

EPIQ III – NEC BUNDLE		
Domain	Interventions	Level of Evidence
<p>Promote human milk*</p> <p>(mother’s own milk, or donor human milk if mother’s own milk is not available or insufficient in volume)</p>	<ul style="list-style-type: none"> • Include breast milk discussion/education and obtain consent for use of donor human milk (if available at institution) in antenatal consults when preterm delivery is anticipated. • Supply colostrum collection kits to birthing units and educate staff and mothers about importance of beginning pumping with 6 hours of delivery and continuing frequently using both electric and hand pumping. + Follow established institutional policies for donor milk use. + 	<p>1B</p> <p>Strong recommendation, moderate quality evidence</p>
<p>Probiotics *</p>	<ul style="list-style-type: none"> • Consider administration of probiotics (Lactobacillus/Bifidobacterium combination) once daily beginning at the time enteral feeds are started. 	<p>1B</p>
<p>Consistent implementation of established feeding guidelines</p>	<ul style="list-style-type: none"> • Introduce minimal enteral nutrition (MEN) within first 24 hours with rare exceptions + • Advance MEN rate as per institutional guidelines + • Follow established milk storage and preparation guidelines • Add fortification (i.e. HMF, other nutrients) as per institutional guidelines + 	<p>2C</p> <p>Weak recommendation, weak quality evidence</p>
<p>Oxygen exposure</p>	<p>Review oxygen saturation targets using the major published RCTs (BOOST II, COT, SUPPORT) comparing low (85-89%) and high (91-95%) as a guide. Individual units may vary in the oxygen saturation target ranges. Of note, two recent meta-analyses of the above RCTs show that the relative risk for NEC is lower in the high oxygen saturation target group</p>	<p>1B</p>
<p>Avoid associated factors</p>	<ul style="list-style-type: none"> • Avoid H2 receptor antagonists and PPIs • Avoid prolonged (>3days) empiric antibiotic therapy • When blood transfusion is indicated, consider discontinuing feeds for a period of time pre and post transfusion • Consider ibuprofen instead of indomethacin for treatment of PDA 	<p>2C</p> <p>2C</p> <p>2C</p> <p>1B</p>
<p>Prevent NI</p>	<ul style="list-style-type: none"> • Implementation of NI intervention bundle 	<p>2C</p>

*priorities

+ Institutional guidelines are available on the EPIQ website as is the World Health Organization’s technical report on Optimal Feeding of Low Birth Weight Infants which provides evidence-based information on mother’s own milk, donor milk and feeding guidelines.

References

Human Milk

1. Arslanoglu S et al. Donor human milk in preterm feeding: evidence and recommendations. *J Perinat Med* 2010;38:347-351.
2. Boyd CA et al. Donor breast milk versus infant formula for preterm infants: systematic review and meta-analysis. *Arch Dis Child Fetal Neonatal Ed* 2007;92:F169-F175.
3. Kim JH et al. Human milk banking. *Paediatr Child Health* 2010;15:595-598.
4. Quigley MA. and McGuire W. Formula milk versus donor breast milk for feeding preterm or low birth weight infants. *Cochrane Database Syst Rev* 2014;(4):CD002971
5. Sisk PM et al. Early human milk feeding is associated with a lower risk of necrotizing enterocolitis in very low birth weight infants. *J Perinatol* 2007;27:428-433.
6. Wight NE. Donor human milk for preterm infants. *J Perinatol* 2001;21:249-254.
7. Ramini M and Ambalavanan N. Feeding Practices and Necrotizing Enterocolitis. *Clin Perinatol* 2013;40:1-10.
8. Deborah L. O'Connor, PhD, RD; Sharyn Gibbins, PhD, RN et al. Effect of Supplemental Donor Human Milk Compared With Preterm Formula on Neurodevelopment of Very Low-Birth-Weight Infants at 18 Months:A Randomized Clinical Trial. *JAMA* 2016; 316(18) p 1897-1905.

Probiotics

1. AlFaleh K and Anabrees J Probiotics for prevention of necrotizing enterocolitis in preterm infants. *Cochrane Database Syst Rev* 2014; (4):CD005496
2. Deshpande GC et al. Evidence-based guidelines for use of probiotics in preterm neonates. *BMC Medicine* 2011;9:92.
3. Jacobs SE et al. Probiotic effects on late-onset sepsis in very preterm infants: A randomized controlled trial. *Pediatrics* 2013;132:1055-1062.
4. Janvier A, Malo J, Barrington KJ Cohort study of probiotics in a North American Neonatal Intensive Care Unit. *J Pediatr* 2014;164:980-s5.
5. Costeloe K et al. The PiPS trial: Early administration of *Bifidobacterium breve* BBG-001 to preterm infants to prevent late-onset sepsis, necrotizing enterocolitis and death. *In press Lancet* 2016; 387(10019): p649-660.

Oxygen exposure

1. Saugstad OD and Aune D. Optimal Oxygenation of Extremely Low Birth Weight Infants: A Meta-Analysis and Systematic Review of the Oxygen Saturation Target Studies. *Neonatology* 2014;105:55-63.
2. Manja V et al. Oxygen Saturation Target Range for Extremely Preterm Infants A Systematic Review and Meta-analysis. *JAMA Pediatr* 2015; 169:332-340.

Avoid associated factors

1. Terrin G et al. Ranitidine is associated with infections, necrotizing enterocolitis, and fatal outcome in newborns. *Pediatrics* 2012;129:e40-e45.
2. Cotten CM et al. Prolonged duration of initial empirical antibiotic treatment is associated with increased rates of necrotizing enterocolitis and death for extremely low birth weight infants. *Pediatrics* 2009;123:58-66.
3. Alexander VN et al. Antibiotic exposure in the newborn intensive care unit and the risk of necrotizing enterocolitis. *J Pediatr* 2011;159:392-7
4. Kirpalani H and Zupancic JAF. Do transfusions cause necrotizing enterocolitis? The complementary role of randomized trials of observational studies. *Semin Perinatol* 2012;36:269-276.
5. Mohamed A and Shah P. Transfusion associated necrotizing enterocolitis: A meta-analysis of observational data. *Pediatrics* 2012;129:529-540.
6. Ohlsson A, Walia R and Shah SS. Ibuprofen for the treatment of patent ductus arteriosus in preterm or low birth weight (or both) infants. *Cochrane Database Syst Rev* 2015; (2):CD003481.