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Croup: Observation Time Post Racemic Epinephrine Dosing in Children with Croup

Children's Mercy Kansas City

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Evidence Based Practice

Critically Appraised Topic (CAT): Observation Time Post Racemic Epinephrine Dosing in Children with Croup

Specific Care Question

In children with croup, is observation time post racemic epinephrine (RE) dosing of two hours versus three or more hours efficacious in preventing treatment failure?

Recommendations from the Croup Care Process Model (CPM) Committee Based on Current Literature

While the Croup CPM Committee recommends a two-hour observation period following the administration of a racemic epinephrine dose (0.5 ml of 2.5% solution via nebulizer) in the emergency department, urgent care clinic, or inpatient settings at Children's Mercy, the committee is unable to recommend for an extended observation period beyond two hours per racemic epinephrine dose, based on the Summary of Outcomes Tables (see Table 1 and Table 2). The overall certainty in the evidence is very low[a].

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

Additional Considerations

While the literature does not support a specific time frame for observation following racemic epinephrine dosing, the Croup CPM Committee recognizes the duration of action for racemic epinephrine is approximately 1.5 hours and that the risk and benefits of prolonged observation must be considered. Prolonged observation time may increase healthcare exposure without necessarily improving the value of care, but truncated observation time may lead to unnecessary hospitalizations. Therefore, the committee recommends a two-hour observation window. In addition, clinicians use clinical reasoning to evaluate a patient's status, including persistent stridor, tachypnea, work of breathing, malaise, and fatigue to comprehensively address the individualized patient's needs.

Literature Summary

Background

Croup, also known as viral laryngotracheitis, is a respiratory infection that affects infants and children three months to six years of age (Bagwell et al., 2020). The clinical presentation often associated with croup is a barking cough, inspiratory stridor, and hoarseness of voice (Cuppari et al., 2022). While many children diagnosed with croup typically demonstrate symptoms that can be managed on an outpatient basis, those children whose symptoms are accompanied by moderate to severe respiratory distress often require hospital admission (Cuppari et al., 2022).

Signs of respiratory distress associated with moderate to severe illness that warrant medical attention are inspiratory stridor at rest, tachypnea, moderate to severe retractions, and hypoxemia in severe cases (Asmundsson et al., 2019). For children with moderate to severe illness, the administration of RE in addition to corticosteroids, specifically dexamethasone, has proven to be an effective short-term treatment; however, there is continued discussion on the appropriate observation time frame following RE dose administration (Rudinsky et al., 2015). Rudinsky et al. (2015) suggested a minimum two-hour observation period following RE dose administration before discharge be considered from the emergency room or an urgent care clinic. Furthermore, Rudinsky et al. (2015) concluded that early medical management (corticosteroid administration) and varying observation periods (two to six hours) following RE administration facilitate outpatient management of croup, reducing the need for hospitalization. Yet, an optimal observation time frame post RE administration for children with croup remains unclear. This review will summarize identified literature to answer the specific care question.

Study characteristics. The search for suitable studies was completed on July 7, 2022. K. Berg, MD and A. Melanson, OTD, OTR/L reviewed the 42 titles and abstracts found in the search and identified[b] 10 single studies believed to answer the question. After an in-depth review of the single studies[b] (Smith et al., 2018; Udoh et al., 2022), two answered the question.

Race/Ethnicity

The literature reviewed did not assess or review race or ethnicity. However, the Croup CPM Committee for this review determined there are no expected differences in the relative effectiveness of the intervention for disadvantaged subgroups. The Croup CPM Committee found no differences in baseline conditions across disadvantaged subgroups that affect the absolute efficacy of the intervention or the importance of the problem.

Question Answered. In children with croup, is observation time post RE dosing of two hours versus three or more hours efficacious in preventing treatment failure?

Smith et al. (2018) completed a retrospective cohort review (*N* = 428) of children with croup following a single RE dose administered in the emergency department of a pediatric hospital. Of the 428 children included in the review, *n* = 163 children were observed for a period of 2.1 to 3 hours, *n* = 136 children were observed for a period of 3.1 to 4 hours, *n* = 92 children were observed for 2 or fewer hours, and *n* = 37 children were observed for greater than 4 hours. Observation time was defined as the time following RE dose administration until the child was discharged from the emergency department or until the child required admittance to the hospital. The study investigators analyzed treatment failure identified as the child requiring a second dose of RE resulting in hospitalization, as indicated by hospital protocol, or the child returned for follow-up care within 24 hours following discharge. Children with observation times of less than 2.1 hours and greater than 4 hours were considered separately. Therefore, limited data was reported for these groups.

Udoh et al. (2022) completed a retrospective cohort review (*N* = 294, 276 unique) of children less than or equal to 12 years of age diagnosed with croup who received RE and were discharged from the emergency department. Of the 294 emergency department visits, *n* = 132 children were observed for less than one hour, *n* = 123 children were observed for 1 to 2 hours, and *n* = 39 children were observed for greater than 2 hours following RE dose administration. Observation time was defined as the time from administration of the first dose of RE until the time of discharge by the clinician. The study investigators analyzed treatment failure, which was described as the need to return for additional care (emergency room, urgent care, or primary care) due to persistent symptoms within 48 hours following emergency department discharge.

Variation across the two studies and missing data limited the ability to make likened comparisons. As a result, a meta-analysis could not be performed to determine the consistency between intervention effects across the studies. Therefore, each study was evaluated separately.

Summary by Outcome

Treatment Failure

Smith et al. (2018) measured treatment failure (hospital admission, child requiring a second dose of RE resulting in hospital admission, return for follow-up care within 24 hours following discharge) when comparing observation times following RE administration, *n* = 299 (subgroup primarily analyzed). For the outcome of treatment failure, the *OR* indicated the intervention of 2.1 to 3 hours observation time following RE dose administration was unfavorable to the comparator of 3.1 to 4 hours observation time following RE dose administration, *OR* = 2.20, 95% CI [1.28, 3.79], *p* = .004 (see *Table 1).*

Udoh et al. (2022) measured treatment failure for which return for additional care within 48 hours was required following discharge when comparing observation times following RE administration, *N* = 294. For the outcome of treatment failure, the *OR* indicated the intervention of 1- to 2- hour observation times following RE dose administration was not different to the comparator of greater than 2-hour observation times following RE dose administration, *OR* = 0.72, 95% CI [0.18, 2.95], *p* = .65 (see *Table 2).*

Certainty of the Evidence for Treatment Failure. The certainty of the body of evidence was very low. The body of evidence was assessed to not have serious risk of bias or indirectness, but serious imprecision. The two studies were assessed to have serious imprecision due to the limited number of events (*n* = 94) and participants (*N* = 593). While each study (Smith et al., 2018; Udoh et al., 2022) addressed the question, the studies were analyzed separately, and consistency could not be assessed.

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) 'racemic epinephrine' OR 'racephedrine'/exp OR racephedrine OR 'epinephrine'/exp OR epinephrine OR 'nebulized adrenaline'
4) #1 AND #2 AND #3
5) #4 AND ([child]/lim OR [infant]/lim OR [preschool]/lim) AND ('article'/lit OR 'article in press'/it OR 'review'/it) AND (2015:py OR 2016:py OR 2017:py OR 2018:py OR 2019:py OR 2020:py OR 2021:py OR 2022:py)

Search Dates: 2015-Current
Records identified through Embase database searching *n* = 42
Additional records identified through other sources *n* = 0

Studies Included in this Review

Citation	Study Type
Smith et al. (2018)	Retrospective cohort
Udoh et al. (2022)	Retrospective cohort

Studies Not Included in this Review with Exclusion Rationale

Citation	Reason for exclusion
Bagwell et al. (2020)	Investigated RE dosing, not observation times
Cuppari et al. (2022)	Background article, describes management of croup in children
Edler & Rao (2019)	Investigated nebulized adrenaline, not RE
Hester et al. (2019)	Investigated preadmission RE doses and additional intervention required
Maalouli & Hodges (2021)	Investigated possible predictors necessitating hospital intervention
Maalouli et al. (2022)	Investigated a predictive model for determining croup admission risk
McCans et al. (2022)	Described variation in pediatric prehospitalization respiratory distress management protocols
Rudinsky et al. (2015)	Investigated interventions and hospital course among asymptomatic and symptomatic children admitted with croup

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.**

Question Originator

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Findings from this review were presented to the question originators and A. Randall, RRT-ACCS, RTT-NPS, C-NPT, C-ELBW, CPPS on November 10, 2022.

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Acronyms Used in this Document

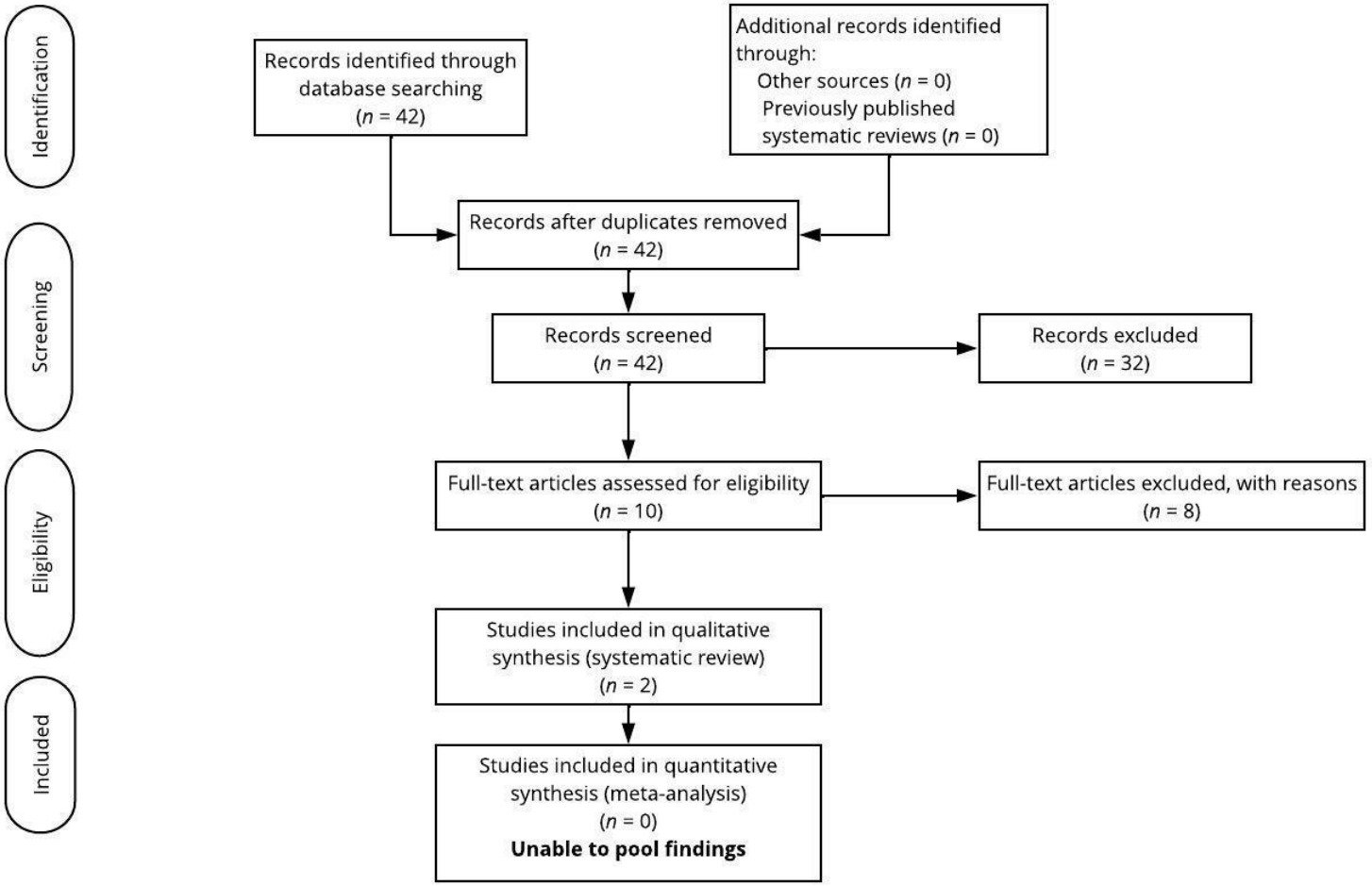
Acronym	Explanation
AGREE II	Appraisal of Guidelines Research and Evaluation II
CAT	Critically Appraised Topic
EBP	Evidence Based Practice
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RE	Racemic Epinephrine

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 Outcomes Table(s)

Table 1

Treatment Failure Comparisons (Smith et al., 2018)

Outcomes	**2.1 to 3 Hours Observation Time** (*n* = 163)	**3.1 to 4 Hours Observation Time** (*n* = 136)
Treatment Failure: Total	54 (33%)	25 (18%)
Treatment Failure: Hospital admission/Treatment failure in emergency room	2 (1%)	2 (~2%)
Treatment Failure: Second dose of RE/Hospital admission	48 (29%)	19 (14%)
Treatment Failure: Return to emergency department within 24 hours following discharge	4 (~3%)	4 (~3%)

Note. Adapted from Smith, N., Giordano, K., Thompson, A., & DePiero, A. (2018). Failure of outpatient management with different observation times after racemic epinephrine for croup. *Clinical Pediatrics, 57*(6), 706-710. https://doi.org/10.1177/0009922817737075

Table 2

Treatment Failure Comparisons (Udoh et al., 2022)

Outcomes	**< 1- Hour Observation Time** (*n* = 132)	**1.0 to 2.0 Hours Observation Time** (*n* = 123)	**>2 Hours Observation Time** (*n* = 39)
Return for additional care within 48 hours of discharge	5 (~4%)	7 (~6%)	3 (~8%)

Note. Adapted from Udoh, I., Heegeman, D., & Ravi, S. (2022). Retrospective evaluation of return rates in pediatric patients treated with inhaled racemic epinephrine for croup. *Wisconsin Medical Journal, 121*(1), 26-29

Characteristics of Intervention Studies
Smith et al., 2018

Methods	Cohort, retrospective
Participants	**Participants**: Children with croup following single racemic epinephrine (RE) dose between March 1, 2012, through May 31, 2014 **Setting**: Single pediatric emergency department (ED; Nemours/Alfred I. duPont Hospital for Children) **Number enrolled into study**: *N* = 428; specific subgroup based on primary analysis* (*N* = 299) • **Group 1**, **Observation period following RE dose of 2.1 to 3 hours*:** *n* = 163 • **Group 2**, **Observation period following RE dose of 3.1 to 4 hours*:** *n* = 136 • **Group 3**, **Observation period following RE dose less than or equal to two hours**: *n* = 92 • **Group 4**, **Observation period following RE dose greater than four hours**: *n* = 37 **Gender, males (%):** • **Group 1:** *n* = ~90 (55%) • **Group 2:** *n* = ~61 (45%) • **Group 3:** Not reported • **Group 4:** Not reported **Race / ethnicity or nationality (as defined by researchers):** • Not reported **Age, mean in months, (SD)** • **Group 1:** 35.2 (± 28) • **Group 2:** 32.5 (± 26) • **Group 3:** Not reported • **Group 4:** Not reported **Inclusion Criteria:** • Patients requiring RE between March 1, 2012, through May 31, 2014 • Patients who required RE for the diagnosis of croup **Exclusion Criteria:** • Patients with history of prematurity (gestational age < 36 weeks) • Patients with underlying cardiopulmonary pathology • Patients with underlying airway disorder • Patients admitted to the hospital for a diagnosis other than croup **Covariates Identified:** None reported
Interventions	**Both:** All patients received steroids and RE within the pediatric ED • 294 of 299 patients received dexamethasone. Five patients received an unknown steroid. Dexamethasone was prescribed per institutional practice of 0.6 mg/kg/dose (maximum dose of 10 mg) orally • A 2.25% solution/dose diluted to 3 ml with normal saline; prescribed as 0.25 ml of RE for patients weighing less than 5 kg and 0.5 ml RE for patients weighing greater than 5 kg within the ED for medical treatment All patients were observed for treatment failure following single RE dose administration until either discharge or hospital admission order was placed.

	• **Group 1**: Observed for treatment failure from 2.1 to 3 hours • **Group 2:** Observed for treatment failure from 3.1 to 4 hours • **Group 3:** Observed for treatment failure for less than or equal to two hours • **Group 4:** Observed for treatment failure greater than four hours
Outcomes	**Primary outcome(s):** • Second dose of RE required (treatment failure); two or more doses of RE required hospital admission based on hospital practices • Return to ED within 24 hours following discharge* (treatment failure) • Comparison of success (discharge following one dose of RE and no readmission to ED within 24 hours) and failure rates (see above) between observation time periods (2.1 to 3 hours; 3.1 to 4 hours) * **Secondary outcome(s):** • None reported **Safety outcome(s):** • None reported *Outcomes of interest to the CMH CPM/CAT development team
Notes	**Results:** • No statistically significant difference between subgroups analyzed (Group 1 and Group 2) regarding treatment success (discharge following one RE dose) • Higher rate of treatment failure (*n* = 54; treatment failure in the ED, second dose of RE required or return to the ED within 24 hours following discharge) reported in Group 1 (2.1 to 3 hours observation time) * • While limited data is reported, 76 patients in Group 3 (Observation time of less than or equal to two hours) were admitted to the hospital and 12 were discharged home and did not return to the ED within 24 hours. • While limited data is reported, 12 patients in Group 4 (Observation time greater than four hours) required a second dose of RE for which hospital admission was required and 25 patients were discharged home and did not return to the ED within 24 hours. • Of the eight patients returning for follow-up care within the 24-hour period, one required hospital admission and was discharged within 24 hours after admission **Limitations:** • Two or more doses of RE in the ED resulted in hospital admission • Patients with observation times less than or equal to two hours and greater than four hours were considered separately, therefore limited data was reported for these groups • The investigators were only able to analyze patient data from their personal institution; data regarding follow-up care received at other institutions was unable to be obtained • The investigators were not able to assess and compare croup symptom severity of patients prior to the initiation of treatment *Contacted author to clarify information found reported in Results section and Table 3. of article. Additional information reported is based on clarification obtained

Udoh et al., 2022

Methods	Cohort, retrospective
Participants	**Participants:** Children diagnosed with croup who received racemic epinephrine (RE) and discharged from the ED from February 2010 through June 2018 **Setting:** Three regional EDs in central Wisconsin (Marshfield Medical Center-Marshfield, Marshfield Medical Center-Eau Claire, and Marshfield Medical Center-Rice Lake) **Number enrolled into study**: *N* = 294; unique patients: *N* = 276 • **Group 1, Observed for less than one hour following RE dose***: n* = 132 • **Group 2, Observed for 1 to 2 hours following RE dose**: *n* = 123 • **Group 3, Observed for more than two hours following RE dose:** *n* = 39 **Gender, males (%):** • **Group 1:** *n* = ~85 (64%) • **Group 2:** *n* = ~82 (67%) • **Group 3:** *n* = ~24 (62%) **Race / ethnicity or nationality (as defined by researchers):** • Not reported **Age, mean in years, (SD):** • **Group 1**: 2.7 (± 2.1) • **Group 2:** 3.0 (± 2.2) • **Group 3:** 2.8 (± 2.2) **Inclusion Criteria:** • Patients less than or equal to 12 years of age • Patients diagnosed with croup (International Classification of Diseases, Ninth Revision [ICD-9] code 464.4) in the ED • Patients discharged from the ED from February 2010 through June 2018 **Exclusion Criteria:** • Patients diagnosed at the same time with asthma, bronchiolitis, and/or pneumonia **Covariates Identified:** • Of the 294 visits identified, all were individual visits and not repeat visits within the 48 hours' time following discharge for one episode of croup
Interventions	**Both:** RE dosing used was 11.25 mg solution nebulizer. Observation time was defined as the time from administration of the first dose of RE until time of discharge by clinician • **Group 1:** Observed for less than one hour following RE dose prior to discharge from ED • **Group 2:** Observed for one to two hours following RE dose prior to discharge from ED • **Group 3:** Observed for greater than two (2.1+) hours following RE dose prior to discharge form ED
Outcomes	**Primary outcome(s):** • Treatment failure resulting in return for additional care within 48 hours from discharge with persistent symptoms between groups (observation less than or equal to two hours versus observation greater than two hours*) **Secondary outcome(s):**

	• If returned patient (within 48 hours following discharge) was treated with steroids, regardless of return to ED, an outpatient clinic, or urgent care • If returned patient (within 48 hours following discharge) was treated with another dose of RE, regardless of return to ED, an outpatient clinic, or urgent care **Safety outcome(s):** • None reported *Outcomes of interest to the CMH CPM/CAT development team
Notes	**Results:** • There was no association between return rates and observation times determined for mild cases of croup (p = .538) or for moderate cases of croup (p = .905) • Average length of observation time in the patient population of the study sample (N = 276 patients or 294 visits) was 1.3 hours (45% observed less than one hour; 42% observed for 1 to 2 hours; and 13% observed for greater than two hours) • Of all the visits (N = 294), the maximum length of observation time was 4.6 hours • Most patients (93%) had mild croup symptoms, whereas patients with moderate croup symptoms (7%) were fewer in number • There were no patients identified with severe croup symptoms • Dexamethasone (0.6 mg/kg) treatment was used with 93% of the patients (87% for those observed less than one hour; 98% for those observed 1 to 2 hours; and 100% for those observed greater than two hours) who returned within 48 hours following discharge for follow-up care **Limitations:** • Limited observational data reported, retrospective study dependent upon chart review • Croup severity score was not assigned/standardized prior to treatment; information was extrapolated based on presenting symptoms documented in the charts • Limited numbers to provide a recommendation for generalization to other populations • RE treatment was not standardized

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Appendix A: Evidence to Decision for RE Observation Time

Should 2 Hours Observation Following RE Dose Administration vs. 3 Hours Observation Following RE Dose Administration be used for Children with Croup?	
POPULATION:	Children with Croup
INTERVENTION:	3 Hours Observation Following RE Dose Administration
COMPARISON:	2 Hours Observation Following RE Dose Administration
MAIN OUTCOMES:	Treatment Failure

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Croup, also known as viral laryngotracheitis, is a respiratory infection that affects infants and children from three months to six years of age (Bagwell et al., 2020). The clinical presentation often associated with croup is a barking cough, inspiratory stridor, and hoarseness of voice (Cuppari et al., 2022). While many children diagnosed with croup typically demonstrate symptoms that can be managed on an outpatient basis, those children whose symptoms are accompanied by moderate to severe respiratory distress often require hospital admission (Cuppari et al., 2022). Signs of respiratory distress associated with moderate to severe illness that warrant medical attention are inspiratory stridor at rest, tachypnea, moderate to severe retractions, and hypoxemia in severe cases (Asmundsson et al., 2019). For children with moderate to severe illness, the administration of racemic epinephrine (RE) in addition to corticosteroids, specifically dexamethasone, has proven to be an effective short-term treatment; however, there is continued discussion on the appropriate observation time frame following RE dose administration (Rudinsky et al., 2015). Rudinsky et al. (2015) suggested a minimum two-hour observation period following RE dose administration before discharge be considered from the emergency room	

	or an urgent care clinic. Furthermore, Rudinsky et al. (2015) concluded that early medical management (corticosteroid administration) and varying observation periods (two to six hours) following RE administration facilitate outpatient management of croup, reducing the need for hospitalization. Yet, an optimal observation time frame post RE administration for children with croup remains unclear.	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	Smith et al. (2018) completed a retrospective cohort review (*N* = 428) of children with croup following a single RE dose administered in the emergency department of a pediatric hospital. Of the 428 children included in the review, *n* = 163 children were observed for a period of 2.1 to 3 hours, *n* = 136 children were observed for a period of 3.1 to 4 hours, *n* = 92 children were observed for 2 or fewer hours, and *n* = 37 children were observed for greater than 4 hours. Observation time was defined as the time following RE dose administration until the child was discharged from the emergency department or until the child required admittance to the hospital. For the outcome of treatment success (not requiring hospitalization or return to the emergency department within 24 hours following discharge), the *OR* indicated the intervention of 2.1 to 3 hours observation time following RE dose administration was no different to the comparator of 3.1 to 4 hours observation time following RE dose administration, *OR* = 0.76, 95% CI [0.45, 1.28], *p* = .30. Udoh et al. (2022) completed a retrospective cohort review (*N* = 294, 276 unique) of children less than or equal to 12 years of age diagnosed with croup who received RE and were discharged from the emergency department. Of the 294 emergency department visits, *n* = 132 children were observed for less than one hour, *n* = 123 children were observed for 1 to 2 hours, and *n* = 39 children were observed for greater than 2 hours following RE dose administration. Observation time was defined as the time from administration of the first dose of RE until the time of discharge by the clinician. For the outcome of treatment success (not requiring hospitalization or return for additional care within 48 hours (about 2 days) following discharge, the *OR* indicated the intervention of 1 to 2 hours observation time following RE dose administration was no	Variation across the two studies and missing data limited the ability to make likened comparisons. As a result, a meta-analysis could not be performed to determine the consistency between intervention effects across the studies. Therefore, each study was evaluated separately.

	different to the comparator of > 2 hours observation time following RE dose administration, *OR* = 1.38, 95% CI [0.34, 5.62], *p* = .65.	
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Large ○ Moderate ○ Small ○ Trivial ● Varies ○ Don't know	***Treatment Failure*** Smith et al. (2018) measured treatment failure (hospital admission, child requiring a second dose of RE resulting in hospital admission, return for follow-up care within 24 hours following discharge) when comparing observation times following RE administration, *n* = 299 (subgroup primarily analyzed). For the outcome of treatment failure, the *OR* indicated the intervention of 2.1 to 3 hours observation time following RE dose administration was unfavorable to the comparator of 3.1 to 4 hours observation time following RE dose administration, *OR* = 2.20, 95% CI [1.28, 3.79], *p* = .004. Udoh et al. (2022) measured treatment failure for which return for additional care within 48 hours (about 2 days) was required following discharge when comparing observation times following RE administration, *N* = 294. For the outcome of treatment failure, the *OR* indicated the intervention of 1- to 2- hour observation times following RE dose administration was not different to the comparator of greater than 2-hour observation times following RE dose administration, *OR* = 0.72, 95% CI [0.18, 2.95], *p* = .65.	Variation across the two studies and missing data limited the ability to make likened comparisons. As a result, a meta-analysis could not be performed to determine the consistency between intervention effects across the studies. Therefore, each study was evaluated separately.
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	**Certainty of the Evidence for Treatment Failure.** The certainty of the body of evidence was very low. The body of evidence was assessed to not have serious risk of bias or indirectness, but serious imprecision. The two studies were assessed to have serious imprecision due to the limited number of events (*n* = 94) and participants (*N* = 593). While each study (Smith et al., 2018; Udoh et al., 2022) addressed the question, the studies were analyzed separately, and consistency could not be assessed.	Minimal evidence exists pertaining to observation times following RE dose administration. Only two studies were identified which addressed the question.

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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		The duration of action for RE is approximately 1.5 hours. Providers must consider the risk and benefits of varying observation times. While parents/families may heavily weigh the risk of treatment failure.
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	Minimal evidence exists for treatment success or treatment failure based on a specific time frame for observation following RE dosing. Only two retrospective cohort studies were identified addressing observation times following RE dose administration for children with croup.	Prolonged observation time may increase healthcare exposure without necessarily improving the value of care, whereas truncated observation time may lead to unnecessary hospitalizations. Prolonged observation time may also lead to unnecessary transfers (increased cost without necessarily continued intervention)
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	Hester et al. (2019) found higher costs associated for children with croup requiring hospital admission as compared to those discharged from the emergency department. The costs associated with hospital admission from the emergency department account for $97 million yearly and an average length of stay in the hospital of 1.7 days without the need for additional treatment (Maalouli et al., 2021). Maalouli et al. (2021) surmised that outpatient medical management for children with croup would decrease medical care cost and improve overall patient and family satisfaction.	
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	No studies comparing the required resources for 2 hours of observation time following RE dose administration versus 3 or more hours of observation time following RE dose administration.	Admission criteria would not be based on observation time alone.
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		Observation time associated with treatment success would determine cost effectiveness. Observation times remain variable among patients treated for croup.
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	The evidence does not support a change in the care process regarding observation times following RE dose administration. Therefore, health equity is not impacted.	
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	The evidence does not support a change in the care process regarding observation times following RE dose administration. Therefore, observation time following RE dose remains the same.	
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	The evidence does not support a change in the care process regarding observation times following RE dose administration. Therefore, feasibility is unchanged.	

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

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	JUDGEMENT						
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

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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
○	●	○	○	○