DATE: October 2012

Pediatric Prehospital Protocols Grant
Post-Resuscitation Management
Evidence-Based Practice Summary

Evidence-Based Practice Summary prepared by Colleen Jones, MS, RN, Research Specialist and Janelle Smith, MSN, RN, Research Specialist.

ASK THE QUESTION

Question 1: In the post-resuscitation management of the pediatric patient in the prehospital setting who has not been previously intubated, how does intubation compare with bag valve mask ventilation in terms of improved outcomes (mortality upon arrival to the EC, 30-day mortality, and neurologic outcome)?

Question 2: Does therapeutic hypothermia compared to no intervention in the post-resuscitation management of the infant (non-neonate) or child in the prehospital setting result in better outcomes (mortality upon arrival to the EC, 30-day mortality, and neurologic outcome)?

Question 3: Does therapeutic hypothermia compared to no intervention in the post-resuscitation of the neonate in the prehospital setting result in better outcomes (mortality upon arrival, 30-day mortality, and neurologic outcome)?

Question 4: Does pulse oximetry monitoring with titration of oxygen delivery improve outcomes (mortality upon arrival to the EC, 30-day mortality, and neurologic outcome) in the post-resuscitation management of the neonatal patient in the prehospital setting?

CRITICALLY ANALYZE THE EVIDENCE

Existing External Order Sets/Guidelines/Clinical Pathways

External Guideline/ Pathway/Order Set	Organization and Author	Last Update
Pediatric Advanced Life Support: 2010 Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care	American Heart Association	2010
Neonatal Resuscitation: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations	American Heart Association	2010

The two published clinical guidelines have been evaluated for this review using the AGREE criteria. AGREE includes evaluation of: Guideline Scope and Purpose,

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Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence. Four reviewers appraised the guideline, and scored each component independently. Domain scores were calculated by summing up all the scores of the individual items in a domain, and standardizing the total as a percentage of the maximum possible score for a particular domain. After appraising the guidelines above using the AGREE instrument, the reviewers recommend using the guidelines with modifications. The reviewers were: Elizabeth Crabtree, MPH; Quinn Franklin, MS, CCLS; Colleen Jones, MS, RN; and Janelle Smith, MSN, RN.

Question 1: In the post-resuscitation management of the pediatric patient in the prehospital setting who has not been previously intubated, how does intubation compare the bag valve mask ventilation in terms of improved outcomes (mortality upon arrival to the EC, 30-day mortality, and neurologic outcome)?

Recommendation: In the post-resuscitation management of the pediatric patient in the prehospital setting, bag valve mask ventilation is preferred over endotracheal intubation to enhance improved outcomes.

Strength of recommendation: Weak
Grade criteria: Very low 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. The Pediatric Basic and Advanced Life Support (Kleinman, et. al. 2010) recommends bag-valve mask over tracheal intubation for children and infants needing ventilatory support in the prehospital setting. This recommendation is supported by evidence via seven studies completed in the prehospital setting. Gausche 2000 and Pitette 2002 found no significant difference between survival to hospital discharge for children intubated or when bag-valve mask was used for ventilatory support. Ehrlic 2004, Gerritse 2008, Garza 2005, Coldwell 2009, and Stockinger 2003 all demonstrated significant clinical data showing children intubated in the field had decreased survival rate to the Emergency Department, lower Glasgow Coma Scale Scores, and no improvement in neurological deficits at discharge.
The three study Lecky 2008 Cochrane Review was not utilized in this evidence summary. Two of the three research trials from this Cochrane review were adult trials for out-of-hospital cardiac arrest. One study compared physician intubation versus a Combitube. The second trial looked at paramedic intubation versus an esophageal gastric airway. Therefore, the Gausche 2000 trial, the third study was reviewed separately, graded, and incorporated into the evidence summary. The Gausche study had the best study design of those reviewed. In this study, there was no significant difference in survival or neurologic outcome between the bag-valve-mask (BVM) and endotracheal intubation (ETI) groups. Since some of the other studies reviewed also demonstrated complications such as malpositioned endotracheal tubes, there is potential risk for harm with ETI in the prehospital setting, when compared to BVM.

Recommendation(s): Very Low Quality Evidence
Number of Studies: Total # 7 ☐ Systematic review /Meta-analysis ☒ **1** RCT ☒ **6** Observational ☐ Case Reports Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	***Inconsistency* of Results**	***Indirectness* of Evidence**	***Imprecision***
☐ None ☐ Insufficient sample size ☒ Lack of blinding (Colwell 2009, Ehrlic 2004, Gerritse 2008, Garza 2005, Pitetti 2002, Stockinger 2003) ☒ Lack of allocation concealment (Colwell 2009, Gausche 2000, Gerritse 2008, Garza 2005, Pitetti 2002, Stockinger 2003)	☒ No inconsistencies (Colwell 2009, Ehrlic 2004, Gausche 2000, Gerritse 2008, Garza 2005, Pitetti 2002, Stockinger 2003) ☐ Wide variation of treatment effect across studies ☐ Populations varied (e.g., sicker, older) ☐ Interventions varied (e.g., doses) ☐ Outcomes varied (e.g., diminishing	☒ Head-to-head comparison in correct population (Ehrlic 2004, Gausche 2000, Pitetti 2002, Stockinger 2003) ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☐ Different populations (Colwell 2009) ☐ Different interventions	**Dichotomous outcomes** ☐ Sample size lower than calculated optimal information size ☒ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes (Ehrlic 2004, Pitetti 2002) ☒ 95% CI includes negligible effect and appreciable benefit or harm (Gausche 2000, Pitetti

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☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g. no effect outcome)	effect over time)	☐ Different outcomes measured ☐ Comparisons not applicable to question/outcome	2002) **Continuous outcomes** ☐ 95% CI includes no effect and the upper or lower limit crosses the minimal important difference (MID), either for benefit or harm ☐ Upper or lower limit crosses an effect size of 0.5 in either direction (if MID is not known or differences in outcomes require the calculation of an effect size)

Sample	CI/RR
Colwell (2009): Prospective, observational chart review on 926 hospital patients for whom prehospital intubation was attempted by emergency personnel in the prehospital setting. **Ehrlic (2004):** 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 ETI's were measured. **Gausche (2000):** Quasi-randomized Control Trial. 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 as compared to treatment group were the main outcomes. **Gerritse (2008):** Prospective observational study analyzed 300 children examined and treated by helicopter-transported medical team (HMT) on scene looking at survival of tracheal intubated vs bag-valve mask ventilation (BVM) by EMS-paramedics. **Garza (2005):** Retrospective, observational study looking at oral endotracheal intubation on pediatric cardiac arrest and intubation nonattempts and endotracheal intubation failures by an ambulance service on pediatric cardiac arrest, adult traumatic arrest, and adult cardiac arrest patients. **Pitetti (2002):** Retrospective chart review of 189 pediatric patients presenting to the Emergency Department (ED) following an out-of-hospital cardiac arrest. The main outcome measured was to compare survival rates among children receiving BLS with bag-valve-mask ventilation or Advanced Life Support (ALS). **Stockinger (2003):** Retrospective chart review of 533 trauma patients from 2 to 97 years old. These patients either received Endotracheal Intubation (ETI) or BVM. Evaluate the efficacy of ETI VS	**Colwell (2009):** • Percentage of patients successfully intubated by the prehospital care givers was 74.8% (617/825), 95% CI: 71.7, 77.7. • Malpositioned tubes including those who were nasally intubated was 8.6% 95% CI: 5.5, 12.0, orally intubated patients with malposition tubes were 3.4%, 95% CI: 2.0, 5.5. 2.4% of all intubations malpositioned into the esophagus 95% CI: 1.5%, 3.9%. **Ehrlic (2004):** • RR of an airway complications was 2.5X 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 Glasgow 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. **Gausche (2000):** • 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 BVM. **Gerritse (2008):** • 155/300 required out of hospital tracheal intubation. EMS-paramedic performed BVM until arrival of HMT (they performed ETI) on 54 children with a survival rate of 63%.

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BVM and the mortality associated with each mode of ventilation of the patient.	• EMS-paramedic performed ETI themselves on 41 children with subsequent correction of tube/ventilation by HMT in 37% and a survival rate of 5%. **Garza (2005):** • 120 pediatric arrests with 86 (71%) had an intubation attempt. • Endotracheal failure for the pediatric population was 44.2% (RR 7.24, 95%, CI 5.73, 9.16 for nonattempt; RR 2.33, 95% CI 1.93, 2.83 for intubation failure) **Pitetti (2002):** • 39/189 or 20.6% of the children were provided BLS (BVM) measures by prehospital personnel. 150/289 or 79.4% received ALS. There was no significant difference between groups in survival to hospital discharge. **Stockinger (2003):** • Patients receiving ETI were significantly more likely to die, 88.9% vs 30.9%, $p < 0.0001$. • ETI patients also had a longer prehospital time, 22.0 vs 20.1 minutes, p= 0.0241.

References:

Colwell, C. B., Cusick, J. M., Hawkes, A. P., Luyte, D. R., McVaney, K. E., et al. (2009). Focus on airway management: A prospective multicenter evaluation of prehospital airway management performance in a large metropolitan region: Denver metro airway study group. *Prehospital Emergency Care, 13*(3), 304-310.

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.

Gausche, M., Lewis, R. J., Stratton, S. J., Haynes, B. E., Gunter, C. S., et al. (2000). Effect of out-of-hospital pediatric endotracheal intubation on survival and neurological outcome. *Journal of American Medical Association, 283*(6), 783-790.

Gerritse, B., Draaisma, J., Schalkwijk, A., van Grunsven, P., & Scheffer, G. J. (2008). Should EMS-paramedics perform paediatric tracheal intubation in the field? *Resuscitation, 79,* 225-229.

Garza, A.G., Algren, D.A., Gratton, M.C., & Ma, O.J. (2005). Populations at risk for intubation nonattempt and failure in the prehospital setting. *Prehospital Emergency Care, 9*(2), 163-166.

Pitetti, R., Glustein, J. Z., & Bhende, M. S. (2002). Prehospital care and outcome of pediatric out-of-hospital cardiac arrest. *Prehospital Emergency Care, 6*(3), 283-290.

Stockinger, Z. T., & McSwain, N. E. (2003). Prehospital endotracheal intubation for trauma does not improve survival over bag-valve-mask ventilation. *The Journal of Trauma, Injury, Infection, and Critical Care, 56*(3), 531-536.

Guideline Reviewed:

Kleinman, M. E., deCaen, A. R., Chameides, L., et. al. (2010). Part 10: Pediatric basic and advanced life support. 2010 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendation. *Circulation, 122*(suppl 2), S466-S515.

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Question 2: Does therapeutic hypothermia compared to no intervention in the post-resuscitation management of the infant (non-neonate) or child in the prehospital setting result in better outcomes (mortality upon arrival to the EC, 30 day mortality, and neurologic outcome)?

Recommendation: Therapeutic hypothermia is not recommended in the post-resuscitation management of the infant (non-neonate) or child in the prehospital setting.

Strength of recommendation: Strong
Grade criteria: Low quality evidence
In an observational study by Doherty, et al., the use of hypothermia was evaluated compared to no intervention in both the Pre-hospital and In-hospital setting. Based on the study results, the use of hypothermia was contraindicated due to the increase mortality rate, 30 day mortality rate and neurologic outcomes of the patients.

Fink, et al. (2010) conducted the largest retrospective cohort study known on the use of therapeutic hypothermia in pediatric cardiac arrest. It was found that the use of therapeutic hypothermia is acceptable if the target temperature was met in less than 3 hours. In this study, the target temperature was set to 34.0°C. Increase cases of mortality was found when the temperature fell below the target.

Recommendation(s): Low Quality Evidence
Number of Studies: Total # 2 ☐ Systematic review ☐ RCT ☒ Observational ☐ Case Reports Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☐ None ☒ Insufficient sample size (Doherty 2009, Fink 2010) ☒ Lack of blinding (Doherty 2009, Fink 2010) ☐ 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 (Doherty 2009, Fink 2010) ☐ 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) (Doherty 2009, Fink 2010)	☒ Head-to-head comparison in correct population (Doherty 2009) ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☐ Different populations ☐ Different interventions ☒ Different outcomes measured (Fink 2010) ☐ 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 includes negligible effect and appreciable benefit or harm **Continuous outcomes** ☐ 95% CI includes no effect and the upper or lower limit crosses the minimal important difference (MID), either for benefit or harm ☐ Upper or lower limit crosses an effect size of 0.5 in either direction (if MID is not known or differences in outcomes require the calculation of an effect size)

Sample	CI/RR
Doherty (2009): Observational Study. 79 patients were enrolled in the study. 29 of 79 patients received hypothermia therapy. 50 of the 79 patients were assigned to the Control (normothermia) group. **Fink (2010):** A Retrospective, cohort study. 181 patients were included in the study. 141	**Doherty (2009):** • Temperature within the first 12 hours after cardiac arrest was significantly lower in the hypothermia therapy group than in the normothermia group (P < 0.001) • Mortality was higher at 6 months in the hypothermia group (69%)

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out of 181 were in the standard therapy group. 40 out of the 181 patients were in the hypothermia group.	than in the normothermia group (38%); P = 0.009 • The 30-day mortality rate was higher in the hypothermia group (58.6%) than in the normothermia group (36%); P = 0.054 • The proportion of patients with a PCPC (Pediatric Cerebral Performance Category) score of 1 to 3 before cardiac arrest who had a PCPC score of 4 to 6 after cardiac arrest was higher in the hypothermia group (65%) than in the normothermia group (37.8%); P = 0.060 • Longer length of stay in the pediatric intensive care unit (PICU) 16.0 days compared to 9.0 days in the hypothermia therapy group than in the normothermia group; P = 0.411 **Fink (2010):** • In the therapeutic hypothermia group, where the temperature fell below < 32°C occurred in 15% of patients and was associated with higher hospital mortality; p = .02. • In the therapeutic hypothermia patients where the temperature stayed within the median target of 34.0, there was no significant difference in the mortality rate; p = 1.0.

References:

Doherty, D. R., Parshuram, C. S., Gaboury, I., et al. (2009). Hypothermia therapy after pediatric cardiac arrest. *Circulation, 119*, 1492-1500.

Fink, E. L., Clark, R. S., Kochanek, P. M., Bell, M. J., & Watson, R. S. (2010). A tertiary care center's experience with therapeutic hypothermia after pediatric cardiac arrest. *Pediatric Critical Care Medicine, 11*(1), 66-74.

Question 3: Does therapeutic hypothermia compared to no intervention in the post-resuscitation of the neonate in the prehospital setting result in better outcomes (mortality upon arrival, 30-day mortality, and neurologic outcome)?

Recommendation: Therapeutic hypothermia is recommended in the post-resuscitation management of the neonate in the prehospital setting.

Strength of recommendation: Strong
Grade criteria: Moderate quality evidence

Several randomized controlled studies evaluated the use of induced hypothermia in neonates for the treatment of neonatal encephalopathy. Based on the study results, the use of induced hypothermia in neonates could improve survival and lead to less neurological long term defects.

Perlman, et al. (2010) discusses in the 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations that infants born at or near term with evolving moderate to severe hypoxic-ischemic encephalopathy should be offered therapeutic hypothermia.

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Recommendation(s): Moderate Quality Evidence
Number of Studies: Total # 4 ☐ Systematic review ☒ **4** RCT ☐ Observational ☐ Case Reports Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	*Inconsistency* of Results	*Indirectness* of Evidence	*Imprecision*
☒ None (Gluckman 2005, Shankaran 2005, Wyatt 2007) ☒ Insufficient sample size (Battin 2003) ☐ 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 (Battin 2003, Gluckman 2005, Shankaran 2005, Wyatt 2007) ☐ 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) (Battin 2003, Gluckman 2005, Shankaran 2005, Wyatt 2007) ☐ 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 includes negligible effect and appreciable benefit or harm **Continuous outcomes** ☐ 95% CI includes no effect and the upper or lower limit crosses the minimal important difference (MID), either for benefit or harm ☐ Upper or lower limit crosses an effect size of 0.5 in either direction (if MID is not known or differences in outcomes require the calculation of an effect size)

Sample	CI/RR
Battin (2003): N = 26 infants. 13 infants received selective head cooling with rectal temperature maintained at 35.0C in 6 infants and at 34.5C in 7 infants. The remaining 13 infants were normothermic. **Gluckman (2005):** N = 234 infants. 116 were randomly allocated cooling; 118 were in the control group. **Shankaran (2005):** N = 208 infants. 102 were assigned to the hypothermia group; 106 were assigned to the control group **Wyatt (2007):** N = 218. 108 were cooled; 110 were in the control group.	**Battin (2003):** • 20 of the 26 infants required respiratory support within the first 72 hours of life. The cooled infants did not have an increased requirement for respiratory support compared with control infants and support was able to be weaned during continued cooling. • Cooled CT results: 6 = WNL, 3 = mild white matter abnormalities, 3 = overt major abnormality; Control CT results: 8 = WNL, 1 = overt major abnormality. • EEG performed within 1 week of CT showed, in cooled infants, 6 cases were WNL, 5 demonstrated either persisting abnormalities of background or excessive sharp waves and 1 died; in the control infants, 7 cases were WNL, 1 was abnormal with an excess of sharp wave and spike activity, and 2 died. **Gluckman (2005):** • In infants with the most severe baseline EEG changes (n = 46), with severe suppression of background activity and seizures, no effect of hypothermia was noted on outcome (p = 0.51).

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	Shankaran (2005): • 24 deaths in the hypothermia group and 38 deaths in the control group; RR, 0.68; p = 0.08. • Death or disability among infants with moderate encephalopathy is 22 (32%) in the hypothermia group and 30 (48%) in the control group. RR=0.69; p=0.09. • Death or disability among infants with sever encephalopathy is 23 (72%) in hypothermia group and 34 (85%) in the control group. RR=0.85; p=0.24. • The rates of disabling cerebral palsy were 19 percent in the hypothermia group and 30 percent in the control group; RR=0.68; p=0.20. **Wyatt (2007):** • Greater severity of EEG background changes, presence of EEG seizures, lower continuous 5-minute Apgar score and greater birth weight were associated with adverse outcomes.

References:

Battin, M., Penrice, J., Gunn, T. R., & Gunn, A. J. (2003). Treatment of term infants with head cooling and mild systemic hypothermia (35.0°C and 34.5°C) after perinatal asphyxia. *Pediatrics, 111*, 244-251.

Gluckman, P. D., Wyatt, J. S., Azzopardi, D., et al. (2005). Selective head cooling with mild systemic hypothermia after neonatal encephalopathy: Multicentre randomized trial. *Lancet*, *365*, 663-70.

Shankaran, S., Laptook, A. R., Ehrenkranz, R. A., et al. (2005). Whole-body hypothermia for neonates with hypoxic-ischemic encephalopathy. *New England Journal of Medicine*, *353*, 1574-84.

Wyatt, J. S., Gluckman, P. D., Liu, P. Y., et al. (2007). Determinants of outcomes after head cooling for neonatal encephalopathy. *Pediatrics*, *119*, 912-921.

Question 4: Does pulse oximetry monitoring with titration of oxygen delivery improve outcomes (mortality upon arrival to the EC, 30 day mortality, and neurologic outcome) in the post-resuscitation management of the neonatal patient in the prehospital setting?

Recommendation: Routine use of pulse oximetry to titrate oxygen delivery to neonates for post-resuscitation management is not recommended for the term infant. For infants with estimated gestational ages of < 32 weeks born in the prehospital setting, pulse oximetry should be used to titrate oxygen delivery to gradually achieve an oxygen saturation of 90-99% over 10 minutes, if pulse oximetry is available.

Recommendation: Strong

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Grade criteria: Low quality evidence

One randomized controlled study and one observational study evaluated the use of Oxygen in neonates (< 32 weeks) after delivery. In the randomized controlled study, it was suggested that room air or 21% oxygen should not be used because it does not successfully oxygenate the infants and SPO_2 levels did not reach targeted ranges until oxygen delivery was increased. In the observational study, it was suggested that excessive oxygen delivery after birth in neonates increases the risk for negative consequences and lower oxygen levels are more beneficial.

Perlman, et al. (2010) discusses in the 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations the use of Supplemental Oxygen in neonates. It is recommended that pulse oximetry be used to guide the delivery of oxygen since most preterm babies (< 32 weeks) will not reach target saturations. However, in term infants who received resuscitation with intermittent positive pressure ventilation (PPV), administration of 100% did not provide an advantage and may be potentially harmful. In addition, infants resuscitated with room air, rather than routine supplemental oxygen, had decreased mortality.

Recommendation(s): Low Quality Evidence
Number of Studies: Total # 2 ☐ Systematic review ☒ RCT [2] ☒ Observational[1] ☐ Case Reports Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	***Inconsistency* of Results**	***Indirectness* of Evidence**	***Imprecision***
☐ None ☒ Insufficient sample size (Escrig 2008, Wang 2008) ☒ Lack of blinding (Escrig 2008) ☐ 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 (Escrig 2008, Wang 2008). ☐ 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 includes negligible effect and appreciable benefit or harm **Continuous outcomes** ☐ 95% CI includes no effect and the upper or lower limit crosses the minimal important difference (MID), either for benefit or harm ☐ Upper or lower limit crosses an effect size of 0.5 in either direction (if MID is not known or differences in outcomes require the calculation of an effect size)
Sample		**CI/RR**	

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Escrig (2008): N = 42 infants. 19 were in the Low-Oxygen group and 23 were in the High Oxygen group **Wang (2008):** N = 43 infants. 23 were in the Oxygen group, 18 were in the room air group and 2 did not require resuscitation.	**Escrig (2008):** • In the first 3 and 4 minutes after birth, FIO_2 in the high-oxygen group was significantly higher than that in the low-oxygen group (P < 0.1). After 4 minutes, there was no significant difference between values. • No deaths occurred in either group in the neonatal period (< 28 days). • 4 infants in the low-oxygen group and 3 in the high-oxygen group died as a result of respiratory or neurologic complications during hospitalization. • No significant difference between the groups in the incidence of acute and/or long-term complications were detected at discharge. **Wang (2008):** • In the room air group, FIO_2 was increased directly to 100% because of bradycardia by 2 minutes of age for 6 patients and FIO_2 was increased incrementally for failure to meet SPO_2 criteria at 3 minutes of life for the remaining 12 patients. • There were no significant differences in any of the evaluated outcomes, including intraventricular hemorrhage, retinopathy of prematurity, necrotizing enter colitis and chronic lung disease. • In the Oxygen group, an infant of 25 weeks of gestation died at 7 days of life as a result of sepsis, respiratory distress syndrome and pneumothorax. • In the Room Air group, an infant of 24 weeks of gestation died at 3 days of life as a result of respiratory failure, pulmonary hemorrhage and grade IV intraventricular hemorrhage.

References:

Escrig, R., Arruza, L., Izquierdo, I., et al. (2008). Achievement of targeted saturation values in extremely low gestational age neonates resuscitated with low or high Oxygen concentrations: A prospective, randomized trial. *Pediatrics*, *121*, 875-881.

Wang, C., Anderson, C., & Leone, T. (2008). Resuscitation of preterm neonates by using room air or 100% Oxygen. *Pediatrics*, *121*, 1083-1089.

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