Integrating Evidence-Based Pediatric Prehospital Protocols into Practice
EMSC Targeted Issues Grant #H34MC19347
Children with Respiratory Distress Prehospital Protocol
Evidence-Based Practice Summary

ASK THE QUESTION

Question 1: In children with respiratory distress, which validated respiratory assessment tools can be used in the prehospital setting?
Question 2: In children with respiratory distress, is pulse oximetry sufficient in monitoring a child's respiratory status in the prehospital setting?
- a. In children with respiratory distress, should pulse oximetry be routinely used?
- b. In children with respiratory distress, what are the limitations of solely utilizing pulse oximetry monitoring?

Question 3: In children with respiratory distress, is it clinically efficacious to use electrocardiogram (ECG) monitoring?
Question 4: In children with respiratory distress, is the routine application of oxygen in the absence of hypoxia clinically effective?
Question 5: In children with respiratory distress, is airway suctioning effective in improving:
- a. Oxygenation
- b. Clinical signs of distress

Question 6: In children with respiratory distress, are the following inhaled medications clinically effective:
- a. Albuterol
- b. Levalbuterol (Xopenex)
- c. Ipratropium (Atrovent)
- d. Hypertonic saline (3%, 5%.)
- e. Racemic epinephrine
- f. Magnesium sulfate
- g. Steam

Question 6a/b: In children with respiratory distress, does the use of inhaled **short-acting beta-agonists (i.e., albuterol or levalbuterol)** in the prehospital setting result in a clinical improvement (i.e., decreased distress, shorter ED length of stay, decreased admission rates to the hospital)?
Question 6c: In children with respiratory distress, does the use of inhaled **anticholinergics (i.e., ipratropium)** in the prehospital setting result in a clinical improvement (i.e., decreased distress, shorter ED length of stay, decreased admission rates to the hospital)?
Question 6d: In children with respiratory distress, does the use of inhaled **hypertonic saline (i.e., 3% or 5%)** in the prehospital setting result in a clinical improvement (i.e., decreased distress, shorter ED length of stay, decreased admission rates to the hospital)?
Question 6e: In children with respiratory distress, does the use of inhaled **racemic epinephrine** in the prehospital setting result in a clinical improvement (i.e., decreased distress, shorter ED length of stay, decreased admission rates to the hospital)?
Question 6f: In children with respiratory distress, does the use of inhaled **magnesium sulfate** in the prehospital setting result in a clinical improvement (i.e., decreased distress, shorter ED length of stay, decreased admission rates to the hospital)?
Question 6g: In children with respiratory distress, does the use of inhaled **steam** in the prehospital setting result in a clinical improvement (i.e., decreased distress, shorter ED length of stay, decreased admission rates to the hospital)?

Question 7: In children with respiratory distress, does the use of **intravenous magnesium sulfate** in the prehospital setting result in clinical improvement (e.g. decreased stress, shorter ED length of stay, decreased admission rates to the hospital)?
Question 8: In children with respiratory distress in the prehospital setting, is it efficacious (e.g., lead to better clinical outcomes) to place an IV?

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Question 9: In children with respiratory distress in the prehospital setting, do steroids (any route) lead to improved clinical outcomes? What is the appropriate timing of steroid administration? What are the indications and contraindications for the use of steroids? What is the preferred route?
Question 10: In children with respiratory distress in the prehospital setting, when are IV fluids clinically effective and useful?
Question 11: In children with respiratory distress in the prehospital setting, does epinephrine (IM/SQ/IV) lead to improved clinical outcomes? What is the appropriate timing of epinephrine use? What are the indications and contraindications for the use of epinephrine?
Question 12: In children with respiratory distress, what are the clinical situations in which the following non-invasive airway adjuncts improve oxygenation and/or respiratory distress:

- **a:** Continuous positive airway pressure (CPAP)
- **b**: Bag valve mask ventilation
- **c:** Heliox

Question 13: In children with respiratory distress in the prehospital setting, do supraglottic devices and intubation lead to improved clinical outcomes? What are the indications and contraindications for using a supraglottic device or intubating?
Question 14: In children with respiratory distress, is the use of capnography efficacious and clinically useful?
Question 15: In children with respiratory distress, are there improved patient outcomes when an online medical direction is contacted versus no online medical direction is contacted?
Question 16: In children with respiratory distress, are there improved patient outcomes when patients are transported by Advanced Life Support (ALS) providers as compared to Basic Life Support (BLS) providers?
Question 17: In children with respiratory distress, is it clinically efficacious to transport with lights and sirens?

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CRITICALLY ANALYZE THE EVIDENCE

Question 1: In children with respiratory distress, which validated respiratory assessment tools can be used in the prehospital setting?
Recommendation: Prehospital providers should be taught to assess and document components of the Respiratory Distress Assessment Instrument (RDAI), Pediatric Asthma Severity Score (PASS), and Westley Croup respiratory scores.
Grade Criteria: Strong recommendation, Moderate quality evidence [1-9]
A review of the literature noted several pediatric respiratory assessment tools used in the emergency department and outpatient setting. No tools were found to be exclusively used or developed in the prehospital setting. Four clinical scores showed high interrater reliability, predictability, and scientific acceptance in the literature by stakeholders and providers for common respiratory diseases (asthma, bronchiolitis, and croup). These scores have been replicated in larger, scientifically accepted studies as outcome measurements to demonstrate clinical improvement after therapies. [2,6] No universal scoring system was found to assess children with respiratory distress for multiple disease processes (i.e., asthma, bronchiolitis, croup).

The RDAI, originally developed in 1987, has been subsequently used in many large pediatric emergency department trials to validate respiratory assessments and improvement in **bronchiolitis**. The original tool was developed in a randomized double blind trial of 30 children < 2 years old, receiving subcutaneous epinephrine for wheezing. The RDAI showed internal validity for three main elements when compared to many other clinical factors, **respiratory rate, wheezing and retractions**. Interobserver agreement was good between two observers (weighted kappa of 0.9). [4] A Respiratory Assessment Change Score (RACS) was calculated as an absolute difference between two RDAI scores to prove clinical improvement. In this study, a clinical improvement was noted to be a change of RACS of 4 units (clinical significance determined a priori). [4] Other studies using the RDAI to assess bronchiolitis have simply measured the average change in RACS as a continuous variable to compare improvement in clinical status from intervention versus another. [2,6]

Although the RDAI is quoted in some reviews as an asthma score, it has only been used in clinical trials for children < 2 years old with wheezing, more likely bronchiolitis than asthma. However, no studies could be found that validated the RDAI as an assessment tool in different populations.

Over half a dozen clinical scores for asthma have been developed in the outpatient setting. A meta-analysis in 2004 of respiratory distress scores for preschool children highlighted the lack of validation, rigorous evaluation, and interobserver agreement when comparing 10 different scores. [7] The PASS and the Preschool Respiratory Assessment Instrument (PRAM) are the only two that showed consistent internal validity, usefulness along age ranges, and easy implementation.

Gorelick et al. (2004) examined 5 clinical factors in 1221 asthma subjects of varying severity. Subset analyses were done on 5-, 4-, and 3-item scales. A 3-item scale looking at **wheezing, work of breathing, and prolonged expiration** showed good performance. High interrater reliability (kappa 0.79), construct validity (degree to which a score correlates with other accepted measures of severity), discriminative validity (c stat of 0.8 or more on ROC curve), and good responsiveness (% change in score and difference between admitted and discharged patients) were all shown. In addition, this score was validated among different providers and varying severities of asthma, as opposed to many other scores found in the literature. [3]

Chalut et al. (2000) performed a prospective cohort study of 217 children < 6 years old with a diagnosis of asthma. A derivation and validation group found a 5-factor scale including **suprasternal retraction, scalene retractions, air entry, wheezing and pulse oximetry** to have the best interrater reliability, predictiveness, and responsiveness. It should be of note that the score excluded patients with severe asthma and children > 6 years old. [1]

Over a dozen clinical croup scores have been reported in the literature. However, the Westley croup score is by far the most utilized, reproduced, and validated croup score for emergency department and outpatient evaluation in the literature. [5,8,9] The Westley croup score is the most common primary outcome used to measure interventions directed at croup. No online access was available to analyze the original study and its validated measurements for this score. The Westley croup score is a 17-point score looking at stridor, retractions, air entry, cyanosis, and level of consciousness. [5]

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Recommendation(s): Strong recommendation with moderate quality evidence that prehospital providers should be taught to assess and document components of the RDAI, PASS, and Westley Croup respiratory scores.

Number of Studies: Total # 5 ☐ Systematic review ☒ RCT [2,4-5] ☒ Cohort [1,3] ☐ Observational ☐ Case Reports Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☐ None ☒ Insufficient sample size [1,4] ☒ Lack of blinding [1,3,5] ☒ Lack of allocation concealment [1,3,5] ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☐ No inconsistencies ☐ Wide variation of treatment effect across studies ☒ Populations varied (e.g., sicker, older) [1-5] ☐ Interventions varied (e.g., doses) ☒ Outcomes varied (e.g., diminishing effect over time) [1-5]	☐ Head-to-head comparison in correct population ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☒ Different populations [1-5] ☒ Different interventions [1-5] ☒ Different outcomes measured [1-5] ☐ Comparisons not applicable to question/outcome	☐ Dichotomous outcomes ☒ Sample size lower than calculated optimal information size [4-5] ☐ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes ☐ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm

Sample	CI/RR
1) A prospective cohort study of children age 3 to 6 with asthma (N=217). Excluded patients needing continuous albuterol. 14 clinical variables assessed for each patient and each child had to be able to perform airway resistance measurement test. Signs with higher associated % predicted resistance measurements were considered discriminative. Signs in which the absolute change corresponded to airway resistance were considered responsive. The final model included: **wheezing, air entry, scalene muscle retraction, suprasternal retractions, and O_2 sat.** 2) Double blind RCT (N=600), comparing single dose oral dexamethasone to placebo for children with Mod-Severe bronchiolitis. Mod-Severe bronchiolitis defined as a RDAI score ≥ 6. Secondary outcome was the RACS. 3) 1221 patients age 1-18 with asthma; 6 clinical factors chosen at first (clinical validity and derivation from other scores), study looked at how factors performed and whether a 3-, 4-, or 5-factor scale would be best. Three factors rose to retain highest reliability (**wheezing, work of breathing, and prolongation of expiration)**. Construct validity measured against pulse ox, PEFR, and hospital admission. Discriminative and predictive ability was examined to determine ability to predict admission vs. discharge. Responsiveness was measured by percent change in the score and its effect size. 4) A double-blinded RCT 30 children < 2 years of age with wheezing, factors were chosen a priori (wheezing, retractions, and resp rate). Other assessment variables measured and proved to not be anymore discriminating than the 3 chosen a priori. Arbitrary change of score of 4 units was deemed clinically significant. 5) RCT of 20 patients looking at improvement of clinical croup score in inpatients receiving saline vs. epinephrine (nebulized and by IPPV).	1) 281 excluded patients (couldn't perform resistance test or were too sick). Group of 142 to develop score, validated in another 78. In the test group, the model was modestly discriminative (r^2 = 0.16, *P* = .001) and responsive (r^2 = 0.13, *P* = .05). The association between the % of predicted Rfo8 and severity appraisal was stronger for physicians (r = 0.32) than for nurses (r = 0.15). **A PRAM score was about as predictive for airway obstruction as a physician assessment of severity.** **No kappa reported – only one trained nurse did assessment.** Because of so few children with severe asthma, they could not determine expected obstruction for a PRAM score of ≥ 9. 2) RDAI score determined by one research assistant at each site. RDAI already previously validated in other studies. **RACS** score difference not significant between two groups, -0.5 (95%CI: -1.3 to 0.3), also no significant difference when RACS values were analyzed in the subgroup with eczema or a family history of asthma (absolute difference, -0.4; 95% CI, -1.3 to 0.6). 3) Kappa of 0.79 between observers, observers varied in training (MD, RN, RT), kappa scores were higher for people of like training (0.83). Scores showed modest correlation with construct validity items – Pearson correlation coefficient with pulse ox: -0.42 (-0.36, -0.47) and with PEFR -0.22 (-0.05, -0.37); all scores were higher with decreasing PEFR for sats < 93% and for admitted patients. 4) Weighted kappa of 0.64 to 0.9 were only between two observers; of patients missed on enrollment, greater % of patients < 4 months (54%).

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1.) Chalut, D. S., Ducharme, F. M., & Davis, G. M. (2000). The Preschool Respiratory Assessment Measure (PRAM): A responsive index of acute asthma severity. *The Journal of Pediatrics, 137*(6), 762-768.
2.) Corneli, H. M., Zorc, J. J., Mahajan, P., Shaw, K. N., Holubkov, R., Reeves, S. D., et al. (2007). A multicenter, randomized, controlled trial of dexamethasone for bronchiolitis. *New England Journal of Medicine, 357*(4), 331-339.
3.) Gorelick, M. H., Stevens, M. W., Schultz, T. R., & Scribano, P. V. (2004). Performance of a novel clinical score, the Pediatric Asthma Severity Score (PASS), in the evaluation of acute asthma. *Academic Emergency Medicine, 11*(1), 10-18.
4.) Lowell, D. I., Lister, G., Von Koss, H., & McCarthy, P. (1987). Wheezing in infants: The response to epinephrine. *Pediatrics, 79*(6), 939-945.Westley, C. R., Cotton, E. K., & Brooks, J. G. (1978). Nebulized racemic epinephrine by IPPB for the treatment of croup: A double-blind study. *132, 5*(484-487).
5.) Westley, C. R., Cotton, E. K., & Brooks, J. G. (1978). Nebulized racemic epinephrine by ippb for the treatment of croup: A double-blind study. *132, 5*(484-487).

Additional References:

6.) Grewal, S., Ali, S., McConnell, D. W., Vandermeer, B., & Klassen, T. P. (2009). A randomized trial of nebulized 3% hypertonic saline with epinephrine in the treatment of acute bronchiolitis in the emergency department. *Archives of Pediatrics & Adolescent Medicine, 163*(11), 1007-1012.
7.) Birken, C. S., Parkin, P. C., & Macarthur, C. (2004). Asthma severity scores for preschoolers displayed weaknesses in reliability, validity, and responsiveness. *Journal of Clinical Epidemiology, 57*(11), 1177-1181.
8.) Ausejo, M., Saenz, A., Pham, B., Moher, D., Chalmers, T. C., Kellner, J. D., et al. (1999). The effectiveness of glucocorticoids in treating croup: Meta-analysis. *The Western Journal of Medicine, 171*(4), 227-232.Birken 2001
9.) Klassen, T. P., Craig, W. R., Moher, D., Osmond, M. H., Pasterkamp, H., Sutcliffe, T., et al. (1998). Nebulized budesonide and oral dexamethasone for treatment of croup. *JAMA: The Journal of the American Medical Association, 279*(20), 1629-1632.

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Question 2: In children with respiratory distress, is pulse oximetry sufficient in monitoring a child's respiratory status in the prehospital setting? **2a.** In children with respiratory distress, should pulse oximetry be routinely used?
There was no relevant literature found that addressed the identified PICO question.

2b. In children with respiratory distress, what are the limitations of solely utilizing pulse oximetry monitoring?
Recommendation: Pulse oximetry should be routinely used in children with respiratory distress as an adjunct to other forms of respiratory monitoring.
Grade Criteria: Strong recommendation, Low quality evidence [1,2]
A review of the literature noted a limited number of studies assessing pulse oximetry's limits in the clinical setting. A few studies looked at how predictive pulse oximetry was by itself for certain clinical outcomes. Mehta et al. (2004) looked at how well pulse oximetry could predict children needing bronchodilators for more than 4 hours. An LR > 10 is deemed clinically significant to change pre-test to post-test probability of an outcome. In this study, only at an initial sat of < 89% did LR get to 12.3 (1.7, 90.1) to predict need for frequent bronchodilator for > 4 hours, and an LR of 9.8 (3.4, 29.5) to predict FBT > 12 hours. Although this may be looked at as being clinically useful, only 15% of patients had a sat of < 91% so it is likely not a sufficient predictor alone for most asthmatic patients in the ED.
Keahey et al. (2002) showed that as a predictor for hospital admission, pulse oximetry alone was not sufficient in predicting admission. In this study, the patient needed a sat of < 88% to have an LR of 12 to predict admission. LR decreased to 2.7 for patients with a sat of 94% or less. With a mean pulse oximetry of 93% for admitted patients, this again showed that as a sole predictor for hospital admission, pulse oximetry is not sufficient for most asthmatics presenting for emergency care.

Recommendation: Strong recommendation with low quality evidence that pulse oximetry should be routinely used in children with respiratory distress, but is not sufficient on its own.
Number of Studies: Total # 2 ☐ Systematic review ☐ RCT ☒ Cohort [1,2] ☐ Observational ☐ Case Reports Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☐ None ☐ Insufficient sample size ☒ Lack of blinding [1,2] ☒ Lack of allocation concealment [1,2] ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☐ No inconsistencies ☐ Wide variation of treatment effect across studies ☒ Populations varied (e.g., sicker, older) [1,2] ☐ Interventions varied (e.g., doses) ☒ Outcomes varied (e.g., diminishing effect over time) [1,2]	☐ Head-to-head comparison in correct population ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☒ Different populations [1,2] ☐ Different interventions ☒ Different outcomes measured [1,2] ☐ Comparisons not applicable to question/outcome	☐ Dichotomous outcomes ☐ Sample size lower than calculated optimal information size ☐ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes ☐ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm

Sample	CI/RR
1) N = 1184; Prospective multicenter study (part of the Multicenter Airway Research Collaboration). Inclusion criteria: acute asthma, age 2-17 years. The association between hospital admission and SaO_2 was examined by using logistic regression. Likelihood ratios were used to assess the diagnostic value of SaO_2. 2) N = 273; Prospective cohort study. Univariate logistic regression of a priori postulated plausible predictors of prolonged FBT for > 4 hours and for > 12 hours, and then a multiple logistic regression analysis.	1) Despite sicker population (57% had been admitted before), only 40% on preventer meds SaO_2 88% or less were 9 times more likely to get admitted than a sat of 100% (CI: 2.2, 36.8). Only at a sat of 88% did an LR approach a clinically useful level (LR = 12, no CI reported). ROC curve for pulse ox as predictor for admission: 0.76. Since 88% of these patients had SaO_2 > 91%, this cutoff was not clinically useful. 92% would be ideal point based on ROC curve but a very poor predictor in this study. 58% of those with SaO_2 < 92% were actually sent home so by itself is a poor predictor to determine admission. 2) LRs approaching 10 or greater were considered clinically significant (how test – pulse ox, changes pre- to post-test probability of an outcome). As the initial SaO_2 increased, the odds of treatment for > 4 hours decreased (OR = 0.73; 95% CI: 0.6, 0.82). After multiple logistic regression analyses, the SaO_2 remained a significant independent predictor of both the > 4-hour therapy (OR = 0.81; 95% CI: 0.71, 0.92) and > 12-hour therapy (OR = 0.84; 95% CI: 0.75, 0.94). Children with the initial SaO_2 < 91% were: 14.7 times (adjusted OR of 14.8, CI: 2.3, 93.4) more likely to require FBT for > 4 hours; LR 6.5 (1.5, 27) 12 times (adjusted OR of 11.8, 95% CI: 1.2, 113.8) more likely to require FBT for > 12 hours than children with SaO_2 between 98% and 100%; LR 3.5 (1.6, 8).

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	ROC for SaO_2 as a predictor for FBT > 4 hours (AUC = 0.70), FBT > 12 hours (AUC = 0.73) Authors concluded that baseline SaO_2 < 91% in acute asthma can be a helpful predictor of prolonged FBT for > 4 hours and that SaO_2 < 89% is strongly associated with FBT for > 12 hours. Authors conclude that as a sole measurement, pulse ox not good enough to predict admission.

1) Keahey, L., Bulloch, B., Becker, A. B., Pollack, C. V., Jr., Clark, S., Camargo, C. A., Jr., et al. (2002). Initial oxygen saturation as a predictor of admission in children presenting to the emergency department with acute asthma. *Annals of Emergency Medicine, 40*(3), 300-7.
2) Mehta, S. V., Parkin, P. C., Stephens, D., & Schuh, S. (2004). Oxygen saturation as a predictor of prolonged, frequent bronchodilator therapy in children with acute asthma. *The Journal of Pediatrics, 145*(5), 641-645.

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Question 3: In children with respiratory distress, is it clinically efficacious to use electrocardiogram (ECG) monitoring?
Recommendation: ECG should not be routinely used for children with respiratory distress. If there are no signs of clinical improvement after treating the respiratory distress, consider ECG monitoring to assess for cardiac concerns.

Grade Criteria: Weak recommendation, Very low quality evidence [(1)]
Freedman et al. (2007) found that children with myocarditis present with symptoms that can often be mistaken for other types of illnesses. Thirty-two percent of patients (N = 10) presented with predominantly respiratory symptoms followed closely by 29% of patients (N = 9) with cardiac symptoms and 6% (N = 2) with gastrointestinal symptoms. In this study, 14 children had previously been seen by a physician before being diagnosed with myocarditis and of those, 57% were originally diagnosed with pneumonia or asthma. Findings suggesting cardiac dysfunction were present in 17 of 31 chest radiographs (sensitivity: 55%; 95% CI: 38, 71). ECG findings potentially indicating myocarditis were reported in 93% of cases (95% CI: 78, 99).

Recommendation: Weak recommendation with very low quality evidence that ECG should not be routinely used for children with respiratory distress. If there are no signs of clinical improvement after treating the respiratory distress, consider ECG monitoring to assess for cardiac concerns.
Number of Studies: Total #1 ☐ Systematic review ☐ RCT ☐ Cohort ☒ Observational [(1)] ☐ Case Reports Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☐ None ☒ Insufficient sample size [(1)] ☒ Lack of blinding [(1)] ☒ Lack of allocation concealment [(1)] ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☐ No inconsistencies ☐ Wide variation of treatment effect across studies ☐ Populations varied (e.g., sicker, older) ☐ Interventions varied (e.g., doses) ☐ Outcomes varied (e.g., diminishing effect over time)	☐ Head-to-head comparison in correct population ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☐ Different populations ☐ Different interventions ☐ Different outcomes measured ☐ Comparisons not applicable to question/outcome	☐ Dichotomous outcomes ☒ Sample size lower than calculated optimal information size [(1)] ☒ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes [(1)] ☐ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm

Sample	CI/RR
1) N = 31 children diagnosed with myocarditis who initially presented to the ED (8.0 ± 6.4 years) 16 cases of definite myocarditis; 15 cases of probable myocarditis	1) 32% of (10) patients presented with predominantly respiratory symptoms followed closely by 29% (9) with cardiac symptoms and 6% (2) with gastrointestinal symptoms. 14 children had previously been seen by a physician before being diagnosed with myocarditis and of those, 57% were originally diagnosed with pneumonia or asthma. Cardiac dysfunction was present in 17/31 chest radiographs (sensitivity: 55%; 95% CI: 38, 71%). ECG findings potentially indicating myocarditis were reported in 93% of cases (95% CI: 78, 99).

1) Freedman, S. B., Haladyn, J. K., Floh, A., Kirsh, J. A., Taylor, G., & Thull-Freedman, J. (2007). Pediatric myocarditis: Emergency department clinical findings and diagnostic evaluation. *Pediatrics, 120*(6), 1278-1285.

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Question 4: In children with respiratory distress, is the routine application of oxygen in the absence of hypoxia clinically effective?
Recommendation: Supplemental oxygen should be provided to all children with respiratory distress.
Grade Criteria: Strong recommendation, Very low quality evidence [(1)]
Fifty-seven percent of the respondents (members of the American Academy of Pediatrics Section of Emergency Medicine) in the survey reported using supplemental oxygen in children with bronchiolitis.

Recommendation: Strong recommendation with very low quality evidence that supplemental oxygen should be provided to all children with respiratory distress.
Number of Studies: Total # 1 ☐ Systematic review/Meta-analysis ☐ RCT ☐ Cohort ☐ Observational [(1)] ☐ Case Reports Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☐ None ☐ Insufficient sample size ☐ Lack of blinding ☐ Lack of allocation concealment ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☐ No inconsistencies ☐ Wide variation of treatment effect across studies ☐ Populations varied (e.g., sicker, older) ☐ Interventions varied (e.g., doses) ☐ Outcomes varied (e.g., diminishing effect over time)	☐ Head-to-head comparison in correct population ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☐ Different populations ☐ Different interventions ☐ Different outcomes measured ☐ Comparisons not applicable to question/outcome	☐ Dichotomous outcomes ☐ Sample size lower than calculated optimal information size ☐ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes ☐ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm

Sample	CI/RR
1) Physicians who were members of the American Academy of Pediatrics Section of Emergency Medicine and lived in the United States were randomized into 4 groups and sent a survey that contained one of four vignettes. The vignettes were identical with the exception of given SpO_2 values (94% or 92%) and RR (50/min or 62/min). Subjects were asked to answer questions regarding laboratory tests, treatment options, and the decision to admit for the patient in their vignette with bronchiolitis. 519 surveys were returned from the 812 physicians contacted (64%).	1) 57% of the respondents recommended supplemental oxygen.

1.) Mallory, M. D., Shay, D. K., Garret, J., & Bordley, W. C. (2003). Bronchiolitis management preferences and the influence of pulse oximetry and respiratory rate on the decision to admit. *Pediatrics, 111*(1), e45-e51.

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Question 5: In children with respiratory distress, is airway suctioning effective in improving:
5a. Oxygenation
5b. Clinical signs of distress
Recommendation: A child's nose and/or mouth should be suctioned (via bulb, Yankauer, suction catheter) if excessive secretions are present.
Grade Criteria: Strong recommendation, Very low quality evidence [(1)]
Eighty-two percent of respondents in the survey reported removing nasal secretions for therapeutic reasons.

Recommendation: Strong recommendation with very low quality evidence that a child's nose and/or mouth should be suctioned (via bulb, xxx, xxx) if excessive secretions are present.
Number of Studies: Total # 1 ☐ Systematic review/Meta-analysis ☐ RCT ☐ Cohort ☒ Observational [(1)] ☐ Case Reports Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☐ None ☐ Insufficient sample size ☐ Lack of blinding ☐ Lack of allocation concealment ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☐ No inconsistencies ☐ Wide variation of treatment effect across studies ☐ Populations varied (e.g., sicker, older) ☐ Interventions varied (e.g., doses) ☐ Outcomes varied (e.g., diminishing effect over time)	☐ Head-to-head comparison in correct population ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☐ Different populations ☐ Different interventions ☐ Different outcomes measured ☐ Comparisons not applicable to question/outcome	☐ Dichotomous outcomes ☐ Sample size lower than calculated optimal information size ☐ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes ☐ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm

Sample	CI/RR
1) Physicians who were members of the American Academy of Pediatrics Section of Emergency Medicine and lived in the United States were randomized into 4 groups and sent a survey that contained one of four vignettes. The vignettes were identical with the exception of given SpO_2 values (94% or 92%) and RR (50/min or 62/min). Subjects were asked to answer questions regarding laboratory tests, treatment options, and the decision to admit for the patient in their vignette with bronchiolitis. 519 surveys were returned from the 812 physicians contacted (64%).	1) 82% of the respondents recommended the use of suctioning.

1.) Mallory, M. D., Shay, D. K., Garret, J., & Bordley, W. C. (2003). Bronchiolitis management preferences and the influence of pulse oximetry and respiratory rate on the decision to admit. Pediatrics, 111(1), e43-e51.

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Question 6a/b: In children with respiratory distress, does the use of inhaled short-acting beta-agonists (i.e., albuterol or levalbuterol) in the prehospital setting result in a clinical improvement (i.e., decreased distress, shorter ED length of stay, decreased admission rates to the hospital)?
Recommendation: Beta-agonists should be administered to all children in respiratory distress with signs of bronchospasm (e.g., known asthmatics, quiet wheezers) in the prehospital setting, either via nebulized route or metered-dose inhaler, by basic life support (BLS) or advanced life support (ALS) providers.
Grade Criteria: Strong recommendation, Moderate quality evidence [1-7]
The use of short-acting beta agonists for respiratory distress in children and adults with known asthma in the emergency department setting is well supported. There is limited literature on its efficacy in the prehospital setting, especially in children, but its routine use for asthma is recommended by expert panel recommendations. [2] Several articles in the prehospital setting, including some with subgroup analysis in children, do note improvements in peak flow and dyspnea when beta-agonists are administered. [4-7] Though some of these articles note a statistically significant improvement in heart rate or respiratory rate, the clinical relevance of this improvement is questionable based on the magnitude of difference and the lack of reporting of 95% confidence intervals. [4,6,7] In an open-label study in adults in the prehospital setting, no difference in effect was noted between levalbuterol and albuterol. [7] The successful administration of nebulized beta-agonists and assessment of bronchospasm by BLS providers in children was noted in 1 study. [4]

For beta agonist use in children < 2 years of age with wheezing and/or bronchiolitis in the hospital setting, no differences in rates of hospital admission, duration of hospitalization, or time to resolution of symptoms existed. [1,3] There were conflicting conclusions regarding change in oxygen saturation but there were improvements in other clinical parameters (heart rate, respiratory rate, use of accessory muscles, and wheezing) noted in both meta-analyses. Treated patients did have increased incidence of tachycardia and tremors, so this risk should be weighed against potential benefit.

Recommendation: Strong recommendation with moderate quality evidence that beta-agonists should be administered to all children in respiratory distress with signs of bronchospasm (e.g., known asthmatics, quiet wheezers) in the prehospital setting, either via nebulized route or meter-dose inhaler, by basic life support (BLS) or advanced life support (ALS) providers.
Number of Studies: Total # 8 ☒ Systematic review/Meta-analysis [2,3] ☐ RCT ☒ Cohort [4-7] ☐ Observational ☐ Case Reports ☒ Clinical Guideline [1] Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☒ None [2,3] ☐ Insufficient sample size ☒ Lack of blinding [6,7] ☒ Lack of allocation concealment [6,7] ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☒ Selective reporting of measured outcomes (e.g., no effect outcome) [6,7]	☒ No inconsistencies [4,5] ☐ Wide variation of treatment effect across studies ☒ Populations varied (e.g., sicker, older) [2,3] ☐ Interventions varied (e.g., doses) ☒ Outcomes varied (e.g., diminishing effect over time) [2-7]	☐ Head-to-head comparison in correct population ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☒ Different populations [1-7] ☐ Different interventions ☐ Different outcomes measured ☒ Comparisons not applicable to question/outcome [6,7]	☐ Dichotomous outcomes ☐ Sample size lower than calculated optimal information size ☒ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes [4,6,7] ☒ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm [1,4-7]

Sample	CI/RR
1) Clinical guideline that references evidence-based recommendations by the National Asthma Education and Prevention Program (NAEPP) on the use of short-acting beta agonists in adults and children in the emergency department. The NAEPP recommendations are also incorporated in another article by Camargo in Prehospital Emergency Care in 2006 that makes the same recommendation, specifically for EMS. 2) 6 RCTs on children < 2 years with recurrent wheezing. One was an ED-based study; none were prehospital; others were at home or in pulmonary function lab. 3) 28 RCTs on children < 2 years with bronchiolitis in the hospital setting. Also included ipratropium	1) N/A 2) **Results from ED based study (Bentur 1992)** • **Respiratory rate:** Decrease of 5.1 breaths/min (0.75-9.45) • **Symptom score** (HR, RR, wheeze, accessory muscle use on 0-3 scale): Improvement by 2.5 points (1.12-3.88) • **Oxygen saturation:** Increased 1.6% (0.33-2.87) • **Hospital admission (OR):** 1.95 (0.27-13.98); no difference **Other studies:** No benefit observed for any outcomes in the home or other settings

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and non-inhaled routes (oral/subcutaneous). Oximetry and clinical score outcomes were heterogeneous; sensitivity analysis performed excluding 1st time wheezers. 4) Prospective cohort of patients with bronchospasm who received nebulized albuterol by an EMT-B after a 4-hour training course. Pre-/Post-treatment comparisons made evaluating several outcomes. Pediatric data (n = 41/190) is shown to the right. No comparison to placebo. 5) Prospective cohort of patients with bronchospasm who received nebulized albuterol by an EMT-B after a 4-hour training course. Pre-/Post-treatment comparisons made evaluating several outcomes. 6) Prospective open label study of nebulized levalbuterol administered to ≥ 16 year olds by ALS providers in the prehospital setting. Data analyzed on 147 complete records. No comparison to placebo. 7) Funded by Sepracor (makers of Xopenex). Prospective open label study comparing nebulized levalbuterol to albuterol administered to ≥ 18 year olds by ALS providers in the prehospital setting before and after a protocol change.	**3) Oxygen saturation (mean difference-MD):** -0.45 (-0.96-0.05); no difference ○ Sensitivity analysis (1st time wheeze excluded): -0.38 (-0.75-0.00) **Overall average clinical score (MD):** -0.37 (-0.62 to -0.13): statistical improvement; limited clinical improvement. ○ Sensitivity analysis (1st time wheeze excluded): -0.26 (-0.44- -0.09) **Hospital admission (OR):** 0.78 (0.47 to 1.29) **Duration of hospitalization (MD):** 0.06 days (-0.27 to 0.39); no difference **Time to resolution of illness at home (MD):** 0.29 (-0.43 to 1.00); no difference. **Adverse effects noted:** tachycardia and tremors → monitoring for this after a trial of a bronchodilator is recommended 4) **Accuracy of EMT-B in assessing bronchospasm:** 90.6% (compared to ED physicians assessment) **Change in HR** (beats/min): -2.20 (p = 0.15) **Change in RR** (breaths/min): -3.00 (p < 0.01) **Change in pulse oximeter:** 0% (n/a) **Change in peak flow** (% improvement): 28.2 % (p < 0.01) **Borg score** (% improvement): 35.7% (p < 0.01) 5)<u>< 15 years only</u> • **Change in peak flow:** +14.9 % (95% CI: 11.8, 18%) • **Borg score:** -2.4 (95% CI: 1.9, 2.9) <u>All patients</u> • **HR:** -0.8 (95% CI: -1.1, -0.4) • **On scene time (min, sec):** +3,51 • **Transport time (min, sec):** no difference • **ALS backup request:** 16% (56% transported by ALS. 42% with ALS assist; 2% refused transport) 6) **Change in HR** (beats/min): -2.2 (+/-9.8); (p = 0.009) **Change in RR** (breaths/min): -4.7 (+/-23.2); (p = 0.02) **Subjective distress** (10 pt scale): -1.8 (+/- 3.3); (p = 0.000) **Change in peak flow** (% seconds): +22.6% (+/-41.2); (p = 0.000) 7) **Change in peak flow:** Albuterol +19.7 (+/- 49.1%) p < 0.01 for change; Levalbuterol +20.4 (+/- 33.7%), p < 0.01 for change. P = 0.9 for comparison between treatments.

1)Camargo, C. A., Jr., Rachelefsky, G., & Schatz, M. (2009). Managing asthma exacerbations in the emergency department: Summary of the National Asthma Education and Prevention Program Expert Panel Report 3 Guidelines for the Management of Asthma Exacerbations. *Journal of Emergency Medicine, 37*(Suppl 2), S6-S17.
2)Chavasse RJPG, Seddon P, Bara A, McKean MC. Short acting beta2-agonists for recurrent wheeze in children under two years of age. *Cochrane Database of Systematic Reviews* 2002, Issue 2. Art. No.: CD002873. DOI: 10.1002/14651858.CD002873.
3)Gadomski AM, Bhasale AL. Bronchodilators for bronchiolitis. *Cochrane Database of Systematic Reviews* 2006, Issue 3. Art. No.: CD001266. DOI: 10.1002/14651858.CD001266.pub2.
4)Markenson, D., Foltin, G., Tunik, M., Cooper, A., Treiber, M., & Caravaglia, K. (2004). Albuterol sulfate administration by EMT-basic: Results of a demonstration project. *Prehospital Emergency Care, 8*(1), 34-40.
5)Richmond, N. J., Silverman, R., Kusick, M., Matallana, L., & Winokur, J. (2005). Out-of-hospital administration of albuterol for asthma by basic life support providers. *Academic Emergency Medicine, 12*(5), 396-403.

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6)Rodenberg, H. (2002). Effect of levalbuterol on prehospital patient parameters. *American Journal of Emergency Medicine, 20*(5), 481-483.
7)Thompson, M., Wise, S., & Rodenberg, H. (2004). A preliminary comparison of levalbuterol and albuterol in prehospital care. *Journal of Emergency Medicine, 26*(3), 271-277.

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Question 6c: In children with respiratory distress, does the use of inhaled anticholinergics (i.e., ipratroprium) in the prehospital setting result in a clinical improvement (i.e., decreased distress, shorter ED length of stay, decreased admission rates to the hospital)?
Recommendation: Nebulized anticholinergic medication (i.e., ipratropium) should be administered in multiple doses with short-acting beta agonist to children ≥ 2 years of age with known asthma who are in severe respiratory distress in the prehospital setting.
Grade Criteria: Strong recommendation, Moderate quality evidence [1-3]
The use of inhaled anticholinergics has been evaluated in wheezing children (< 2 years) and known asthmatics (18 months-17 years) in the emergency department and inpatient settings. [2,3] In the younger age group, there was no improvement in respiratory rate, oxygen saturation, duration of hospital stay, or effect on symptoms in children < 2 years of age who received ipratropium. [2] In children 18 months-17 years, a single dose of ipratropium did not make a difference in reducing the risk of hospital admission or improving pulmonary function tests. [3] In severe asthmatics, however, multiple doses of ipratropium reduced hospital admission rates and improved pulmonary function tests at both 1- and 2-hour intervals after treatment with no increase in nausea, vomiting, or tremors. [3]

Ipratropium use has not been studied in children in the prehospital setting, but one retrospective cohort comparing adult patients before and after the addition of ipratropium to a prehospital reactive airway disease protocol showed no difference in admission rates or vital signs after treatment. [1] This study had several flaws (inadequate sample size, heterogeneous population, adult population, before and after comparison) that makes it difficult to determine whether or not children may benefit from prehospital treatment with ipratropium. Due to the compelling evidence of benefit in the emergency department and inpatient settings for children with severe asthma exacerbations, this higher quality data should be considered in making a recommendation.

Recommendation(s): Strong recommendation with moderate quality evidence that nebulized anticholinergic medication (i.e., ipratropium) should be administered in multiple doses with short acting beta-agonist to children ≥ 2 years of age with known asthma who are in severe respiratory distress in the prehospital setting.
Number of Studies: Total # 3 ☒ Systematic review/Meta-analysis [2,3] ☐ RCT ☒ Cohort [1] ☐ Observational ☐ Case Reports Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☒ None [2,3] ☐ Insufficient sample size ☒ Lack of blinding [1] ☐ Lack of allocation concealment ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☐ No inconsistencies ☐ Wide variation of treatment effect across studies ☒ Populations varied (e.g., sicker, older) [1-3] ☒ Interventions varied (e.g., doses) [2,3] ☒ Outcomes varied (e.g., diminishing effect over time) [2,3]	☐ Head-to-head comparison in correct population ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☒ Different populations [1,2,3] ☐ Different interventions ☐ Different outcomes measured ☐ Comparisons not applicable to question/outcome	☒ Dichotomous outcomes [2,3] ☒ Sample size lower than calculated optimal information size [1] ☐ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes ☒ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm [1]

Sample	CI/RR
1) Before/After comparison of ipratropium use for prehospital reactive airway disease in ≥ 18 year olds. 2) 6 RCTs found on children < 2 years with wheezing, excluding patients with bronchiolitis and chronic lung disease. Included studies of patients 1) at home, 2) in the accident/emergency department, and 3) in the hospital who received nebulized or metered dose inhaler ipratropium vs. placebo or beta agonist. Both ED studies (Naspitz 1992, Schuh 1992) used ipratropium with a beta agonist. ED and hospital data noted to the right. 3) 6 RCTs in children (18 months – 17 years) who received a single or multiple doses of ipratropium.	**1) Admission rate:** 53% vs. 56% (p = 0.596); no difference **Change in HR:** -3 vs. -6 (p = 0.474); no difference **Change in BP:** -7 vs. -10 (p = 0.523); no difference **Change in RR:** 0 vs. -4 (p = 0.055); no difference **Oxygen saturation:** 8 vs. 8 (p = 0.581); no difference **2) Requirement for additional inhaled therapy after 45 minutes (OR):** 0.22 (0.08-0.61) in one study; decreased need with ipratropium **Decrease in respiratory rate:** -2.00 (-6.77-2.77); no difference **Increase in oxygen sat in ED (MD):** 0.08 (-0.84-1.00); no difference **Oxygen sat at discharge or HD#3 (MD):** -0.90 (-2.80-1.00); no difference **Observed response (OR for "excellent response"):** 0.96 (0.37-2.47) **Effect on symptom scores at discharge or HD#3 (MD):** 0.65 (-0.29-1.59); no difference **Effect on duration of hospital stay (MD):** -0.4 days (-1.4-0.61); no difference

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	3)**Hospital admission (RR):** 0.93 (0.65-1.32); no difference (single dose); 0.72 (0.53-0.99); favors ipratropium (multiple dose for severe exacerbations). NNT = 11 (5-250) **Pulmonary function tests (MD):** at 60 min: -0.57 (-0.93 to -0.21); favors use of ipratropium; at 120 min: 0.53 (-0.90 to -0.17); favors ipratropium **Adverse effects:** nausea: 0.59 (0.30-1.14); vomiting: 1.03 (0.37-2.87); tremor: 1.02 (0.63-1.64); no difference in any adverse effects with multiple doses (or single dose)

1)Davis, D. P., Wiesner, C., Chan, T. C., & Vilke, G. M. (2005). The efficacy of nebulized albuterol/ipratroprium bromide versus albuterol alone in the prehospital treatment of suspected reactive airways disease. *Prehospital Emergency Care, 9*(4), 386-390.

2)Everard M, Bara A, Kurian M, N'Diaye T, Ducharme F, Mayowe V. Anticholinergic drugs for wheeze in children under the age of two years. *Cochrane Database of Systematic Reviews* 2005, Issue 3. Art. No.: CD001279. DOI: 10.1002/14651858.CD001279.pub2.

3)Plotnick, L. H., & Ducharme, F. M. (1998). Should inhaled anticholinergics be added to beta-2 agonists for treating acute childhood and adolescent asthma? A systematic review. *BMJ, 317*(7164), 971-977.

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Question 6d: In children with respiratory distress, does the use of inhaled hypertonic saline (i.e., 3% or 5%) in the prehospital setting result in a clinical improvement (i.e., decreased distress, shorter ED length of stay, decreased admission rates to the hospital)?
Recommendation: Hypertonic saline should not be administered to children in respiratory distress in the prehospital setting.
Grade Criteria: Weak recommendation, Low quality evidence [1-3]
Two studies evaluating the use of hypertonic saline the emergency department for infants with respiratory distress due to bronchiolitis showed differing results in improvement in respiratory scores, but no difference in revisit rates to the emergency department. [1,2] For the one study that did show a difference in respiratory scores at 48 hours, there was no significant difference at 24 hours.[1] This study also showed no difference in mean length of stay. The other study showed no difference in rate of hospital admission or change in oxygen saturation. [2] Use of 3% saline in the inpatient setting reduced hospital length of stay. [3]

Recommendation: Weak recommendation with low quality evidence that hypertonic saline should not be administered to children in respiratory distress in the prehospital setting.
Number of Studies: Total # 3 ☒ Systematic review/meta-analysis [3] ☒ RCT [1,2] ☐ Cohort ☐ Observational ☐ Case Reports Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	**Summary of *Consistency***	***Indirectness* of Comparison**	***Imprecision* of Results**
☐ None ☐ Insufficient sample size ☐ Lack of blinding ☒ Lack of allocation concealment [3] ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☐ No inconsistencies ☐ Wide variation of treatment effect across studies ☒ Populations varied (e.g., sicker, older) [1-3] ☒ Interventions varied (e.g., doses) [1] ☒ Outcomes varied (e.g., diminishing effect over time) [1-3]	☐ Head-to-head comparison in correct population ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☒ Different populations [1-3] ☐ Different interventions ☐ Different outcomes measured ☐ Comparisons not applicable to question/outcome	☐ Dichotomous outcomes ☐ Sample size lower than calculated optimal information size ☐ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes ☐ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm

Sample	**CI/RR**
1) RCT of 171 infants < 18 months old with moderate to severe bronchiolitis who received either 5 ml of 5%, 3%, or 0.9% saline with 1.5 ml epinephrine every 4 hours in a short-stay unit. 2) RCT of 46 infants 6 weeks to 12 months with mild to moderate bronchiolitis who received 1-2 doses of either 2.5 ml of nebulized 3% hypertonic saline or 0.9% saline, both with 3 ml of 2.25% racemic epinephrine, in the emergency department. 3) 4 RCTs of infants with bronchiolitis (189 inpatients; 65 outpatients) treated with nebulized 3% saline vs. 0.9% saline.	1) **Wang bronchiolitis severity score improvement at 48 hours (diff b/t 5% and 0.9%):** 0.43 (0.02-0.88); there is a trend toward significance between 8-72 hours after administration, but it was not significant at 24 hours. **Mean length of stay:** 1.56 +/-1.38 days (5%); 1.4 +/-1.41 days (3%); 1.88 (+/-1.76 days (0.9%), p = 0.36 (no difference) **Revisit rates:** no difference (61%, 59%, 63%, respectively) 2) **Respiratory Assessment Change Score (RACS-mean):** 0.74 (-1.45-2.93); no difference **Change in oxygen saturation (mean):** 1.78 (-0.50-4.06); no difference **Rate of hospital admission (RR):** 0.61 (0.22-1.19); no difference, though there was a trend towards decreased admission in the hypertonic saline group that may have been significant if treatment had been provided for a longer duration of time. **Return to the ED (RR):** 0.74 (0.11-2.91): no difference 3) **Length of hospital stay (MD):** -0.94 days (-1.48 to -0.40; p = 0.0006); shorter LOS favoring 3% saline **Post-inhalation clinical scores over 3 days (MD):** • Day 1: -0.75 (-1.38 to -0.12; p = 0.02) • Day 2: -1.18 (-1.97 to -0.39; p = 0.003) • Day 3: -1.28 (-2.57 to 0.00; p = 0.05) **Rate of hospitalization (RR):** 0.67 (0.12-3.75); no difference

1)Al-Ansari, K., Sakran, M., Davidson, B. L., El Sayyed, R., Mahjoub, H., & Ibrahim, K. (2010). Nebulized 5% or 3% hypertonic or 0.9% saline for treating acute bronchiolitis in infants. *Journal of Pediatrics, 157*(4), 630-634.
2)Grewal, S., Ali, S., McConnell, D. W., Vandermeer, B. V., & Klassen, T. P. (2009). A randomized trial of nebulized 3% hypertonic saline with epinephrine in the treatment of acute bronchiolitis in the emergency department. *Archives of Pediatrics & Adolescent Medicine, 163*(11), 1007-1012.

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3)Zhang L, Mendoza-Sassi RA, Wainwright C, Klassen TP. Nebulized hypertonic saline solution for acute bronchiolitis in infants. *Cochrane Database of Systematic Reviews* 2008, Issue 4. Art. No.: CD006458. DOI: 10.1002/14651858.CD006458.pub2.

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Question 6e: In children with respiratory distress, does the use of inhaled racemic epinephrine in the prehospital setting result in a clinical improvement (i.e., decreased distress, shorter ED length of stay, decreased admission rates to the hospital)?
Recommendation: Nebulized epinephrine should be administered to children in severe respiratory distress with presumed croup (e.g., have stridor at rest or barking cough) or refractory bronchiolitis (e.g. coarse breath sounds) in the prehospital setting if other treatments (e.g., suctioning, oxygen) fail to result in clinical improvement.
Grade Criteria: Strong recommendation, Moderate quality evidence [1,2]
There are no studies to date on the use of racemic epinephrine in children in the prehospital setting for any respiratory condition; however, two meta-analyses exist for the use of nebulized epinephrine for both croup and bronchiolitis in the emergency department setting. [1,2]

For emergency department patients with croup, croup scores were improved at 30 minutes and 6 hours with the use of nebulized epinephrine; no difference in return visits, readmission, or length of hospitalization existed when compared to placebo. [1] In addition, there was no difference between racemic and L-epinephrine, and the addition of IPPB (intermittent positive pressure breathing) made no difference. [1]

For emergency department and inpatients with bronchiolitis, nebulized epinephrine improved clinical scores when compared to placebo (but not salbutamol), oxygen saturation in some instances (30 minutes for outpatients), short term respiratory rate (30-60 minutes in outpatients), and subjective improvement. [2] There were no differences in rates of admission to the hospital or length of hospital stay. [2]

Recommendation: Strong recommendation with moderate quality evidence that nebulized epinephrine should be administered to children in severe respiratory distress with presumed croup (e.g., coarse breath sounds and have stridor at rest or barking cough) or refractory bronchiolitis in the prehospital setting if other treatments (e.g., suctioning, oxygen) fail to result in clinical improvement.
Number of Studies: Total # 2 ☒ Systematic review [1,2] ☐ RCT ☐ Cohort ☐ Observational ☐ Case Reports Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☐ None ☐ Insufficient sample size ☒ Lack of blinding [1] ☒ Lack of allocation concealment [1,2] ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☐ No inconsistencies ☐ Wide variation of treatment effect across studies ☒ Populations varied (e.g., sicker, older) ☐ Interventions varied (e.g., doses) ☒ Outcomes varied (e.g., diminishing effect over time) [2]	☐ Head-to-head comparison in correct population ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☒ Different populations [1,2] ☐ Different interventions ☐ Different outcomes measured ☐ Comparisons not applicable to question/outcome	☐ Dichotomous outcomes ☐ Sample size lower than calculated optimal information size ☐ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes ☐ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm

Sample	CI/RR
1) 8 RCTs or quasi-RCTs evaluating the use of nebulized racemic epinephrine for croup in emergency department or admitted patients with 3 different comparisons: • Nebulized epinephrine vs. placebo • Nebulized racemic epinephrine vs. L-epinephrine • Nebulized epinephrine with IPPB (intermittent positive pressure breathing) vs. without IPPB 2) 14 RCTs evaluating the use of nebulized racemic epinephrine for bronchiolitis in emergency department patients and inpatients	1) • **Nebulized epinephrine vs. placebo** ○ **Change in croup score (baseline to 30 minutes):** -0.94 (-1.37 to -0.51); favors epinephrine ○ **Change in croup score (baseline to 2 hours):** -0.15 (-1.03 to 0.73); no difference ○ **Change in croup score (baseline to 6 hours):** -0.60 (-1.12 to -0.08); favors epinephrine ○ **Return visits/readmission:** 0.0 (-0.07 to 0.07); no difference ○ **Length of hospitalization (hours):** -1.80 (-4.07 to 0.47); no difference ○ **Improvement (risk ratio):** 1.46 (0.82 to 2.60); no difference • **Nebulized racemic epinephrine vs. L-epinephrine** ○ **Change in croup score (baseline to 30 minutes):** 0.33 (-0.42 to 1.08); no difference ○ **Change in croup score (baseline to 2 hours):** 0.87 (0.09 to 1.65); favors L-epinephrine ○ **Intubation:** 0.19 (-0.03 to 0.40); no difference • **Nebulized epinephrine with IPPB (intermittent positive pressure breathing) vs. without IPPB**

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	○ **Change in croup score (baseline to 30 minutes):** -0.14 (-1.24 to 0.95); no difference ○ **Change in croup score (baseline to 2 hours):** -0.72 (-1.86 to 0.42); no difference ○ **Intubation:** 0.0 (-0.26 to 0.26); no difference 2) • **Nebulized epinephrine vs. placebo** ○ **Clinical score (baseline to 30 min) (MD):** -0.28 [-0.54, -0.02]; favors epinephrine ○ **Clinical score (baseline to 60 min) (MD):** -0.63 [-0.98, -0.28]; favors epinephrine ○ **Oxygen saturation (baseline to 30 minutes) (MD):** 0.85 [-0.94, 2.64]; no difference; outpatient data only favored epinephrine: 2.79 [1.50, 4.08] ○ **Oxygen saturation (baseline to 60 minutes) (MD):** 0.55 [-0.29, 1.40]; no difference ○ **Admission to hospital (OR):** 0.51 [0.18, 1.42]; no difference ○ **Length of hospital stay (MD-hours):** -5.90 [-16.23, 4.43]; no difference ○ **Respiratory rate (at 30 min) (MD):** -1.84 [-4.63, 0.94]; no difference; outpatient data only favored epinephrine: -4.54 [-8.89, -0.19] ○ **Respiratory rate (at 60 min) (MD):** -1.76 [-6.65, 3.13]; no difference; no outpatient data available ○ **Heart rate (at 30 min) (MD):** 1.79 [-4.28, 7.85]; no difference ○ **Heart rate (at 60 min) (MD):** 8.40 [-0.13, 16.92]; no difference; outpatient data only favored placebo: 11.80 [5.20, 18.40] ○ **Improvement (OR):** 25.06 [4.95, 126.91]; favors epinephrine (outpatient data only) ○ **Pallor (OR):** 4.73 [0.46, 48.77]; no difference • **Nebulized epinephrine vs. salbutamol** ○ **Clinical score (baseline to 30 min) (MD): -**0.20 [-0.56, 0.16]; no difference ○ **Clinical score (baseline to 60 min) (MD):** -0.16 [-0.61, 0.29]; no difference ○ **Clinical score (baseline to 90 min) (MD): -**0.32 [-0.82, 0.19]; no difference ○ **Clinical score (baseline to 24 hours) (MD):** 0.11 [-0.61, 0.83]; no difference ○ **Clinical score (baseline to 36 hours) (MD):** 0.55 [-0.18, 1.29]; no difference ○ **Oxygen saturation (baseline to 30 min) (MD):** 0.31 [-0.88, 1.49]; no difference ○ **Oxygen saturation (baseline to 60 min) (MD):** 1.91 [0.38, 3.44]; favors epinephrine ○ **Oxygen saturation (baseline to 90 min) (MD):** -0.68 [-2.39, 1.03]; no difference ○ **Admission to hospital (OR):** 0.40 [0.12, 1.33]; no difference ○ **Length of hospital stay (MD-hours):** -3.96 [-25.55, 17.62]; no difference ○ **Respiratory rate (at 30 min) (MD):** -5.15 [-6.83, -3.46]; favors epinephrine ○ **Respiratory rate (at 60 min) (MD): -**7.76 [-11.35, -4.17]; favors epinephrine ○ **Respiratory rate (at 90 min) (MD): -**5.00 [-12.04, 2.04]; no difference ○ **Heart rate (at 30 min) (MD):** 0.33 [-5.12, 5.78]; no difference ○ **Heart rate (at 60 min) (MD):** 6.25 [-3.64, 16.13]; no difference ○ **Heart rate (at 90 min) (MD): -**14.00 [-22.95, -5.05]; favors epinephrine ○ **Improvement (OR):** 4.51 [1.93, 10.53]; favors epinephrine ○ **Pallor (OR-30 min):** 6.00 [1.33, 27.00]; favors salbutamol

1) Bjornson C, Russell KF, Vandermeer B, Durec T, Klassen TP, Johnson DW. Nebulized epinephrine for croup in children. *Cochrane Database of Systematic Reviews* 2011, Issue 2. Art. No.: CD006619. DOI: 10.1002/14651858.CD006619.pub2.
2) Hartling L, Russell KF, Patel H, Klassen TP, Liang Y. Epinephrine for bronchiolitis. *Cochrane Database of Systematic Reviews* 2004, Issue 1. Art. No.: CD003123. DOI: 10.1002/14651858.CD003123.pub2.

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Question 6f: In children with respiratory distress, does the use of inhaled magnesium sulfate in the prehospital setting result in a clinical improvement (i.e., decreased distress, shorter ED length of stay, decreased admission rates to the hospital)?
Recommendation: Inhaled magnesium sulfate should not be administered to children in respiratory distress in the prehospital setting.
Grade Criteria: Weak recommendation, Low quality evidence [(1)]
There is no significant improvement in pulmonary function or hospitalization rates between pediatric patients who received nebulized magnesium sulfate and those who did not. In adult patients with severe asthma, there was a significant difference in admission rates favoring the use of inhaled magnesium, but the data present for pediatric patients showed no difference in mild to moderate asthma exacerbations.

Recommendation: Weak recommendation with low quality evidence that inhaled magnesium sulfate should not be administered to children in respiratory distress in the prehospital setting.
Number of Studies: Total # 1 ☒ Systematic review/meta-analysis [(1)] ☐ RCT ☐ Cohort ☐ Observational ☐ Case Reports Publication Bias Evident ☐ Yes ☐ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☐ None ☐ Insufficient sample size ☐ Lack of blinding ☒ Lack of allocation concealment [(1)] ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☐ No inconsistencies ☐ Wide variation of treatment effect across studies ☐ Populations varied (e.g., sicker, older) [(1)] ☐ Interventions varied (e.g., doses) ☐ Outcomes varied (e.g., diminishing effect over time)	☐ Head-to-head comparison in correct population ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☒ Different populations [(1)] ☐ Different interventions ☒ Different outcomes measured [(1)] ☐ Comparisons not applicable to question/outcome	☐ Dichotomous outcomes ☐ Sample size lower than calculated optimal information size ☐ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes ☐ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm

Sample	CI/RR
1) Six RCTs involving 296 patients were included. Three studies enrolled only adults and 2 enrolled exclusively pediatric patients; three of the studies enrolled severe asthmatics. Subgroup analysis was done on the pediatric population and this data is noted to the right when available.	1) **Pediatric Data Only** **Pulmonary function testing (MD):** 0.36 [-0.14, 0.86]; no difference **Admission to the hospital (RR):** 2.00 [0.19, 20.93]; no difference

1.) Blitz M, Blitz S, Beasely R, Diner B, Hughes R, Knopp JA, Rowe BH. Inhaled magnesium sulfate in the treatment of acute asthma. *Cochrane Database of Systematic Reviews* 2005, Issue 4. Art. No.: CD003898. DOI: 10.1002/14651858.CD003898.pub4.

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Question 6g: In children with respiratory distress, does the use of inhaled steam in the prehospital setting result in a clinical improvement (i.e., decreased distress, shorter ED length of stay, decreased admission rates to the hospital)?
Recommendation: Inhaled steam via a mist tent should not be administered to children in respiratory distress in the prehospital setting.
Grade Criteria: Weak recommendation, Moderate quality evidence [1]
Only one randomized trial has evaluated the use of a mist tent for bronchiolitis in children < 3 years of age. [1] This showed that mist therapy is ineffective for improving respiratory distress scores in children.

Recommendation: Weak recommendation with moderate quality evidence that inhaled steam via a mist tent should not be administered to children in respiratory distress in the prehospital setting.
Number of Studies: Total # ☒ Systematic review/meta-analysis [1] ☐ RCT ☐ Cohort ☐ Observational ☐ Case Reports Publication Bias Evident ☐ Yes ☐ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☐ None ☐ Insufficient sample size ☒ Lack of blinding [1] ☒ Lack of allocation concealment ☐ Large losses to F/U ☐ Incorrect analysis of ITT [1] ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☐ No inconsistencies ☐ Wide variation of treatment effect across studies ☐ Populations varied (e.g., sicker, older) ☐ Interventions varied (e.g., doses) ☐ Outcomes varied (e.g., diminishing effect over time)	☐ Head-to-head comparison in correct population ☒ Indirect comparisons (e.g., interventions to placebo but not each other) [1] ☒ Different populations [1] ☐ Different interventions ☐ Different outcomes measured ☐ Comparisons not applicable to question/outcome	☐ Dichotomous outcomes ☐ Sample size lower than calculated optimal information size ☐ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes ☐ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm

Sample	CI/RR

1) Randomized controlled trials involving children up to three years old with bronchiolitis comparing steam inhalation (or cool mist) or humidified oxygen against bronchodilators, corticosteroids or placebo; alone or in combination; only 1 study met criteria for inclusion, which enrolled 104 patients ages 7 weeks to 24 months.	1)
	• **Steam inhalation vs. nebulized salbutamol**
	  ○ **Change in respiratory distress score (30 min):** 3.80 [2.51, 5.09]; favors salbutamol
	  ○ **Change in respiratory distress score (60 min):** 4.40 [3.35, 5.45]; favors salbutamol
	• **Steam inhalation vs. nebulized saline**
	  ○ **Change in respiratory distress score (30 min):** 1.10 [-0.30, 2.50]; no difference
	  ○ **Change in respiratory distress score (60 min):** -0.60 [-1.93, 0.73]; no difference

1)Umoren R, Odey F, Meremikwu MM. Steam inhalation or humidified oxygen for acute bronchiolitis in children up to three years of age. *Cochrane Database of Systematic Reviews* 2011, Issue 1. Art. No.: CD006435. DOI: 10.1002/14651858.CD006435.pub2.

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Question 7: In children with respiratory distress, does the use **of** intravenous magnesium sulfate **in** the prehospital setting result in a clinical improvement (e.g., decreased distress, shorter ED length of stay, decreased admission rates to the hospital)?
Recommendation: Administer intravenous magnesium sulfate to children with presumed asthma in impending respiratory failure.
Grade Criteria: Strong recommendation, moderate quality of evidence [1-3]

Recommendation: Strong recommendation with moderate quality evidence that intravenous magnesium sulfate should be administered to children with presumed asthma in impending respiratory failure.
Number of Studies: **Total # 3** ☒ Systematic review/Meta-analysis [1,2,3] ☐ ☐ Cohort ☐ Observational ☐ Case Reports ☐ Clinical Guideline Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☒ None [1,3] ☒ Insufficient sample size [2] ☐ Lack of blinding ☐ Lack of allocation concealment ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g. no effect outcome)	☐ No inconsistencies ☐ Wide variation of treatment effect across studies ☒ Populations varied (e.g. sicker, older) [1-3] ☒ Interventions varied (e.g. doses) [1-3] ☐ Outcomes varied (e.g. diminishing effect over time)	☒ Head-to-head comparison in correct Population [1] ☐ Indirect comparisons (e.g. interventions to placebo but not each other) ☒ Different populations [2,3] ☒ Different interventions [2] ☐ Different outcomes measured ☐ Comparisons not applicable to question/outcome	☐ Dichotomous outcomes ☐ Sample size lower than calculated optimal information size ☐ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes ☒ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm [1-3]

Sample	CI/RR
1) Meta-analysis of 9 studies with 859 pediatric patients given a bolus of IV $MgSO_4$ in the ED for acute bronchospasm. 2) Cochrane Review of 6 trials involving 296 patients with asthma exacerbations treated with $MgSO_4$. Two of the studies enrolled exclusively pediatric patients, and three studies enrolled only adults. 3) Cochrane Review of 7 trials involving 665 patients receiving $MgSO_4$ in the emergency department for acute asthma. Five adult trials and two pediatric trials were included.	1) • **Posttreatment Effect Size**: 0.162 for patients treated with $MgSO_4$ (95% CI: 0.028 to 0.297; p = 0.02) • **Sensitivity Analysis**: summary effect ranged from 0.127 to 0.206 • **Adverse Events**: no serious adverse events were reported 2) • **Pulmonary Function:** non significant improvement in pulmonary function between patients whose treatments included nebulized $MgSO_4$ in addition to β_2 agonist (SMD:0.23; 95% CI: -0.03 to 0.50) • **Hospitalizations**: similar between the groups treated with $MgSO_4$ and β_2 agonist s (RR: 0.69; 95% CI: 0.42 to 1.12) • **Lung Function:** significantly different for patients given $MgSO_4$ (SMD: 0.55; 95% CI: 0.12 to 0.98) 3) • **Peak Expiratory Flow:** Non significant improvement in peak expiratory flow rates for pts receiving $MgSO_4$ (WMD: 29.4 L/min; 95% CI: -3.4 to 62) • In pts with acute asthma, peak expiratory flow rate improved by 52.3 L/min (95% CI: 27 to 77.5) • **Admission:** Overall admission to the hospital was not reduced (OR 0.31; 95% CI: 0.09 to 1.02) • For patients with severe asthma, hospital admission reduced for those receiving $MgSO_4$ (OR 0.10; 95% CI: 0.04 to 0.27)

1)Alter, H. J., Koepsell, T. D., & Hilty, W. M. (2000). Intravenous magnesium as an adjuvant in acute bronchospasm: A meta-analysis. *Annals of Emergency Medicine, 36*(3), 191-197.
2)Blitz M, Blitz S, Beasely R, Diner B, Hughes R, Knopp JA, Rowe BH. Inhaled magnesium sulfate in the treatment of acute asthma. Cochrane Database of Systematic Reviews 2005, Issue 4. Art. No.: CD003898. DOI: 10.1002/14651858.CD003898.pub4.
3)Rowe BH, Bretzlaff J, Bourdon C, Bota G, Blitz S, Camargo CA. Magnesium sulfate for treating exacerbations of acute asthma in the emergency department. Cochrane Database of Systematic Reviews 2000, Issue 1. Art. No.: CD001490. DOI: 10.1002/14651858.CD001490.

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Question 8: In children with respiratory distress in the prehospital setting, is it efficacious (e.g., lead to better clinical outcomes) to place an IV?
Recommendation: IVs should only be placed in children with respiratory distress for clinical concerns of dehydration, or when administering IV medications.
Grade Criteria: Weak recommendation, Very low quality evidence [1-3]
Evidence from three observational studies offered differing results. One study found that EMS responders had a 98.3% success rate in obtaining IV line access in the prehospital setting. [2] A second observational study found a significant reduction in mortality after the implementation of advanced life support practices (i.e., starting IVs and intubating patients). [3] However, one study found that IV catheters, when placed, were used only 17% of the time. [1]
All three of the studies included adults as well as pediatric patients.

Recommendation: Weak recommendation with very low quality evidence that IVs should only be placed in children with respiratory distress for clinical concerns of dehydration, or when administering IV medications.
Number of Studies: Total # 3 ☐ Systematic review/Meta-analysis ☐ RCT ☐ Cohort ☒ Observational [1-3] ☐ Case Reports ☐ Clinical Guideline Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☐ None ☒ Insufficient sample size [2] ☒ Lack of blinding [1-3] ☐ Lack of allocation concealment ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☒ No inconsistencies [1-3] ☐ Wide variation of treatment effect across studies ☐ Populations varied (e.g., sicker, older) ☐ Interventions varied (e.g., doses) ☐ Outcomes varied (e.g., diminishing effect over time)	☐ Head-to-head comparison in correct population ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☒ Different populations [1-3] ☐ Different interventions ☐ Different outcomes measured ☐ Comparisons not applicable to question/outcome	☐ Dichotomous outcomes ☐ Sample size lower than calculated optimal information size ☐ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes ☒ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm [1-3]

Sample	CI/RR
1) Retrospective observational study of 34,585 prehospital patients. 2) Prospective observational study of 58 patients encountered by participating emergency medical service agencies who had at least one IV line placement. 3) Retrospective observational study of 8,138 patients provided advanced life support for out-of-hospital respiratory distress.	1) **Line access and utilization:** IV catheters were placed in 60% of patients but only 17% of the IVs were utilized; 82% of patients with bradycardia received an IV (OR:1.5888, p < 0.00001), 51% were utilized 2) • **Line Access:** rate of 98.3% in obtaining IV line access in the prehospital • **Procedure intervals:** mean IV line procedure intervals were 1.6 minutes in urban and 1.4 minutes in non-urban settings (p = 0.408) 3) • **IV drug administration rate:** 15.1% after advanced life support training, baseline comparison not available • **Mortality:** reduced 1.9% after advanced life support training (training on IV administration and endotracheal intubation), p = 0.01; 95% CI: 0.4-3.4; OR: 1.3; 95% CI: 1.1, 1.5

1)Kuzma, K., Sporer, K. A., Michael, G. E., & Youngblood, G. M. (2009). When are prehospital intravenous catheters used for treatment? *Journal of Emergency Medicine, 36*(4), 357-362.
2)Spaite, D. W., Valenzuela, T. D., Criss, E. A., Meislin, H. W., & Hinsberg, P. (1994). A prospective in-field comparison of intravenous line placement by urban and nonurban emergency medical services personnel. *Annals of Emergency Medicine, 24*(2), 209-214.
3)Stiell, I. G., Spaite, D. W., Field, B., Nesbitt, L. P., Munkley, D., Maloney, J., et al. (2007). Advanced life support for out-of-hospital respiratory distress. *The New England Journal of Medicine, 356*(21), 2156-2164.

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Question 9: In children with respiratory distress in the prehospital setting, **do steroids lead** to improved clinical outcomes? What is the appropriate timing of **steroid** administration? What are the indications and contraindications for the use of **steroids**? What is the preferred route?
Recommendation: Oral or parenteral steroids should be administered to children in respiratory distress with presumed asthma in the prehospital setting.
Grade Criteria: Strong recommendation, Moderate quality evidence [1-14]
Two Cochrane Reviews and one meta-analysis found that early administration of corticosteroids in pediatric patients with asthma in the ED resulted in a reduction in the hospital admission rate. [10, 11,14]

One Cochrane Review evaluating the benefit of systemic corticosteroids compared to placebo in acute pediatric asthma found that administration of corticosteroids was associated with a reduction in length of stay. [14] However, a RCT conducted in children age 10-60 months who presented to the ED with wheezing found there to be no significant difference in mean length of stay for those children receiving oral steroids, compared to controls. [9]

An RCT in 49 children presenting to the ED with asthma evaluated admission rate and pulmonary function for IV methylprednisolone vs. oral methylprednisolone. It found no significant difference between the two groups in regard to respiratory rates, oxygen saturation, and PISs and FEV_1 values four hours after treatment. There was also no difference in admission rates between the two groups. [2]

One RCT evaluated length of stay, hospital admission rates, and adverse effects of prednisolone and dexamethasone for children presenting to the ED with asthma. The study found that hospital admission rates were higher and length of stay was longer for patients treated with prednisolone. [13]

Recommendation: Strong recommendation with moderate quality evidence that steroids should be administered to children in respiratory distress with presumed asthma in the prehospital setting.
Strong recommendation with moderate quality evidence that steroids administered either IV or IM are no more effective than steroids administered orally in improving pulmonary function, asthma scores, and reducing readmission rates.
Number of Studies: Total # 14 ☒Systematic review/Meta-analysis [3,4,5,8,10,11,12,14] ☒RCT [1,2,6,7,9,13] ☐Cohort ☐Observational ☐Case Reports Publication Bias Evident ☐Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☒ None [3,4,8,10-12] ☒ Insufficient sample size [1,2,6,7,13] ☐ Lack of blinding ☐ Lack of allocation concealment ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☒ Selective reporting of measured outcomes (e.g. no effect outcome) [9,14]	☐ No inconsistencies ☐ Wide variation of treatment effect across studies ☒ Populations varied (e.g. sicker, older) [1-14] ☐ Interventions varied (e.g. doses) ☐ Outcomes varied (e.g. diminishing effect over time)	☐ Head-to-head comparison in correct population ☐ Indirect comparisons (e.g. interventions to placebo but not each other) ☒ Different populations [1-14] ☒ Different interventions [1-14] ☒ Different outcomes measured [1-14] ☐ Comparisons not applicable to question/outcome	☐ Dichotomous outcomes ☐ Sample size lower than calculated optimal information size ☐ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes ☒ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm [1-14]

Sample	CI/RR

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1) RCT of 96 children (age 3-84 months) presenting to the ED with moderate-to-severe group 2) RCT of 49 pediatric patients who presented to the ED with moderate to severe asthma. 3) Cochrane Review of 48 studies with 15,155 patients (including 1155 children) that compared the combination of inhaled LABA and ICS to a higher dose of inhaled corticosteroids for asthma 4) Cochrane Review of 77 studies with 21,248 patients (including 4625 children) that compared the addition of inhaled LABA to inhaled corticosteroids to same dose inhaled corticosteroids for asthma 5) Cochrane Review of 10 studies with 587 patients (including 5 pediatric studies) that presented to the ED with asthma 6) RCT of 86 children (age 18 months - 6 years) who presented to the ED with clinical asthma score 3-7 7) RCT of 144 children with moderate-to-severe croup 8) Cochrane Review of 9 trials with 344 adult patients with acute severe asthma 9) RCT of 687 children (age 10 months - 60 months) who presented to an ED with an attack of wheezing associated with a viral infection. 10) Meta-analysis of 30 RCTs with patients presenting to the ED for asthma exacerbations. Several of the studies involved pediatric patients; none of the studies were in the prehospital setting. 11) Cochrane Review of 9 RCTs on participants > 2 presenting to an ED with signs and symptoms of asthma. 5 of the studies involved pediatric patients; none of the studies were in the prehospital setting. 12) Cochrane Review of 31 studies with 3736 children with croup 13) A RCT of 111 children (age 1-17 yrs) who presented to ED with acute asthma. 14) Cochrane Review of 7 RCTs that included 426 children (age 1-18 yrs) with severe acute asthma that received oral, inhaled, IV or intramuscular corticosteroids. None were prehospital studies, and all participants were assessed in the ED and admitted to the hospital with asthma.	1) • No statistical difference between the group that received IM dexamethasone and the one that received oral dexamethasone for the proportion of stridor, expiratory sounds, barky cough, sleep pattern, the degree of improvement or proportion with complete resolution after 1 day 2) • **Pulmonary function:** 4 hrs after treatment both groups (IV methylprednisolone and oral methylprednisolone) had similar respiratory rates, oxygen saturation, PISs, and FEV1 values (p = not significant) • **Admission rate:** 48% of patients in the oral group and 50% of patients in the IV group were admitted to the hospital (p = 0.88) 3) • **Exacerbations:** lower risk in patients treated with LABA and ICS (RR 0.88; 95% CI: 0.78 to 0.98) • **Admission rate:** no statistically significant difference overall (RR 1.02; 95% CI: 0.67 to 1.56); but a trend toward increased hospital admission associated with combination therapy in pediatric patients (RR 2.21; 95% CI: 0.74 to 6.64) • **Adverse Events:** no statistically significant difference between the groups (RR 1.125; 95% CI: 0.91 to 1.37) 4) • The addition of LABA to ICS reduced the risk of exacerbations requiring oral steroids by 23% from 15% to 11% (RR 0.77; 95% CI: 0.68 to 0.87); subgroup estimate for pediatric pts was not statistically significant (RR 0.89; 95% CI: 0.58 to 1.39) 5) • **Hospital Admission**: pts administered ICS were less likely to be admitted (OR:0.32; 95% C:I 0.18 to 0.54) • **PEFR and FEV1**: pts administered ICS saw improvement (WMD 7%; 95% CI 4 to 11%); and (WMD 6%; 95% CI: 2 to 10%), respectively 6) • **Asthma Score:** mean change at 4 day FU was 3.6 in IM dexamethasone group and 3.4 in 5 day oral prednisolone group (difference 0.2; 95% CI: -0.4 to 0.7) • **Re-Admission rate:** 5.9% of IM dexamethasone patients and 4.1% of prednisolone patients were admitted before the 2 week FU (difference 1.8%; 95% CI: -5.4 to 9.0%) 7) • **Hospital Admission:** rates of admission were 71% in placebo group, 38% in nebulized budesonide group, and 23% in IM dexamethasone group (p= 0.001 for comparison of budesonide with placebo, p < 0.001 for comparison of dexamethasone with placebo, and p = 0.18 for comparison of budesonide with dexamethasone) • **Croup Scores**: children treated with budesonide or dexamethasone had greater improvement in croup scores than those given placebo (p = 0.03 and p < 0.0001); pts treated with dexamethasone (-2.9) had a greater improvement than those treated with budesonide (-2) (p = 0.003)

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	8) • **FEV1:** no significant difference between the comparison groups of different doses of corticosteroids after 24, 48 of 72 hrs; at 48 hrs, the WMD was -3.3% predicted (95% CI: -12.4 to 5.8) for the low vs. medium dose comparison, -1.9% predicted (95% CI: -8.1 to 4.3) for the medium vs. high dose comparison and 0.5% predicted (95% CI: -7.8 to 8.8) for the low vs. high dose comparison 9) • **Length of stay:** no significant difference between the placebo group and the prednisolone group (13.9 hrs vs. 11.0 hrs; ratio of geometric means, 0.90, 95% CI: 0.77-1.05) • **Albuterol actuations administered:** not significant • **PRAM scores at 4-24 hrs:** not significant 10) • **Hospital admission following the early use of corticosteroids (any route) in the ED**: OR: 0.50 (95% CI: 0.31-0.81) - there was no difference in the magnitude of the reduction in admission rates between studies of children (OR: 0.40, 95% CI: 0.17-0.94) and adults (OR: 0.58, 95% CI: 0.32-1.07) - early outcomes (< 2 hr) were not significant (OR:1.38, 95% CI: 0.41-4.67); at 4 hrs the benefit of CS was (OR: 0.48, 95%: 0.24-0.97); and at 6 hrs (OR:0.28, 95% CI: 0.09-0.84) - admission rates appeared greater with oral route (OR: 0.24, 95% CI: 0.11-0.53) than IV (OR: 0.68, 95% CI: 0.39-1.21) 11) • **Admission rate:** use of steroids early in the treatment of asthmatic exacerbations reduces admissions in adults (OR: 0.47, 95% CI: 0.27-0.79); and in children (OR : 0.06-0.42) • **Pulmonary function:** Oral and IV steroids have equivalent effects on pulmonary function in acute exacerbations (ES: -0.07; 95% CI: -0.39-0.25) 12) • **Westley Score:** glucocorticosteroid treatment associated with an improvement in score at 6 hours (WMD -1.2; 95% CI -1.6 to -0.8) and at 12 hours (WMD -1.9; 95% CI: -2.4 to -1.3) • **Readmissions:** Fewer return visits and readmissions occurred in its treated with glucocorticosteroids (RR 0.50; 0.36 to 0.70) • **LOS in ED:** decreased for patients with glucocorticosteroids (WMD 12 hours; 95% CI: 5 to 19 hours) • **Epi Use:** decreased for patients with glucocorticosteroids (risk difference 10%; 95% CI 1 to 20) • **Croup Score:** no mean difference between oral vs. IM dexamethasone • **Readmissions:** reduced risk in oral group (RR 0.80; 95% CI: 0.58 to 1.12) 13) • **Hospital admission for patients treated with oral prednisone vs. nebulized dexamethasone:** 21% of patients treated with dexamethasone required hospitalization, compared with 31% of those treated with prednisone (p = 0.26) • **Length of Stay:** 23% of patients treated with dexamethasone were discharged home within 2 hrs, vs. 7%

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	of those treated with prednisone (p = 0.02) • **Adverse Effects:** fewer patients treated with dexamethasone vomited (0% vs. 15%, p = 0.001) • **Relapse:** fewer patients treated with dexamethasone relapsed within 48 hrs of ED discharge (0% vs. 16%, p = 0.008). 14) • **Length of Stay:** WMD: -8.75 hours; 95% CI: -19.23 – 1.74 in favor of treating with corticosteroids • **% Predicted PEFR:** WMD: 7.21; 95% CI: 7.01-21.25; no significant difference between placebo and corticosteroid treatment group • **Relapse rate following discharge:** treatment group less likely to relapse within 3 months of discharge (OR: 0.19; 95% CI: 0.07-0.55) • **Nebulized steroids vs. systemic steroids:** 1 study (Matthews 1999) found that severity of shortness of breath decreased more in patients who received budesonide than those receiving prednisolone (WMD: -0.77; 95% CI: -1.34-.0.20)

1)Amir, L., Hubermann, H., Halevi, A., Mor, M., Mimouni, M., & Waisman, Y. (2006). Oral betamethasone versus intramuscular dexamethasone for the treatment of mild to moderate viral croup: A prospective, randomized trial. *Pediatric Emergency Care, 22*(8), 541-544.
2)Barnett, P. L. J., Caputo, G. L., Baskin, M., & Kuppermann, N. (1997). Intravenous versus oral corticosteroids in the management of acute asthma in children. *Annals of Emergency Medicine, 29*(2), 212-217.
3)Ducharme, F. M., Chalut, D., Plotnick, L., Savdie, C., Kudirka, D., Zhang, X., et al. (2008). The pediatric respiratory assessment measure: A valid clinical score for assessing acute asthma severity from toddlers to teenagers. *The Journal of Pediatrics, 152*(4), 476-480.e471.
4)Ducharme FM, Ni Chroinin M, Greenstone I, Lasserson TJ. Addition of long-acting beta2-agonists to inhaled corticosteroids versus same dose inhaled corticosteroids for chronic asthma in adults and children. *Cochrane Database of Systematic Reviews* 2010, Issue 5. Art. No.: CD005535. DOI: 10.1002/14651858.CD005535.pub2.
5)Edmonds M, Camargo CA, Pollack CV, Rowe BH. Early use of inhaled corticosteroids in the emergency department treatment of acute asthma. *Cochrane Database of Systematic Reviews* 2003, Issue 3. Art. No.: CD002308. DOI: 10.1002/14651858.CD002308.
6)Gordon, S., Tompkins, T., & Dayan, P. S. (2007). Randomized trial of single-dose intramuscular dexamethasone compared with prednisolone for children with acute asthma. *Pediatric Emergency Care, 23*(8), 521-527.
7)Johnson, D. W., Jacobson, S., Edney, P. C., Hadfield, P., Mundy, M. E., & Schuh, S. (1998). A comparison of nebulized budesonide, intramuscular dexamethasone, and placebo for moderately severe croup. *New England Journal of Medicine, 339*(8), 498-503.
8)Manser R, Reid D, Abramson MJ. Corticosteroids for acute severe asthma in hospitalised patients. *Cochrane Database of Systematic Reviews* 2001, Issue 1. Art. No.: CD001740. DOI: 10.1002/14651858.CD001740.
9)Panickar, J., Lakhanpaul, M., Lambert, P. C., Kenia, P., Stephenson, T., Smyth, A., et al. (2009). Oral prednisolone for preschool children with acute virus-induced wheezing. *New England Journal of Medicine, 360*(4), 329-338.
10) Rowe, B. H., Keller, J. L., & Oxman, A. D. (1992). Effectiveness of steroid therapy in acute exacerbations of asthma: A meta-analysis. *The American Journal of Emergency Medicine, 10*(4), 301-310.
11) Rowe BH, Spooner C, Ducharme F, Bretzlaff J, Bota G. Early emergency department treatment of acute asthma with systemic corticosteroids. *Cochrane Database of Systematic Reviews* 2001, Issue 1. Art. No.: CD002178. DOI: 10.1002/14651858.CD002178.
12) Russell KF, Wiebe N, Saenz, A, Ausejo Segura M, Johnson DW, Hartling L, Klassen TP. Glucocorticoids for croup. *Cochrane Database of Systematic Reviews* 2004, Issue 1. Art. No.: CD001955. DOI: 10.1002/14651858.CD001955.pub2.
13) Scarfone, R. J., Loiselle, J. M., Wiley Ii, J. F., Decker, J. M., Henretig, F. M., & Joffe, M. D. (1995). Nebulized dexamethasone versus oral prednisone in the emergency treatment of asthmatic children. *Annals of Emergency Medicine, 26*(4), 480-486.
14) Smith M, Iqbal SMSI, Rowe BH, N'Diaye T. Corticosteroids for hospitalised children with acute asthma. Cochrane Database of Systematic Reviews 2003, Issue 1. Art. No.: CD002886. DOI: 10.1002/14651858.CD002886.

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Question 10: In children with respiratory distress in the prehospital setting, when are IV fluids clinically effective and useful? **There was no relevant literature found that addressed the identified PICO question.**
Recommendation: IVs should only be placed in children with respiratory distress for clinical concerns of dehydration, or when administering IV medications.
Grade Criteria: Weak recommendation, Very low quality evidence

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Question 11: In children with respiratory distress in the prehospital setting, does epinephrine (IM/SQ/IV) lead to improved clinical outcomes? What is the appropriate timing of epinephrine use? What are the indications and contraindications for the use of epinephrine?
Recommendation: Epinephrine should only be administered to children with impending respiratory failure as adjunct therapy to albuterol when there are no clinical signs of improvement.
Grade Criteria: Strong recommendation, Moderate quality evidence [1-3]
Two RCTs in children presenting to the ED with asthma found no significant difference in clinical respiratory scores, respiration rates, PFT, or pulmonary function between patients who received albuterol and patients who received subcutaneous epinephrine. [1,2] Admission rates were also similar for the two groups. Adverse events were significantly higher in the epinephrine group, however. [1]

One RCT evaluating children with asthma found that 65% of patients receiving epinephrine experienced improved respiratory status compared to 7% of patients receiving placebo. [3]

None of the above studies were in the prehospital setting, and all had sample sizes less than 45.

Recommendation: Strong recommendation with moderate quality evidence that epinephrine should only be administered to children with respiratory distress as adjunct therapy to albuterol when there are no clinical signs of improvement.
Number of Studies: Total # 5 ☐ Systematic review/Meta-analysis ☒ RCT [1-5] ☐ Cohort ☐ Observational ☐ Case Reports ☐ Clinical Guideline Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☐ None ☒ Insufficient sample size [1-5] ☒ Lack of blinding [4] ☐ Lack of allocation concealment ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☒ No inconsistencies [1-5] ☐ Wide variation of treatment effect across studies ☐ Populations varied ☐ Interventions varied (e.g., doses) ☐ Outcomes varied (e.g., diminishing effect over time)	☐ Head-to-head comparison in correct population ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☒ Different populations [1-5] ☐ Different interventions ☐ Different outcomes measured ☐ Comparisons not applicable to question/outcome	☐ Dichotomous outcomes ☐ Sample size lower than calculated optimal information size ☐ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes ☒ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm [1-5

Sample	CI/RR
1) RCT of 40 children with acute asthma. 2) RCT of 43 children (age 3-12 years) presenting to the ED with acute asthma. 3) RCT of 30 children (age < 24 months) who presented to the ED with wheezing. 4) RCT of 154 adult patients (age 18-50 years) who presented to paramedics with shortness of breath and wheezing. 5) RCT of 19 children presenting to the ED with acute asthma (age 2-18 years).	1) • **Respiratory Status:** no difference in clinical score, RR, or PFT between group randomized to receive inhaled albuterol and group randomized to receive subcutaneous epinephrine • **Admission rates:** no difference in admission rates or return to ED between group that received albuterol and group that received epinephrine • **Adverse events:** increased adverse events among epinephrine group (p < 0.01) 2) • **Respiratory Status:** no difference at 20 minutes and 2 hours post-treatment in clinical score, peak flow, or RR between the group randomized to receive subcutaneous, long-lasting epinephrine and albuterol, and the group randomized to receive only albuterol 3) • **Respiratory Status:** 65% of patients receiving epinephrine experienced improved respiratory status, compared to 7% of patients receiving placebo (p = 0.0067) 4) • **PEFR:** the mean difference between pre-treatment and post-treatment PEFR was 73 l/min and did not vary significantly between the

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	subcutaneous epinephrine, nebulized metaproterenol and subcutaneous epinephrine and nebulized metaproterenol groups 5) • **Pulmonary Function (FEV1, FVC, FEF):** measures at 20 minutes and 1 hour post-treatment were not significantly different between group randomized to subcutaneous epinephrine and group randomized to receive nuebulized terbutaline

1)Becker, A. B., Nelson, N. A., & Simons, F. E. R. (1983). Inhaled salbutamol (albuterol) vs injected epinephrine in the treatment of acute asthma in children. *The Journal of Pediatrics, 102*(3), 465-469.
2)Kornberg, A. E., Zuckerman, S., Welliver, J. R., Mezzadri, F., & Aquino, N. (1991). Effect of injected long-acting epinephrine in addition to aerosolized albuterol in the treatment of acute asthma in children. *Pediatric Emergency Care, 7*(1), 1-3.
3)Lowell, D. I., Lister, G., Von Koss, H., & McCarthy, P. (1987). Wheezing in infants: The response to epinephrine. *Pediatrics, 79*(6), 939-945.
4)Quadrel, M., Lavery, R. F., Jaker, M., Atkin, S., Tortella, B. J., & Cody, R. P. (1995). Prospective, randomized trial of epinephrine, metaproterenol, and both in the prehospital treatment of asthma in the adult patient. *Annals of Emergency Medicine, 26*(4), 469-473.
5)Uden, D. L., Goetz, D. R., Kohen, D. P., & Fifield, G. C. (1985). Comparison of nebulized terbutaline and subcutaneous epinephrine in the treatment of acute asthma. *Annals of Emergency Medicine, 14*(3), 229-232.

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Question 12: In children with respiratory distress, what are the clinical situations in which the following non-invasive airway adjuncts improve oxygenation and/or respiratory distress:

Question 12a: Continuous positive airway pressure (CPAP)
Recommendation: CPAP for bronchospasm should be administered to children in severe respiratory distress..
Grade Criteria: Strong recommendation, Low quality evidence
The use of CPAP or Bilevel Positive Airway Pressure in children with asthma, bronchiolitis, and respiratory distress both in the emergency center and the prehospital setting was statistically significant in decreasing work of breathing and improving oxygenation thereby decreasing the need for intubation. [1-5] Although these studies showed significant differences, all of the studies did not report 95% confidence intervals, therefore questioning the strength of clinical significance. The one pediatric prehospital study found that when CPAP was applied in the field there was a decrease in the need for intubation both in the field and in the emergency department. [5]

Recommendation: Strong recommendation with low quality evidence that CPAP for bronchospasm should be administered to children in severe respiratory distress.
Number of Studies: Total # 5 ☐ Systematic review ☒ RCT [4] ☐ Cohort ☒ Observational [1-3,5] ☐ Case Reports Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☒ None (4) ☒ Insufficient sample size [1-3,5] ☒ Lack of blinding [1-3,5] ☐ Lack of allocation concealment [1-3,5] ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☒ No inconsistencies [1-5] ☐ Wide variation of treatment effect across studies ☐ Populations varied (e.g., sicker, older) ☐ Interventions varied (e.g., doses) ☐ Outcomes varied (e.g., diminishing effect over time)	☒ Head-to-head comparison in correct Population [1-5] ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☐ Different populations ☐ Different interventions ☐ Different outcomes measured ☐ Comparisons not applicable to question/outcome	☐ Dichotomous outcomes ☒ Sample size lower than calculated optimal information size [1-5] ☒ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes [1-5] ☐ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm

Sample	CI/RR
1) Retrospective chart review. 83 pediatric patients (2 to 17 years old) presenting to Emergency Department with status asthmaticus refratory to conventional pharmacological treatment. All were placed on **BiPap** with beta 2 agonist. 2) Prospective, observational study. Twelve Infants < 3 months with a diagnosis of bronchiolitis, confirmation of RSV and severe respiratory distress as defined by a PCO_2 > 50 mmHg with a respiratory assessment score (m-WCAS) > 5. The patients were excluded if the received a bronchodialator treatment within the first 2 hours of enrollment or had a pneumothorax on chest x-ray. Nasal continuous positive airway pressure **(nCPAP)** was instituted in the PICU. Outcomes measured were the effect of nCPAP on respiratory distress, breathing pattern, and respiratory effort. 3) Retrospective chart review. 79 children (2 to18 years old) admitted to the Pediatric ICU for treatment of status asthmaticus, 5 children (6%) received NPPV and 8 (10%) children were intubated. 4 of the 5 **NPPV** patients had BMI of 32 ± 5. 4) Randomized control trial. 29 children < 1 year with bronchiolitis and capillary PCO_2 > 45 mmHg (> 6 kPa) were randomized and treated with **CPAP** and standard therapy then crossed over to the alternative treatment after 12 hours.	1) Immediate improvement in clinical status upon initiation of BiPAP with 77% had a decrease in respiratory rate with an average decrease of 23.6% (range 4% to 50%), 88% had improvement in oxygen saturation of 6.6%. No adverse events noted. 2) Respiratory accessory muscle used significantly decreased from 1.7 (± 0.08) to 0.8 (± 0.13) P = 0.0002 and expiratory wheezing from 1.3 (± 0.18 to 0.3 (± 0.13) P = 0.002 after the placement of nCPAP. Also reduction of inspriatory effort, 53% (± 5%) decrease in Pes swings, reduction of 58% (± 4%) of $PTPes_{insp}$/min. 3) Statistically significant improvement in respiratory rate (43 ± 20 vs. 31 ± 12/min, P = .03) 4) When CPAP was used first followed by standard treatment there was a statistically significant reduction of PCO_2 (-1.35 change in PCO_2, SD 1.37; SE 0.34). 5) 18.9% of the patients received CPAP in the field. No patient who received CPAP in the prehospital setting required intubation in the field or emergency department. 17% were continued on CPAP upon admission with the average length of stay in the ICU being 3.0 days (1-6 days).

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5) Observational study. In the prehospital setting, **CPAP** was applied to106 patients ≥12 years old deemed in acute respiratory distress (dysnpnea, RR ≥ 25/min, and/or retractions or accessory muscle use, arterial hypoxemia as evidenced by O_2 sats of 95% in spite of supplemental oxygen administration). Outcomes measured included: intubation in the field and/or emergency department and length of stay in the hospital.	

1) Beers, S.L., Abramo, T.J., Bracken, A., & Wiebe, R.A. (2007). Bilevel positive airway pressure in the treatment of status asthmaticus in pediatrics. *American Journal of Emergency Medicine, 25*(1), 6-9.
2) Cambonie, G., Milesi, C., Jaber, S., Amsallem, F., Barbotte, E., Picaud, J. C., et al. (2008). Nasal continuous positive airway pressure decreases respiratory muscles overload in young infants with severe acute viral bronchiolitis. *Intensive Care Medicine, 34*(10), 1865-1872.
3) Carroll, C. L., & Schramm, C. M. (2006). Noninvasive positive pressure ventilation for the treatment of status asthmaticus in children. *Annals of Allergy, Asthma & Immunology, 96*(3), 454-459.
4) Thia, L. P., McKenzie, S. A., Blyth, T. P., Minasian, C. C., Kozlowska, W. J. & Carr, S. B. (2008). Randomised controlled trial of nasal continuous positive airways pressure (CPAP) in bronchiolitis. *Archives of Diseases in Children, 93*(1), 45-47.
5) Warner, G. S. (2010). Evaluation of the effect of prehospital application of continuous positive airway pressure therapy in acute respiratory distress. *Prehospital and Disaster Medicine, (25)*1, 87-91.

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Question 12b: Bag-valve-mask ventilation
Recommendation: Bag-valve-mask ventilation should be utilized in children with respiratory failure.
Grade Criteria: Strong recommendation, Moderate quality evidence
The use of bag-valve mask in the prehospital setting has been shown to improve oxygenation and/or ventilation to help prevent the need for endotracheal intubation. Two studies completed in the prehospital setting both demonstrated significant clinical data showing children intubated in the field had lower Glascow Coma Scale Scores and lack of improvement in neurological deficits at discharge. Both studies also found no advantage in adding endotracheal intubation skills to the scope of practice of the paramedics where BVM was already in use. (1,2)

Recommendation: Strong recommendation with moderate quality evidence that bag-valve-mask ventilation should be utilized in children with respiratory failure.
Number of Studies: Total # 2 ☐ Systematic review ☒ RCT (2) ☐ Cohort ☒ Observational (1) ☐ Case Reports Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☒ None (2) ☐ Insufficient sample size ☒ Lack of blinding (1) ☐ Lack of allocation concealment ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☒ No inconsistencies (1,2) ☐ Wide variation of treatment effect across studies ☐ Populations varied (e.g., sicker, older) ☐ Interventions varied (e.g., doses) ☐ Outcomes varied (e.g., diminishing effect over time)	☒ Head-to-head comparison in correct Population (1,2) ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☐ Different populations ☐ Different interventions ☐ Different outcomes measured ☐ Comparisons not applicable to question/outcome	☐ Dichotomous outcomes ☐ Sample size lower than calculated optimal information size ☒ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes (1) ☒ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm (2)

Sample	CI/RR
1) Retrospective chart review. 105 pediatric trauma patients < 18 years old in whom endotracheal intubation (ETI) was attempted either in the field, hospital, or trauma center emergency department. Subsequent ETI attempts had failure rates of 50% in the field and 0% in hospital or trauma center. Effectiveness of field ETIs were measured. 2) RCT. 830 children < 12 years old, < 40 kg requiring airway management. Bag-valve-mask (BVM) was assigned on odd days and BVM followed by ETI was assigned on even days in the prehospital setting of 2 large, urban, rapid-transport emergency medical services (EMS) systems. Survival to hospital discharge and neurological status at discharge from hospital as compared to treatment group.	1) 9.5% could not be oxygenated by bag-valve-mask before ETI. 23% of children had complications related to ETI (aspiration). RR of airway complications was 2.5 X higher with more than one ETI attempt (P < 0.05). 4% of airway complications occurred in trauma center, 29% in hospital, and 66% in the field (P < 0.05). Multiple ETI attempts were related to transport delay, lower Glascow Coma Scale, longer hospital stays, and lower GCS at discharge independent of injury (P <0.001). 9.3% could not be oxygenated or ventilated before ETI by bag-valve-mask. 2) No significant difference in survival between BVM group (123/404 [30%]) and the ETI group (110/416 [26%]) OR 0.82; 95% CI: 0.61, 1.11 or in achieving good neurological outcome (BVM, 92/404 [23%] vs ETI, 85/416 [20%] OR, 0.87; 95% CI: 0.62, 1.22). The survival rate or neurological outcome of pediatric patients did not improve by adding out-of-hospital ETI to paramedic scope of practice that already includes the BMV.

1) Ehrlic, P.F., Seidman, P.S., Atallah, O., Haque, A., & Heimkamp, J. (2004). Endotracheal intubations in rural pediatric trauma patients. *Journal of Pediatric Surgery, 39*(9), 1376-1380.
2) Gausche, M., Lewis, R.J., Stratton, S.J., Haynes, B.E., Gunter, C.S., Goodrich, S. M., et al. (2000). Effect of out-of-hospital pediatric endotracheal intubation on survival and neurolgical outcome. *Journal of American Medical Association, 283*(6), 783-790.

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Question 12c: Heliox
Recommendation: Heliox should not be routinely administered to children with respiratory distress.
Grade Criteria: Strong recommendation, Moderate quality evidence

Heliox was studied in pediatric patients diagnosed with acute asthma, bronchiolitis, and croup admitted to the emergency department and the pediatric intensive care unit. Two Cochrane Reviews looking at adults and children with acute asthma determined there was no significant data supporting the use of heliox in all asthma patients in the emergency department. Heliox did not improve pulmonary function or peak flow and increased heart rate and respiratory rate. [4,5] In two studies patients with bronchiolitis showed an improvement in clinical respiratory scores in the first hour of administration of heliox in the pediatric intensive care unit. [4,5] In the two studies looking at croup, there was no significant change in clinical respiratory scores during treatment or post-treatment using heliox as compared with the oxygen group. There was also no change in admission rates or length of hospital stay.

Recommendation: Strong recommendation with moderate quality evidence that heliox should not be routinely administered to children with respiratory distress.
Number of Studies: Total # 6 ☒ Systematic review [2,4-6] ☐ RCT ☐ Cohort ☒ Observational [1,3] ☐ Case Reports Publication Bias Evident ☒ Yes ☐ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☒ None [2,4,5] ☒ Insufficient sample size [1,2,6] ☐ Lack of blinding [1,3] ☐ Lack of allocation concealment [1,2] ☐ Large losses to F/U ☒ Incorrect analysis of ITT [6] ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☒ No inconsistencies [2- 6] ☐ Wide variation of treatment effect across studies ☐ Populations varied (e.g., sicker, older) ☒ Interventions varied (e.g., doses) [1] ☐ Outcomes varied (e.g., diminishing effect over time)	☒ Head-to-head comparison in correct Population [1-4] ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☒ Different populations [5] ☒ Different interventions [2] ☒ Different outcomes measured [4] ☐ Comparisons not applicable to question/outcome	☐ Dichotomous outcomes ☒ Sample size lower than calculated optimal information size [1,3,6] ☒ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes [1-3,6] ☒ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm [2,4,5]

Sample	CI/RR
1) Observational study. 42 children 1 week to 14 years old who were admitted to the hospital for upper airway obstruction received helium-oxygen therapy. Response from therapy was determined by decrease in work of breathing (decrease of subcostal, substernal, or supraclavicular retractions and elimination of stridor) within 5 to 10 minutes. Patients received 80/20, 70/30, or 60/40 percent of mixture of helium/oxygen. 2) Cochrane Systematic Review. 4 trials involving 84 infants less than 2 years of age with respiratory distress related to bronchiolitis which was positive for RSV (none of these infants were intubated). All infants were admitted to the pediatric intensive care unit. All infants were treated with heliox versus oxygen or room air. 3) Observational study. 38 infants from 1 month to 2 years old admitted to the PICU for treatment of moderate to severe bronchiolitis, positive for RSV. 19 patients received supportive therapy with nebulized epinephrine. 19 patients received heliox therapy administered via a non-rebreather mask. Reduction of clinical respiratory score and PICU length of stay were measured. 4) Cochrane Systematic Review. Ten trials with 544 acute asthma patients, 3 studies were pediatric specific. Admission to the hospital was the outcome measured. 5) Systematic Review. Seven studies were analyzed, 6 adult studies and 1 pediatric study with 392 total patients. These studies compared heliox to a placebo, oxygen or air, in conjunction with other	1) 32 (72.7%) treatments had an immediate response and 12 treatments had no response. 2) Infants treated with heliox had significantly lower mean clinical respiratory score within the first hour after the implementation of therapy when compared to the infants receiving oxygen or air inhalation. Mean Difference (MD) -1.15, 95% CI: -1.98, -0.33, P = 0.006, n = 69. There was no reduction in rate of intubation (RR 1.38, 95% CI 0.41 to 4.56, P = 0.60, n = 58) or in length of stay in PICU (MD = -0.15 days, 95% CI: -0.92, 0.61, P = 0.69, n = 58). 3) After 1 hour of heliox therapy the clinical score improved significantly as compared to the oxygen group (3.6 ± 1.16 vs 5.5 ± 0.89) continuing to be significant at the end of the observation period. No statistics were provided for length of stay in PICU. 4) There was not clear benefit of administering helium-oxygen mixtures to all emergency department patients. Heliox may improve clinical respiratory scores on the most severe asthma cases. 5) No significant differences between heliox or oxygen/air group for peak flow (SMD -0.20; 95%CI: 1.27, 16.8; p=0.02). Also a nonsignificant increase in pulmonary function (SMD, -0.21; 95% CI: -0.43, 0.01; p = 0.06). Significant increase in heart rate weighted mean difference, 9.0; 95% CI: 1.27, 16.8; p = 0.02). Nonsignificant difference in hospital admissions (ORn, 1.07; 95% CI: 0.46, 2.48; p = 0.9). 6) Only one study included data for analysis: no significant change in croup score after 20 minutes (MD 0.83;

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standard treatments. 6) Cochrane Systematic Review. Two studies were analyzed with 44 pediatric patients, 22 patients received heliox and the other 22 patients received either 30% oxygen or 100% oxygen in conjunction with racemic epinephrine.	95% CI: -0.9, 2.56); no significance in post-treatment croup score 9MD -0.57; 95% CI: -1.54, 0.4); no significant influence on heart rate (MD 14.5; 95% CI: -5.4, 34.5) or respiratory rate (MD 6.3; 95% CI: -2.1, 14.8) or oxygen saturation (MD -0.4; 95% CI: -1.8, 1.0)

1) Grosz, A. H, Jacobs, I. N., Cho, C., & Schears, G.J. (2001). Use of helium-oxygen mixture to relieve upper airway obstruction in a pediatric population. *Laryngoscope*, *111*(9), 1512-1514.
2) Liet JM, Ducruet T, Gupta V, Cambonie G. Heliox inhalation therapy for bronchiolitis in infants. *Cochrane Database of Systematic Reviews* 2010, Issue 4. Art. No.: CD006915. DOI: 10.1002/14651858.CD006915.pub2.
3) Martinon-Torres, F., Rodriguez-Nunez, A. & Martinon-Sanchez, J. M. (2002). Heliox therapy in infants with acute bronchiolitis. *Pediatrics, 109(1),* 68-73.
4) Rodrigo GJ, Pollack CV, Rodrigo C, Rowe BH. Heliox for non-intubated acute asthma patients. *Cochrane Database of Systematic Reviews* 2006, Issue 4. Art. No.: CD002884. DOI: 10.1002/14651858.CD002884.pub2.
5) Rodrigo, G. J., Rodrigo, C., Pollack, C. V., & Rowe, B. (2003). Use of helium-oxygen mixtures in the treatment of acute asthma. *Chest, 123*(3), 891-896.
6) Vorwerk C, Coats T. Heliox for croup in children. *Cochrane Database of Systematic Reviews* 2010, Issue 2. Art. No.: CD006822. DOI: 10.1002/14651858.CD006822.pub2.

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Question 13: In children with respiratory distress in the prehospital setting, do supraglottic devices and intubation lead to improved clinical outcomes? What are the indications and contraindications for using a supraglottic device or intubating a patient?
Recommendation: Supraglottic devices and intubation should be utilized only if bag-valve-mask ventilation fails. The airway should be managed in the least invasive way possible.
Grade Criteria: Weak recommendation, Very low quality evidence
One observational study of patients in the prehospital setting who had attempted intubation found that only 74.8% of transported patients were intubated successfully, and that malpositioned tubes were more commonly found in children than adults. (1)
A second observational study found a significant reduction in mortality after the implementation of advanced life support practices (i.e., starting IVs and intubating patients). (3)
A RCT in pediatric patients in the prehospital setting found no significant difference in survival or in the rate of good neurological outcomes between patients randomized to an endotracheal group and those randomized to a bag-valve-mask ventilation group. (2)

Recommendation: Supraglottic devices and intubation should be utilized only if bag-valve-mask ventilation fails. The airway should be managed in the least invasive way possible.
Grade Criteria: Weak Recommendation, Very Low Quality Evidence
Number of Studies: Total # 3 ☐ Systematic review/Meta-analysis ☒ RCT (2) ☐ Cohort ☒ Observational (1,3) ☐ Case Reports ☐ Clinical Guideline Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☐ None ☐ Insufficient sample size ☒ Lack of blinding (1-3) ☐ Lack of allocation concealment ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☒ No inconsistencies (1-3) ☐ Wide variation of treatment effect across studies ☐ Populations varied (e.g., sicker, older) ☐ Interventions varied (e.g., doses) ☐ Outcomes varied (e.g., diminishing effect over time)	☒ Head-to-head comparison in correct Population (2) ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☒ Different populations (1,3) ☐ Different interventions ☐ Different outcomes measured ☐ Comparisons not applicable to question/outcome	☐ Dichotomous outcomes ☐ Sample size lower than calculated optimal information size ☐ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes ☒ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm (1-3

Sample	CI/RR
1) Prospective observational study of 825 patients who had attempted prehospital intubation.	1)**Rate of successful intubation:** 74.8% of transported patients were successfully intubated, 20% had failed intubation and 5.2% had malpositioned tube on arrival to the ED - Malpositioned tubes were significantly more common in children (13% compared with 4% for non-pediatric patients)
2) RCT of 830 pediatric patients (< 12 years) who required airway management in the prehospital setting.	2)**Survival to hospital discharge:** no significant difference in survival between the bag-valve-mask ventilation group (30%) and the endotracheal intubation group (26%); OR: 0.82; 95% CI: 0.61, 1.11 **Neurological outcomes:** no significant difference in achieving good neurological outcomes between the bag-valve-mask ventilation group (23%) and the endotracheal intubation group (20%); OR: 0.87; 95% CI: 0.62,1.22
3) Retrospective observational study of 8138 patients provided advanced life support for out-of-hospital respiratory distress	3)**Intubation administration rate:** 1.7% after advanced life support training, baseline comparison not available **Mortality:** reduced 1.9% after advanced life support training (training on IV administration and endotracheal intubation), p = 0.01; 95% CI: 0.4, 3.4; OR: 1.3; 95% CI: 1.1, 1.5

1)Denver Metro Airway Study Group. (2009). A prospective multicenter evaluation of prehospital airway management performance in a large metropolitan region. *Prehospital Emergency Care, 13*(3), 304-310.
2)Gausche, M., Lewis, R. J., Stratton, S. J., Haynes, B. E., Gunter, C. S., Goodrich, S. M., et al. (2000). Effect of out-of-hospital pediatric endotracheal intubation on survival and neurological outcome. *JAMA: The Journal of the American Medical Association, 283*(6), 783-790.
3)Stiell, I. G., Spaite, D. W., Field, B., Nesbitt, L. P., Munkley, D., Maloney, J., et al. (2007). Advanced life support for out-of-hospital respiratory distress. *The New England Journal of Medicine, 356*(21), 2156-216.

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Question 14: In children with respiratory distress, is the use of capnography efficacious and clinically useful?
Recommendation: Measuring end-tidal CO_2 ($ETCO_2$) is safe, reliable and non-invasive and demonstrates a strong correlation with pulse oximetry; it should used as an adjunct to other forms of respiratory monitoring.
Grade Criteria: Strong recommendation, Low quality evidence [1-4]
Four studies were found that noted $ETCO_2$ to be a feasible and non-invasive measurement tool in children; however there is no evidence that either proves or disproves the use as being efficacious within the prehospital setting. Noninvasive $ETCO_2$ monitoring is safe and reliable, and has shown good correlation with capillary refill and CO_2. [1,4] $ETCO_2$ measurements do not distinguish between children in severe distress versus those in moderate distress. [2,3]

Abramo et al (1996) found in a prospective, observational study of 85 nonintubated children with upper and lower respiratory distress that measuring $ETCO_2$ is safe and efficacious and as reliable as arterial partial pressure of CO_2 ($CapCO_2$; t = 14.9, P < 0.0001, r = 0.87 with a 95% CI for prediction of ± 5 mmHg). In 2005, a prospective cohort study was conducted to evaluate the utility of $ETCO_2$ as a predictor for hospital admission in children with acute asthma exacerbation. [3] This pilot study suggests that baseline $ETCO_2$ measurement is helpful in predicting admission. The odds of being admitted were found to be 18.77 times higher for patients with a baseline capnography ratio less than 0.15. In addition, this ratio was a highly sensitive and moderately specific indicator of admission (See Table 2 below). Guthrie et al. (2007) found that after evaluating the association between children's $ETCO_2$ and asthma disease severity that $ETCO_2$ values do not distinguish between children with mild and with more severe asthma. Lastly, a retrospective study investigating the relationship and level of agreement between $ETCO_2$ and $vpCO_2$ in nonintubated, admitted children with moderate to severe respiratory distress found that $ETCO_2$ and $vpCO_2$ are highly correlated; however, $ETCO_2$ cannot replace a blood gas evaluation. [4]

TABLE 2. Disposition and Test Performance Characteristics by Capnography Ratio

	Hospitalized (n = 12)	Discharged (n = 25)
Capnography ratio	**%**	**%**
<0.15	83.3	32.0*
≥0.15	16.7	68.0

Sensitivity, 83.3% (95% CI, 50.9–97.1); specificity, 68.0% (95% CI, 46.4–84.3); PPV, 55.6% (95% CI, 31.3–77.6); NPV, 89.5% (95% CI, 65.5–98.2); relative risk, 5.28 (95% CI, 1.34–20.86). CI indicates confidence interval; PPV, positive predictive value; NPV, negative predictive value.
*$P < 0.05$ by χ^2.

Kunkov, 2005

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Recommendation(s): Strong recommendation with low quality evidence to utilize capnography in conjunction with pulse oximetry.
Number of Studies: Total #4 ☐ Systematic review ☐ RCT ☒ Cohort [3] ☒ Observational [1-2,4] ☐ Case Reports Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☐ None ☒ Insufficient sample size [1-4] ☒ Lack of blinding [1-3] ☒ Lack of allocation concealment [1-4] ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☐ No inconsistencies ☐ Wide variation of treatment effect across studies ☒ Populations varied (e.g., sicker, older) [1,4] ☐ Interventions varied (e.g., doses) ☐ Outcomes varied (e.g., diminishing effect over time)	☒ Head-to-head comparison in correct Population [2-3] ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☒ Different populations [4] ☒ Different interventions [4] ☐ Different outcomes measured ☐ Comparisons not applicable to question/outcome	☐ Dichotomous outcomes ☒ Sample size lower than calculated optimal information size [1-4] ☒ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes [1-4] ☐ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm

Sample	CI/RR
1) N = 85 non-intubated children presenting to the EC with upper and lower respiratory distress (mean 5.42 years) 2) N = 100 children with acute asthma presenting to the EC (mean age 8.3 years) 3) N = 37 children with acute asthma exacerbation presenting to the EC Hospitalized children- N = 12 Discharged children- N = 25 4) N = 62 non-intubated children admitted to an intermediate care unit with moderate to severe respiratory distress (mean 5.7 years) with 80 paired $ETCO_2$ and $vpCO_2$ values	1) Mean $ETCO_2$ = 33± 4.6 mmHg and $CapCO_2$ of 36 ± 4.5 mmHg. The relationship between $CapCO_2$ and $ETCO_2$ was statistically significant with a 95% CI for prediction of ± 5 mmHg (t = 14.9, p < 0.0001, r = 0.87). 2) Children admitted, at presentation, had an $ETCO_2$ values that were slightly lower than those discharged (mean 32.9; 95% CI: 31, 34.6; mean 35.6; 95% CI: 34.6, 36.6; p < 0.02, respectively). Similar findings were found at disposition. 3) The odds of being admitted were 18.77 times higher for patients with a baseline capnography ratio < 0.15. Baseline capnography ratio of < 0.15 was highly sensitive and a moderately specific indicator of admission. See Table 2 below. TABLE 2. Disposition and Test Performance Characteristics by Capnography Ratio Hospitalized (n = 12) Discharged (n = 25) Capnography ratio % % < 0.15 83.3 32.0* ≥ 0.15 16.7 68.0 Sensitivity, 83.3% (95% CI, 51.6–97.9); specificity, 68.0% (95% CI, 46.6–84.8); PPV, 31.6% (95% CI, 31.3–77.6); NPV, 96.3% (95% CI, 65.1–99.9); relative risk, 5.25 (95% CI, 1.34–20.56). CI indicates confidence interval; PPV, positive predictive value; NPV, negative predictive value. *P < 0.05 by χ². 4) The mean ± SD for $ETCO_2$ and $vpCO_2$ was 35.7 ± 10.1 mmHg and 39.4 ± 10.9 mmHg, respectively. $ETCO_2$ and $vpCO_2$ were highly correlated (r = 0.90, P < 0.0001). The correlations for asthma, bronchiolitis, and pneumonia were 0.74 (P < 0.0001), 0.832 (PP = 0.0002), and 0.98 (p < 0.0001), respectively.

1)Abramo, T. J., Wiebe, R. A., Scott, S. M., Primm, P. A., McIntyre, D., & Mydlyer, T. (1996). Noninvasive capnometry in a pediatric population with respiratory emergencies. *Pediatric Emergency Care, 12*(4), 252-254.
2)Guthrie, B. D., Adler, M. D., & Powell, E. C. (2007). End-tidal carbon dioxide measurements in children with acute asthma. *Academic Emergency Medicine, 14*, 1135-1140.
3)Kunkov, S., Pinedo, V., Johnson Silver, E., & Crain, E. F. (2005). Predicting the need for hospitalization in acute childhood asthma using end-tidal capnography. *Pediatric Emergency Care, 21*(9), 574-577.
4)Moses, J. M., Alexander, J. L., & Agus, M. S. (2009). The correlation and level of agreement between end-tidal and blood gas pCO_2 in children with respiratory distress: A retrospective analysis. *BMC Pediatrics, 9*, 20.

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Question 15: In children with respiratory distress, are there improved patient outcomes when an online medical direction is contacted versus no online medical direction is contacted? **There was no relevant literature found that addressed the identified PICO question.**

Question 16 In children with respiratory distress, are there improved patient outcomes when patients are transported by Advanced Life Support (ALS) providers as compared to Basic Life Support (BLS) providers?
There was no relevant literature found that addressed the identified PICO question.

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Question 17: In children with respiratory distress, is it clinically efficacious to transport with lights and sirens?
Recommendation: Routine use of lights and sirens (Code 3 transport) is not recommended during transport.
Grade Criteria: Strong recommendation, Low quality evidence [1-3]
Three studies were found evaluating the use of lights and sirens for transport. Lacher et al. (1997) specifically looked at 622 pediatric EMS calls of which 312 utilized L&S for transport to evaluate the appropriateness of L&S in the pediatric EMS transport. Basic units were more likely to utilize L&S inappropriately for stable patients in comparison to paramedic units (P < 0.15). Patients transported inappropriately were more likely to be discharged home in comparison to patients whose medical needs warranted L&S transport (74% versus 41%, P < 0.001). Lastly, patients with cardiovascular and respiratory chief complaints were more likely to be transported with appropriate L&S than those children with general medical, trauma, or central nervous system complaints. However, a previous study prospectively studied 50 EMS calls (not pediatric specific) to determine whether or not transporting with L&S was faster. [2] It found that although it was faster by 43.5 seconds, it was not clinically relevant except for in rare circumstances. Ho and Casey (1998) examined the speed of response to a call with L&S, in an urban setting. They found that it was significantly faster to travel with L&S in comparison to without (4.46 vs. 7.48 minutes).

Recommendation: Strong recommendation with low quality evidence that routine use of lights and sirens (Code 3 transport) is not recommended during transport.
Number of Studies: Total # 3 ☐ Systematic review ☐ RCT ☐ Cohort ☒ Observational [1-3] ☐ Case Reports Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☐ None ☒ Insufficient sample size [1,2] ☒ Lack of blinding [1-3] ☒ Lack of allocation concealment [1-3] ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☐ No inconsistencies ☐ Wide variation of treatment effect across studies ☒ Populations varied (e.g., sicker, older) [1-3] ☐ Interventions varied (e.g., doses) ☐ Outcomes varied (e.g., diminishing effect over time)	☐ Head-to-head comparison in correct population ☒ Indirect comparisons (e.g., interventions to placebo but not each other) [1-3] ☒ Different populations [1-3] ☐ Different interventions ☐ Different outcomes measured ☐ Comparisons not applicable to question/outcome	☐ Dichotomous outcomes ☒ Sample size lower than calculated optimal information size [1,3] ☐ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes ☐ 95% CI (or alternate measure) includes negligible effect and appreciable benefit or harm

Sample	CI/RR
1) N = 64 EMS runs (Urban setting) Group 1: Lights and sirens group (L&S; Code 3) Group 2: non-Lights and sirens group (non-L&S; Code 2) 2) N = 50 transport times Group 1: Lights and sirens group (L&S) Group 2: non-Lights and sirens group (non-L&S) 3) N = 504 pediatric EMS calls Lights and sirens (L&S) were used in 312 (62%) of the EMS calls	1) Average Code 3 response was 4.46 minutes versus 7.48 minutes. The 3.02 minutes (95% CI: 0.8 to 5.24 minutes; P < 0.01) saved presents a significant time savings of 38.5% (95% CI: 35.7, 41.3%; P < 0.01). 2) The time differences between the two groups ranged from 311 seconds faster in the L&S to 169 seconds slower with L&S. 38 (76%) of the transport times were faster with L7S, 11 (22%) were faster with non-L&S and 1 (2%) was the same for both groups. On average, L&S transports are 43.5 seconds faster although this is not clinically significant except in rare circumstances. 3) Basic units were more likely to utilize L&S inappropriately for stable patients in comparison to paramedic units (P < 0.15). Patients transported inappropriately were more likely to be discharged home in comparison to patients whose medical needs warranted L&S transport (74% vs. 41%, P < 0.001).

1)Ho, J., & Casey, B. (1998). Time saved with use of emergency warning lights and sirens during response to requests for emergency medical aid in an urban environment. *Annals of Emergency Medicine, 32*(5), 585-588.
2)Hunt, R. C., Brown, L. H., Cabinum, E. S., Whitley, T. W., Prasad, N. H., Owens, C. F., Jr., et al. (1995). Is ambulance transport time with lights and siren faster than that without? *Annals of Emergency Medicine, 25*(4), 507-511
3)Lacher, M. E., & Bausher, J. C. (1997). Lights and siren in pediatric 911 ambulance transports: Are they being misused? *Annals of Emergency Medicine, 29*(2), 223-227.

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