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# Beating the bugs: what works and what does not against nosocomial infections?

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# Nosocomial Infections in Neonates

- Sepsis claims > 1 million neonatal deaths/year worldwide
- Nosocomial sepsis 100 times more common than EO sepsis
- 7-24 % of NICU patients
  - Blood stream infections 55%
  - Pneumonia 30%
- Incidence varies inversely with gestational age
- Huge burden of mortality, morbidity and cost

# Common Organisms

## Developed world

- Gram +ve – 70%, mainly CONS
- Gram –VE – 18%
- Fungi – 15%
- Staph Aureus
- Enterococci
- Viruses –RSV and Rotavirus
- Fungal

## Developing world

- Klebsiella
- Staph Aureus
- Acenatobacter
- E coli
- Fungal
- Enterococci
- Gram +ve

# Hand Hygiene

- Simplest Most effective method for reducing nosocomial infections
- High compliance lowers rate of blood stream infection
- Antiseptic Hand wash vs Alcohol hand rub *(Larson et al 2005)*

  No significant differences
  - Any Neonatal infections *(OR 0.98 95% CI 0.77-1.25)*
  - Mean microbial counts on nurses' hands (*3.21 and 3.11 log10 CFU for handwashing and alcohol, respectively; P=.38)*

*Larson et al . Effect of antiseptic handwashing vs alcohol sanitizer on health care-associated infections in neonatal intensive care units. Arch Pediatr Adolesc Med. 2005 Apr;159(4):377-83.*

# Hand Hygiene

- AAP Perinatal Care Guidelines 6th ed (2007) recommends
  - When hands are visibly contaminated, they should first be washed

Antiseptic Hand Wash and Alcohol Hand Rub equally effective

# Gowning by Staff and visitors

- No significant effects on *(Cochrane review 2013)*
  - Incidence of systemic nosocomial infection
  - Colonization
  - Length of hospital stay
- Not required routinely in NICU's
- Wear doing procedures or handling neonate for isolation

*Webster J, Pritchard MA. Gowning by attendants and visitors in newborn nurseries for prevention of neonatal morbidity and mortality. Cochrane Database of Systematic Reviews 2013*

THE COCHRANE COLLABORATION®

# Central Venous Catheter Related Infections

- CRBSI - Most common nosocomial infection
- Usually because of
  - Breach of asepsis during insertion
  - Poor insertion technique
  - Lack of Ongoing care of catheter
  - Hub manipulation and contamination
- After 2 weeks odds of infection ↑ *(Advani et al 2011)*
  - Extraluminal – Ist week
  - Intraluminal and hub colonization - > Ist week

# Risk factors for CVC-associated bloodstream infections in NICU

- ELBW *(OR = 5.13, CI = 2.1 to 12.5)*
- Catheter hub colonization *(OR = 44.1, 95% CI = 14.5 -134.4)*
- Exit site colonization *(OR = 14.4, CI = 4.8-42.6)*
- Duration of parenteral nutrition *(OR=1.04, CI=1.0-1.08)*
- Catheter insertion after Ist week of life *(OR = 2.7, CI = 1.1-6.7)*

*Mahieu et al* ***Risk factors for central vascular catheter-associated bloodstream infections among patients in a neonatal intensive care unit.*** *J Hosp Infect. 2001 Jun;48(2):108-16.*

# CVC Protocol

- Maximal sterile barrier precautions during insertion (cap, mask, glove, gown) reduce infection *(Raad et al 1995)*
- Asepsis by Chlorhexidine vs Povidone –Iodine
  - Equally efficacious *(Garland et al 1995)*
  - Chlorhexidine impregnated dressing *(Garland et al 2001)*
- In line filters *(Jack et al 2012)*
  - No impact on sepsis

# Antimicrobial-impregnated CVC for prevention of CRBI - Cochrane review 2015

- 1 small trial(N=98)

Needs more data before Routine use

*benefit 6)*

*Balain M, Oddie SJ, McGuire W. Antimicrobial-impregnated central venous catheters for prevention of catheter-related bloodstream infection in newborn infants. Cochrane Database of Systematic Reviews 2015*

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# Proactive Management of CVC

- Dedicated task force for CVC management – 2/3rd reduction in CRBSI *(Costa et al 2007)*

Dedicated CVC management team reduces CRBSI

- 43% lower risk of CRBSI in patients who had a central line in place for more than 30 days *(Taylor et al 2011)*

# Antibiotic lock for prevention of catheter related infection - Cochrane Review 2015

- 3 trials (271 infants)
- ↓ confirmed CRI's *(RR 0.15, 95% CI 0.06 - 0.40)*

Appears to be effective but concern of antibiotic resistance
Needs more data before routine recommendations

- ↓ combined confirmed and suspect infection rates *(RR 0.25, 95% CI 0.12 0.49)*
- ARR was 20.5% and the NNTB was 5
- However, No difference for mortality due to sepsis

*Taylor JE, Tan K, Lai NM, McDonald SJ. Antibiotic lock for the prevention of catheter-related infection in neonates. Cochrane Database of Systematic Reviews 2015*

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# Antibiotics Use and Misuse

- Use is universal and Misuse is very common
- Alteration of neonatal microflora
- Development of antibiotics resistance
- Use of 3 rd Gen cephalosporin as empirical therapy increase drug resistance
- Increase fungal infections

# Prophylactic Antibiotics

- Central Catheters - ↓ rate of proven bacterial sepsis but no

DON'T Use Prophylactic Antibiotics

- UAC - Insufficient evidence *(Cochrane Review 2010)*
- ICD - Insufficient evidence *(Cochrane Review 2010)*
- Ventilation - Insufficient evidence *(Cochrane Review 2010)*
- Proph Vancomycin - Not recommended *(Cochrane Review 201*

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*J Pediatr*. 2011 November ; 159(5): 720–725. doi:10.1016/j.jpeds.2011.05.033.

# Prolonged Initial Empirical Antibiotic Treatment is Associated with Adverse Outcomes in Premature Infants

**Venkata S Kuppala, MD**[1], **Jareen Meinzen-Derr, PhD**[1,2,3], **Ardythe L. Morrow, PhD**[1,2,3], and **Kurt R. Schibler, MD**[1,3]

**Results**—Of the 365 premature infants surviving 7 days free of sepsis or NEC, 36% received prolonged initial empirical antibiotics, which was independently associated with subsequent outcomes: LOS (odds ratio [OR] 2.45, 95% confidence interval [CI] 1.28–4.67) and the combination of LOS, NEC, or death (OR 2.66, 95% CI 1.12–6.3).

**Conclusions**—Prolonged administration of empirical antibiotics to premature infants with sterile cultures in the first week of life is associated with subsequent severe outcomes. Judicious

# Probiotics for prevention of NEC in preterm infants - Cochrane Review 2014

- Significantly ↓ severe NEC (≥stage II ) *(RR 0.43, 95% CI 0.33 to 0.56)*

**Probiotics prevents Severe NEC and Mortality**
**Recommended, if right preparation is available**

- Concerns
  - Most effective preparations
  - Timing, Dose and duration
  - Preparations available in India

*AlFaleh K, Anabrees J. Probiotics for prevention of necrotizing enterocolitis in preterm infants. Cochrane Database of Systematic Reviews 2014*

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# A Randomized Study of a Monoclonal Antibody (Pagibaximab) to Prevent Staphylococcal Sepsis

- 80 patients received pagibaximab at 90 (*n*22) or 60 (*n* 20)

Not enough data for recommendation
Promising Future

high-risk neonates, seemed safe and well tolerated

- No staphylococcal sepsis occurred in infants who received 90 mg/kg

*Weisman e al Pediatrics* 2011;128:271–279

# Immunoprophylaxis

- IVIG – No Role *(INIS 2011)*
- Antistaph Immunoglobulin – No Role *(Lyon et al 2000)*

Immunoprophylaxis Doesn't Work

- G –CSF and GM – CSF – No role *(Cairo et al 1999)*
- Glutamine Supplementation – No Role *(Cochrane 2012)*

# Prophylactic Fluconazole in VLBW – Cochrane Review 2013

- 7 trials involving 880 infants compared systemic antifungal

Can be considered in settings of high incidence of fungal infections and In neonates with multiple risk facors

*95% CI 0.27 - 0.61)* Risk of death not different

- High Incidence of Fungal infection in control
- Concerns
  - Emergence of fluconazole resistant strains of Candida

*Austin N, McGuire W. Prophylactic systemic antifungal agents to prevent mortality and morbidity in very low birth weightinfants. Cochrane Database of Systematic Reviews 2013,*

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# Breast Milk

- Anti-infective properties – Lactoferrin, lysozyme, IgA, IgG cytokines interferons, bifidogenic factors, PAF
- BM feeding associated with decreased gut permeability
- Reduction of Late onset Sepsis and NEC *(Schanler et al, Pedaitrics 1999)*
- Fresh Breast milk of > 50 ml/kg/day reduces sepsis by 0.27 *(Furman 2003)*

ORIGINAL ARTICLE

# Impact of early human milk on sepsis and health-care costs in very low birth weight infants

AL Patel[1,2], TJ Johnson[2,3], JL Engstrom[2,4], LF Fogg[2], BJ Jegier[2], HR Bigger[1] and PP Meier[1,2]

**OBJECTIVE:** To study the incidence of sepsis and neonatal intensive care unit (NICU) costs as a function of the human milk (HM) do

**ST** daily

nu te a

pr

**RE** Days

1–28 was 54 ± 39 ml kg$^{-1}$ day$^{-1}$ (range 0–135). Binary logistic regression analysis controlling for propensity score revealed that increasing ADDHM-Days 1–28 was associated with lower odds of sepsis (odds ratio 0.981, 95% confidence interval 0.967–0.995, $P = 0.008$). Increasing ADDHM-Days 1–28 was associated with significantly lower NICU costs.

**CONCLUSION:** A dose–response relationship was demonstrated between ADDHM-Days 1–28 and a reduction in the odds of sepsis and associated NICU costs after controlling for propensity score. For every HM dose increase of 10 ml kg$^{-1}$ day$^{-1}$, the odds of sepsis decreased by 19%. NICU costs were lowest in the VLBW infants who received the highest ADDHM-Days 1–28.

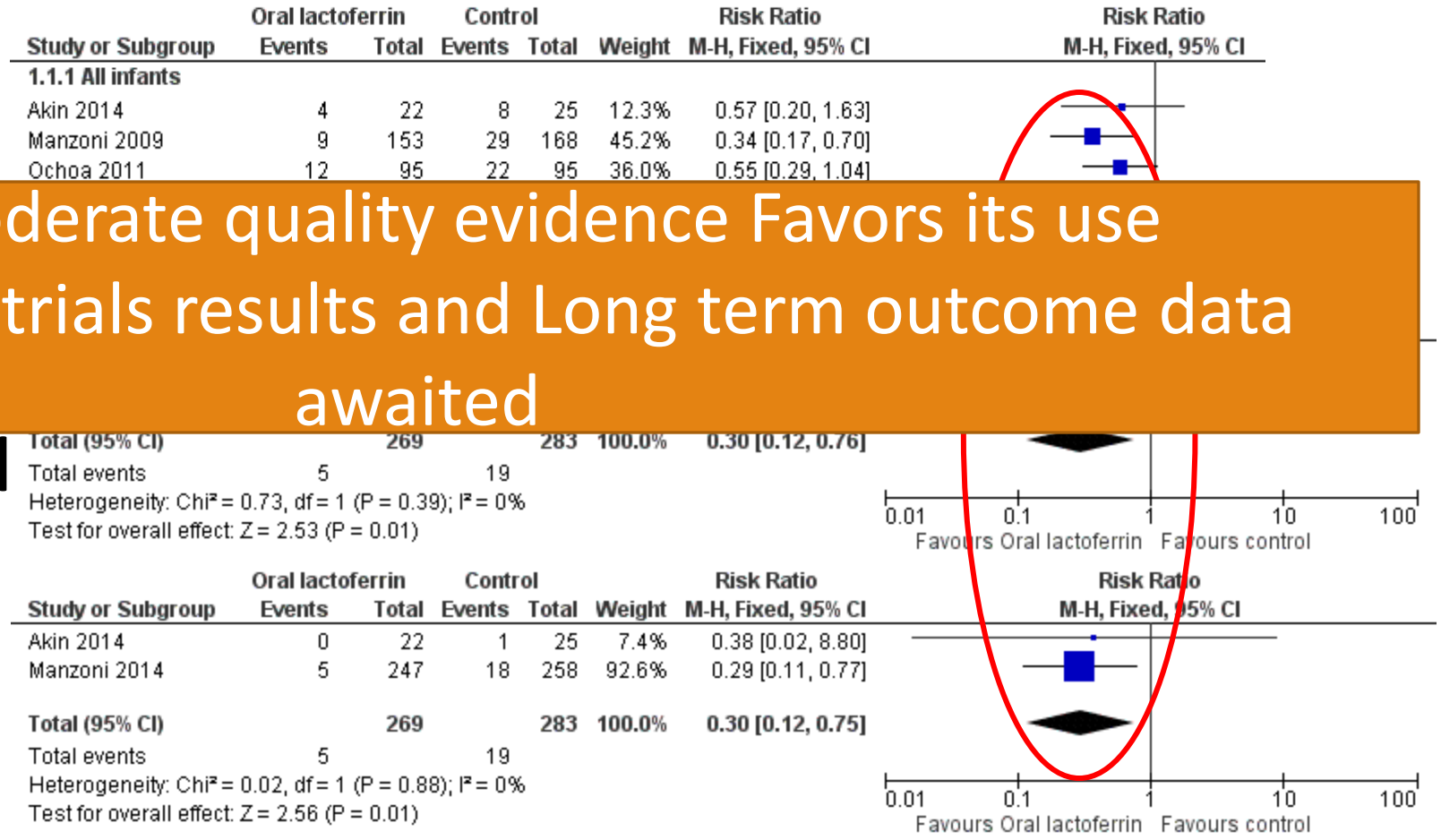
*Journal of Perinatology* (2013) **33,** 514–519; doi:10.1038/jp.2013.2; published online 31 January 2013

Always Use Breast Milk – Fresh whenever possible

# Oral lactoferrin for prevention of sepsis and NEC in preterm infants – Cochrane 2015

- ↓Late onset
- ↓NEC ≥ Stage II
- ↓All Cause mortality

**Low to Moderate quality evidence Favors its use**
**Large Ongoing trials results and Long term outcome data awaited**




*PammiM, Abrams SA.Oral lactoferrin for the prevention of sepsis and necrotizing enterocolitis in preterm infants. Cochrane Database of Systematic Reviews 2015*

# KMC and nosocomial infection – Cochrane Review 2014

- ↓ Nosocomial infection/sepsis *(RR 0.45, 95% CI 0.27-0.76)*

**KMC should be encouraged**

- ↓ Length of hospital stay *(MD 2.2 days, 95% CI 0.6 to 3.7*)
- Better infant growth, breastfeeding, and mother-infant attachment

*Conde-Agudelo A, Díaz-Rossello JL. Kangaroo mother care to reduce morbidity and mortality in low birthweight infants. Cochrane Database of Systematic Reviews 2014*

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# Use of H2 Blockers

- Impairs Acid gastric barrier
- ↑Risk of infections
- 7 times greater risk of LO Sepsis *(Bianconi et al , J P Med 2007)*

# Ranitidine is Associated With Infections, Necrotizing Enterocolitis, and Fatal Outcome in Newborns

H2 Blockers are Harmful

exposed to ranitidine and 18 (9.8%) of the 183 not exposed to ranitidine had contracted infections (odds ratio 5.5, 95% confidence interval 2.9–10.4, $P < .001$). The risk of NEC was 6.6-fold higher in ranitidine-treated VLBW infants (95% confidence interval 1.7–25.0, $P = .003$) than in control subjects. Mortality rate was significantly higher in newborns receiving ranitidine (9.9% vs 1.6%, $P = .003$).

*Terrin et al. Pediatrics Ranitidine is Associated With Infections, Necrotizing Enterocolitis, and Fatal Outcome in Newborns2012;129:e40–e45*

# Ventilator Associated Pneumonia - VAP

- Risk Factors *( Garland 2009)*
  - <28 weeks/ELBW
  - Duration of venti
  - No of reintubations
  - ET Suction
  - Opiate use
- Position *(Torres 1992)*
  - Lateral vs Supine – Lateral better
- Suctioning systems
  - Closed vs suction – Equal

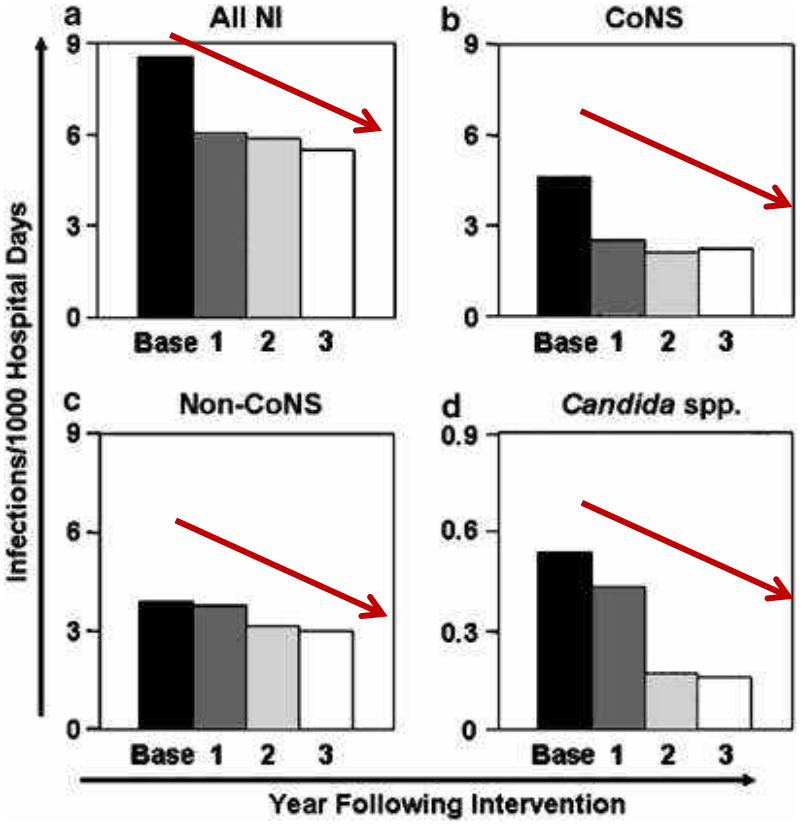
ORIGINAL ARTICLE

Journal of Perinatology (2006) 26, 176–179


# Sustained reductions in neonatal nosocomial infection rates following a comprehensive infection control intervention

RL Schelonka, S Scruggs, K Nichols, RA Dimmitt and WA Carlo

- Baseline infection rate was 8.5 /1000 hospital days
- NI rate fell 26% (*P*=0.002) from baseline in Ist year and 29% (*P*<0.001) in 2nd and 3rd years after the CIC intervention
- CIC measures can reduce bacterial and fungal NI rates. This effect has been sustained for 3 years following the intervention




*Schelonka et al Journal of Perinatology (2006) 26, 176–179*

# Efficacy of an infection control programme in reducing nosocomial bloodstream infections in a Senegalese neonatal unit

C. Landre-Peigne [a,b], A.S. Ka [b], V. Peigne [c], J. Bougere [d], M.N. Seye [b], P. Imbert [e,*]

Table 1

Main results of the infection control programme in the neonatal unit of Hôpital Principal de Dakar, Senegal

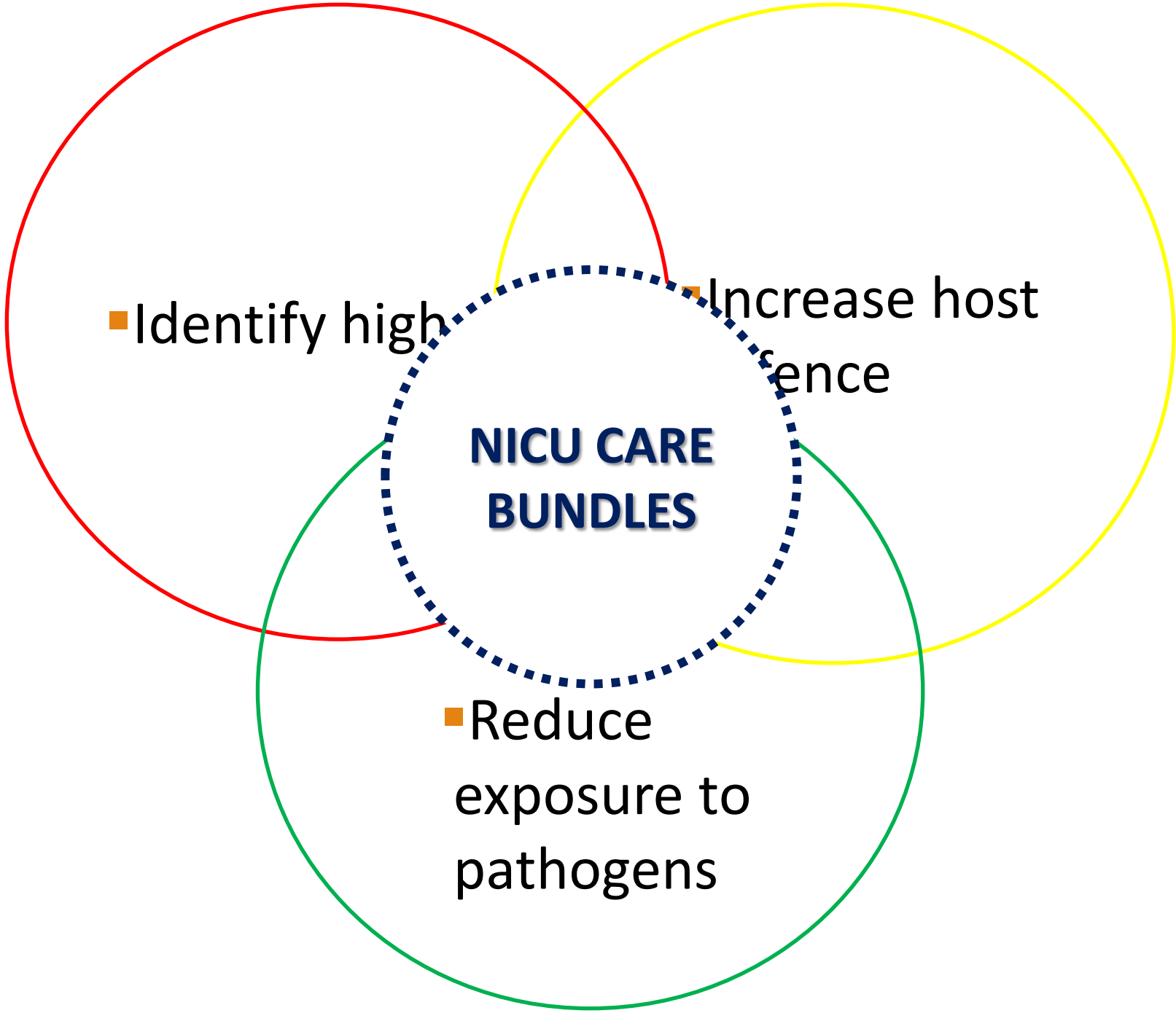
| Variable | Period 1 Jan–Feb 2005[a] | Period 2 Jun–Jul 2005[b] | RR | 95% CI | *P*-value |
|---|---|---|---|---|---|
| No. of neonates | 125 | 148 | | | |
| No. of neonates with birth weight <2500 g (%) | 32 (25.6) | 36 (24.3) | | | NS |
| No. of neonates with birth weight <1500 g (%) | 8 (6.4) | 9 (6.1) | | | NS |
| Median birth weight (g) | 3050 | 3140 | | | |
| No. of NI (%) | 11 (8.8) | 3 (2.0) | 0.23 | 0.07–0.81 | 0.01 |
| NI/1000 patient-days | 10.9 | 2.9 | 0.27 | 0.08–0.97 | 0.03 |
| No. of deaths (%) | 4 (3.2) | 8 (5.4) | | | NS |
| No. of deaths after 48 h (%) | 3 (2.4) | 3 (2.1) | | | NS |
| No. of NI-related deaths | 1 | 1 | | | |
| No. of infants treated with antibiotics for suspected early-onset sepsis (% of admissions for suspected early-onset sepsis) | 88 (100) | 64 (51) | 0.5 | 0.43–0.61 | <0.0001 |
| No. of infants with proven or possible early-onset sepsis (% of admissions) | 41 (33) | 45 (30) | | | NS |
| Ratio of drug-resistant bacteria/all positive cultures (%) | 34/43 (79) | 4/33 (12) | 0.15 | 0.06–0.39 | <0.001 |

RR, relative risk; CI, confidence interval; NI, nosocomial bloodstream infections; NS, non-significant.

[a] Immediately before implementation of the infection control programme.

[b] Immediately after implementation of the infection control programme.

*Landre-Peigne. J Hospital Infection . 2011*


Identify high
Increase host
ence
NICU CARE BUNDLES
Reduce exposure to pathogens

# Potentially Best Practices – PBP's

- Hand Washing
  - Initial hand wash till elbows with soap and water
  - Follow 6 steps of Hand Washing
  - Soap and water/Alcohol hand rub for routine asepsis
  - Hand hygiene even touching the inanimate object or surface
  - Gloves don't replace the hand hygiene need
  - Ensure Compliance
  - Regular Education, Monitoring

# Potentially Best Practices – PBP's

- Gowning
  - Daily washed dress
  - Routine gowning not required
  - Gowning for Procedures
- Prevent understaffing and Overcrowding
- Routine Disinfection Policy
- Decrease no of venipunctures and heel pricks

# Potentially Best Practices – PBP's

- CVC Bundles
  - Strict Asepsis during insertion
  - Topical antiseptic – Chlorhexidine/Povidone-Iodine
  - Sterile dressing –Transparent
  - Daily visual inspection
  - Minimum hub manipulation
  - Separate medication line for reducing repeated hub entry
  - Alcohol wipes rubbing of hub for 10 sec before entry

# Potentially Best Practices – PBP's

- CVC Bundles
  - Careful preparation of TPN and fluids
  - Change fluids and sets every 72 hours
  - Change lipids every 24 hours
  - Catheter removal at the earliest - 100 ml/kg feeds
  - Dedicated CVC team

# Potentially Best Practices – PBP's

- VAP Policy
  - Change position regularly – Lateral/Prone preferred
  - Sterile disposable circuits
  - Change circuits when visibly soiled
  - No routine suction
  - Strict asepsis during suction
  - Extubate at the earliest
  - Aggressive use of NIV - CPAP/HHHFNC

# Potentially Best Practices – PBP's

- Nutritional policy
  - Use Fresh Breast milk
  - Promote KMC
  - Promote enteral feeding
  - Probiotics can be used
  - NO H2 blockers

# Potentially Best Practices – PBP's

- Antibiotic stewardship
  - Make your own Antibiotic Policy
  - Develop Clinical Guidelines for Sepsis
  - Authorization for High end antibiotics
  - Limit antibiotics where infection is likely
  - Specific plans for Streamlining  antibiotics – Braod spectrum to narrow spectrum
  - Deescalating antibiotics
  - Treat for appropriate duration

# Potentially Best Practices – PBP's

- Antibiotic stewardship
  - Discontinue empirical treatment when infection not identified
  - No routine prophylaxis
  - No prophylaxis in invasive devices
  - No Immunoprophylaxis
  - Know your NICU cultures
- Antifungal Policy
  - Consider Fluconazole prophylaxis only if incidence is high

# Potentially Best Practices – PBP's

- Participate in the surveillance program *(NEOKISS 2007 Germany)*
- Quality improvement Program


Thank You

# Reducing neonatal nosocomial bloodstream infections through participation in a national surveillance system

- NEO-KISS 2000 in Germany
- 48 NICUs
- Incidence density of BSIs decreased significantly by 24% from 8.3 BSIs per 1000 patient-days in the first year to 6.4 in the third year
- Participation in ongoing surveillance of nosocomial infections in NICUs, requiring individual units to feedback data, may lead to a reduction in BSI rates

The NEW ENGLAND JOURNAL of MEDICINE

# Treatment of Neonatal Sepsis with Intravenous Immune Globulin

The INIS Collaborative Group*

- 113 hospitals in 9 countries, 3493 infants receiving antibiotics for suspected or proven serious infection
- Polyvalent IgG immunoglobulin-500 mg/kg 48 hours apart
- No effect on the outcomes of suspected or proven neonatal sepsis

*INIS Collaborative group N Engl J Med 2011;365:1201-11.*