute for Health Research (NIHR) supported this project, via Cochrane Infrastructure funding to the Cochrane Airways Group.

Normansell, 2016

Methods	Systematic Review (meta-analysis)
Objective	To assess the efficacy and safety of any dose or duration of oral steroids versus any other dose or duration of oral steroids for adults and children with an asthma exacerbation.

Methods	**Criteria for considering studies for this review**
	• **Types of studies:**
	  ○ RCTs
	• **Participants:**
	  ○ Adults
	  ○ Children
	• **Target Condition(s):**
	  ○ Acute Asthma Attack
	
	Search methods for identification of studies
	• **Electronic databases searched:** the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), the Allied and Complementary Medicine Database (Alangari et al.) and PsycINFO, and by handsearching of respiratory journals and meeting abstracts
	• **Search strategy employed:** Mesh terms (see study for full list)
	• **Searching other resources:** Handsearching of respiratory journals and meeting abstracts
	
	Data collection and analysis
	• **Inclusion criteria:**
	  ○ Randomized controlled trials (RCTs), irrespective of blinding or duration, that evaluated one dose or duration of oral steroid versus any other dose or duration, for management of asthma exacerbations.
	  ○ Both adults and children with asthma of any severity, in which investigators analyzed adults and children separately.
	  ○ Other co-intervention in the management of an asthma exacerbation, provided it was not part of the randomized treatment.
	• **Exclusion criteria:**
	  ○ Wrong comparator
	  ○ Wrong intervention
	  ○ Not randomized
	• **Population:**
	  ○ Adults and children with an acute exacerbation of asthma
	• **Setting:**
	  ○ Inpatient
	  ○ Emergency department
	• **Study Design:**
	  ○ Systematic review and meta-analysis
	• **Data collection process:**
	  ○ Data collection form designed by two of the investigators

	• **Assessment of the certainty of the evidence:**
	  ○ GRADE
	• **Data Synthesis (what statistical plan do the authors establish a priori):**
	  ○ **Overall Effect Size (just state what is being used in the study)**
	  ▪ OR
	  ▪ RD
	  ▪ CI
	  ○ **Heterogeneity**
	  ▪ Cochran's Q statistic
	  ▪ I^2 statistic

Results	**Study Selection (actual results/data)** **Number of articles identified:** *N* = 1406 **Full-text articles assessed for eligibility:** *n* = 71 ○ **Studies included in qualitative synthesis:** *n* = 18 **Synthesis of quality of evidence** (strength of evidence): • Low to very low certainty **Synthesis of quantitative evidence:** • Prednisolone vs dexamethasone, outcome: Admission during follow-up ○ OR = .09 (-0.07, 0.26), *p*-value = .9 ○ *n* = 3 studies (985 patients) ○ I^2 = 0% • Prednisolone vs dexamethasone, outcome: Re-admission during follow-up ○ OR = .44 (0.15, 1.33), *p*-value = .14 ○ *n* = 3 studies (985 patients) ○ I^2 = 0% • Prednisolone vs dexamethasone, outcome: Asthma symptoms: Pulmonary Index Score ○ *MD* = -.1 (0.45, 0.25), *p*-value = .58 ○ *n* = 1 study (100 patients) • Prednisolone vs dexamethasone, outcome: Asthma symptoms: Patient Self-Assessment Score ○ *MD* = .1 (-0.67, 0.69), *p*-value = .98 ○ *n* = 1 study (100 patients) • Prednisolone vs dexamethasone, outcome: Asthma symptoms: Pediatric Respiratory Assessment Measure ○ *MD* = 0 (-0.36, 0.36), ○ *n* = 1 study (218 patients) • Prednisolone vs dexamethasone, outcome: New exacerbation during follow-up period: unscheduled visit to healthcare provider ○ OR = .85 (0.54, 1.34), *p*-value = .48 ○ *n* = 4 study (981 patients) ○ I^2 = 0% • Prednisolone vs dexamethasone, outcome: New exacerbation during follow-up period: oral corticosteroids prescribed ○ OR = .29 (0.1, 0.81) ○ *n* = 1 study (242 patients)

Discussion	**Summary of evidence** • There was difficulty to combine the results of studies in a useful way because investigators used a variety of doses and durations of steroids and measured their results in different ways. Also, events such as hospital admissions and serious side effects happened very rarely in these studies, making it difficult to tell whether longer or shorter courses or higher or lower doses are better or safer, or if prednisolone is generally better or worse than dexamethasone. Some studies were old and did not use steroid doses or durations used by medical practitioners today. **Limitations** • Evidence presented in the review is generally considered to be of low or very low certainty, which means there is a great amount of uncertainty of whether the results are accurate, mostly because the authors could not combine many studies. Some studies did not clearly explain how trial organizers decided which people would receive which dose of steroids, and in some studies, both participants and trial organizers knew which dose they were getting.
Funding	**Funding** • Cochrane Collaborative

Paniagua, 2017

Methods	**Randomized Control Trial**
Participants	**Participants:** Children with asthma exacerbation who presented to the emergency department (ED) Sept 2014-October 2015 **Setting:** Acute care teaching tertiary hospital, Spain (Basque Country) **Randomized into study:** *N* = 590 • **Group 1:** Dexamethasone, *n* = 294 • **Group 2:** Prednisolone, *n* = 296 **Completed Study:** *N* = 557 • **Group 1:** *n* = 281 • **Group 2:** *n* = 276 **Gender, males: mean, (%)** • **Group 1:** *n* = 169 (60.1%) • **Group 2:** *n* = 166 (60.1%) **Race / ethnicity or nationality:** • Not reported **Age, years** (mean) (Einarsdottir et al.): • **Group 1:** 4.7 (3.4) • **Group 2:** 4.5 (3.4) **Inclusion Criteria:** • Aged 1-14 years • History of previous diagnosis of asthma or at least 2 previous episodes responsive wheeze or first wheezing episode in a child > 2 years with history of atopy • Respiratory symptoms- ○ Acute cough, shortness of breath, tachypnea attributed to bronchospasm (wheezing, prolong expiration), increased work of breathing, and/or increased bronchodilator requirements from baseline **Exclusion Criteria:** • Other airway pathology • Other diseases that require hospitalization for safety • Children with life-threatening asthma exacerbation • Use of oral or parenteral corticosteroids in past 4 weeks **Power Analysis:** Sample size calculation was based on a Pediatric Asthma Control Tool (PACT) score at day seven for the dexamethasone group would not be more than 6% greater than the prednisolone group score; a sample size of at least 556 subjects was required to detect a difference.

Interventions	**Both groups:** received the first 2-3 β_2-agonist treatments at 20-minute intervals with the addition of ipratropium bromide prescribed per attending provider. • **Group 1:** Dexamethasone*, oral, (1 mg/ml), 0.6 mg/kg, maximum 12 mg, one dose received in the ED, a second dose was administered 24 hours later. • **Group 2:** Prednisone/prednisolone*, oral, 1.5 mg/kg, maximum 60 mg, one dose in the ED, followed by 1 mg/kg/d, maximum 60 mg, twice daily on days 2 - 5. Choice of liquid or tablet formulate was based on the subject's age. ○ *If either treatment was vomited within 30 minutes, the dose was re-administered. Subjects were contacted by phone at day 7 and 15 in which PACT questionnaire and the asthma related quality of life (ARQoL) instrument was completed. Both instruments are validated.
Outcomes	**Primary outcome(s):** • Percent of subjects with symptoms at 7 days [PACT score] * and their quality of life score [ARQoL score]. **Secondary outcome(s):** • Vomiting • Adherence to treatment • Parent satisfaction • Admission rate* • Unscheduled returns to ED* • Hospital re-admissions • Visits to Primary Care Provider • School and work absenteeism **Safety outcome(s):** • Not reported *Outcomes of interest to the CMH CPG team
Notes	Trial registered - clinicaltrialsregister.eu: 2013-003145-42, the registry states it is ongoing July 2, 2018,

Risk of bias table

Bias	**Judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Statisticians performed the randomization
Allocation concealment (selection bias)	Low risk	allocation concealment was maintained by the use of sequentially numbered opaque envelopes containing a letter A (experimental treatment) or B (conventional treatment), following the randomization list.
Blinding of participants and personnel (performance bias)	High risk	Open label, with subjective outcomes
Blinding of outcome assessment (detection bias)	Unclear risk	Data managers and the statistical team were blinded but bias could have occurred during interview with family.
Incomplete outcome data (attrition bias)	Low risk	Used a per-protocol analysis, Met sample size needed to detect inferiority between interventions.
Selective reporting (reporting bias)	Low risk	All outcomes were reported
Other bias	High risk	Treating physician was permitted to exclude patients if time constraints made enrollment unfeasible. The PACT tool used in a six-item inventory. References were found to the 10 and 3 item PACT, not the 6 item PACT. Self-reported response to both the PACT and the quality-of-life inventories.

Volk, 2019

Methods	**Retrospective Cohort**
Participants	**Participants:** Pediatric patients with Asthma or wheezing, **Setting:** Ambulatory Setting between August 2013 to July 2015 **Number enrolled into study:** *N* = 63 • **Group 1, Prednisone:** *n = 40* • **Group 2, Dexamethasone:** *n = 23* **Gender, males (as defined by researchers):** • **Group 1:** *n* = 31 (78%) • **Group 2:** *n = 23* (78%) **Race / ethnicity or nationality (as defined by researchers):** • **Group 1:** Non-Hispanic *n* = 16 (40%) • **Group 1**: Hispanic *n* = 24 (60%) • **Group 2**: Non-Hispanic *n* = 6 (26%) • **Group 2:** Hispanic *n* = 17 (74%) **Age, mean (years)** • **Group 1:** 6.4 • **Group 2:** 7.8 **Inclusion Criteria:** • ≥ 3 years of age • Primary visit diagnosis of "wheezing" (ICD9 786.07), "asthma unspecified type with exacerbation" (ICD9 493.92), "asthma with status asthmaticus" (ICD9 493.91), or "cough variant asthma" (ICD9 493.82) **Exclusion Criteria:** • Received steroid treatment from an outside health facility within 1-week of presentation to the Center **Covariates Identified:** • Not reported
Interventions	**Both:** inhaled ß-agonist treatment prior to corticosteroid with supplemental oxygen is oxygen saturations fall below 94%. • **Group 1:** Oral Prednisone-a single dose of weight-based prednisolone as either an oral tablet or liquid solution. Additional daily single doses are prescribed and completed at home over 5 days. • **Group 2:** Oral Dexamethasone-single dose of a dissolvable oral tablet using a weight-based formula at the Center. A second dose is prescribed and given within 24 hrs. (typically at home) to complete the 2-day course

Outcomes	**Primary outcome(s):** • ED visits • Hospital admissions • Return clinic visits within 1 week for recurrent • *Persistent symptoms *Outcomes of interest to the CMH CPG development team
Notes	**Results:** • The rates of hospital admissions, ED visits, and symptom follow-up were similar between the 2 groups (P > .05). • The cost for a course of dexamethasone was US $1.28 versus US $16.20 for prednisolone. The average cost for an asthma exacerbation office visit was US $79.89 compared with US $3113.28 for an ED visit. **Limitations:** • As the EMR was surveyed, errors may exist in coding and documentation • Unable to determine the true illness severity as measured by the number of previous exacerbations and the dose or duration of inhaled corticosteroids • Call backs were not done to determine medication compliance or medication adverse effects • Insurance claims from outside health facilities could not be tracked for 16% of patients, do not know if they were treated for wheezing elsewhere

Watnick, 2016

Methods	**Cohort**
Participants	**Participants:** patients 3 to 17 years old with acute asthma exacerbations **Setting:** urban tertiary care children's hospital ED **Number enrolled into study:** *N* =13,518 (4,749 excluded because they did not receive corticosteroid) **number included into study:** 8,769 • **Group 1, prednisone/prednisolone:** *n = 7130* • **Group 2, dexamethasone:** *n = 1639* **Gender, males (as defined by researchers)-not described per study group but overall patients compared to those with corticosteroids and relapse:** • *n* = 8,281 (61%) (all patients with & without corticosteroid treatment) • *n* = 109 (60 %) (patients with relapse) **Race / ethnicity or nationality (as defined by researchers):** • 4,783 (35%) White (all patients with & without corticosteroid treatment) 63 (34%) White (patients with relapse) • 7,701 (57%) Black (all patients with & without corticosteroid treatment) 108 (59%) Black (patients with relapse) • 119 (1%) Asian (all patients with & without corticosteroid treatment) 1 (1%) Asian (patients with relapse) • 36 (0%) American Indian or Alaskan (all patients with & without corticosteroid treatment) 0 (0%) American Indian or Alaskan (patients with relapse) • 1 (0%) Pacific Islander (all patients with & without corticosteroid treatment) 0 (0%) (patients with relapse) • 878 (7%) unknown or declined (all patients with & without corticosteroid treatment) 11 (6%) (patients with relapse) **Age, mean/median in months/years, (range/IQR** • **Group 1:** 7 (4-10) (all patients with & without corticosteroid treatment) • **Group 2:** 7 (4-11) (patients with relapse) **Inclusion Criteria:** • Patients 3 to 17 years old • Seen in ED, treated with systemic corticosteroids and subsequently discharged • Those that returned within 72 hours with continued asthma symptoms **Exclusion Criteria:** • Patients in ED for asthma exacerbation not receiving corticosteroids or IV formulation of corticosteroids • For patients with multiple return trips to the ED within 72 hours, only the first return visit was analyzed. **Covariates Identified:** • None identified
Interventions	• **Group 1:** oral prednisone or prednisolone-2 mg/kg for 3 to 5 days • **Group 2:** oral dexamethasone 0.6mg/kg given in a single dose

Outcomes	**Primary outcome(s):** • *Relapse rates of patients receiving oral dexamethasone with those receiving oral prednisone or prednisolone. **Secondary outcome(s):** • None described **Safety outcome(s):** • None *Outcomes of interest to the CMH CPG development team
Notes	**Results:** • **Group 1:** 143 cases of relapse of symptoms • **Group 2:** 21 cases of relapse of symptoms **Limitations:** • Lack of information available on patient's severity of asthma exacerbation • Lack of information on detailed asthma characteristics, patient's exposure to smoke, and flu vaccine status • Potential loss of patients that would have qualified for the study inclusion, however, may have been classified incorrectly from the International Classification of Diseases, nineth edition

References

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Appendix. Evidence to Decision for Dexamethasone

Should 1-2 doses of dexamethasone vs. 5-day course of prednisolone be used for children greater than 2 years old with an acute asthma exacerbation?	
POPULATION:	children greater than 2 years old with an acute asthma exacerbation
INTERVENTION:	1-2 doses of dexamethasone
COMPARISON:	5-day course of prednisolone
MAIN OUTCOMES:	Relapse of symptoms (1 day Dexamethasone vs. 3-5 days Prednisolone); Relapse of symptoms (1 day Dexamethasone vs. 3-5 days Prednisolone); Relapse of symptoms (1 day Dexamethasone vs. 3-5 days Prednisolone); Relapse of symptoms (2 days Dexamethasone vs. 5-6 days Prednisolone); Relapse of symptoms (2 days Dexamethasone vs. 5-6 days Prednisolone); Relapse of symptoms (2 doses Dexamethasone vs. 5 doses Prednisolone during hospitalization); Relapse of symptoms (1-3 doses Dexamethasone vs. 1-3 doses Prednisolone before hospital arrival);

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Since the last review of asthma exacerbations in pediatrics, there has been an uptick in literature measuring the efficacy of 1-2 doses of dexamethasone compared to a 5-day course of prednisolone. Dexamethasone is less expensive with a long half-life compared to prednisolone. In addition, prednisolone's poor can make compliance with a five-day course challenging, especially with children. Thus, the question becomes a priority if providers have an alternative systemic corticosteroid that demonstrates similar recovery of symptoms yet is both less expensive and requires fewer doses.	

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know	In review of all studies, the test for overall effect showed the intervention (dexamethasone) and the control (prednisolone) were effective and equivalent in reducing relapse of symptoms regardless of dosing provided.	The desired anticipated effect is substantial considering the consequences of relapse of symptoms. Relapse may lead to missed school/work, repeat ambulatory visits, repeat ED visits, or readmission.

Undesirable Effects
How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ● Moderate ○ Small ○ Trivial ○ Varies ○ Don't know	Nausea, vomiting, and GI distress are noted undesirable effects of both dexamethasone and prednisolone. Side effects (SMD 0.03; 95% CI (-0.38, 0.44) in the first 7-10 days, while rarely reported, showed no differences between the treatment groups (Rowe, B. H., Spooner, C. H., Ducharme, F. M., Bretzlaff, J. A., & Bota, G. W., 2001).	Theoretically, a longer treatment course may increase the risk of adrenal suppression. Anecdotally, the committee notes more neuropsychiatric side effects (labile mood, poor sleep) with prednisolone compared to dexamethasone.

Certainty of evidence
What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	While systemic corticosteroids are standard of care for asthma exacerbation, the overall certainty of the evidence is low to very low that dexamethasone vs prednisolone show differences in relapse of symptoms.	None identified

Values
Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	As there was no substantial difference with effect on relapse of symptoms for dexamethasone compared to prednisolone and the variability between studies reflects a 'no difference' in outcome, clinicians are left to determine best choice of corticosteroid for their setting based on ease of provision and likelihood of compliance. However, there is probably no important variability as to how much clinicians value to outcome of no relapse of symptoms.	None identified

Balance of effects
Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ● Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know	No difference in desirable or undesirable effects were found to support either dexamethasone or prednisolone within the literature reviews.	Consideration of additional effects (other than relapse of symptoms) favors the intervention (dexamethasone). Dexamethasone is easier to administer (often 1 dose in the care setting before discharge home), less expensive, and essentially eliminates the issue of non-compliance. Non-compliance with prednisolone could be related to treatment duration, poor palatability, side effects, cost and/or the process of filling the prescription.

Resources required
How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ● Moderate savings ○ Large savings ○ Varies ○ Don't know	Outside of CM, prednisolone costs for a five-day course can range from $18.00 to $48.00 compared to dexamethasone pricing for a one-to-two-day course costs $11.00 to $32.00 based on insurance and pharmacy.	Overall, dexamethasone cost for the treatment course is less than that of prednisolone. According to CM standard charges for 2022, the self-pay costs per unit are as follows: Dexamethasone 12mg/12ml oral solution - $11.77 Dexamethasone 4mg tablet - $8.29 Prednisolone 3mg/ml oral solution - $4.16 x 5 days Prednisone 10mg tab - $3.88 x 5 days Prednisone 20mg tab - $3.97 x 5 days Additional costs include the time, effort, and transportation needed to get a prednisolone prescription filled at a pharmacy, compared to receiving dexamethasone in the care setting prior to discharge.

Certainty of evidence of required resources
What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	The majority of patients will take either dexamethasone or the first dose of prednisolone in the care setting (urgent care, emergency department, inpatient) so cost for initial dosing would be the same in regard to resources of staff and staging. The only difference would be the cost in drug pricing.	None identified

Cost effectiveness
Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ● Favors the intervention ○ Varies ○ No included studies	The cost effectiveness would favor the dexamethasone (intervention) with average of $7.00 to $16.00 less, depending on insurance and pharmacy. Additional cost savings for dexamethasone include no need for time or transportation to go to a pharmacy.	None identified

Equity
What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Fifty percent to 70% of participants were either of black race or Hispanic ethnicity. Majority of initial visits were through a medical care settings' emergency department. The use of dexamethasone allows for equal efficacy (based on relapse of symptoms) without the impact of inequalities potentially posed by prednisolone. Some subpopulations may have more challenges related to transportation to a pharmacy and medication costs/medical insurance. Literacy or language barriers may impact efficacy of prescription instructions.	None identified

Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	It is acceptable to key stakeholders to use an equally effective, yet less expensive medication. Stakeholders also value the increased ease of administration (fewer doses, better palatability) of the intervention (dexamethasone) which may improve compliance.	None identified
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	The intervention is feasible to implement. It is available in CM urgent care, emergency department, and inpatient settings. The first dose of systemic corticosteroid is already given in the care setting, so the use of dexamethasone does not create additional processes. Medication access and administration of dexamethasone is more feasible than prednisolone for patients and their families.	None identified

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	Large	**Moderate**	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	**Moderate savings**	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	**Moderate**	High			No included studies
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	**Favors the intervention**	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○