NICU Infection Prevention Guideline Update

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Overview

- Stakeholder Engagement
- Key Questions
- Search Strategies
- Abstract Review
- Inclusion Criteria

Stakeholders

- American Academy of Pediatrics
- Society for Healthcare Epidemiology of America
- Association for Professionals in Infection Control
- Vermont Oxford Network
- National Association of Neonatal Nurses (NANN)

Guideline Team

- Core Writing Group
  - Alexis Elward
  - Martha Iwamoto
  - Craig Umscheid
  - Amanda Paschke
  - Gretchen Kuntz
  - Michael Brady
- Expert Reviewers
  - Lisa Saiman, Charlie Huskins, Susan Dolan, Richard Polin, Wanda Barfield, David Kaufman, Susan Huang, David Pegues, Suzanne Frey, Gautham Suresh, Russ Olmstead, Pablo Sanchez, Rachel Gorwitz

Stakeholder Engagement

- Conference calls with core writing group and expert reviewer group
- Key Questions reviewed
- Broad list of potential topics generated
- Initial literature searches performed
  - Existing or developing guidelines addressing topics
  - Adequate literature to include as key question
- Key Questions triaged and consolidated

Key Questions: Viral Infections

Viral Infections	
Initial Questions	*Revised Questions*
What are the best methods for control of respiratory viral pathogens in the NICU? What are the best pathogen specific prevention measures of RSV, Pertussis, VZV?	What are the **most effective** methods of prevention and control of viral respiratory illnesses in the NICU? What are the **most effective** methods for preventing transmission of RSV, Pertussis and VZV in the NICU? **Should transmission-based precautions be modified for patients in isolettes?**
What are the best diagnostic modalities for detection of an outbreak of respiratory viral pathogens in the NICU?	What is the **most effective diagnostic approach** to identifying respiratory viral outbreaks in the NICU?

Key Questions: Central Line Associated Bloodstream Infections (CLABSI)

CLABSI	
Initial Questions	*Revised Questions*
What are the best strategies to prevent CLABSI in NICU patients?	What are the **most effective** strategies to prevent CLABSI in the NICU?

Key Questions: Methicillin Resistant Staphylococcus aureus (MRSA)

MRSA	
Initial Questions	*Revised Questions*
What are the risk factors for MRSA and MSSA colonization in NICU patients?	What are the risk factors for **MRSA** colonization in NICU patients?
What are the most effective strategies to identify MRSA and MSSA colonization in NICU patients?	What are the most effective strategies to screen for **MRSA** colonization in NICU patients? **Does screening of MRSA colonization result in fewer MRSA infections?**
What are the most effective measures to prevent hospital-acquired infection or colonization with MRSA and MSSA?	What are the most effective measures to prevent hospital-acquired infection or colonization with **MRSA**?

Invasive fungal disease	
Initial questions	*Revised Questions*
What are the risk factors for invasive candidal infections?	No change
What are the most effective prevention strategies to prevent colonization or invasive infection with Candida?	What are the **most effective strategies to prevent invasive infection with Candida**? **What are the most effective strategies to prevent colonization with Candida?** **Does prevention of Candidal colonization result in fewer invasive Candidal Infections?**
What are the best diagnostic modalities for detection of invasive fungal infection in NICU patients?	What are the **most effective methods of identifying invasive fungal infections (Candida, Aspergillus, Zygomycoses, Pichia, Malassezia)** in NICU patients?

Key Questions: *Clostridium difficile*

Other	
Initial Questions	*Revised Questions*
What are the most effective strategies for *C difficile* testing in NICU patients?	What are the most effective strategies for *C difficile* testing in NICU patients? **When should testing for *C difficile* be performed in NICU patients?** **What is the significance of a positive *C difficile* test in a NICU patient?**
What is the most effective way to perform hand hygiene to prevent infection in NICU patients?	
What is the optimal architectural design for NICU to prevent infection transmission?	

Search Strategies

Databases

- MEDLINE
- Cochrane Library
- Excerpta Medica Database (EMBASE)
- Cumulative Index to Nursing and Allied Health Literature (CINAHL)
- National Guideline Clearinghouse
- Professional Societies: SHEA, IDSA, APIC, HICPAC, AAP

Respiratory Viruses and RSV

#	Search History	Results
1	exp Intensive Care Units, Neonatal/ or exp Intensive Care, Neonatal/	10481
2	Infant, Newborn/	440263
3	1 or 2	440999
4	exp Respiratory Tract Infections/	249278
5	exp Virus Diseases/	614076
6	4 and 5	54452
7	exp Respiratory Syncytial Virus Infections/ or exp Respiratory Syncytial Viruses/	7292
8	6 or 7	59287
9	3 and 8	3846
10	exp Infection Control/	43521
11	exp Cross Infection/	39370
12	exp Communicable Disease Control/	207284
13	10 or 11 or 12	236787
14	9 and 13	432
15	limit 14 to (english language and humans)	341

Medline results only shown, same search strategy for other databases

Study Selection Agreement Among Reviewers

Sampling Strategy

- Screening of titles and abstracts
  - Single author – 100%
  - Two authors – 20% sample
- Inter-reviewer comparison of 20% sample using kappa statistic
- Calculating change agreement
  - Formula for calculating kappa
    (Observed agreement – agreement expected by chance) / (100% - agreement expected by chance)

Measures of Observer Variability (Kappa Statistic)

Table 1: Qualitative classification of kappa values as degree of agreement beyond chance[3]

Kappa value	Degree of agreement beyond chance
0	None
0–0.2	Slight
0.2–0.4	Fair
0.4–0.6	Moderate
0.6–0.8	Substantial
0.8–1.0	Almost perfect

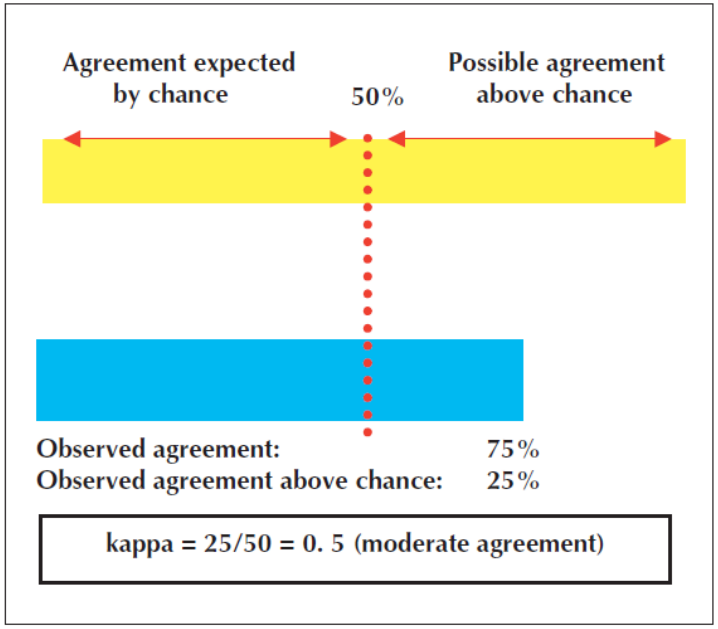

Fig. 1: Two observers independently assess the presence or absence of a finding or outcome. Each observer determines that the finding is present in exactly 50% of the subjects. Their assessments agree in 75% of the cases. The yellow horizontal bar represents potential agreement (100%), and the turquoise bar represents actual agreement. The portion of each coloured bar that lies to the left of the dotted vertical line represents the agreement expected by chance (50%). The observed agreement above chance is half of the possible agreement above chance. The ratio of these 2 numbers is the kappa score.

Agreement Between Reviewers

Key question	Observed agreement	Kappa statistic
Respiratory viral	.84	0.69
Varicella	.90	0.80
Pertussis	.83	0.67
CLABSI	.86	0.71
MRSA	.88	0.75
Fungal	.89	0.74
C. difficile	.78	0.58

Results of the Study Selection Process

Respiratory Viral Infections

Literature search

513 references identified for title and abstract screening

Study selection

207 references selected for full-text review

16 narrative reviews
19 outbreak reports
6 existing guidelines

Varicella

Literature search

98 references identified for title and abstract screening

Study selection

32 references selected for full-text review

2 narrative reviews
3 outbreak reports

Pertussis

Literature search

147 references identified for title and abstract screening

Study selection

31 references selected for full-text review

6 outbreak reports

CLABSI

Literature search

499 references identified for title and abstract screening

Study selection

295 references selected for full-text review

26 narrative reviews
7 existing guidelines

MRSA

Literature search

663 references identified for title and abstract screening

Study selection

346 references selected for full-text review

6 existing guidelines

C. difficile

Literature search

160 references identified for title and abstract screening

Study selection

105 references selected for full-text review

General Inclusion Criteria

- **Include**
  - Original data
  - Systematic review
- **Exclude**
  - Non-U.S. descriptive epidemiology only
  - Mixed patient population without NICU or infant subgroup analysis
  - Studies that do not include NICU patients or infants
  - General hospital-aquired infection surveillance

Respiratory Pathogen Exclusion Criteria

- Immunization
- Non-respiratory viruses in NICU population (Enteroviruses, Herpes Simplex Virus, Cytomegalovirus)

CLABSI Exclusion Criteria

- Treatment only
- Catheter removal for documented infections
- Peripheral IV studies
- Endocarditis

MRSA: Exclusion Criteria

- Molecular epidemiology study, only
- Endocarditis
- Japan MRSA neonatal toxic-shock entity (only reported in Japan, very specific syndrome)
- Case reports of single-site infections (such as case report of periorbital cellulitis)
- Community-acquired or community-onset infections
  - WILL include infections in NICU patients with CA- MRSA strains
- Treatment only

Fungal Infections Exclusion Criteria

- Treatment only
- Pharmacokinetics studies of antifungals in neonates
- Case Reports except for non-Candidal fungal infections
- Case series with n <10
- Vaginitis without infant colonization/infection outcome
- Nonclinical (immunologic) studies

Clostridium difficile Exclusion Criteria

- Molecular biology of *Clostridium difficile*
- Molecular epidemiology without clinical information

Timeline

- January 2010 Tentative guideline team and key questions
- April 2010 Final guideline team
- June 2010 Key questions finalized
- July 2010 Literature search performed
- **September 2010 Abstract and full text review**
- November 2010 Data extracted into draft evidence tables
- February 2011 Extraction finalized, evidence quality graded using GRADE approach, and narrative summaries drafted
- June 2011 Narrative summaries finalized and recommendations drafted using GRADE approach
- November 2011 Recommendations finalized

Next Steps

- Identify replacement for Amanda Paschke
- Finalize inclusion and exclusion criteria for full text review
- Begin full text review

Public Comment

"*The first thing we need is a definition*."

Ben, age 10 years

"*Sometimes when babies come out they are not fully done.*"

Katie, age 7 years