




Neonatal Sepsis & Overview of Current NICU QI Projects

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Pediatrics

Premature infants & Health Care Dollars - 2013

- Estimated expenditures: First Year
  - Employer Sponsored Health Plans: $6 billion to $14 billion
    - $78,000 per preterm infant @ the high end.

Grosse SD, Waitzman NJ, Yang N, et al. Employer Sponsored Plan Expenditures for Infants Born Preterm. Pediatrics. 2017;140(4):e20171078

Nosocomial Infection (HAC)

- Huge burden of morbidity and mortality
  - Causes
    - Antibiotic Overuse
    - Formula Feeding
    - Use of H2 Blockers
    - Poor Central Catheter Care
    - Handwashing

Manzoni P, De Luca D, Stronati M, et al. Prevention of nosocomial infections in neonatal intensive care units. Am J Perinatol. 2013;30(2):81-8

Antibiotic Overuse

Bacterial Resistance

- Multiple etiologies
  - Acquisition of enzymes that alter antibiotic structure and function (e.g., β-lactamases);
  - Mutations in bacterial targets such as penicillin-binding proteins,
  - Changes in efflux pumps: allow removal of antibiotics from bacteria or decreased entry sites (porins) which prevent antibiotics from entering bacteria.

Bacterial Resistance

- Mechanisms
  - Underdosing
  - Use of specific antibiotics (i.e., 3rd generation cephalosporin)
    - Cephalosporin use also associated with increased candida infection*, NEC^ & mortality*^
  - Overuse/prolonged use

*Pediatrics. 2010 Oct;126(4):e865-73; ^Pediatrics. 2009 Jan;123(1):58-66.

Antibiotic Overuse

- Bacterial Interference: The More Different Species of Bacteria = Less Risk of Infection
  - S. pneumoniae produces NanA – strips sialic acid from LPS of H influenzae & N. meningitidis (destroys biofilm capacity)
  - H influenzae may promote local inflammation – recruits neutrophils that selectively eliminate S. pneumoniae

Antibiotic Overuse

- Translocation of bacteria from the GI tract 2^{o} to changes in the intestinal microbiome.
  - Early postnatal as well as prenatal antibiotic exposure for GBS prophylaxis: Associated with alterations of the microbiome
  - Shorter courses of antibiotics (1–3 days vs. 5–7 days)
    - Associated with suppression and alteration of the microbiome for several weeks
    - Recovery occurred after the third postnatal week.
    - The CDC estimates that nearly 50% of antibiotics are unnecessary or suboptimally effective as prescribed

Antibiotic Overuse

- ≥ 5 days of antibiotics associated with increased incidence of LOS, NEC & death*
  - ~7% increase in the odds of developing NEC for each additional day of empiric antibiotics beyond 5 days^

*Kuppala VS, Meinzen-Derr J, Morrow, AL, et al. Prevention of nosocomial infections in neonatal intensive care units. J Pediatr. 2011; 159(5): 720–725.

^Cotten CM, Taylor S, Stoll B, 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(1):58–66.

Antibiotic Overuse

- Antibiotic Stewardship
  - Who to treat: Maternal chorioamnionitis
    - On line “risk tool” for EOS: ≥34 weeks’ gestation
      - Reduced number of patients treated (99.7% to 2.5%)*
      - Missed asymptomatic infants with positive blood culture

*Money N, Newman J, Demissie S, et al. Anti-microbial stewardship: antibiotic use in well-appearing term neonates born to mothers with chorioamnionitis. J Perinatol. 2017;37:1304-9

Antibiotic Overuse

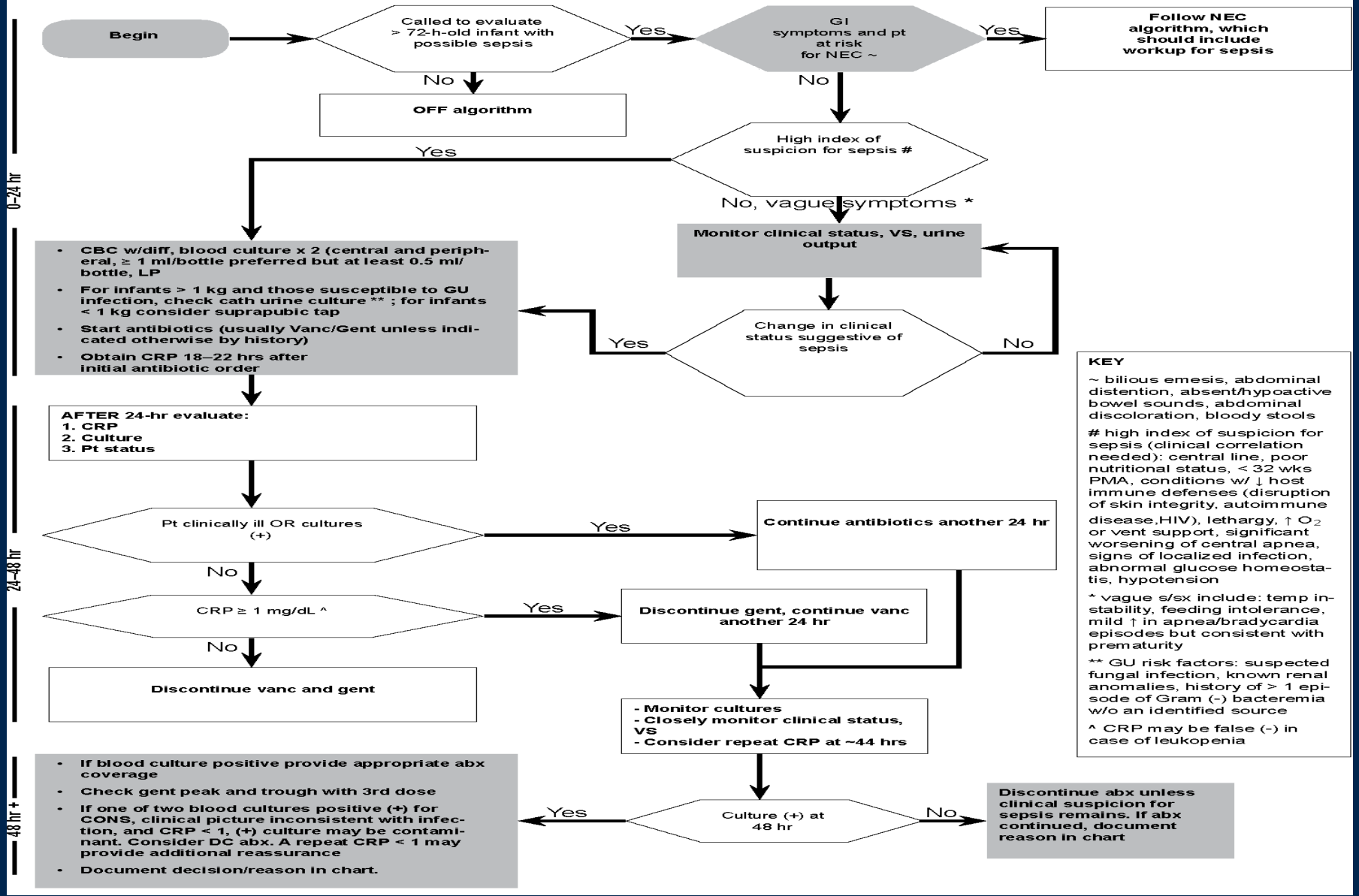
- Antibiotic Stewardship
  - How long to treat: DUE
    - EOS: if patient is not symptomatic of infection ≤ 48 hours*
    - LOS: no recommendations
      - Use of an algorithm to reduce antibiotic use to ≤48 hours has been successful
      - Questionable duration when treating NEC
  - Avoid overly broad spectrum antibiotics (e.g., 3rd generation cephalosporin)

*Benitz WE, Wynn JL, Polin RA. Reappraisal of guidelines for management of neonates with suspected early-onset sepsis. J Pediatr. 2015 Apr; 166(4):1070-4.

Antibiotic Stewardship

- Methodology:
  - Prescriber audit and feedback
  - Preauthorization and formulary restriction of selected antibiotics
  - Education and computerized decision support.
  - Metrics to evaluate antimicrobial stewardship programs include
    - Measurements of patient safety and quality:
      - Rates of adverse drug events,
      - Appropriate dosing and timing of perioperative prophylaxis.

Figure 8–2. Late-onset Sepsis in Newborn Center Patients, Level 2 and 3



Feeding

Relationship between mode of delivery and microbiome

- Cesarean section: Colonized by organisms in the environment

- Vaginal: Colonized by maternal organisms

Feeding and the Microbiome

- Breast Milk
  - Human milk oligosaccharides
    - Directly interact with the surface of pathogenic bacteria,
    - Inhibit the binding of pathogens and toxins to host cell receptors
  - Secretory IgA confers a protective effect against pathogens
  - Non-digestible carbohydrates ferment in the colon and promote further growth of probiotic *Bifidobacterium* and *Bacteroides* species
  - Lower gastric pH

Gritz EC, Bhandari V. The Human Neonatal Gut Microbiome: A Brief Review. Front Pediatr. 2015; 3: 17.

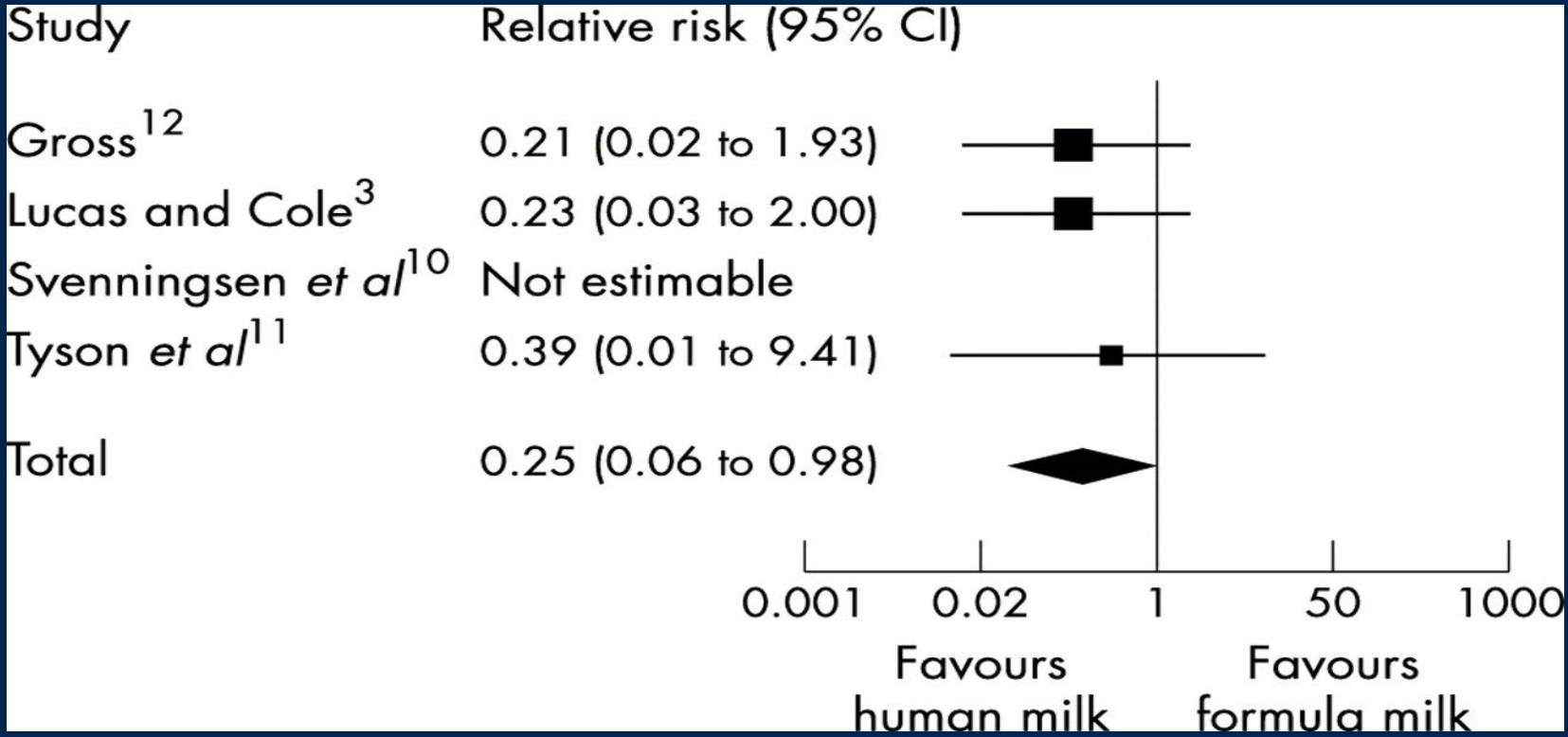
Feeding and the Microbiome

- Differing microbiota

Major differences in neonatal gut colonization by type of feeding.

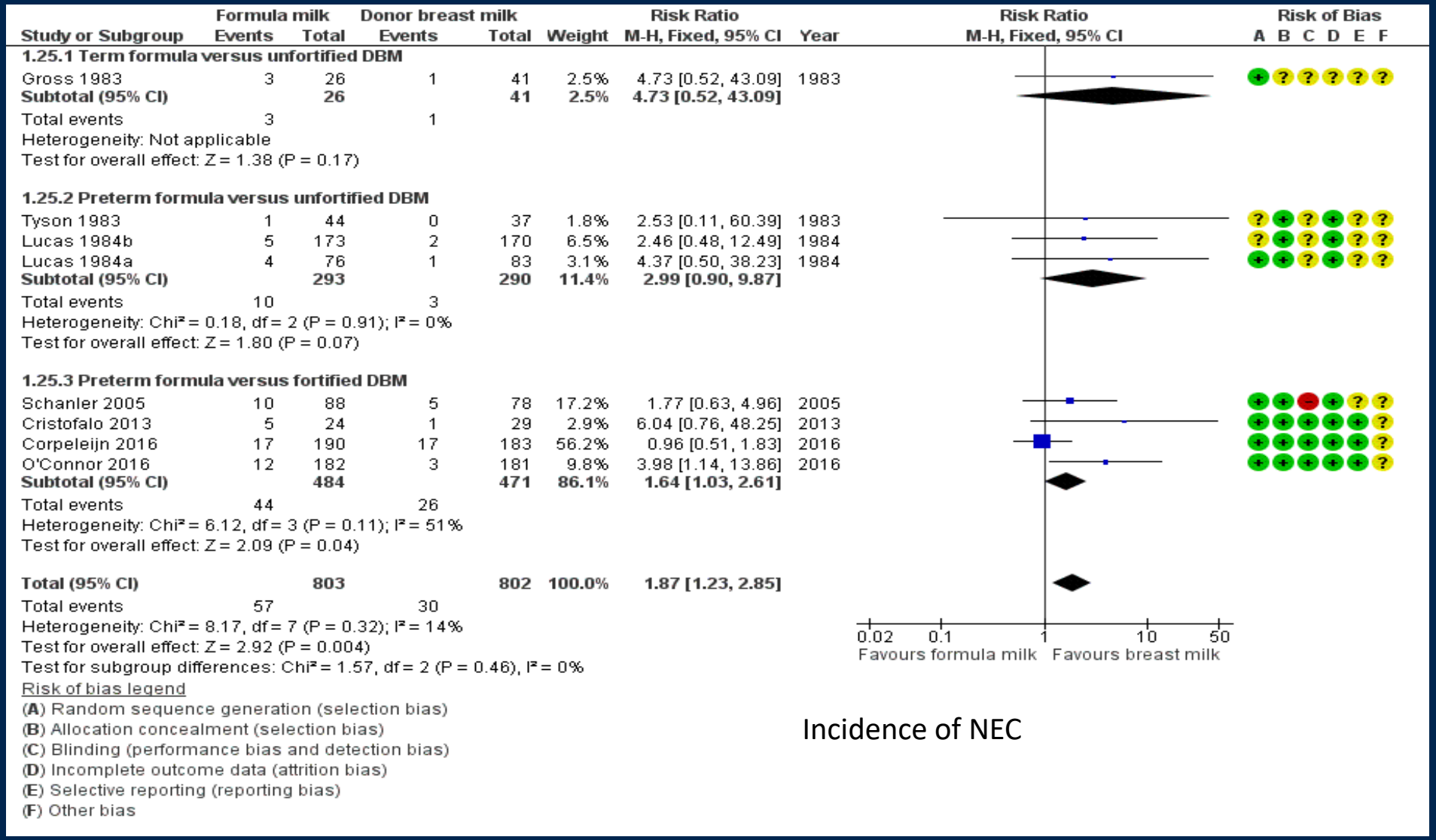
Breast fed	Formula fed
Bifidobacteria	*Bifidobacteria* species
Enterobacteria species	*Escherichia coli*
	Clostridium difficile
	Bacteroides species
	Prevotella species
	Lactobacillus species

Type of Feeding and NEC



- Donor breast milk vs. formula & confirmed NEC

McGuire W, Anthony MY. Donor human milk versus formula for preventing necrotising enterocolitis in preterm infants: systematic review. Archives of Disease in Childhood - Fetal and Neonatal Edition 2003;88:F11-F14



Incidence of NEC

Quigley M, Embleton ND, McGuire W. Formula versus donor breast milk for feeding preterm or low birth weight infants. Cochrane Database of Systematic Reviews 2018, Issue 6. Art. No.: CD002971. DOI: 10.1002/14651858.CD002971.pub4

Type of feeding and NEC

- Estimated number needed to treat with breast milk to prevent 1 case of NEC: 10

Sullivan S, Schanler RJ, Kim JH et al. An exclusively human milk-based diet is associated with a lo wer rate of necrotizing enterocolitis than a diet of human milk and bovine milk-based products. J Pediatr.2010;156(4):562–567.

H2 Blockers

Infection & H2 Blockers

- Two Observational Studies
  1. National Institute of Child Health and Human Development Neonatal Research Network*:
     - BW: 401 – 1500 gms
     - Case-control methodology
     - 11,072 Infants
     - H2-blocker use was associated with an increased incidence of NEC (odds ratio [OR]: 1.71; 95% confidence interval [CI]: 1.34–2.19; P < .0001

Guillet R et al. Association of H2-blocker therapy and higher incidence of necrotizing enterocolitis in very low birth weight infants. Pediatrics. 2006;117(2):e137-42

Infection & H2 Blockers

- Two Observational Studies

2. Multicenter, observational study
   - BW: 401 – 1500 gms or GA between 24 & 32 weeks
   - Rates of infectious diseases, NEC, and death
   - 274 VLBW infants: 91 received ranitidine and 183 had not
   - Results:
     - Increased rate of infection (odds ratio 5.5, 95% confidence interval 2.9-10.4, P < .001); 6.6 fold increase in NEC
     - Increased mortality x 6

Terrin G et al. Ranitidine is associated with infections, necrotizing enterocolitis, and fatal outcome in newborns. Pediatrics. 2012;129(1):e40-5.

CLABSI
(Central Line Associated Bloodstream Infection)

CLABSI Impact

- CDC Estimate: 2002, ~250,000 CLABSI in US hospitals
  - -> 30,000 deaths
- Risk Factors (Neonatal)
  - Catheter hub and exit site colonization
  - ELBW (< 1000 g)
  - Duration of parenteral nutrition (Dwell time)*
  - Catheter insertion after first week of life

*Milstone AM et al. **Catheter dwell time and CLABSIs in neonates with PICCs: a multicenter cohort study.** Pediatrics. 2013;132(6):e1609-15.

Dwell Time

- Retrospective cohort study of 13 327 infants with 15 567 catheters (93% peripherally inserted central catheters [PICCs], 7% tunneled catheters) and 256 088 catheter days cared for in 141 NICUs.
  - incidence of CLABSI was 0.93 per 1000 catheter days.
  - No relationship to dwell time for PICC.

Rachel G. Greenberg et al. Effect of Catheter Dwell Time on Risk of Central Line–Associated Bloodstream Infection in Infants. Pediatrics. 2015 Dec; 136(6): 1080–1086.

Central Line Care Bundles

- 2008, all 18 regional referral NICUs in New York state
  - Prospective cohort study
  - Pre-intervention (January to December 2007) versus the post-intervention (March to December 2009)
  - Each study period: >55,000 central-line days and >200,000 patient-days

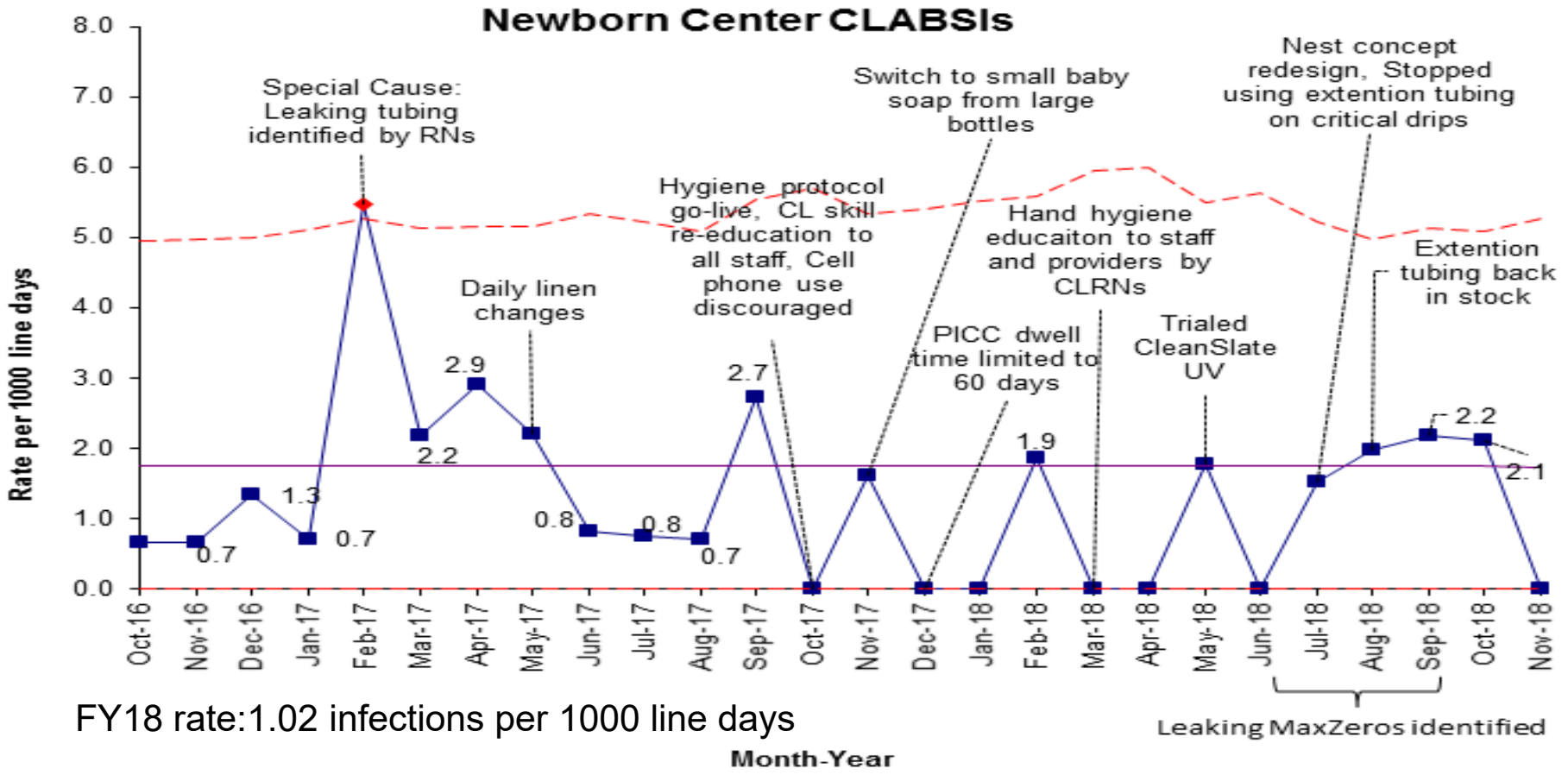
Schulman J et al. Statewide NICU central-line-associated bloodstream infection rates decline after bundles and checklists. Pediatrics. 2011 Mar;127(3):436-44.

Central Line Care Bundles

- Results
  - 40% decrease over all (RR: 0.60 [95% CI: 0.48-0.75]; P < .0005
  - Use of Check-lists with the Bundles improved outcome
  - Large interfacility variation
    - incidence rate ratio: 0.044 to 2.87

Schulman J et al. Statewide NICU central-line-associated bloodstream infection rates decline after bundles and checklists. Pediatrics. 2011 Mar;127(3):436-44.

Central Line Bundles



FY18 rate:1.02 infections per 1000 line days

HANDWASHING

Handwashing

- Soaps with no Residual Antimicrobial Activity
  - Iodophores: water-soluble material that releases free iodine when in solution.

- Soaps with residual antibacterial activity
  - ≤ 3% Hexachoraphene
  - 4% Chlorhexidine gluconate

Hand Hygiene

- 60% - 70% Alcohol/water: As effective or more effective than hand washing in normal circumstances
  - If hands are soiled, use soap and water
  - Ineffective against C. difficile and other spore producing pathogens as well as human norovirus (i.e., Norwalk virus)

https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5116a1.htm