
Systematic Review

AARC Clinical Practice Guideline Management of Pediatric Patients with Oxygen in the Acute Care Setting

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AARC Clinical Practice Guideline

Management of Pediatric Patients with Oxygen in the Acute Care Setting

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Abstract

Oxygen therapy is one of the most important therapeutics offered in the clinical management of pediatric patients suffering from cardiopulmonary disease. As the medical community seeks to ensure evidence-based management of clinical interventions, we conducted a systematic review with the goal of providing evidence-based clinical practice guidelines to answer questions surrounding the use of simple oxygen therapy to improve oxygenation including comparison of delivery devices, the efficacy of humidification, comparison of flows, and goals for hemoglobin oxygen saturation in children. Using a modification of the RAND/UCLA Appropriateness Method, four recommendations were developed to assist clinicians in the utilization of oxygen therapy in hospitalized children: (1) The use of an oxygen hood or tent in lieu of a low-flow oxygen device for consistent oxygen delivery is not recommended; (2) The use of HFNC is safe and more effective than low flow oxygen to treat infants with moderate to severe bronchiolitis; (3) The application of humidification with low flow oxygen delivery is not recommended; (4) Targeting hemoglobin oxygenation saturation of 90% -97% for infants and children suffering from bronchiolitis is recommended, however no specific target can be recommended for pediatric patients suffering from respiratory diseases outside of bronchiolitis and establishing a patient/disease oxygen therapy target upon admission is considered best practice.

Key Words

Oxygen, Pediatric, Child, Infant

Introduction

Oxygen is one of the most commonly delivered medications to children for the treatment of hypoxemia caused by many acute conditions such as lower respiratory tract infections, sepsis, or shock. Oxygen is widely considered to have many benefits and is applied liberally in clinical practice because it is cheap and the fear of chronic and intermittent hypoxemia causing long term brain injury including developmental and behavioral conditions.^{1,2} It also does, however, have consequences of overuse and hyperoxia resulting in oxygen toxicity and absorption atelectasis.³⁻⁵ The delivery of oxygen in pediatric requires appropriate selection of delivery device, concentration, and flow for the most effective therapy in order to avoid hypo and hyperoxia.^{6,7}

The World Health Organization recommends oxygen delivery for hemoglobin oxygen saturation (SpO₂) level < 90% for children with signs of respiratory distress.⁸ American Heart Association 2020 Pediatric Advance Life Support Guidelines state oxygen should be administered and weaned to achieve SpO₂ levels of between 94% and 99%.⁹ The liberal use of oxygen in pediatric emergencies is not often questioned, however, how it is administered and the therapeutics goals are illusive. Therefore, we set out to help guide clinicians to evidence-based practices that will help provide the best treatment of hypoxemia while limiting the adverse effects of oxygen therapy.

We conducted a systematic review of peer-reviewed literature to develop clinical practice guidelines to answer the current pressing questions in the management of pediatric patients with oxygen in the acute care setting. The following questions were developed to guide the systematic review:

1. In hospitalized pediatric patients, does the use of oxygen tents and hoods versus low-flow oxygen systems (nasal cannula, simple face mask) provide a more consistent oxygen delivery?
2. In hospitalized pediatric patients, does the use of high-flow oxygen systems versus low-flow oxygen systems increase the FDO₂ or decrease escalation of therapy (NIV or intubation)?
3. In hospitalized pediatric patients, does adding humidification to supplemental oxygen as compared to no humidification improve comfort or reduce infection risk?
4. In hospitalized pediatric patients, does establishing disease-specific oxygenation targets reduce oxygen use, decrease the length of stay, or prevent escalation of therapy as compared to prescribed or no disease-specific oxygen targets?

Committee composition

Committee was selected by the American Association for Respiratory Care (AARC) leadership based on their known experience related to the topic, their interest in participating in the project, and their commitment to the process details. The committee first met face-to-face, where they were introduced to the process of developing clinical practice guidelines. At that time, the committee selected a chair and wrote a first draft of Patient, Intervention, Comparison, Outcome (PICO) questions. Subsequent meetings occurred as needed by conference call. Frequent email communications occurred among committee members and AARC staff. The committee members received no remuneration for their participation in the process, though their expenses for the face-to-face meeting were covered by the AARC.

Search strategy

A literature search was conducted using the PubMed, CINAHL via EBSCOhost, and Scopus.com databases for studies on oxygen therapy in pediatric patients. The search strategies used a combination of relevant controlled vocabulary (i.e., Medical Subject Headings and CINAHL Headings) and keyword variations that were related to oxygen therapy, oxygenation techniques, pediatrics, and outcomes. The searches were limited to English language studies about human populations. The searches were also designed to filter out citations indexed as commentaries, editorials, interviews, news, or reviews. No date restrictions were applied to the searches. Refer to the online supplemental material for the complete search strategy executed in each database on January 10, 2020. Cited reference searching was completed for all included studies as well as for studies that were topically relevant but excluded based on study design. Duplicate citations were identified and removed using the EndNote X8 citation management software.

Study selection

Two reviewers independently assessed study eligibility in the Covidence systematic review software. Inclusion criteria used to assess eligibility were: 1) oxygen therapy; 2) pediatric population, including neonates, infants, and children; and 3) clinical outcomes. The exclusion criteria used were: 1) not oxygen therapy; 2) adult population; 3) preterm newborn; 4) no clinical outcomes relevant to oxygen therapy; 5) not empirical research (e.g., theory, opinion, or review articles); and 6) published prior to 1987.

Development of recommendations

A modification of the RAND/UCLA Appropriateness Method¹⁰ was used to combine the best available evidence with the collective experience of committee members. The literature was

condensed into evidence tables according to PICO question (Table 1). Individual panel members were assigned the task of writing a systematic review of the topic, drafting 1 or more recommendations, and suggesting the level of evidence supporting the recommendation:

A: Convincing scientific evidence based on randomized controlled trials of sufficient rigor.

B: Weaker scientific evidence based on lower levels of evidence such as cohort studies, retrospective studies, case-control studies, and cross-sectional studies.

C: Collective experience of the committee.

Committee members reviewed the first draft of evidence tables, systematic reviews, recommendations, and evidence levels. Each committee member rated each recommendation using a Likert scale of 1 to 9, with 1 meaning expected harms greatly outweigh the expected benefits and 9 meaning expected benefits greatly outweigh the expected harms. The ratings were returned to the committee chair. The first ratings were done with no interaction among committee members. A conference call was convened, during which time the individual committee ratings were discussed. Particular attention was given to any outlier scores and the justification. Recommendations and evidence levels were revised with input from the committee members. After discussing each PICO question, committee members re-rated each recommendation. The final median and range of committee members' scores are reported (Table 2). Strong agreement required that all committee members rank the recommendation 7 or higher, weak agreement meant that one or more committee members ranked the recommendation below 7, but the median vote was at least 7. For recommendations with weak agreement, the percentage of committee members who rated 7 or above was calculated and reported after each weak

recommendation. Figure 1 illustrates the process flow the panel used to rate the appropriateness and quality of the literature selected through the search process.

Drafts of the report were distributed among committee members in several iterations. When all committee members were satisfied, the document was submitted for publication. The report was subjected to peer review before the final publication.

Assessment and recommendations

The search strategies retrieved a total of 3,312 articles. The team also identified 1,413 articles through the cited references of articles assessed for full text eligibility and 1 relevant article through other methods. After removal of duplicates, 4,116 articles remained for screening. In the title and abstract screening phase, 3,950 articles were excluded. Of the remaining 166 articles, 153 were excluded following full text review against the inclusion and exclusion criteria (Figure 2).

Oxygen tents and hoods versus low-flow oxygen systems in hospitalized pediatric patients

Oxygen can be delivered to hospitalized pediatric patients in a variety of ways. Most pediatric patients receive supplemental oxygen via low-flow nasal cannula devices or via simple face mask. The inspired oxygen provided to the patient is dependent upon gas flow, the patient's inspiratory demand, and the diameter of the nares. A simple facemask may deliver more inspired oxygen to the pediatric patient, but the mask is harder to secure to the patient's face and it is imperative that a minimum flow is used to flush exhaled carbon dioxide.⁶

Historically, hospitalized pediatric patients received oxygen via humidified tent or hood. The oxygen tent, also called a mist tent or croup tent, consists of clear plastic sheeting that hangs over the patient's hospital bed. The tent allows for an input of cool, humidified oxygen from high-pressure gas sources. Popular for its ability to allow the child movement within the tent in

the hospital bed, there are many disadvantages to this method of oxygen delivery: the maximum FiO_2 achieved is around 0.4 and is dependent upon how well the tent is secured around the patient and bed; children could bring spark-emitting toys within the tent environment, which could support combustion; and the plastic could be a source of suffocation. In addition, these large tents are difficult to set up and maintain, as microbial contamination is likely.^{6, 11-13}

An oxygen tent can also consist of a collapsible plastic cube that is connected to a humidified oxygen source. Oxygen hoods consist of a collapsible plastic cube that surrounds the head of the infant. Both devices function in the same way and may theoretically deliver an FiO_2 up to 1.0 with appropriate gas flow and both devices require a minimum gas flow to flush exhaled carbon dioxide from the device. Similar to the tent, the efficacy of oxygen delivery with this device is dependent upon the seal of the device around the patient's head. The larger the unsealed area, the less likely the target FiO_2 will be reached.¹¹

The mist tents, smaller oxygen tents, and oxygen hoods are all subject to lower delivered FiO_2 due to structural issues with creating a sealed environment. Though there are limitations to achieving consistent oxygen delivery with low-flow devices such as the nasal cannula and simple face mask, there is a lack of evidence comparing the consistency of oxygen delivery between the oxygen hood, oxygen tent, and low-flow devices. As such, the committee does not recommend using an oxygen hood or tent in lieu of a low-flow oxygen device for consistent oxygen delivery (Evidence level C, median appropriateness score 8).

High-flow oxygen versus low-flow oxygen in hospitalized pediatric patients

The use of HFNC systems to provide respiratory support to children has increased over the past decade. These systems have the potential to provide washout of the nasopharyngeal dead space; decrease inspiratory resistance; improve airways conductance and pulmonary compliance;

and decrease metabolic work by providing heated and humidified gas.¹⁴ Finally, the generation of positive pressure is a more controversial mechanism. Although these systems were initially used in PICU settings, they have transitioned to the acute care setting. Few studies have compared the use of low flow and HFNC systems for the treatment of respiratory conditions in infants and children. One of the challenges in analyzing the published data is that the definition of HFNC varies among publications. Another limitation is that with few exceptions most studies are retrospective and have a small sample size. Another confounder is that all the reported studies included infants diagnosed with either moderate or severe bronchiolitis. Therefore, it is not completely clear if the benefits of HFNC arise from improved oxygenation only or by also providing a more robust ventilatory support.

Franklin et al, reported a multicenter, randomized, controlled clinical trial comparing low flow oxygen (up to 2 L/min) and HFNC (2 L/kg/min) to treat 1472 infants younger than 12 months admitted to the Pediatric Ward with diagnosis of bronchiolitis who needed supplemental oxygen therapy.¹⁵ This is the largest reported study to date comparing low flow and HFNC therapies. The primary outcome was need for escalation of care defined as the present of 3 out of 4 criteria (unchanged or elevated heart rate and respiratory rate, hypoxemia at 2 L/min or 40% with HFNC, triggering of early warning tool). Subjects assigned to HFNC had a lower rate of escalation of care than those on the low flow oxygen arm (12 versus 23% respectively).¹⁵ A large percentage of subjects (61%) who failed low flow oxygen responded to HFNC. Hospital stay, duration of oxygen therapy, and incidence of pneumothorax (0.1%) were similar between groups.¹⁵

Ergul et al, reported a randomized trial comparing an oxygen mask (30 subjects) to HFNC (30 subjects) in the treatment of infants 1-24 months admitted to PICU with diagnosis of

moderate to severe bronchiolitis.¹⁶ Subjects in the HFNC group required almost 50% less time of supplemental oxygen support, did not experience treatment failure (escalation of care, lack of improvement in heart and respiratory rate, and persistent hypoxemia), and had shorter PICU and hospital stay than subjects in oxygen mask group.¹⁶ Uygur et al, reported a prospective clinical trial in children age 3-36 months admitted to a Pediatric Ward with hypoxemic acute lower respiratory infection.¹⁷ The subjects were randomized to simple mask (32 subjects) or air entrainment mask (33 subjects). Although both groups improved, those in the venturi mask group had a greater reduction in respiratory rate at 24 hours than those in the simple mask group. In addition, those in the venturi group had a 50% reduction in the length of time requiring supplemental oxygen.¹⁷

Milani et al, compared in non-formally randomized clinical trial the use of HFNC ($L/min = 8 * weight * respiratory\ rate * 0.3$, 20 subjects) versus low flow oxygen (no upper limit defined, 20 subjects) to treat infants younger than 12 months admitted to the Pediatric Ward with diagnosis of moderate to severe bronchiolitis who needed supplemental oxygen therapy.¹⁸ Those receiving HFNC experienced faster reduction in respiratory rate, regained their ability to feed faster, and required less time on supplemental oxygen and hospitalization than those receiving low flow oxygen. None of the subjects required PICU admission.¹⁸

Mayfield et al, in a pilot study compared use of HFNC (2 L/kg/min) (61 subjects) with low flow oxygen (31 subjects) in infants younger than 12 months admitted to Pediatric Ward with diagnosis of bronchiolitis who needed supplemental oxygen therapy. Subjects enrolled in a HFNC pilot study, and the low flow group was retrospectively identified. Subjects in the HFNC were less likely to require transfer to PICU (13 vs. 30 % respectively).¹⁹ The authors found that

lack of decrease of respiratory rate and heart rate at the first hour of HFNC was associated with treatment failure. Hospital length of stay was similar between groups.¹⁹

Daverio et al, retrospectively reviewed their 5-year experience using a 2-tiered HFNC (2 L/kg/min) protocol in 211 infants younger than 12 months admitted to the Pediatric Ward of tertiary care hospital with a diagnosis of bronchiolitis.²⁰ The authors used a standardized score to decide type of respiratory support (low versus HFNC). Most subjects (83%) were started on low flow oxygen (< 2 L/min), but 41% of them required the use of rescue HFNC.²⁰ These subjects had shorter duration of illness, lower body weight Z-score, lower SpO₂ on arrival, received more epinephrine treatments, and were more likely to have cardiac comorbidity than those who did not need escalation. Air leaks were reported in 1.9% of subjects receiving HFNC. Transfer to PICU was low for both groups (5 and 3% for low flow and HFNC groups respectively).²⁰

McKiernan et al, retrospectively review the intubation rate in infants younger than 24 months of age admitted to PICU with a diagnosis of bronchiolitis. The authors compared 2 treatment periods: before (57 subjects) and after (58) use of HFNC for treatment of bronchiolitis. They found a 68% reduction in intubation rate after HFNC was used.²¹ The reduction remained statistically significant after adjusting for age, weight, and RSV status.²¹ Similar to Mayfield et al., these authors found that infants who did not reduce their respiratory rate after starting HFNC therapy were more likely to be intubated.

Baudin et al, retrospectively reviewed the safety of using HFNC in pediatric patients admitted to a PICU a tertiary care hospital. The authors reviewed 177 episodes corresponding to 145 subjects (median IQR 8 2-28 months) over a 1-year data period.²² The system was used for de-escalation of support (36% and 18% after extubation and NIV respectively) and as primary support (31%).²² The maximum flow used was < 2 L/kg/min and a 22% failure rate was reported.

The authors reported a low rate of complications (1 and 0.6% for pneumothorax and epistaxis respectively).²²

In summary, the use of HFNC (2 L/kg/min or less) appears to be safe and more effective than low flow oxygen (< 2 L/min) to treat infants with moderate to severe bronchiolitis in the Pediatric Ward and PICU setting (Evidence level B, median appropriateness score 7.5).

Humidification of oxygen in hospitalized pediatric patients

The use of humidification for low flow oxygen therapy is a common practice with little evidence to support its use or that it is harmful to stop its use. Complications of dry oxygen delivery have been linked to the use of high flow oxygen delivery and are perceived to be present with lower severity with low flow oxygen delivery. There are two different options for humidification of low flow oxygen. The first and most common is unheated humidification, also referred to as bubble or passover, and the second is heated and humidified humidification via active humidification device.

The evidence to support the use of humidification of any kind versus dry delivery of low flow oxygen delivery to impact comfort or infection risks is scant. There are three studies to date to investigate this comparison. Scolnik et al, concentrated on the croup population in the emergency room and performed a randomized, single-blinded controlled trial to deliver three levels of humidity for 30 minutes in the emergency department.²³ The three groups were blow-by therapy, controlled 40% humidity, and controlled 100% humidity; all delivered with 40% oxygen, with the pre- and post-assessment with the Westley Croup Score. The results showed that there was no significant difference with either level of humidity in the Westley score or any of the secondary outcomes of vital signs and hospitalization rate thus not supporting the use of humidification in the emergency department for the treatment of croup.²³ The HHOT AIR study

by Chen, et al performed a prospective, randomized pilot study comparing dry vs heated and humidified low flow oxygen defined as < 4 L/min in children < 24 months of age with mild to moderate bronchiolitis admitted to the general pediatric ward.²⁴ Patients that required oxygen therapy were randomized to the control or heat and humidification for oxygen delivery. The respiratory distress assessment instrument (RDAI) was used to score comfort and distress to compare for each group. Although the investigators saw a quicker change in the RDAI over time (1-hour vs 12-hours), there was not a significant difference in the score when comparing the 2 groups at the same timeframes. Although there was a trend in a quicker improvement of RDAI over time with the heated and humidified oxygen group, this did not show a significant difference in length of stay or vital signs. This may be a result of small sample size, however at this time does not support the use of heated and humidified oxygen over dry gas for the treatment of bronchiolitis. Lorente Sánchez, et al also investigated the use of humidification of low flow oxygen therapy in children with mild to moderate bronchiolitis admitted to the general pediatric ward in a pre-post interventional trial.²⁵ They implemented the use of unheated humidification and compared the number of nasal lavages pre- and post-universal use of bubbler humidifier as well as change in bronchiolitis score, vital signs and hospital length of stay.²⁵ There was not a statistical difference in any outcome measure indicating that the use of unheated humidification was not beneficial.

In summary, low level of evidence does not support the use of heated or unheated humidification with low flow oxygen delivery (Evidence level B, median appropriateness score 8.25). More robust research is needed to make a clear determination.

Oxygenation targets in hospitalized pediatric patients

Normoxia, or a pulse oximetry reading of 94% or higher, is often the recommended target for oxygen therapy in children. There are several clinical practice guidelines that recommend pulse oximetry targets by disease yet practice and even recommendations vary between national guidelines. Current oximetry target recommendations for children with pneumonia is > 92% and for asthma is > 90% using the 2007 NHLBI National Asthma Education and Prevention Program (NAEPP) or 94-98% if using the revised 2019 British guideline on the management of asthma.²⁶⁻
²⁸ We only found one category of respiratory disease in which there was enough evidence of specific oxygen targets in the pediatric population. This respiratory disease was acute lower respiratory tract infection (LRTI) or often referred to as bronchiolitis.

LRTI accounts for about 128,000 hospitalizations of children < 2 years of age each year in the US at an estimated cost of \$1.73 billion, which is an estimated 30% increase over the nine years studied.²⁹ While trends in hospitalization for LRTI have decreased from 17.9 to 14.9 per 1,000 persons from 2000-2009, there was a 34% increase in admission of children with high-risk medical conditions and a 21% increase in use of mechanical ventilation.²⁹ The American Academy of Pediatrics and the World Health Organization both recommend permissive hypoxemia of an oxygen saturation of 90% for children suffering with lower respiratory tract infections based largely on expert opinion and consideration of resource limited areas as there was not a high-level evidence presented in their publications.^{30, 31}

Since the publication of those national clinical practice guidelines on the management of bronchiolitis, there has been a single double-blind, randomized, equivalence trial using two oximetry targets (< 90% modified vs < 94% standard) for oxygen therapy.³² Cunningham et al were able to demonstrate the modified target of 90% or higher is as safe and clinically effective

as the standard practice of 94% or higher.³² Additionally, they were able to observe a significantly lower time to fit to discharge (44.2h vs 30.2h, $p < 0.0001$), time to actual discharge (50.9h vs 40.9h, $p=0.003$) and time to no further supplemental oxygen (27.6h vs 5.7h, $p=0.0021$) in the modified oxygen saturation group.³² This was all accomplished without any differences in adverse events and safety outcomes.

In hospitalized pediatric patients suffering from bronchiolitis, evidence supports an oxygenation target of 90% or greater (Evidence level C, median appropriateness score 7). However, in hospitalized pediatric patients suffering from respiratory diseases outside of bronchiolitis, establishing a patient/disease oxygen therapy target upon admission is best practice, but a specific target cannot be recommended (Evidence level C, median appropriateness score 7).

Summary

The results of this systematic review are summarized in Table 1. Disappointingly, the evidence available to answer the PICO questions is minimal. The recommendations in Table 2 are based on low-level evidence and strongly reflects committee experience. The PICO questions were developed from the aspects of oxygen use that were perceived to have the highest variability in clinical practice and the greatest chance of reducing the efficiencies in care of pediatric patients. Unfortunately, the result of this evidence-based review identified more needs for future research than evidence-based recommendations for clinical practice. The lack of evidence to support the consistency of oxygen delivery via oxygen tents and hoods over the use of low-flow oxygen devices is overwhelmed by the potential risks.

The use of HFNC (2 L/kg/min or less) appears to be safe and more effective than low flow oxygen (< 2 L/min) to treat infants with moderate to severe bronchiolitis in the Pediatric

Ward and PICU setting. Practitioners need to use appropriate size cannulas that block around 50% of naris opening. Larger sizes increase the risk of inadvertently creating PEEP and pressure ulcers. Also, the cannulas should not exceed the manufacturers' recommended maximum flow. Exceeding these flows results in back pressure build-up. It is important to understand the role of HFNC in pediatric oxygenation and be mindful of its limitations. Protocols that include indications, contraindications, escalation and de-escalation of care, scheduled monitoring of occurrence of pressure ulcers, recommendations for obtaining a blood gas, transfer to PICU if used in the ward, should be used. Monitoring adverse events that occur during the use of HFNC should be included in the protocols. In addition, when HFNC is used in pediatric wards patients should be monitored with continuous pulse oximetry, staff need to be appropriately trained to use the devices, and to recognize complications. Although studies done in conditions other than bronchiolitis are lacking, these systems are used in clinical practice. This is an area that needs to be studied in the future. In the meantime, if used careful monitoring is of the utmost importance.

There are few investigations into the benefit of adding humidification (heated or unheated) for low flow oxygen delivery. None of the studies identified showed a difference in the defined outcomes. From these results the committee cannot recommend the routine use of humidification for low flow oxygen delivery, however the need for future research into the efficacy of short and long-term outcomes for each type of humidification is needed.

Titration of oxygen to a therapeutic goal in the treatment of hypoxemia would appear to be a best practice within many of the disease specific clinical practice guidelines today, however apart from bronchiolitis this practice has not been evaluated scientifically. In hospitalized patients suffering from bronchiolitis, targeting a lower than normal oxygen saturation results in less time receiving oxygen therapy and earlier discharge. In hospitalized pediatric patients

suffering from bronchiolitis, evidence supports an oxygenation saturation target of 90% to 98%.

While expert clinicians recommend therapeutic oxygenation targets for respiratory diseases, we could find little evidence these targets are correct. In hospitalized pediatric patients suffering from respiratory diseases outside of bronchiolitis, establishing a patient/disease oxygen therapy target upon admission is best practice, but a specific target cannot be recommended.

References

1. Subhi R, Adamson M, Campbell H, Weber M, Smith K, Duke T. The prevalence of hypoxemia among ill children in developing countries: a systematic review. *Lancet infect dis* 2009;9(4):219-27.
2. Bass JL, Corwin M, Gozal D, Moore C, Nishida H, Parker S, et al. The effect of chronic intermittent hypoxemia on cognition in childhood: a review of the evidence. *Pediatrics* 2004;114(5):805-816.
3. Kacmarek RM, Stoller JK, Heur AJ. Egan's fundamentals of respiratory care, 10th edition. St Louis: Mosby|Elsevier; 2013:321, 322, 914.
4. Nunn JF. Conscious volunteers developed hypoxemia and pulmonary collapse when breathing air and oxygen at reduced lung volumes. *Anesthesiology* 2003;98(1):258-259.
5. Saugstad OD. Bronchopulmonary dysplasia-oxidative stress and antioxidants. *Semin Neonatol* 2003;8(1):39-49.
6. Walsh BK, Smallwood CD. Pediatric oxygen: a review and update. *Respir Care* 2017;62(6):645-661.
7. Rojas-Reyes MX, Granados Rugeles C, Charry-Anzola LP. Oxygen therapy for lower respiratory tract infections in children between 3 months and 15 years of age. *Cochrane Database of Systematic Reviews* 2014, Issue 12.
8. WHO. Guideline: Updates on Paediatric Emergency Triage, Assessment and Treatment. Geneva: World Health Organization, 2016.
9. Topjian AA, Raymond TT, Atkins D, Chan M, Duff JP, Joyner BL, et al. on behalf of Pediatric Basic and Advanced Life Support Collaborators. *Circulation* 2020;142(supp 2):S469-S523.

10. Fitch K, Bernstein SJ, Aguilar MD, Burnand B, LaCalle JR, Lazaro P, et al. The RAND/UCLA Appropriateness Method User's Manual. Santa Monica, CA: RAND;2001.
11. Walsh BK, Brooks TM, Grenier BM. Oxygen therapy in the neonatal care environment. *Respir Care* 2009;54(9):1193-1202.
12. Rubin BK, Haynes JM. Myths, misunderstandings, and dogma in respiratory care. *Respir Care* 2012;57(8):1314-1324.
13. Volsko TA. Cystic fibrosis and the respiratory therapist: a 50-year perspective. *Respir Care* 2009;54(5):587-594.
14. Dysart K, Miller TL, Wolfson MR, Shaffer TH. Research in high flow therapy: mechanisms of action. *Respir Med*, 2009: 103(10):1400-1405.
15. Franklin D, Babl F, Schlapbach L, Oakely E, Craig S, Neutze J, et al. A randomized trial of high-flow oxygen therapy in infants with bronchiolitis. *N Engl J Med* 2018;378(12):1121-1131.
16. Ergul AB, Caliskan E, Samsa H, Gokcek I, Kaya A, Zararsiz GE, Torun YA. Using a high-flow nasal cannula provides superior results to OxyMask delivery in moderate to severe bronchiolitis: a randomized controlled study. *Eur J Pediatr* 2018;177(8):1299-1307.
17. Uygur P, Oktem S, Boran P, Tutar E, Tokuc G. Low- versus high-flow oxygen delivery systems in children with lower respiratory infection. *Pediatr Int* 2016;58(1):49-52.
18. Milani GP, Plebani AM, Arturi E, Brusa D, Esposito S, Dell'Era L, et al. Using a high-flow nasal cannula provided superior results to low-flow oxygen delivery in moderate to severe bronchiolitis. *Acta Paediatr* Aug;105(8):e368-372.

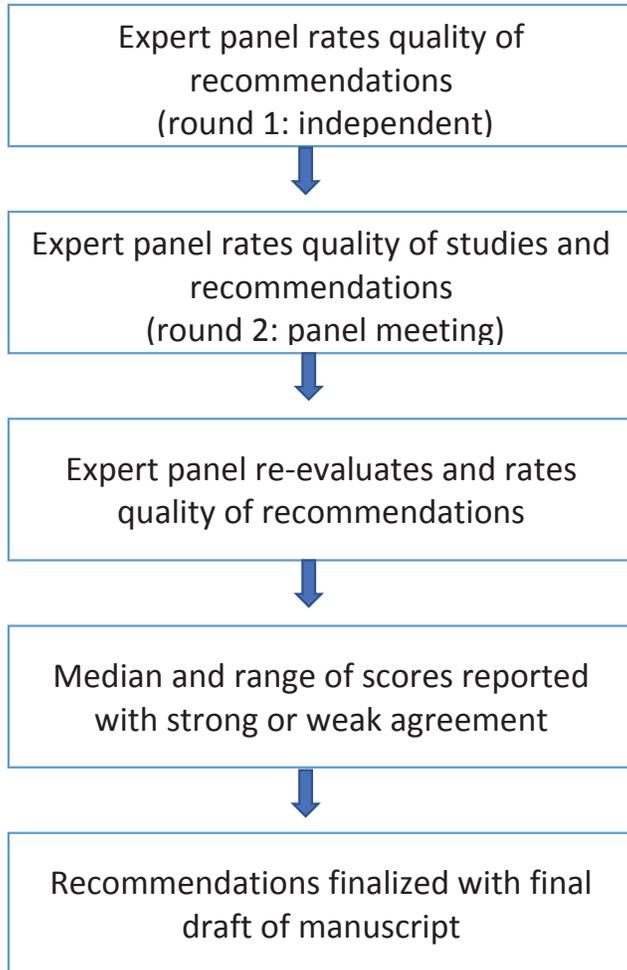
19. Mayfield S, Bogossian F, O'Malley L, Schibler A. High-flow nasal cannula oxygen therapy for infants with bronchiolitis: pilot study. *J Paediatr Child Health* 2014;50(5):373-378.
20. Daverio M, Da Dalt L, Panozzo M, Frigo AC, Bressan S. A two-tiered high-flow nasal cannula approach to bronchiolitis was associated with low admission rate to intensive care and no adverse outcomes. *Acta Paediatr* 2019;108(11):2056-2062
21. McKiernan C, Chua LC, Visintainer PF, Allen H. High flow nasal cannulae therapy in infants with bronchiolitis. *J Pediatr* 2010;156(4):634-638.
22. Baudin F, Gagnon S, Crulli B, Proulx F, Jovet P, Emeriaud G. Modalities and Complications Associated With the Use of High-Flow Nasal Cannula: Experience in a Pediatric ICU. *Respir Care* 2016;61(10):1305-1310.
23. Scolnik D, Coates AL., Stephens D, Da Silva Z, Lavine E, Schuh S. Controlled delivery of high vs low humidity vs mist therapy for croup in emergency departments: a randomized controlled trial. *Jama* 2006;295(11):1274-1280.
24. Chen DY, Zee ED, Gildengorin G, Fong EW. A pilot study of heated and humidified low flow oxygen therapy: an assessment in infants with mild and moderate bronchiolitis (HHOT AIR study). *Pediatr Pulmonol* 2019;54(5):620-627.
25. Lorente Sánchez S, Gimeno R, Losilla JM, Garzon S, Vives J. Benefits of the humidified low-flow oxygen therapy in infants with mild-moderate bronchiolitis. *J Clin Nurs* 2018;27(5-6):1125-1133.
26. Harris M, Clark J, Coote N, Fletcher P, Harnden A, McKean M, et al. British Thoracic Society guidelines for the management of community acquired pneumonia in children: update 2011. *Thorax* 2011;66 Suppl 2:ii1-23

27. National Asthma E, Prevention P. Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma-Summary Report 2007. *J Allergy Clin Immunol* 2007;120(5 Suppl):S94-138
28. British Thoracic Society Scottish Intercollegiate Guidelines N. SIGN158 British guideline on the management of asthma. *British Thoracic Society* 2019:172
29. Hasegawa K, Tsugawa Y, Brown DF, Mansbach JM, Camargo CA, Jr. Trends in bronchiolitis hospitalizations in the United States, 2000-2009. *Pediatrics* 2013;132(1):28-36.
30. Ralston SL, Lieberthal AS, Meissner HC, Alverson BK, Baley JE, Gadomski AM, et al. Clinical practice guideline: the diagnosis, management, and prevention of bronchiolitis. *Pediatrics* 2014;134(5):e1474-1502
31. Organization WH. WHO Pocket book of hospital care for children. WHO Publications; 2013:412
32. Cunningham S, Rodriguez A, Adams T, Boyd KA, Butcher I, Enderby B, et al. Oxygen saturation targets in infants with bronchiolitis (BIDS): a double-blind, randomized, equivalence trial. *Lancet* 2015;386(9998):1041-1048.

Figure Legends:

Figure 1: A flow diagram outlining the process used by the committee to appraise the literature.

Figure 2: PRISMA Diagram. *From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement.* PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097. **For more information, visit www.prisma-statement.org.**



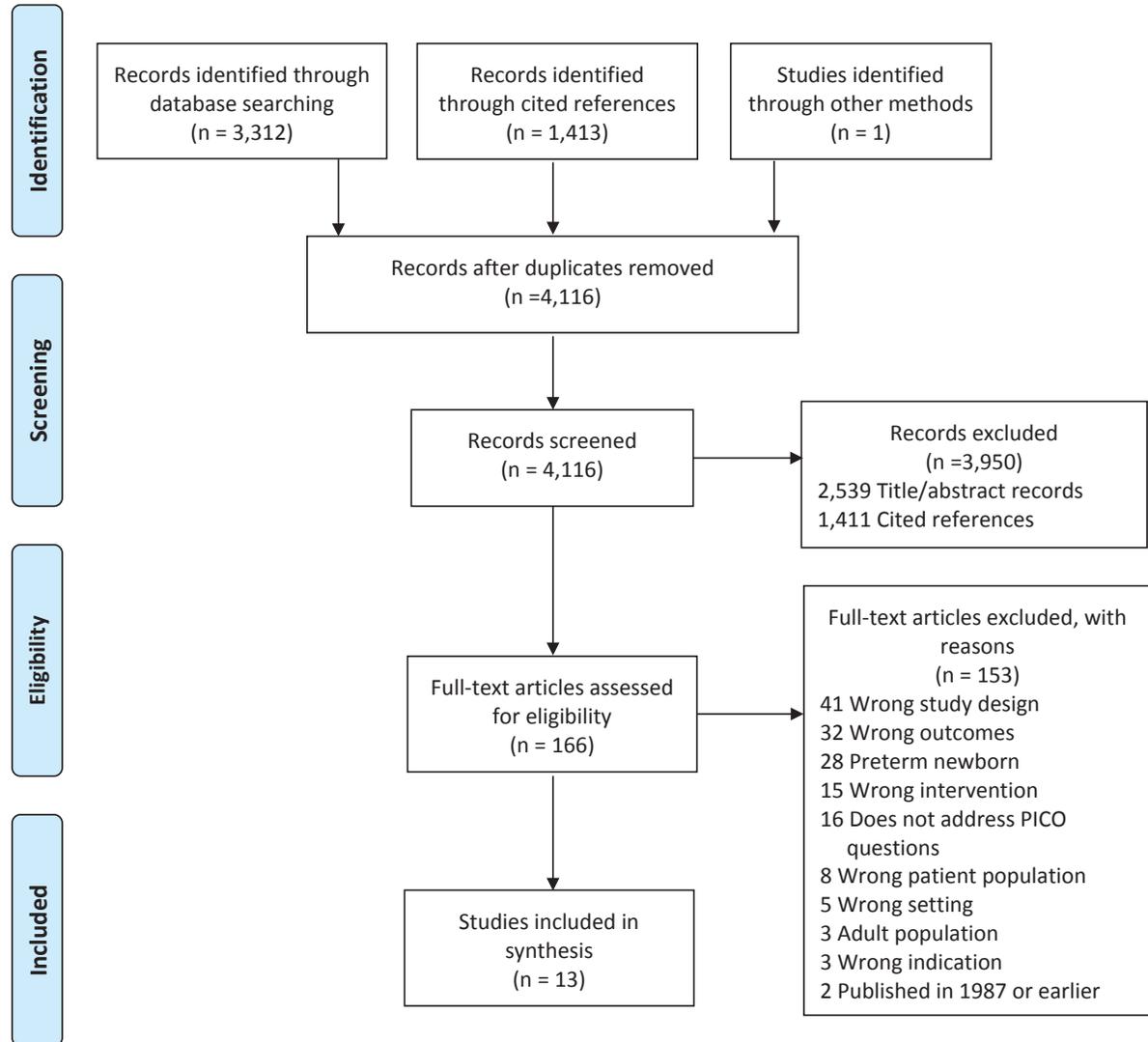


Table 1. Summary of Evidence for Each PICO Question Included in the Systematic Review

PICO Question	Study	Intervention	Outcomes
1. In hospitalized pediatric patients, does the use of oxygen tents and hoods versus low-flow oxygen systems (nasal cannula, simple face mask) provide a more consistent oxygen delivery?	No published evidence identified.		
2. In hospitalized pediatric patients, does the use of high-flow oxygen systems versus low-flow oxygen systems increase the FDO ₂ or decrease escalation of therapy (NIV or intubation)?	Baudin et al ²²	HFNC in pediatric patients	Escalation of therapy to NIV or intubation occurred in 22% of subjects
	Daverio et al ²⁰	First-line HFNC vs low-flow oxygen vs rescue HFNC in infants with bronchiolitis	HFNC as initial treatment had less therapy escalation rate than conventional oxygen therapy (3% vs. 41.5%)
	Ergul et al ¹⁶	HFNC vs conventional oxygen therapy in patients with moderate to severe acute bronchiolitis	Use of HFNC reduced weaning time ($P < .001$) and treatment failure rate ($P = .011$) over conventional oxygen therapy
	Franklin et al ¹⁵	HFNC vs low-flow oxygen in pediatric patients	HFNC reduced escalation of care over conventional oxygen therapy ($P < .001$)
	Mayfield et al ¹⁹	HFNC vs low-flow oxygen in pediatric patients with bronchiolitis	Oxygenation did not significantly differ between groups ($P = .17$) though fewer patients in the HFNC group required escalated therapy over the conventional oxygen therapy group ($P = .043$)
	McKiernan et al ²¹	Introduction of HFNC vs baseline	HFNC in children with bronchiolitis may reduce rates of intubation ($P = .043$) and PICU LOS ($P = .0058$) but results not statistically significant
	Milani et al ¹⁸	HFNC vs low-flow oxygen in pediatric patients with bronchiolitis	HFNC may reduce escalation of therapy over conventional oxygen therapy ($P = .043$)
	Uygur et al ¹⁷	Venturi mask vs low-flow oxygen mask in pediatric patients with bronchiolitis	Venturi mask reduced oxygen usage time ($P = .03$) and need for supplemental oxygen after 12 hours ($P = .03$)
3. In hospitalized pediatric patients, does adding active or	Chen et al ²⁴	Low-flow oxygen with heated humidification vs low-flow oxygen	No significant difference in RDAI score between groups ($P = .56$)

supplemental oxygen as compared to no humidification improve comfort or reduce infection risk?		with no humidification in pediatric patients with bronchiolitis	
	Lorente et al ²⁵	Low-flow oxygen with bubble humidification vs low-flow oxygen with no humidification in children	No difference found in respiratory rate at 24, 48 and 72 hours ($P=.852$, $P=.405$, $P=.336$, respectively), median (IQR) need for nasal lavages (3 (2-9) vs 3 (1-5), $P=.467$), length of hospital stay (5 (4-7) vs 5 (4-6), $P=.467$), or length of time on Oxygen (3 (2-5) vs 3 (2-4), $P=.174$)
	Scolnik et al ²³	100% humidity vs 40% humidity via nebulizer vs blowby in ED in children with croup	30 min difference in Wesley score blow-by vs. low-humidity was 0.03 (95% CI, -0.72 to 0.66), low- vs. high-humidity, 0.16 (95% CI, -0.86 to 0.53), and blow-by vs. high-humidity, 0.19 (95% CI, -0.87 to 0.49). Mean (SD) change in respiratory rate at 60 min (blow-by 30 (7), Low-humidity 30 (6), high-humidity 30 (9)). Number (%) of hospitalization of 1(2.1) for blow-by vs. 2 (4.3) for low-humidity vs 0 for high-humidity.
4. In hospitalized pediatric patients, does establishing disease-specific oxygenation targets reduce oxygen use, decrease the length of stay, or prevent escalation of therapy as compared to prescribed or no disease-specific oxygen targets?	Cunningham et al ³²	Discharge oxygenation goals of 90% SpO ₂ vs discharge oxygenation goal of 94% SpO ₂ in pediatric patients with bronchiolitis	Discontinuing supplemental oxygen at stable 90% SpO ₂ rather than 94% SpO ₂ could result in a median discharge from hospital 22 h (IQR 7h-39h) earlier.
	Cunningham et al ³³	90% or higher SpO ₂ target vs 94% or higher SpO ₂ target for infants with bronchiolitis	Lower SpO ₂ target range resulted in less time to further supplemental oxygen (27.6h vs 5.7h, $P=.0021$), fitness to discharge (44.2 vs 30.2h, $P<.0001$), and less time to discharge (50.9h vs 40.9h, $P=.003$)

HFNC = high flow nasal cannula

LOS = length of stay

ED = emergency department

CI = confidence interval

SD = standard deviation

IQR = interquartile range

Table X. Summary of Recommendations for Each PICO Question.

1. In hospitalized pediatric patients, does the use of oxygen tents and hoods versus low-flow oxygen systems (nasal cannula, simple face mask) provide a more consistent oxygen delivery?
 - The committee does not recommend using an oxygen hood or tent in lieu of a low-flow oxygen device for consistent oxygen delivery (Evidence level C, median appropriateness score 8).
2. In hospitalized pediatric patients, does the use of high-flow oxygen systems versus low-flow oxygen systems increase the FDO₂ or decrease escalation of therapy (NIV or intubation)?
 - The use of HFNC appears to be safe and more effective than low flow oxygen to treat infants with moderate to severe bronchiolitis in the Pediatric Ward and PICU setting (Evidence level B, median appropriateness score 7.5).
3. In hospitalized pediatric patients, does adding heated or non-heated humidification to supplemental oxygen as compared to no humidification improve comfort or reduce infection risk?
 - Low level of evidence does not support the use of heated or non-heated humidification with low flow oxygen delivery (Evidence level B, median appropriateness score 8.25).
4. In hospitalized pediatric patients, does establishing disease-specific oxygenation targets reduce oxygen use, decrease the length of stay, or prevent escalation of therapy as compared to prescribed or no disease-specific oxygen targets?
 - In hospitalized pediatric patients suffering from bronchiolitis, evidence supports an oxygenation target of 90% or greater (Evidence level C, median appropriateness score 7).

- In hospitalized pediatric patients suffering from respiratory diseases outside of bronchiolitis, establishing a patient/disease oxygen therapy target upon admission is best practice, but a specific target cannot be recommended (Evidence level C, median appropriateness score 7).