Children's Mercy KANSAS CITY
Evidence Based Practice

Critically Appraised Topic (CAT): Predictors of admission for patients with Croup

Specific Care Question

In patients 6 months to 6 years of age with croup (viral laryngotracheitis) seen in an acute care setting or emergency department (ED), which patient characteristics are indicative for hospital admission (i.e., requiring an intervention once admitted rather than observation alone)?

Recommendations from the Croup CPG Committee Based on Current Literature (Best Evidence) Only

A conditional recommendation is made for use of racemic epinephrine (RE) dosing as a predictor for hospital admission requiring additional treatment (three or more doses were predictive of additional treatments to the patient once hospitalized), based on the GRADE Evidence to Decision instrument[a] and the Summary of Findings Table[a]. The overall certainty in the evidence is very low[a]. Two cohort studies support the use of RE as standard treatment for croup and demonstrate the need for admission to receive additional interventions once three or more doses of RE are provided.

A conditional recommendation is made against use of patient characteristics of age or stridor as predictors for hospital admission requiring additional treatment based on the GRADE Evidence to Decision instrument[a] and the Summary of Findings Table[a]. The overall certainty in the evidence is very low[a]. Two cohort studies demonstrate no difference using age as a predictor for hospital admission needing further intervention for croup. However, two cohort studies showed using the patient characteristic of stridor was a poor predictor for hospital admission needing further intervention.

When there is a lack of scientific evidence, standard work should be developed, implemented, and monitored.

Recommendations from the Croup CPG Committee

Following a review of additional considerations using the GRADE Evidence to Decision instrument[a] (see Appendix), a conditional recommendation is made for dosing of RE (three or more doses) as a predictor for hospital admission in need of further intervention based on feasibility, value, and compliance of all stakeholders.

Literature Summary

Background

Croup, or viral laryngotracheitis, is characterized by a barking cough and may be accompanied by hoarseness or inspiratory stridor. When severe, it may lead to respiratory distress due to upper airway obstruction (Woods, 2015). In North America, it is the second most common cause of respiratory distress in children three months to six years of age with peak incidence at 6-36 months of age (Bagwell et al., 2020). Other signs and symptoms of viral upper respiratory illness, such as rhinorrhea, can be associated with croup. However, these other symptoms are temporary in most cases and spontaneously resolve (Bjornson & Johnson, 2013).

The diagnosis of croup and assessment of the severity of symptoms are based on clinical evaluation (Bagwell et al., 2020). There is strong evidence for the use of corticosteroids and racemic epinephrine (RE), though the effect of RE only lasts 1 to 2 hours (Bjornson & Johnson, 2013; Petrocheilou et al., 2014). Although the safety of discharging a patient from the emergency department following administration of corticosteroids and one dose of RE have been established, there has been little evidence to suggest the risk stratification for two or more doses of RE (Bjornson & Johnson, 2013; Petrocheilou et al., 2014). Additional questions remain on how to determine which patients will benefit most from additional care received as an inpatient. Admissions to the hospital in which additional medical interventions (e.g., repeat RE or corticosteroids) are required represent high-value care. For admission involving observation only, it may have been more beneficial for these patients to have been discharged to home from the ED. Identifying patient characteristics that predict need for intervention once admitted may guide medical decision making prior to hospitalization. This review will summarize identified literature to answer the specific care question on the topic.

Study characteristics. The search for suitable studies was completed on April 27, 2022. Amanda Nedved, MD and Donna Wyly, MSN, RN, APRN, CPNP-AP, PPCNP-CB, ONC reviewed the 50 titles and/or abstracts found in the search and identified[b] 11 single studies believed to answer the question. After an in-depth review of the single studies[b], three cohort studies (Asmundsson et al., 2019; Elder & Rao, 2019; Hester et al., 2019) answered the question.

Race/Ethnicity
While the literature reviewed did not assess or review race or ethnicity, the content experts from the subcommittee on this review determined there are no expected differences in the relative effectiveness of the intervention for disadvantaged subgroups or different baseline conditions across disadvantaged subgroups that affect the absolute effectiveness of the intervention or the importance of the problem.

Summary by Predictor
Data Summary by Predictor (rationale for evidence certainty rating[a] provided for each predictor)

Age in Months
Two cohort studies (Asmundsson et al., 2019; Elder & Rao, 2019) measured age in months as a possible predictor for patients requiring admission for additional treatment for croup (*N* = 736). Based on the mean difference in months, age was not a predictor for receipt of additional treatment while an inpatient, the *MD = 0.62,* 95% CI [-1.89, 0.64], *p = .01*, (see Figure 2 & *Table 1*).

Certainty Of The Evidence For Age In Months. The certainty of the body of evidence was very low. The body of evidence was assessed to not have serious risk of bias, nor serious indirectness, or serious imprecision, however, serious inconsistency was assessed. Inconsistency was serious due to a substantial heterogeneity of 83 percent.

Stridor
Two cohort studies (Elder & Rao, 2019; Hester et al., 2019) measured stridor as a possible predictor for patients requiring admission for additional treatment for croup (*N* = 696). Based on the odds ratio, stridor was not a predictor for receipt of additional treatment while an inpatient, the *OR = 4.89,* 95% CI [2.45, 9.74], *p = .00001*, (see Figure 3 & *Table 1*).

Certainty Of The Evidence For Stridor. The certainty of the body of evidence was very low. The body of evidence was assessed to not have serious risk of bias, nor serious inconsistency, or serious indirectness, however, serious imprecision was assessed. Imprecision was serious due to a low number of events.

One dose of racemic epinephrine
Two cohort studies (Asmundsson et al., 2019; Hester et al., 2019) measured one dose of RE as a possible predictor for patients requiring admission for additional treatment for croup (*n* = 1,216). Based on the odds ratio, one dose of RE was not a predictor for receipt of additional treatment while an inpatient, the *OR = 0.80,* 95% CI [0.56, 1.15], *p = .23*, (see Figure 4 & *Table 1*).

Certainty Of The Evidence For One Dose Of Racemic Epinephrine. The certainty of the body of evidence was very low. The body of evidence was assessed to not have serious risk of bias, nor serious inconsistency, or serious indirectness, however, serious imprecision was assessed. Imprecision was serious due to a low number of events.

Two doses of racemic epinephrine

Two cohort studies (Asmundsson et al., 2019; Hester et al., 2019) measured two doses of RE as a possible predictor for patients requiring admission for additional treatment for croup (*n* = 1,216). Based on the odds ratio, two doses of RE was not a predictor for receipt of additional treatment while an inpatient, the *OR = 0.79,* 95% CI [0.58, 1.06], *p = .12*, (see Figure 4 & *Table 1*).

> **Certainty Of The Evidence For Two Doses of Racemic Epinephrine.** The certainty of the body of evidence was very low. The body of evidence was assessed to not have serious risk of bias or serious indirectness, however, serious inconsistency and serious imprecision was assessed. Inconsistency was serious due to a moderate heterogeneity of 69 percent and imprecision was serious due to a low sample size.

Three doses of racemic epinephrine

Two cohort studies (Asmundsson et al., 2019; Hester et al., 2019) measured three doses of RE as a possible predictor for patients requiring admission for additional treatment for croup (*n* = 1,216). Based on the odds ratio, three doses of RE was a predictor for receipt of additional treatment while an inpatient, the *OR = 1.78,* 95% CI [1.18, 2.69], *p = .006*, (see Figure 4 & *Table 1*).

> **Certainty Of The Evidence For Three Doses of Racemic Epinephrine.** The certainty of the body of evidence was very low. The body of evidence was assessed to not have serious risk of bias, nor serious inconsistency, or serious indirectness, however, serious imprecision was assessed. Imprecision was serious due to a low number of events.

Potential predictors found in the literature but not reviewed	**Reason not analyzed**
Gender	Provided as demographic data
Tachycardia	Provided as baseline demographic
Tachypnea	Provided as baseline demographic
Fever	Not identified by the CPG committee
Oxygen saturation <92%	Not identified by the CPG committee
Croup score	Not identified by the CPG committee
History of prematurity	Not identified by the CPG committee
Time in ED to dose of Decadron given	Data available in only one study

Identification of Studies

Search Strategy and Results (see Figure 1)

1)'laryngotracheobronchitis'/exp OR laryngotracheobronchitis OR 'laryngotracheitis'/exp OR laryngotracheitis OR 'croup'/exp OR croup,
2) 'emergency care'/exp OR 'emergency care' OR 'emergency ward'/exp OR 'emergency ward' OR 'urgent care'/exp OR 'urgent care' OR 'emergency health service'/exp OR 'emergency health service' OR 'emergency department'/exp OR 'emergency department' OR 'ambulatory care'/exp OR 'outpatient department'/exp OR 'ambulatory care' OR 'outpatient department',
3) 'hospital admission'/exp OR 'hospital admission' OR 'treatment outcome'/exp OR 'treatment outcome' OR 'outcome'/exp OR 'outcome' OR 'patient assessment'/exp OR 'patient assessment' OR 'treatment failure'/exp OR 'treatment failure' OR 'time factor'/exp OR 'time factor',
4) 'racemic epinephrine' OR 'racephedrine'/exp OR racephedrine OR 'epinephrine'/exp OR epinephrine OR 'nebulised adrenaline',
5) #3 OR #4
6) #1 AND #2 AND #5
7) #6 AND ([child]/lim OR [infant]/lim OR [preschool]/lim) AND ('article'/it OR 'article in press'/it OR 'review'/it) AND (2016:py OR 2017:py OR 2018:py OR 2019:py OR 2020:py OR 2021:py OR 2022:py)
8) #7 AND (2016:py OR 2017:py OR 2018:py OR 2019:py OR 2020:py OR 2021:py OR 2022:py)

Records identified through database searching *n* = 50
Additional records identified through other sources *n* = 0

Studies Included in this Review

Citation	Study Type
*Asmundsson (2019)	cohort
*Elder & Rao (2019)	cohort
*Hester (2019)	cohort

Studies marked with an asterisk are included in the meta-analysis

Studies Not Included in this Review with Exclusion Rationale

Citation	Reason for exclusion
Bagwell (2020)	Wrong comparison
Chiang (2019)	Wrong comparison
Hanna (2019)	Wrong comparison
Maalouli & Hodges (2021)	Wrong comparison
Smith (2018)	Wrong outcome
Syamkumar (2022)	Wrong comparison
Yang (2017)	Wrong outcome
Yang (2019)	Wrong outcome

Methods Used for Appraisal and Synthesis

[a]The GRADEpro Guideline Development Tool (GDT) is the tool used to create the Summary of Findings (SOF) table(s) for this analysis. Using the GDT, the author of this CAT rates the certainty of the evidence based on four factors: *within-study risk of bias*, *consistency among studies, directness of evidence*, and *precision of effect estimates*. Each factor is subjectively judged against the author's confidence of the estimated treatment effect. Confidence is assessed as not serious, serious or very serious. If the attribute of serious or very serious is assessed, the author will provide an explanation.

[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

[c]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

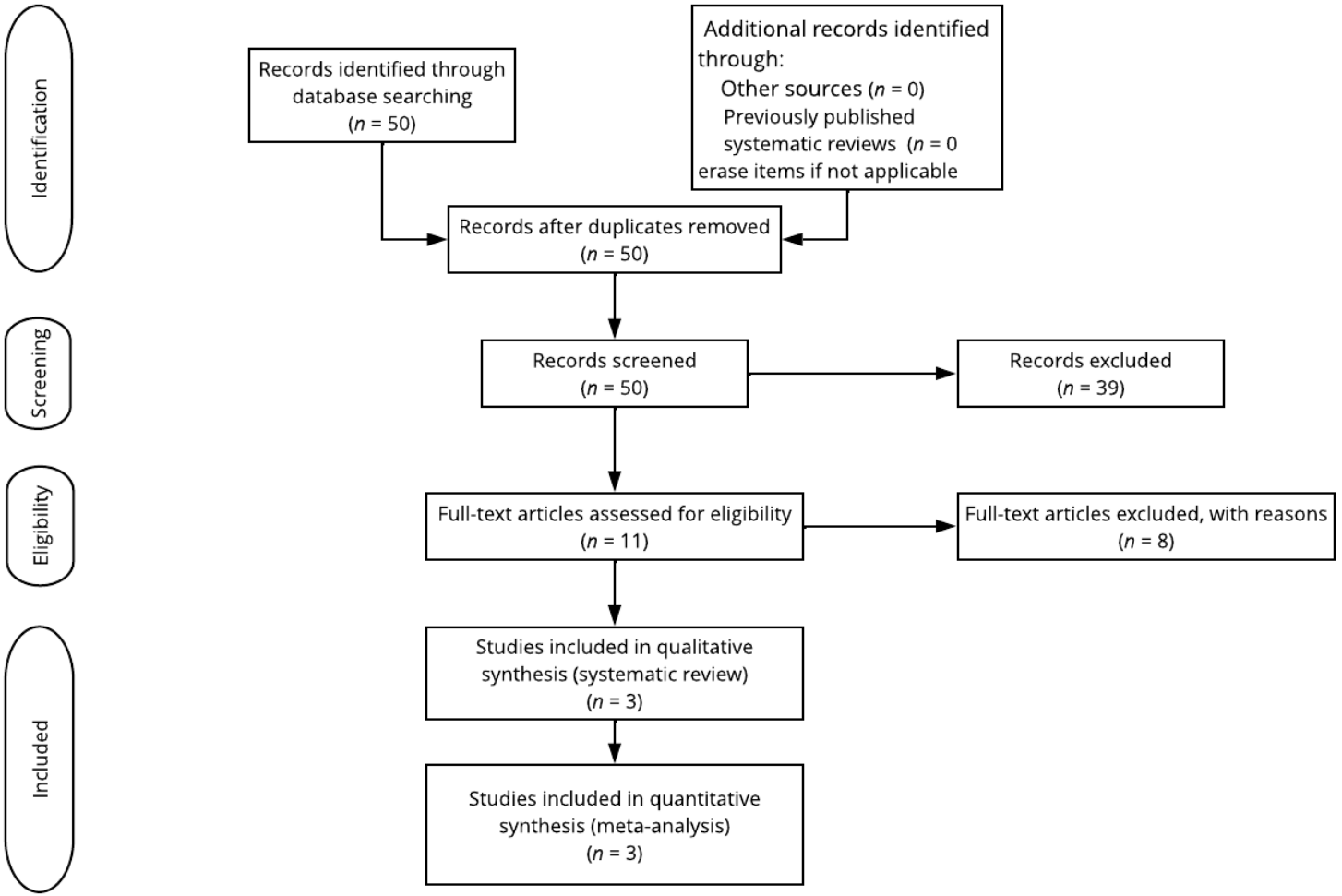
Acronym	Explanation
AGREE II	Appraisal of Guidelines Research and Evaluation II
CAT	Critically Appraised Topic
EBP	Evidence Based Practice
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RE	Racemic Epinephrine

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
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(s)
Table 1
Summary of Findings Table[a]: Predictors of admission requiring additional interventions

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With observation	With intervention		Risk with observation	Risk difference with intervention
Age in months											
682 (2 observational studies)	not serious	serious[a]	not serious	not serious	none	⨁◯◯◯ Very low	530	152	-	The mean age in months was **0**	MD **0.62 lower** (1.89 lower to 0.64 higher)
Stridor											
502 (2 observational studies)	not serious	not serious	not serious	serious[b]	none	⨁◯◯◯ Very low	52/410 (12.7%)	23/92 (25.0%)	**OR 4.89** (2.45 to 9.74)	127 per 1,000	**288 more per 1,000** (from 136 more to 459 more)
Doses of racemic epinephrine before admission - One dose RE											
1022 (2 observational studies)	not serious	not serious	not serious	serious[b]	none	⨁◯◯◯ Very low	205/798 (25.7%)	50/224 (22.3%)	**OR 0.80** (0.56 to 1.15)	257 per 1,000	**40 fewer per 1,000** (from 95 fewer to 28 more)
Doses of racemic epinephrine before admission - Two doses of RE											
1022 (2 observational studies)	not serious	serious[c]	not serious	serious[d]	none	⨁◯◯◯ Very low	486/798 (60.9%)	123/224 (54.9%)	**OR 0.79** (0.58 to 1.06)	609 per 1,000	**57 fewer per 1,000** (from 134 fewer to 14 more)
		Inconsistency	**Indirectness**	**Imprecision**	**Publication bias**	**Overall certainty**	**Study event rates (%)**		**Relative effect**	**Anticipated absolute effects**	

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	**Risk of bias**					**of evidence**	**With observation**	**With intervention**	**(95% CI)**	**Risk with observation**	**Risk difference with intervention**
Doses of racemic epinephrine before admission - Three doses of RE											
1022 (2 observational studies)	not serious	not serious	not serious	serious[b]	none	⨁◯◯◯ Very low	89/798 (11.2%)	40/224 (17.9%)	**OR 1.78** (1.18 to 2.69)	112 per 1,000	**71 more per 1,000** (from 17 more to 141 more)

Notes

a. Substantial heterogeneity
b. Low number of events
c. Moderate heterogeneity
d. Low sample size

Meta-analysis(es)

Figure *2*
Comparison: Additional intervention vs. observation only after admission, Predictor: Age in months

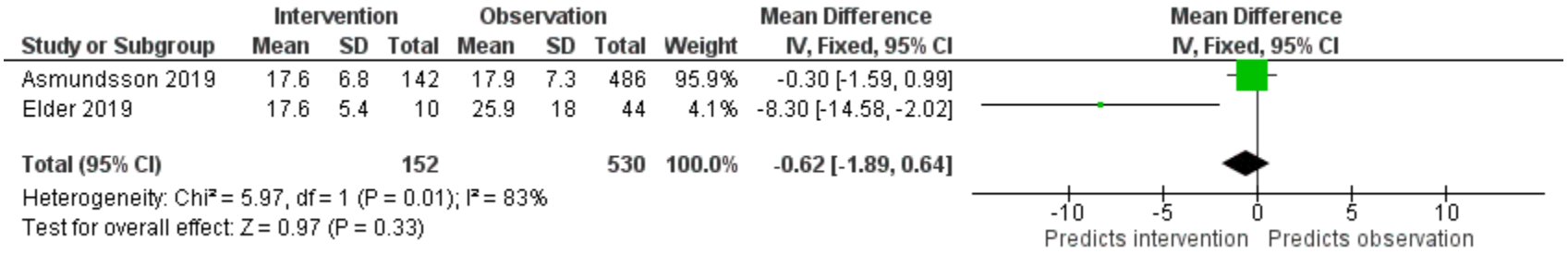


Figure *3*
Comparison: Additional intervention vs. observation only after admission, Predictor: Stridor

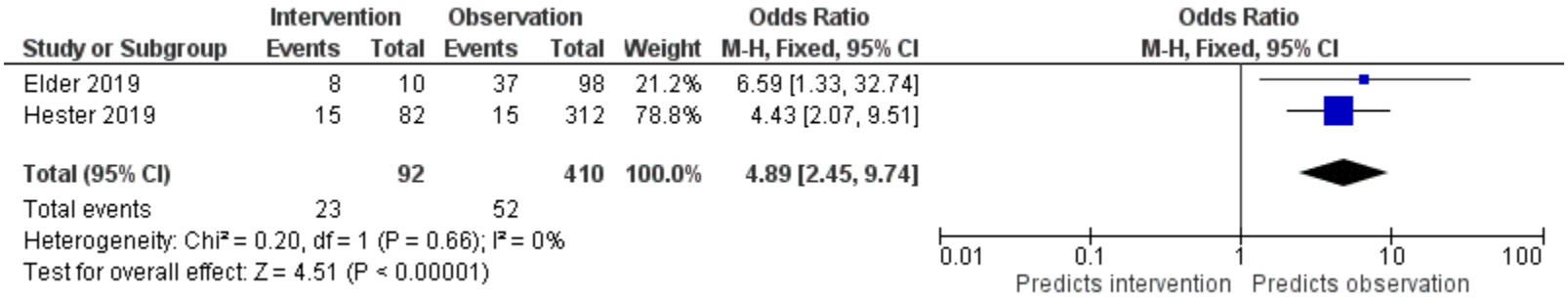
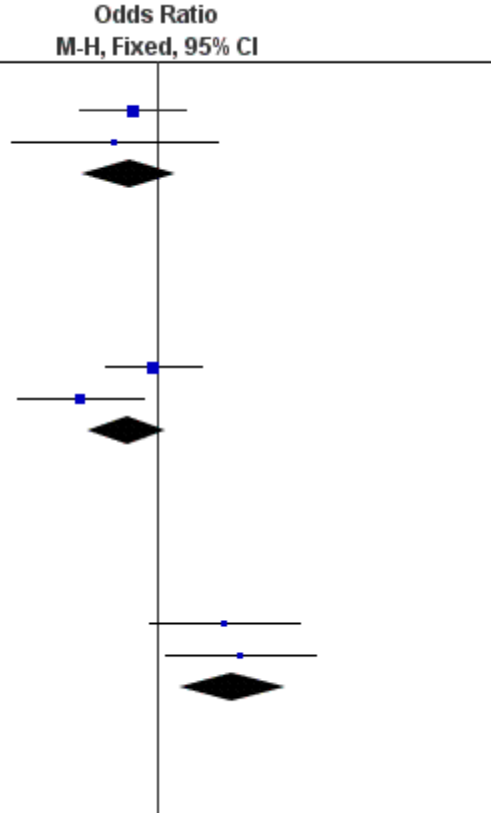


Figure *4*

Comparison: Additional intervention vs. observation only after hospital admission, Predictor: Doses of racemic epinephrine

Study or Subgroup	Intervention Events	Intervention Total	Observation Events	Observation Total	Weight	Odds Ratio M-H, Fixed, 95% CI
2.1.1 One dose RE						
Asmundsson 2019	42	142	164	486	26.8%	0.82 [0.55, 1.24]
Hester 2019	8	82	41	312	7.9%	0.71 [0.32, 1.59]
Subtotal (95% CI)		**224**		**798**	**34.7%**	**0.80 [0.56, 1.15]**
Total events	50		205			
Heterogeneity: Chi² = 0.10, df = 1 (P = 0.75); I² = 0%						
Test for overall effect: Z = 1.21 (P = 0.23)						
2.1.2 Two doses of RE						
Asmundsson 2019	81	142	281	486	28.0%	0.97 [0.66, 1.41]
Hester 2019	42	82	205	312	21.4%	0.55 [0.34, 0.90]
Subtotal (95% CI)		**224**		**798**	**49.4%**	**0.79 [0.58, 1.06]**
Total events	123		486			
Heterogeneity: Chi² = 3.24, df = 1 (P = 0.07); I² = 69%						
Test for overall effect: Z = 1.58 (P = 0.12)						
2.1.3 Three doses of RE						
Asmundsson 2019	19	142	41	486	8.2%	1.68 [0.94, 2.99]
Hester 2019	21	82	48	312	7.6%	1.89 [1.06, 3.39]
Subtotal (95% CI)		**224**		**798**	**15.9%**	**1.78 [1.18, 2.69]**
Total events	40		89			
Heterogeneity: Chi² = 0.08, df = 1 (P = 0.77); I² = 0%						
Test for overall effect: Z = 2.75 (P = 0.006)						



Characteristics of Intervention Studies
Asmundsson et al., 2019

Methods	Multicenter, cross-sectional observational study based on retrospective chart review
Participants	**Setting:** USA, Minnesota, three pediatric tertiary care children's hospitals, March 2011 to September 2015 **Number enrolled into study:** *N* = 628 • **Group 1, Patients with no significant interventions** *n* = 486 • **Group 2, Patients with significant intervention** *n* = 142 **Gender, males (as defined by researchers):** • **Group 1:** *n* = (%) 321 (66.0) • **Group 2:** *n* = (%) 82 (57.7) **Race / ethnicity or nationality (as defined by researchers):** No information **Age, mean/median (SD), months** • **Group 1:** 17.9/17.1 (7.3) • **Group 2:** 17.6/16.5 (6.8) **Inclusion Criteria:** • Evaluated by the participating ED • Treated with at least 1 RE dose • Age 6 months to 5 years • Admitted to the hospital **Exclusion Criteria:** • History of congenital anomalies of the airway • Previous tracheal surgery • Required supplemental oxygen in the ED due to saturation < 90% • Patients directly admitted to the pediatric intensive care unit (ICU) **Covariates Identified:** This study took place in Minnesota; croup tends to be worse in the winter.
Interventions	**Group 1:** Patient admitted to the hospital for croup, no significant intervention after hospital admission **Group 2:** Patient admitted to hospital for croup, patient required one or more significant interventions: • More than 1 RE treatments • Helium-oxygen (Heliox) use • PICU transfer after hospital admission

Outcomes	**Primary outcome(s)/predictors:** • Tachycardia • Tachypnea • Fever (>/= 38°C) • Abnormal pulse oximetry (<95% on room air) • Doses of RE **Secondary outcome(s):** • Significant interventions (any number of inpatient RE doses, Heliox treatment, transfer to pediatric ICU) **Safety outcome(s):** • None reported
Notes	**Results:** • Of the patients admitted, those that received significant interventions demonstrated age-defined tachypnea (83.9%) in the ED compared to those that did not receive any significant interventions (68.9%) p = < .0012. • Of the patients admitted, those that received significant interventions demonstrated age-defined tachycardia (55.1%) compared to those that did not receive any significant interventions (45.5%) p = 0.483. • ED temperature ≥ 38°C and O_2 saturation did not demonstrate significant differences between the two groups of admitted patients (p = .843 and .728, respectively). • Authors report that tachypnea in the ED and use of radiograph were associated with an increased use of significant interventions **Limitations:** • Of the 628 patients, 40 had multiple visits during the study period, of which, one visit was randomly selected to be in the study. • The number of ED initial vitals is <628 because of missing data for some patients • It is unclear if the need for radiograph equaled causation for or correlation with the need for hospital admission • The authors did not report race or ethnicity data

Elder & Rao, 2019

Methods	Cohort, retrospective

Participants	**Participants:** Patients between 6 months and 6 years of age (inclusive) who presented to the ED with croup and had received two doses of nebulized adrenaline within the ED or prior to arrival.
	Setting: Single tertiary pediatric referral hospital in Sydney, Australia between January 2011 and August 2016
	Number enrolled into study: *N* = 108
	• **Group 1, Admit intervention:** *n* = 10
	• **Group 2, Admit no intervention + ED discharge:** *n* = 98
	Gender, males (%):
	• **Group 1:** *n* = 6 (60)
	• **Group 2:** *n* = 75 (77)
	Race / ethnicity or nationality (as defined by researchers):
	• Not reported
	Age, mean in months (SD)
	• **Group 1:** 17.6 (5.4)
	• **Group 2:** 29.4 (16.1)
	
	Inclusion Criteria:
	• Patients aged 6 months to 6 years
	• Must have received 2 doses of nebulized adrenaline within the ED or prior to arrival
	• Diagnosis of croup
	
	Exclusion Criteria:
	• Patients were excluded from the study if they received further medical interventions within 2 hours of the second dose of adrenaline including:
	  ○ Supplemental oxygen
	  ○ Intravenous (IV) fluids
	  ○ Respiratory support
	  ○ Salbutamol administered more frequently than every 3 hours
	
	Covariates Identified:
	• History of chronic medical condition

Interventions	**Both: 2 doses of nebulized adrenaline in the ED or prior to arrival**
	• **Group 1: Admit and additional interventions required including:**
	  ○ Additional doses of nebulized adrenaline (10/10 patients)
	  ○ IV antibiotics (2/10 patients)
	  ○ IV steroids (1/10 patients)
	  ○ Admission to ICU (1/10 patients)
	• **Group 2: No additional interventions**

Outcomes	**Primary outcome(s):**
	• Factors which may predict need for further interventions in children with croup:
	  ○ Heart rate
	  ○ Respiratory rate
	  ○ Fever (temperature > 38° Celsius)
	  ○ Stridor at rest
	
	Secondary outcome(s):
	• None requested
	
	Safety outcome(s):
	• None requested

Notes	**Results:** • Authors concluded older patients with no history of a chronic medical condition who have a normal heart rate, temperature and no evidence of stridor at rest two hours after the second dose of adrenaline may be suitable for outpatient management • Patients who were discharged from the ED (the 'ED discharge' group) were significantly older (*M* age 32.3 ± 14.0 months vs. 25.9 ± 18.0 months for the 'Admit no-intervention' group and 17.6 ± 5.4 months for the 'Admit intervention' group, $p = .010$) and were less likely to have a chronic medical condition (9% for both the 'Admit no-intervention' group and ED discharge group vs. 50% for the 'Admit intervention' group, $p = .001$). **Limitations:** • Small sample size • Single center • Retrospective review • Subjective outcomes (work of breathing/stridor)

Hester, 2019

Methods	Cohort, retrospective
Participants	**Participants:** Children ages 3 months to 8 years **Setting:** 430 bed tertiary children's hospital **Number enrolled into study:** *N* = 588 • **Group 1, admitted inpatient with no inpatient airway intervention:** *n* = 312 • **Group 2, admitted inpatient airway intervention:** *n* = 82 • **Group 3, discharged from emergency department (ED):** *n* = 194 **Gender, males (as defined by researchers):** • **Group 1:** *n* = 205 (65.7%) • **Group 2:** *n* = 48 *(58.5%)* • **Group 3:** *n* = 129 (66.5%) **Race / ethnicity or nationality (as defined by researchers):** • See Table 1: Race **Age, median in months, (IQR):** Statistically significant differences in pairwise comparisons. Significance was adjusted for multiple comparisons using Holm-Sidak • **Group 1:** *n* = 17 (10.5-25) • **Group 2:** *n* = 16.5 (11-25) • **Group 3:** *n* = 24 (14-43) **Inclusion Criteria:** • Patients aged 3 months to 8 years with an ED, observation, or inpatient encounter (observation/inpatient) **Exclusion Criteria:** • Patients <3 months of age • Patients with diagnosis of asthma/bronchiolitis/pneumonia • Patients with an alternate primary reason for stridor (e.g., post extubation). • Patients directly admitted to the ICU • Complex Chronic Condition • Concurrent ICD for asthma/bronchiolitis • Repeat visit within 7 days • Diagnosed with non-croup illness **Covariates Identified:** • All demographic covariates in the final adjusted model • Because it represented the largest group, used 2 eRE doses as the reference group in the multivariate model
Interventions	• **Group 1:** admission without airway intervention

	• **Group 2:** admission with airway intervention • **Group 3:** discharged from ED
Outcomes	**Primary outcome(s):** • To describe initial RE use, including doses at an outside hospital (OSH) and the ED • Admission decisions for patients presenting with croup at a large children's hospital **Secondary outcome(s):** • Describe the rate of inpatient RE (IRE)/inpatient airway interventions (IAIs) in patients with croup in the ED and inpatient settings • Examine potential factors associated with IRE/IAI in admitted patients **Safety outcome(s):** • To provide a more comprehensive assessment of croup outcomes after initial stabilization at an OSH or ED to be used by clinicians in admission decision making
Notes	**Results:** • Of admitted patients, 20.8% (82/394) had IRE and/or IAI, most commonly additional RE (20.6%, 81/394). • Only 3 patients (0.76%, 3/394) had IAI; 2 required oxygen and 1 required ICU transfer. • No patients required Heliox, intubation, or died. • Overall, 3 patients (3/588 [0.5%]) were treated with antibiotics for suspected concurrent bacterial tracheitis. • Of the sample of patients initially discharged from the ED, 3 had ED revisits within 24 hours: 1 of whom received an additional single RE dose, 2 of whom received no further treatments, and none of whom were readmitted. • Admitted patients without IAI had a 3.1 times greater median cost than patients discharged from the ED. **Limitations:** • Reflects practice at a single tertiary children's hospital and thus results may not be generalizable. • Unable to incorporate standardized respiratory scores (e.g., Westley score); therefore, indications for RE or admission were unknown. • Alternative reasons for admission, such as dehydration, or family preferences were not assessed. • Patients discharged from the ED were, by definition, not able to have an outcome of IRE/IAI. • Dosing for OSH medications was not verified. • This study was underpowered to detect differences in variables of low frequency, such as certain demographic or medical history categories. • To focus on patients whose disposition decision in the ED was discharge vs. hospital admission, excluded patients whose initial disposition was ICU.

References

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Appendix
Evidence to Decision for Croup Predictors

Should intervention vs. observation be used for patients 6 months to 6 years with a dx of croup based on patient characteristics or doses of racemic epinephrine?	
POPULATION:	patients 6 months to 6 years with a dx of croup based on patient characteristics or doses of racemic epinephrine
INTERVENTION:	intervention
COMPARISON:	observation
MAIN OUTCOMES:	Age in months; Stridor; Doses of racemic epinephrine before admission - One dose RE; Doses of racemic epinephrine before admission - Two doses of RE; Doses of racemic epinephrine before admission - Three doses of RE;

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 Croup in children 6 months to 6 years of age, there has been additional literature reviewing the management of the disease while in the ED. There is strong evidence for the use of corticosteroids and racemic epinephrine (RE), though the effect of RE only lasts 1-2 hours (Bjornson & Johnson, 2013; Petrocheilou et al., 2014). Although the safety of discharging a patient from the emergency department (ED) following administration of corticosteroids and one dose of racemic epinephrine (RE) have been established, there has been little evidence to suggest the risk stratification for two or more doses of RE (Bjornson & Johnson, 2013; Petrocheilou et al., 2014). Thus, the question becomes a priority if we can determine an effective course of management when additional doses of RE are necessitated.	Unnecessary hospitalizations are a major burden to patients, patients' families, and the hospital system. However, unplanned return visits with or without need for subsequent hospitalization are also problematic.
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small ○ Moderate • **Large**	For one and two doses of RE, the literature demonstrates use of one to two doses of RE as a predictor for hospitalization with additional treatment as unreliable ($p = 0.23$ *and* 0.12, respectively).	Avoiding unnecessary admissions has a substantial effect on all parties.

○ Varies ○ Don't know	For three doses of RE, the literature indicates use of three doses of RE as a predictor for hospitalization with additional treatment as favorable (*p = 0.006*).	
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
• **Large** ○ Moderate ○ Small ○ Trivial ○ Varies ○ Don't know	Undesirable effects of using age, stridor or RE doses as predictors for hospital admission for additional treatment include: 1. Pt. discharged too early from ED returns needing additional treatment or is then admitted. 2. Pt admitted but only needed longer observation In a study by Udoh et al. (2022), only 8% (3/294) of children returned to the ED for recurrence of Croup symptoms if they were initially observed in the ED for greater than 2 hours prior to discharge.	Not hospitalizing when it would be beneficial may lead to clinical deterioration and return visits, though this is rare. Providing more doses of RE in the ED or UC settings requires more time spent in that location with at least 2 hrs. of observation following each administration. This can impact patient throughput. UC closes in 1700, therefore transfer to the ED may be needed. If the patient is ultimately admitted that extra transfer may have been avoided. Would add return visit numbers from the newer article you discussed.
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 using doses of RE as predictors for hospital admission for additional treatment, the overall certainty of evidence is very low that three doses or more of RE in the ED indicates need for hospital admission to receive additional intervention/treatment. Some of the undesirable effects of admitting a patient with Croup is that they end up only needing more observation vs. medical/medicinal treatments.	
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 one to two doses of RE showed no substantial predictive value in hospitalization with additional treatment, three or more doses did predict and support hospital admission for patient to receive additional treatment.	Providers and patients' families share similar values about the need to carefully consider admission, avoiding admission for those unlikely to need additional treatments. However, comfort with the uncertainty varies significantly.
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**	Not provided by the available research evidence.	
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	Estimate costs for hospitalization for Croup without any additional interventions (one article shows costs differences and will report that here). Can we also include what it would cost through CM? Cost analysis from Bagwell et al., 2020 demonstrates cost of ED patients d/c from EDs with dx of croup and received both dexamthasone and RE, 2004-2014 compared to patients with dx of croup admitted to the hospital and received both dexamethasone and RE: 1. ED patients mean adjusted billed charges (SE): single dose RE- $1,525.9 (5.4); multidose RE - $4,357.1 (67.8) 2. Admitted patients mean adjusted billed charges (SE): single does RE - $9,800.3 (335.2); multidose RE - $23,460.1 (880.9)	Beyond monetary cost savings, additional cost savings for the family may include decreased stress, less time away from work, and less time away from other children. Additional cost savings for the hospital include increased bed availability and avoidance of insurance denials for admissions requiring observation only. While likely outweighed by above, increased costs may be increased time in the ED or UC.

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 cost differences would be most significant when moving a patient from the ED to the inpatient setting. Cost analysis from Bagwell et al., 2020 demonstrates cost of ED patients d/c from EDs with dx of croup and received both dexamthasone and RE, 2004-2014 compared to patients with dx of croup admitted to the hospital and received both dexamethasone and RE: 1. ED patients mean adjusted billed charges (SE): single dose RE- $1,525.9 (5.4); multidose RE - $4,357.1 (67.8) 2. Admitted patients mean adjusted billed charges (SE): single does RE - $9,800.3 (335.2); multidose RE - $23,460.1 (880.9)	
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	Favors RE doses as a predictor of hospitalization with additional treatments.	Avoiding unnecessary admission by waiting until a patient requires a third dose of RE is likely more cost effective than admitting at 1-2 doses of RE when no additional medical treatments may be needed.
Equity What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced	**Bagwell et al., 2020** Single dose RE Multi dose RE	Hospitalization may be a greater burden for families with challenges related to

○ Probably no impact ○ Probably increased ○ Increased ○ Varies • **Don't know**	White 57,081 (65.4%) 4776 (59.1%) Black 11,982 (13.7%) 1584 (19.6%) Other 13,405 (15.4%) 1303 (16.1%) **Hester et al., 2019** D/c from ED Admit, no airway intervention Admit, airway intervention White 99 (51%) 166 (53.2%) 38 (46.3%) Black 30 (15.5%) 57 (18.3%) 13 (15.9%) Asian 15 (7.7%) 34 (10.9%) 15 (18.3%) Hispanic/Latino 23 (11.9%) 19 (6.1%) 5 (6.1%) **Maalouli, 2022** Admit not needed Admit needed Asian 204 (7.1%) 6 (8.8%) Black 516 (18%) 10 (15%) Hispanic/Latino 264 (9.2%) 2 (2.9%) White 1409 (49%) 41 (60%)	transportation, childcare for other children, employment, access to FMLA, etc. Hispanics are more likely to be discharged vs. admitted per the data.

Acceptability
Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no • **Probably yes** ○ Yes ○ Varies ○ Don't know	Not provided by the available research evidence.	Providing additional RE in the ED or UC setting with longer observation in effort to avoid admission if possible is likely acceptable to providers and patients' families. However, it does require more time to determination of disposition which may be tolerated more by some stakeholders than others.

Feasibility
Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no • **Probably yes** ○ Yes ○ Varies ○ Don't know	Not provided by the available research evidence.	Providing additional RE in the ED or UC setting with longer observation is feasible. One barrier is time, particularly if the UC is closing.

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
○	○	○	●	○