Neonatal Prophylaxis: Current Recommendations and Trends

ELIZABETH E. GALLARDO, M.D., FPPS, FPIDSP
Professor and Chair
Department of Pediatrics
Saint Louis University , Baguio City

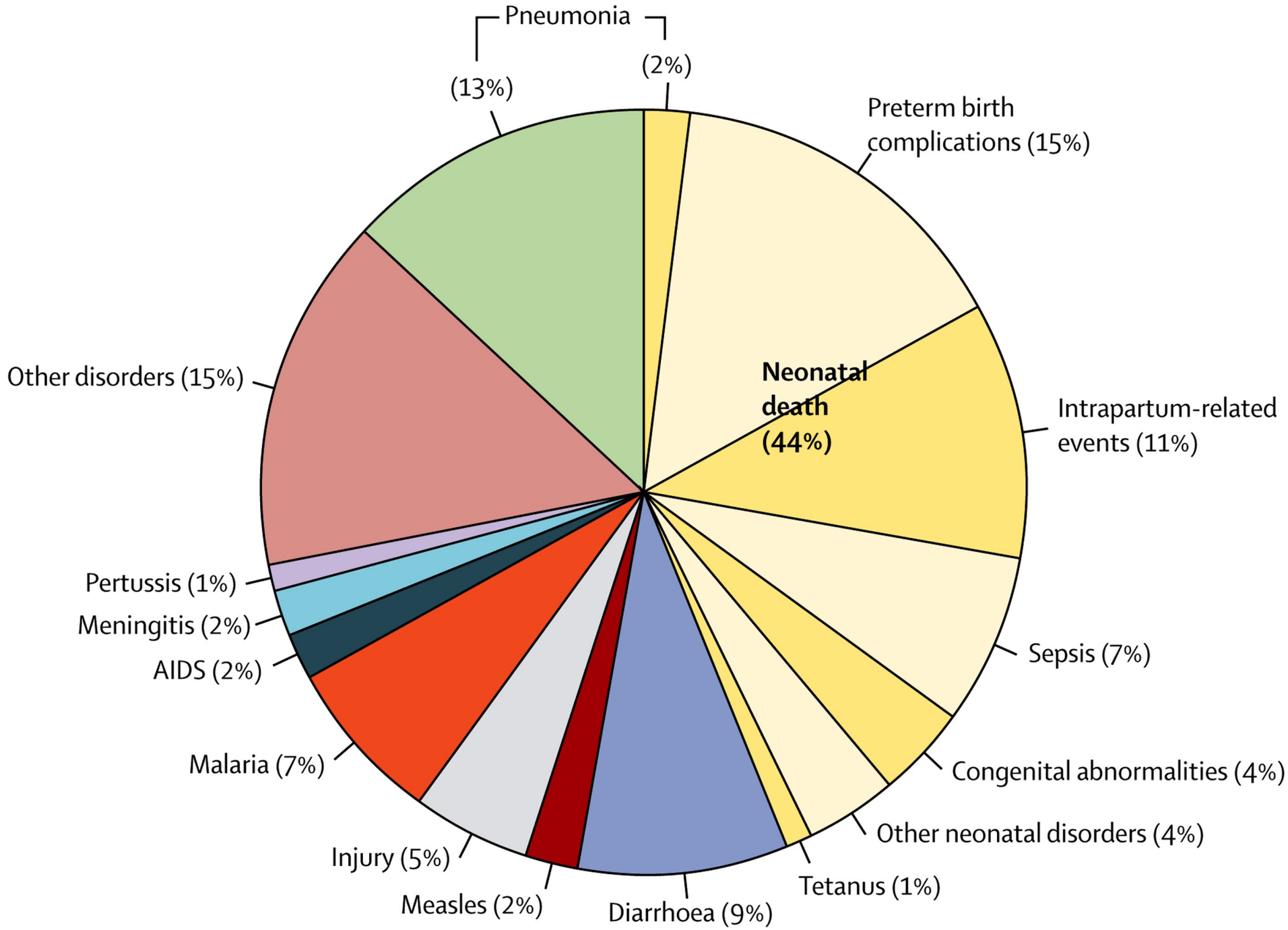
OBJECTIVES

- To discuss current recommendations on the prevention of common infectious diseases in the neonate
- To review relevant researches on prophylaxis for neonatal infections and identify potential areas for research

OUTLINE

- Introduction
- Current Recommendations on Post-exposure Prophylaxis for Hepatitis B and Varicella in neonates
- Possible interventions to prevent neonatal infections
- Summary

Global causes of under-five child deaths 2013



The Lancet
Volume 385, Issue 9966, Pages 430-440 (January 2015)
DOI: 10.1016/S0140-6736(14)61698-6

Risk factors for Neonatal Infections

1. **Host factors**

   - Prematurity, anatomic abnormalities

2. **Environmental risk factors**

   - Maternal risk factors - PROM, maternal intrapartum fever, maternal UTI

   - Admission in NICU

3. **Virulence of the organism**

   - Maternal colonization with pathogens such as GBS, HSV, etc.

Case 1

You are called to attend to the delivery of a 26 year old G2P1 mother who is **HepBsAg (+)**.

The baby is born term at 38 weeks AOG, with a birth weight of 2.9 kg and an APGAR score of 8 and 9.

How can perinatal Hepatitis B virus infection be prevented?

Hepatitis B Immunoprophylaxis Scheme for Infants based on Maternal HBsAg Status

Maternal Status	Infants > 2000 g	Infants < 2000 g
HBsAg (+)	**Hep B vaccine + HBIG**, (w/in 12 hrs of birth) * HBIG not later than 7 days of age	
HBsAg unknown	**Hep B vaccine**, (w/in 12 hrs of birth) *determine maternal HBsAg status ASAP *If (+), give HBIG ASAP, not later than 7 days of age	**Hep B vaccine + HBIG**, w/in 12 hrs of birth *Immunize with 4 vaccine doses
HBsAg (-)	Hep B vaccine at birth or before hospital discharge	**Delay Hep B vaccine dose 1 until 30 days of chronologic age** or at hospital discharge if discharge occurs before 30 days of age Counted as part of 3-dose primary series

CDC Epidemiology and Prevention of Vaccine-Preventable Diseases. The Pink Book. 13th edition (2015)

Immunoprophylaxis for Infants of HBsAg (+) Mothers

- Risk of perinatal transmission without immunoprophylaxis as high as 90%

- Infants should receive monovalent Hep B vaccine and HBIG 0.5 ml as soon after delivery as possible (preferably within 12 hours), **regardless of birthweight**

- Breastfeeding poses no additional risk of Hep B acquisition in an infant with appropriate administration of Hep B vaccine and HBIG

Nelson NP, Jamieson DJ, Murphy TV. **Prevention of Perinatal Hepatitis B Virus Transmission.** J Pediatric Infect Dis Soc 2014; 3 Suppl 1:S7.

Infants of HBsAg (+) Mothers

- The schedule for subsequent doses depends upon the **infant's birth weight**:

  - **Birth weight ≥ 2 kg**- The second and third doses should be given at 1-2 and at 6 months of age, respectively

  - **Birth weight < 2 kg** - Three additional doses should be given (1, 2-3, and 6 months of age OR at 2, 4, and 6 months of age)

    ** The final dose in the vaccine series should not be administered before 24 weeks (6 months) of age.

CDC Epidemiology and Prevention of Vaccine-Preventable Diseases. The Pink Book. 13th edition (2015)

Hepatitis B vaccine response of infants born to HepBsAg(+) mothers

- 95% of uninfected infants born to HBsAg-positive mothers in the United States responded to primary Hep B vaccine series

- **Vaccine non-responder**: infant with anti-HBs < 10 mIU/ml at Post-vaccination Serologic Testing (PVST) after receiving ≥ 3 vaccine doses

Hepatitis B vaccine response among infants born to hepatitis B surface antigen-positive women.
Ko SC, Schillie SF, Walker T, Veselsky SL, Nelson NP, Lazaroff J, Crowley S, Dusek C, Loggins K, Onye K, Fenlon N, Murphy TV
Vaccine. 2014 Apr;32(18):2127-33. Epub 2014 Feb 22.

Factors associated with Hepatitis B vaccine non-response

- Gestational age < 37 weeks
- Vaccine birth dose > 12 hours after birth
- Timing of final dose < 6 months after birth
- Receipt of 3 vs 4 vaccine doses
- PVST interval > 6 months from final vaccine dose

Hepatitis B vaccine response among infants born to hepatitis B surface antigen-positive women.
Ko SC, Schillie SF, Walker T, Veselsky SL, Nelson NP, Lazaroff J, Crowley S, Dusek C, Loggins K, Onye K, Fenlon N, Murphy TV
Vaccine. 2014 Apr;32(18):2127-33. Epub 2014 Feb 22.

Factors associated with Hepatitis B vaccine non-response

- PVST interval **> 6 months from final vaccine dose** (OR=2.7, CI=2.0, 3.6) was significantly associated with anti-HBs<10mIU/mL

- The proportion of non-responders increased from 2% at 1-2 months to 21.6% at 15-16 months after the final dose.

- Receipt of a 4th dose improved the response rate (OR=0.5, CI=0.3, 0.8).

Hepatitis B vaccine response among infants born to hepatitis B surface antigen-positive women.
Ko SC, Schillie SF, Walker T, Veselsky SL, Nelson NP, Lazaroff J, Crowley S, Dusek C, Loggins K, Onye K, Fenlon N, Murphy TV
Vaccine. 2014 Apr;32(18):2127-33. Epub 2014 Feb 22.

Factors associated with Hepatitis B vaccine non-response

- CONCLUSIONS: The proportion of infants with anti-HBs<10mIU/mL increased with **longer interval** between the final vaccine dose and PVST.

- Optimal timing of PVST is **within 1-2 months of final vaccine dose** to avoid unnecessary revaccination.

Hepatitis B vaccine response among infants born to hepatitis B surface antigen-positive women.
Ko SC, Schillie SF, Walker T, Veselsky SL, Nelson NP, Lazaroff J, Crowley S, Dusek C, Loggins K, Onye K, Fenlon N, Murphy TV
Vaccine. 2014 Apr;32(18):2127-33. Epub 2014 Feb 22.

Post-vaccination Serologic Testing (PVST) of Infants of HBsAg (+) Mothers

- Testing for **HBsAg** and **anti-HBs** should be done after completion of at least 3 doses of the vaccine at age **9-12 months** (or 1-2 months after the final dose of the vaccine series, if the series is delayed)

- Infants with HBsAg (-) with anti-HBs concentrations < 10 mIU/ml require **revaccination** with a second 3- dose vaccine series followed by PVST for anti-HBs 1 to 2 months after the final vaccine dose

CDC MMWR October 9, 2015/ 64(39); 1118-20
Robinson CL. Advisory Committee on Immunization Practices Recommended Immunization Schedules for Persons Aged 0 Through 18 Years — United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:86–87.

Protective efficacy of immunoprophylaxis to infants born to HBsAg (+) Mothers

- **Hepatitis B vaccination + HBIG within 24 hours after birth, followed by completion of the vaccine series:** 85-95% effective in preventing both acute and chronic HBV infection

- **Hepatitis B vaccine administered alone beginning within 24 hours after birth:** 70-95% effective in preventing perinatal HBV infection

CDC Epidemiology and Prevention of Vaccine-Preventable Diseases. The Pink Book. 13th edition (2015)

Protective efficacy of immunoprophylaxis to infants born to HBsAg (+) Mothers

- Compared with placebo/no intervention, the combination of **HepB vaccine and HBIG reduced HBV infection** in infants born to HBsAg-positive women (RR 0.08, 95% CI 0.03-0.17, 3 trials)

- Combination of **HepB vaccine and HBIG** was **superior to HepB vaccine alone** in reducing perinatal HBV infection (RR 0.54, 95% CI, 0.41-0.73, 10 trials).

Hepatitis B immunisation for newborn infants of hepatitis B surface antigen-positive mothers.
Lee C, Gong Y, Brok J, Boxall EH, Gluud C
Cochrane Database Syst Rev. 2006;

Case 2

RG is a full-term baby boy born to a G3P3 mother by normal spontaneous delivery.

At the time of birth, mother was noted to hav generalised vesiculo-pustular lesions which apparently started 3 days before delivery.

Her 7 year-old child was diagnosed to hav chickenpox about 2 weeks ago.

How can varicella infection be prevented in this newborn?

Neonatal Varicella

- Acquired following vertical transmission from the mother during pregnancy or delivery, or acquired after birth from the environment or infected healthcare providers

- Varicella can develop between **2 and 16 days** after birth in infants born to mothers with active varicella around the time of delivery

- Usual interval from onset of rash in a mother to onset in her neonate is **9 to 15 days**

American Academy of Pediatrics. Varicella-zoster virus infections. In: Red Book: 2015 Report of the Committee on Infectious Diseases, 30th ed, Kimberlin DW, Brady MT, Jackson MA, Long SS (Eds), American Academy of Pediatrics,Elk Grove Village, IL 2015.

Neonatal Varicella

- **Premature infants** are at increased risk for nosocomial acquisition of VZV compared with term infants because active transfer of maternal IgG antibodies occurs primarily during the **third trimester of pregnancy**

Saji F, Samejima Y et al. **Dynamics of immunoglobulins at the feto-maternal interface**. Rev Reprod 1999; 4:81

Management of Varicella Exposure

- Specific intervention depends upon:
    - timing of exposure
    - the mother's serologic status
    - gestational age
- Varicella vaccination to prevent infection has not been tested in newborns

Timing of Exposure

- Risk of infection and case fatality rate significantly increases when symptoms of maternal infection occur **less than 5 days prior to delivery to 2 days after delivery**

- Infants born to mothers with onset of maternal varicella **5 days or more prior to delivery** usually have a benign course, presumably due to passive transfer of maternal antibody across the placenta.

CDC Epidemiology and Prevention of Vaccine-Preventable Diseases. The Pink Book. 13th edition (2015)

Post-exposure Prophylaxis (PEP) against VZV Infection

- Varicella-zoster immune globulin (VariZIG) 125 units (1 vial) IM given ASAP **within 96 hours (4 days)** and **no later than 10 days after exposure**

CDC. FDA approval of an extended period for administering VariZIG for post exposure prophylaxis of varicella. . MMWR 2012; 61:212

- PEP has been shown to prevent varicella in exposed neonates, ameliorate the course, or delay the disease in patients in whom the infection was not fully prevented

Tebruegge M, Pantazidou A, Curtis N. Towards evidence based medicine for paediatricians. How effective is varicella-zoster immunoglobulin (VZIG) in preventing chickenpox in neonates following perinatal exposure? Arch Dis Child 2009; 94:559.

Current ACIP and CDC Recommendations for VariZIG

- Neonates whose mothers have signs and symptoms of varicella around the time of delivery **(within five days before to two days after)**
- Hospitalized **premature infants born at ≥ 28 weeks of gestation or more** whose mothers lack evidence of immunity against varicella

American Academy of Pediatrics. Varicella-zoster virus infections. In: Red Book: 2015 Report of the Committee on Infectious Diseases, 30th ed, Kimberlin DW, Brady MT, Jackson MA, Long SS (Eds), American Academy of Pediatrics,Elk Grove Village, IL 2015, p 846

CDC. MMWR. Updated recommendations for use of VariZIG- United States, 2013

Current ACIP and CDC Recommendations for VariZIG

- Hospitalized premature infants born at **< 28 weeks of gestation or who weigh < 1000 grams at birth** regardless of maternal history of varicella or vaccination

- * Exposed infants within the first two weeks of life whose mothers do not have evidence of immunity to VZV

American Academy of Pediatrics. Varicella-zoster virus infections. In: Red Book: 2015 Report of the Committee on Infectious Diseases, 30th ed, Kimberlin DW, Brady MT, Jackson MA, Long SS (Eds), American Academy of Pediatrics,Elk Grove Village, IL 2015, p 846

CDC. MMWR. Updated recommendations for use of VariZIG- United States, 2013

Unavailability of Varicella-zoster Immune Globulin

- Consider **Intravenous immunoglobulin (IVIG)**
- Recommended dose for PEP of varicella: **400 mg/kg**, intravenously administered once
- No clinical data available demonstrating effectiveness of IVIG for PEP of varicella

American Academy of Pediatrics. Varicella-zoster virus infections. In: Red Book: 2015 Report of the Committee on Infectious Diseases, 30th ed, Kimberlin DW, Brady MT, Jackson MA, Long SS (Eds), American Academy of Pediatrics,Elk Grove Village, IL 2015, p 846

Isolation
for Mother and Infant

- Depends upon whether there is active disease or the timing of exposure

- Mothers with active disease must be isolated. Treat infant with VariZIG if onset of maternal varicella is within 5 days before or 2 days after delivery.

- Isolate any infant who develops varicella.

American Academy of Pediatrics. Varicella-zoster virus infections. In: Red Book: 2015 Report of the Committee on Infectious Diseases, 30th ed, Kimberlin DW, Brady MT, Jackson MA, Long SS (Eds), American Academy of Pediatrics,Elk Grove Village, IL 2015, p 846

Isolation
for Mother and Infant

- Mothers who are seronegative with a history of exposure **6 to 21 days before admission** must be isolated from other patients and the nursery.

- Her infant, if born at term, should be isolated with the mother and both should be discharged ASAP

American Academy of Pediatrics. Varicella-zoster virus infections. In: Red Book: 2015 Report of the Committee on Infectious Diseases, 30th ed, Kimberlin DW, Brady MT, Jackson MA, Long SS (Eds), American Academy of Pediatrics,Elk Grove Village, IL 2015, p 846

Isolation
for Mother and Infant

- All infants exposed to VZV who remain in the hospital should be **cohorted** and placed in protective isolation **from 7 to 21 days after exposure (up to 28 days if given VariZIG)**

- Breastfeeding is encouraged in newborns exposed to or infected with varicella because antibody in breast milk may be protective.

American Academy of Pediatrics. Varicella-zoster virus infections. In: Red Book: 2015 Report of the Committee on Infectious Diseases, 30th ed, Kimberlin DW, Brady MT, Jackson MA, Long SS (Eds), American Academy of Pediatrics,Elk Grove Village, IL 2015, p 846

Case 3

A 32 week, 1.5 kg baby was born to a primigravid mother by vaginal delivery. The mother had preterm premature rupture of membranes of 12 hours duration. Amniotic fluid was clear. APGAR score was 8 and 9 at 1 and 5 mins. of life.

What interventions can be done to prevent neonatal infections in this baby?

Prevention of Neonatal Infections

INTERVENTIONS	EXAMPLES
Feeding-related interventions	Breast milk, Early enteral feeding, Probiotics, Prebiotics
Infection control measures	Hand hygiene, gowning, clusters of infection control interventions (e.g. sepsis bundles)
Physical interventions	Umbilical cord care, Skin barrier therapy, Kangaroo care, Delayed cord clamping
Immunomodulatory agents	Polyclonal IVIG, anti-staphylococcal immunoglobulins, G-CSF or GM-CSF, Lactoferrin

Isaacs, D. Evidence-based Neonatal Infections. 1st ed. BMJ Publishing Book Ltd. 2014, pp 468-84.

Prevention of Neonatal Infections

INTERVENTIONS	EXAMPLES
Immunization	**Maternal** immunization (Influenza vaccine, pertussis vaccine, pneumococcal vaccine, tetanus vaccine) **Neonatal** immunization (BCG vaccine, Polio vaccine, Hepatitis B vaccine, PCV, Pertussis vaccine)
Prophylactic antibiotics	Central venous catheters, Umbilical venous catheters, Umbilical arterial catheters, Mechanical ventilation, Neutropenia
Maternal antibiotics for preterm rupture of membranes	

Isaacs, D. Evidence-based Neonatal Infections. 1st ed. BMJ Publishing Book Ltd. 2014, pp 468-84.

Probiotics to prevent late-onset sepsis in preterm infants

PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Probiotic Supplementation and Late-Onset Sepsis in Preterm Infants: A Meta-analysis

Shripada C. Rao, Gayatri K. Athalye-Jape, Girish C. Deshpande, Karen N Simmer and Sanjay K. Patole

Pediatrics 2016;137;; originally published online February 12, 2016;
DOI: 10.1542/peds.2015-3684

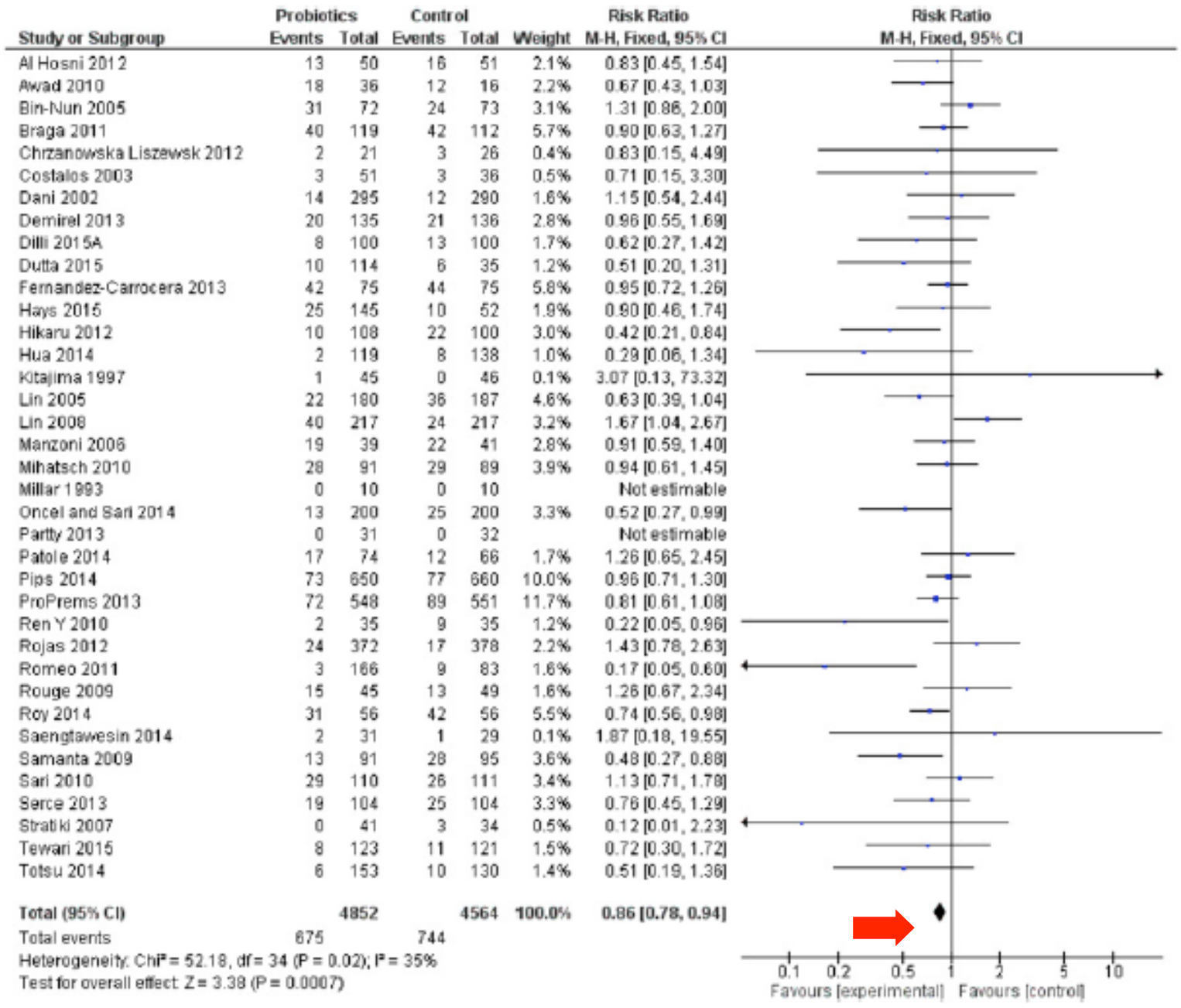
Probiotics to prevent late-onset sepsis(LOS) in preterm infants

- Pooled meta-analysis of 37 RCTs (n = 9416) that compared “probiotics” with “placebo” or “no probiotics” in decreasing the risk of LOS in preterm infants < 37 weeks or < 2500 g

- Largest meta-analysis of probiotic supplementation in preterm neonates

PEDIATRICS Volume 137 , number 3 , March 2016

Forest plot: Probiotic supplementation to reduce LOS in preterm infants. M-H, Mantel–Haenszel



Outcome: probiotic supplementation resulted in a statistically significant **reduction in the incidence of LOS** [13.9%] vs [16.3%] RR 0.86; 95% CI, 0.78–0.94; P_{36}= .0007

PEDIATRICS Volume 137 , number 3 , March 2016

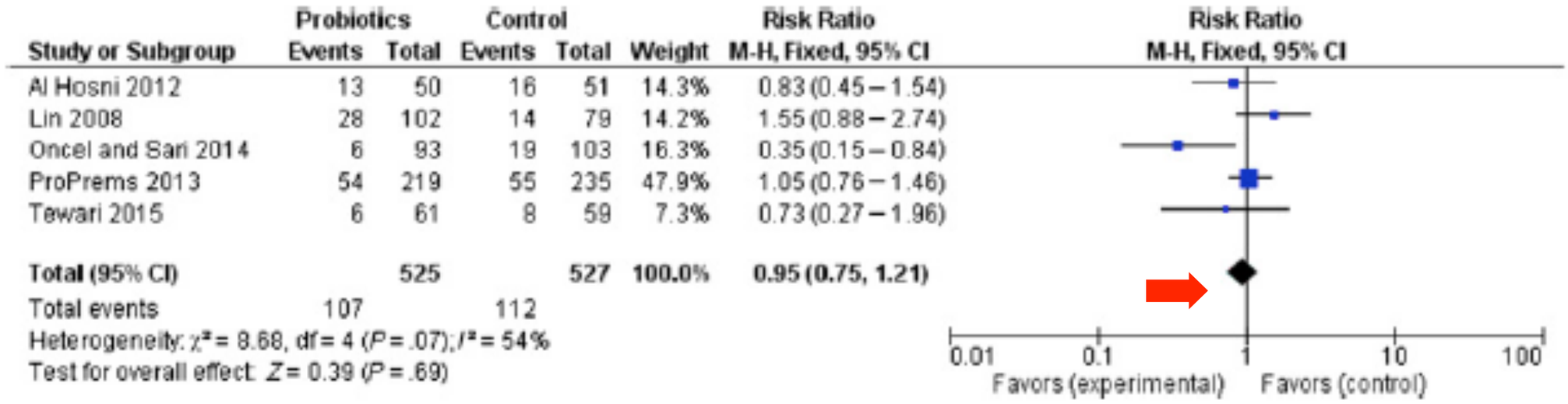


FIGURE 4

Probiotic supplementation in infants born at <28 weeks or <1000 g. M-H, Mantel–Haenszel.

Subgroup analysis of **infants born at <28 weeks' gestation or <1000 g** revealed **no significant benefits** of probiotic supplementation in reducing LOS

PEDIATRICS Volume 137 , number 3 , March 2016

Table 1. Characteristics of included trials

Study	Neonates on probiotics, n	Controls, n	Birth weight or gestational age	Probiotic agent	Primary outcome	NOS score
Bonsante [15], 2013 France	347	783	>24 and <31 weeks	*L. casei* rhamnosus	NEC; sepsis; mortality	7
Dang [16], 2015 USA	128	135	<1,250 g and/ or <28 weeks	*L. rhamnosus* GG/ *B. infantis*	NEC; mortality	7
Härtel [17], 2014 Germany	2,566	1,043	>22+6 and <32 weeks or <1,500 g	*L. acidophilus/B. infantis*	NEC; sepsis; mortality	8
Hoyos [18][a], 1999 Colombia	102	103	<1,500 g	*L. acidophilus/B. infantis*	NEC; mortality	8
Hunter [19], 2012 USA	79	232	<1,500 g	*L. reuteri*	NEC; sepsis	7
Janvier [20], 2014 Canada	294	317	<32 weeks	Mixture of *Bifidobacterium* and *Lactobacillus*[b]	NEC; sepsis; mortality	7
Lambæk [21], submitted, Denmark	333	381	<30 weeks	*Bifidobacterium/L. rhamnosus*	NEC; mortality	7
Li [22], 2013 California	291	289	<1,500 g	Mixture of *Streptococcus* and *Bifidobacterium*[c]	NEC; mortality	7
Luoto [23], 2010 Finland	418	1,900	<30 weeks or <1,500 g	*Lactobacillus* GG	NEC	8
Repa [24], 2014 Austria	230	233	<34 weeks	*L. acidophilus/B. infantis*	NEC; sepsis; mortality	6
Yamashiro [25], 2010 Japan	338	226	<1,500 g	*B. breve*	NEC; sepsis; mortality	6
Zampieri [26], 2013 Japan	18	14	<1,500 g	*L. paracasei* subsp. Paracasei F19	NEC	3

[a] Data for <1,500 g obtained by contacting the authors. [b] Mixture of *Bifidobacterium (breve, bifidum, infantis* and *longum)* and *L. rhamnosus*. [c] Mixture of *S. thermophilus, B. infantis* and *B. bifidum*.

Deshpande *et al. BMC Medicine* 2011, **9**:92
http://www.biomedcentral.com/1741-7015/9/92

BMC Medicine

CORRESPONDENCE Open Access

Evidence-based guidelines for use of probiotics in preterm neonates

Girish C Deshpande[1,2], Shripada C Rao[3,4,5], Anthony D Keil[3,6] and Sanjay K Patole[3,5*]

SPECIFIC RECOMMENDATIONS		LEVEL OF EVIDENCE
Selection of strains	Combination containing *Lactobacillus* and at least one *Bifidobacterium* species is preferable *Lactobacillus GG* alone may not be effective	I, II III
Dose	3 x 10 organisms per day, preferably in a single dose	I, II

Deshpande et al. BMC Medicine 2011, 9:92
http://www.biomedcentral.com/1741-7015/9/92

BMC Medicine

CORRESPONDENCE Open Access

Evidence-based guidelines for use of probiotics in preterm neonates

Girish C Deshpande[1,2], Shripada C Rao[3,4,5], Anthony D Keil[3,6] and Sanjay K Patole[3,5*]

SPECIFIC RECOMMENDATIONS		LEVEL OF EVIDENCE
When to start?	When the neonate is ready for enteral feeds, preferably within the first 7 days of life	I, II, III
How long to continue?	At least until 35 weeks corrected age, or discharge	II
Supplementation during acute illness	Stopping the supplementation during an acute illness such as sepsis, NEC, or perinatal asphyxia may be safe	IV

Research Gaps

- Further studies are needed to address the optimal probiotic organism, dosing, timing, and duration of supplementation
- High-quality and adequately powered RCTs regarding the efficacy and safety of the use of probiotics in extremely low birth weight infants are still warranted

Probiotics for Preventing Late-Onset Sepsis in Preterm Neonates: A PRISMA-Compliant Systematic Review and Meta-Analysis of Randomized Controlled Trials. Zhang GQ[1], Hu HJ, Liu CY, Shakya S, Li ZY. Medicine (Baltimore). 2016 Feb;95(8):e2581. doi: 10.1097/MD.0000000000002581.

Immunomodulatory Interventions

- Nosocomial infections are significant causes of morbidity and mortality among preterm and/or low birth weight (LBW) infants.

- Preterm infants are deficient in immunoglobulin G (IgG) → administration of intravenous immunoglobulin (IVIG) may have the potential of preventing or altering the course of nosocomial infections.

Intravenous immunoglobulin for preventing infection in preterm (<37 weeks) and/or low birthweight infants (<2500 g BW)

INTERVENTION	LEVEL OF EVIDENCE	NO. OF INFANTS	OUTCOMES	AUTHOR'S CONCLUSIONS
IVIG (polyclonal)	Cochrane systematic review of RCTs in pre-term infants (19 studies)	4986	3% reduction in sepsis and 4% reduction in one or more episodes, of any serious infection No effect on mortality Cost-effectiveness unknown	Not recommended Unlikely to be cost-effective No further similar RCTs needed

C

Intravenous immunoglobulin for preventing infection in preterm and/or low birth weight infants.
Ohlsson A1, Lacy JB.

G-CSF and GM-CSF for preventing systemic infections in high-risk neonates

INTERVENTION	LEVEL OF EVIDENCE	NO. OF INFANTS	OUTCOMES	AUTHOR'S CONCLUSIONS
G-CSF or GM-CSF	Cochrane systematic review of 3 prophylactic RCTs	359	No difference in mortality or sepsis	Not recommended More RCTs needed
GM-CSF	Multicenter RCT	280	No significant difference in sepsis-free survival	Not recommended

Cochrane Database Syst Rev. 2003;(3):CD003066.
G-CSF and GM-CSF for treating or preventing neonatal infections.
Carr R1, Modi N, Doré C.

Carr R, Brockelhurst P et al. **GM-CSF administered as prophylaxis for reduction of sepsis in extremely preterm, SGA neonates (the PROGRAMS trial): a single-blind, multi centre, randomised controlled trial.** Lancet 2009; 373:226-233.

Prophylactic Use of Antibiotics

- **Prophylactic** antibiotic use

    - giving antibiotics to an **uninfected baby with risk factors for infection** in order to prevent the baby from developing an infection

- **Empiric** antibiotic use

    - giving antibiotics to babies who **may already be infected** due to the presence of one or more **maternal risk factors**, e.g. PROM, maternal fever or UTI

Isaacs, D. Evidence-based Neonatal Infections. 1st ed. BMJ Publishing Book Ltd. 2014, pp 468-84.

Prophylactic antibiotics in neonates with umbilical artery catheters

RISK FACTOR	LEVEL OF EVIDENCE	OUTCOME	AUTHOR'S CONCLUSIONS
Umbilical artery catheter	Cochrane systematic review (2 quasi-randomized trials)	No significant differences in morbidity and mortality	Insufficient evidence to support or refute the routine use of prophylactic antibiotics

Cochrane Database Syst Rev. 2007 Oct 17;(4):CD004697.
Prophylactic antibiotics to reduce morbidity and mortality in neonates with umbilical artery catheters.
Inglis GD1, Jardine LA, Davies MW.

Prophylactic antibiotics in neonates with umbilical venous catheters

RISK FACTOR	LEVEL OF EVIDENCE	OUTCOME	AUTHOR'S CONCLUSIONS
Umbilical venous catheter	Cochrane systematic review (1 study of poor quality)	No effect of a short 3 day course of Penicillin and gentamicin on preventing catheter-related blood stream infection	Insufficient evidence to support or refute the use of prophylactic antibiotics

Cochrane Database Syst Rev. 2005 Oct 19;(4):CD005251.
Prophylactic antibiotics to reduce morbidity and mortality in neonates with umbilical venous catheters.
Inglis GD1, Davies MW.

Prophylactic antibiotics in neonates with central venous catheters

RISK FACTOR	LEVEL OF EVIDENCE	OUTCOME	AUTHOR'S CONCLUSIONS
Central venous catheter	Cochrane systematic review (3 RCTs: Vancomycin, Amoxicillin)	Decreased rate of proven or suspected sepsis but no effect on over-all mortality	Routine use is not recommended No data on selection of resistant organisms

Cochrane Database Syst Rev. 2008 Jan 23;(1):CD006179. doi: 10.1002/14651858.CD006179.pub2.
Prophylactic systemic antibiotics to reduce morbidity and mortality in neonates with central venous catheters.
Jardine LA1, Inglis GD, Davies MW.

Prophylactic antibiotics in intubated, ventilated newborn infants not known to have an infection

RISK FACTOR	LEVEL OF EVIDENCE	OUTCOME	AUTHOR'S CONCLUSIONS
Mechanical ventilation	Cochrane systematic review (1 trial of fair quality)	No effect on mortality and morbidity Rates of septicaemia not reported	Insufficient evidence to support or refute the use of prophylactic antibiotics when starting mechanical ventilation in NB infants

Cochrane Database Syst Rev. 2007 Jul 18;(3):CD004338.
Prophylactic antibiotics to reduce morbidity and mortality in ventilated newborn infants.
Inglis GD1, Jardine LA, Davies MW.

Prophylactic Antibiotics

- Current available data do not support nor refute the use of prophylactic antibiotics to reduce morbidity and mortality in neonates with umbilical arterial catheters, umbilical venous catheters, central venous catheters or on mechanical ventilation

- Potential harmful effects include selection of resistant organisms, development of fungal infections, increased mortality and added cost of antibiotics

Should **asymptomatic term** newborn infants born to **mothers with one or more risk factors** for early-onset bacterial infection receive **prophylactic** vs **selective** antibiotics once clinical or microbiological evidence of sepsis emerges?

- Insufficient data from randomised controlled trials to guide clinical practice

- Large, well-designed RCTs are needed in asymptomatic term infants born to mothers with risk factors for infection in their babies to compare prophylactic vs selective antibiotics on morbidity, mortality and costs

Cochrane Neonatal Group.DOI: 10.1002/14651858.CD003957.pub2. **Prophylactic versus selective antibiotics for term newborn infants of mothers with risk factors for neonatal infection**.
Regina LS Ungerer, Ornella Lincetto,, William McGuire, et al. 18 October 2004

Maternal Antibiotics for pre-term rupture of membranes (PROM)

- Prophylactic maternal antibiotics for PROM were associated with statistically significant **reductions in chorioamnionitis** (average RR 0.66%, 95% CI 0.46-0.96) and in **neonatal infections** (RR 0.67%, 95% CI 0.52-0.85) vs no antibiotics or placebo

- No significant reduction in perinatal mortality nor long-term benefit in childhood

Cochrane Database Syst Rev. 2013 Dec 2;(12):CD001058. doi: 10.1002/14651858.CD001058.pub3.
Antibiotics for preterm rupture of membranes.
Kenyon S1, Boulvain M, Neilson JP.

Newborn chemoprophylaxis for Group B Streptococcal Disease

- Efficacy of newborn chemoprophylaxis is **controversial**

    - Observational studies: Administration of intramuscular penicillin to newborns immediately after delivery **may reduce** early-onset GBS disease

    - Nonblinded randomised trial: **No benefit** in outcome of GBS disease or neonatal mortality

Cochrane Neonatal Group DOI: 10.1002/14651858.CD003667.pub2. 19 April 2004.
Penicillin for the prevention of early onset group B streptococcal infection in newborn infants
Paul G Woodgate,Vicki Flenady,Peter A Steer

Prevention of perinatal Group B Streptococcal Disease

- The primary intervention to prevent neonatal sepsis is the use of **intrapartum antibiotic prophylaxis (IAP) in mothers** with group B streptococcal (GBS) colonization and other risk factors

- Good quality trials are needed to prove efficacy of preventive strategies targeting newborns rather than maternal colonization

CDC. Prevention of perinatal group B streptococcal disease. MMWR Recommendations and Reports 2010; (59RR-10):1-32

Neonatal group B streptococcal disease: Prevention. Carol J Baker. https://www.uptodate.com. December 12, 2016

SUMMARY

- Neonatal infections are important causes of morbidity and mortality globally
- Timely and appropriate post-exposure prophylaxis can protect neonates exposed to maternal infections like Hepatitis B and Varicella
- Prevention of neonatal infections can be achieved through multiple interventions/ preventive strategies
- More research is needed to identify effective, safe and low-cost health measures to prevent neonatal infections

Thank You