Clinical Practice Guidelines

Prevention and Surveillance of Healthcare Associated Infections

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National Neonatology Forum, India

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Executive summary

Neonatal sepsis is an important cause of morbidity and mortality, especially in low and middle-income countries. Infections contribute to 20.8% of neonatal mortality in India (1). The morbidities related to neonatal infections include prolonged hospital stay, increased cost of care, retinopathy of prematurity, periventricular leukomalacia, and abnormal neurodevelopment. Neonatal sepsis is classified as early onset sepsis (EOS) for symptom onset before 72 hours of birth, and as late onset sepsis (LOS) for symptoms beginning 72 hours after birth. EOS is related to maternal infection and LOS is often hospital acquired. Hospital/health care associated infections (HAIs) are potentially preventable. Various principles underline formulation of infection prevention and control strategies. These include, but not limited to improving hand hygiene practices, good housekeeping practices, improving nurse to patient ratio, human milk usage, probiotics, kangaroo mother care, decreasing use of invasive devices and antibiotic prophylaxis,

The objective of this guideline is to improve the quality of care and outcomes for preterm and term infants by providing recommendations on infection prevention and control strategies. The guideline development group short-listed 12 research questions to be of the highest priority for development of recommendations.

A separate search strategy was used for each of the priority questions to identify studies for inclusion in this review. At least two or more databases were searched to identify eligible studies. Search was restricted to studies in English language. A standardized form was used to extract relevant information from studies. Systematically extracted data included: study identifiers, setting, design, participants, sample size, intervention or exposure, control or comparison group, outcome measures and results. The following quality characteristics were recorded for all randomized controlled studies: allocation concealment, blinding of intervention, loss to follow up, and intention to treat analysis. Standard methods were used for quality assessment of observational studies.

We used the GRADE approach for assessing the quality of evidence and the recommendations. The quality of the studies reporting results for an outcome was graded as: high, moderate, low or very low. The strength of a recommendation reflects the degree of confidence that the desirable effects of adherence to a recommendation outweigh the undesirable effects. The decisions were made on the basis of evidence of benefits and harms; quality of evidence; values and preferences of policymakers, health-care providers and parents; and whether costs are qualitatively justifiable relative to benefits in low- and middle- income countries. Each recommendation was graded as ***strong*** when there was confidence that the benefits clearly outweigh the harms, or ***weak*** when the benefits probably outweigh the harms, but there was uncertainty about the trade-offs. A strong or weak recommendation was further classified as ***situational*** if the benefits outweigh the harms in some situations but not in others. For example, some recommendations were considered relevant only to settings where resources were very limited while others were considered relevant only to settings where certain types of facilities were available.

Table 1 summarizes the key recommendations for prevention and surveillance of infections in neonates.

Table 1: Summary of recommendations for prevention and surveillance of healthcare associated infections in neonates

S. No.	Recommendations	Strength of recommendation	Certainty of evidence
1.	Asepsis should be maintained during the birthing process by following the clean birth practices.	Strong	Very low
2.	Pregnant women with preterm premature rupture of membranes should be prescribed antibiotics.	Strong	High
3.	Regular system-based and behavioral interventions should be undertaken to improve compliance to hand hygiene.	Strong	High
4.	Hand hygiene should be practiced by either hand washing or using alcohol-based hand-rub. Hand washing should be followed at the time of entry to neonatal intensive care unit/special newborn care unit or when hands are visibly soiled.	Strong Strong	Moderate Very low
5.	Aseptic non-touch technique (ANTT) should be followed during invasive procedures like central or peripheral vascular cannulation, intravenous fluid or medication preparation or administration and endotracheal tube insertion or suction.	Strong	Moderate
6.	Neonatal units should implement Central line insertion and care bundle to reduce catheter-related bloodstream infections.	Strong	High
7.	Neonatal units should implement Ventilator-associated pneumonia (VAP) prevention bundle in neonates on invasive and non-invasive respiratory support.	Strong	Not graded
8.	Regular educational activities about prevention of healthcare associated infections should be conducted for healthcare professionals.	Strong	Low
9.	Optimum nurse patient ratio should be ensured in the neonatal units to prevent healthcare associated infections.	Strong	Low

10.	Regular antibiotic stewardship program should be implemented in neonatal units.	Strong	Moderate
11.	Routine environmental surveillance cultures should not be done in the neonatal unit. *Surveillance cultures should be taken only while for outbreak investigation, specific research question, potentially hazardous environmental condition and quality assurance of a sterile process.*	Strong, conditional	Not graded
12.	Routine organism-specific surveillance is unlikely to be beneficial in overcrowded and busy facilities. *Surveillance for Methicillin resistant Staphylococcus aureus may have a role in set-ups with adequate isolation and lab facilities.*	Weak, Conditional	Low

Introduction

Healthcare associated infections (HAI) are an important cause of mortality and morbidity in neonates. A significant proportion of these can be prevented by appropriate health-care practices including hand hygiene, minimizing the use of invasive lines/devices, breast milk feeding and others. The financial burden imposed on health-care due to HAIs is extremely high. Preventing HAIs is more cost-effective than treating neonates with infections. But, the infection control practices across units vary and so does the incidence and prevention strategies for HAIs.

Most of the existing international guidelines are more inclined toward developed, high-resource settings. The evidence and the measures needed to employ in developing countries may differ. Hence, it is important to review the available evidence and formulate national guidelines to increase awareness and knowledge about the evidence-proven strategies to decrease HAIs.

Scope of guidelines and target audience

Aim

The primary aim of this guideline is to improve the quality of care and outcomes of preterm and term neonates by providing recommendations on prevention and control of hospital acquired infections.

Target audience

The primary audience for this guideline includes health-care professionals (neonatologists, pediatricians, nurses and other practitioners) who are responsible for delivering care for neonates in different levels of heath care as well health program managers and policy makers in all settings. The information in this guideline will be useful for developing job aids and tools for training of health professionals to enhance the delivery of neonatal care. These guidelines may also be used by health policy makers to set up facilities in special care newborn units for optimal care of infants.

Population of interest

The guidelines focus on prevention and control of hospital-acquired infections in neonates admitted to healthcare settings.

How to use these guidelines

This systematic review on prevention and control of hospital acquired infections led to the development of 12 sets of recommendations. Each recommendation was graded as **strong** when there was confidence that the benefits clearly outweigh the harms, or **weak** when the benefits probably outweigh the harms, but there was uncertainty about the trade-offs. A strong or weak recommendation was further classified as **situational** if the benefits outweigh the harms in some situations but not in others. For example, some recommendations were relevant only to settings in low- and middle-income countries where resources are very limited while others were considered relevant only to settings where certain types of facilities were available. To ensure that each recommendation is correctly understood and applied in

practice, the context of all context-specific recommendations is clearly stated within each recommendation, and additional remarks are provided where needed. Users of the guideline should refer to these remarks, which are presented along with the evidence summaries within the guideline.

Methodology

Questions relevant to clinical practice

The guideline development group (GDG) short-listed 12 research questions after a process which included listing of all possible questions, rating on a scale by members of GDG and also by a wider group of National Neonatology Forum (NNF) members. A list of potential outcomes of interest for each question was circulated to all members of the GDG, who scored the importance of each outcome on a scale of 1 to 9: 1–3: not important; 4–6: important; and 7–9: critical. The average of the scores for each outcome was used to prioritize the outcome and to select the most important outcomes for each PICO question.

The following questions have been addressed in this set of recommendations:

1. In mothers with preterm premature rupture of membranes (PPROM), does antibiotic use compared to no antibiotics, decrease the incidence of neonatal sepsis?
2. In delivery room, does adherence to clean birth practices decrease the incidence of neonatal HAIs?
3. In neonates admitted to NICU, does CLABSI bundle approach compared to routine care decrease the incidence of CLABSI?
4. In neonates admitted to NICU, does VAP bundle approach compared to routine care decrease the incidence of VAP?
5. In neonates admitted to NICU, does ANTT approach compared to routine care decrease the incidence of HAI?
6. In neonates admitted to neonatal unit, what interventions can result in improved compliance to hand hygiene?
7. In neonatal units, is hand rub as effective as hand wash in decreasing neonatal infections?
8. In neonatal ICUs, does optimizing nurse to patient ratio decrease the incidence of HAI?
9. In neonatal units, does education of health care workers and patients result in reduced HAIs?
10. In neonatal units, does adherence to antibiotic stewardship policies result in decreased incidence of HAI?
11. In neonatal units, does active surveillance compared to no surveillance decrease the rate of HAIs?
12. In neonatal units, does organism specific surveillance help in reducing the rates of HAI?

Outcomes of interest

For each question, the following outcomes were considered to be *critical*:

1. Mortality
2. Healthcare associated infection (HAI)- Blood culture positive sepsis in neonates after 48 hours of hospital admission
3. Central line associated blood stream infection (CLABSI)

4. Ventilator associated pneumonia (VAP)

The following outcomes were considered to be *important*:

1. Duration of hospitalization
2. Costs

The details of the outcomes and their definitions are available in the online annexures. Benefits and harms in critical outcomes formed the basis of the recommendations for each question.

A systematic review of literature was done and a standardized form was used to extract relevant information from studies. Systematically extracted data included: study identifiers, setting, design, participants, sample size, intervention or exposure, control or comparison group, outcome measures and results. The following quality characteristics were recorded for all studies: allocation concealment or risk of selection bias (observational studies), blinding of intervention or observers or risk of measurement bias, loss to follow up, intention to treat analysis or adjustment for confounding factors, and analysis adjusted for cluster randomization (the latter only for cluster-randomized controlled trials, RCTs).

We used GRADE approach for assessing the quality of evidence and the recommendations. The quality of the set of included studies reporting results for an outcome was graded as: high, moderate, low or very low. The strength of a recommendation reflects the degree of confidence that the desirable effects of adherence to a recommendation outweigh the undesirable effects. The decisions were made on the basis of evidence of benefits and harms; quality of evidence; values and preferences of policy-makers, health-care providers and parents; and whether costs are qualitatively justifiable relative to benefits in low- and middle- income countries.

Evidence review

We searched all published randomized, quasi-randomized and observational studies for information related to priority questions. Recent systematic reviews, meta-analyses and review articles were initially looked for, and they were included if they were recently published (last 1-2 years). In cases where they were not available, we retrieved the studies and pooled the available data. For epidemiology of the neonatal sepsis in India, we used recently published data for the country.

Type of participants

Full term and preterm neonates with hospital acquired infections before 28 days of life (44 weeks post-conception) were included.

Search strategy, data abstraction and synthesis of evidence

Literature search was performed using a separate search terminology for each of the research question. The search terminology used, and databases searched are provided in the Appendix. Studies were stratified according to the study design, population characteristics and place of conduct of the study. Effects were expressed as relative risk (RR) and odds ratio (OR) for categorical data and mean difference (MD) and weighted mean

difference (WMD) for continuous data. When available, results were adjusted for potential confounders. All studies included in the analysis and also studies that reported a critical outcome, but could not be pooled in meta-analysis are summarized in the table of individual studies (online annexure)

Grading the quality of evidence

Pooled effects were used for developing recommendations and pooling of available data from individual studies were done using RevMan software (version 5). When 3 or more RCTs were available for an outcome, the quality of evidence was rated at least "low" by GRADE approach. When a meta-analysis was already available and data from newer studies had to be added, the data from existing meta-analysis was entered or imported into RevMan and newer data was added to the existing data. For pooling data, we used author reported data, and requested authors for additional data when it was not available in published study. When pooling of results was not possible, we used the range of effect sizes observed in the individual studies in developing recommendations. Pooled data were later exported to GRADEPro for generation of recommendations.

All relevant reviews were summarized, and the evidence was synthesized using the GRADE methodology where possible. In case it was not possible to GRADE the evidence, a study-by-study table was developed to summarize and assess the quality of the evidence. Online annexure provides the details of evidence synthesis.

The GRADE handbook was distributed to all members before the process was initiated. The following five aspects were rated in the quality assessment: (1) limitations (risk for bias); (2) inconsistency; (3) indirectness; (4) imprecision; (5) reporting bias. The quality of the set of studies included – reporting results for an outcome – was graded as: high, moderate, low or very low.

High: One can be sure that the intervention is beneficial, has no effect or is harmful. Results, including the magnitude of the pooled effect, are unlikely to change with new studies.

Moderate: One can be reasonably sure that the intervention is beneficial, has no effect or is harmful. However, the magnitude of the pooled effect may change with new studies.

Low: Although it is likely, one cannot be sure the intervention is beneficial, has no effect or is harmful. The magnitude of the pooled effect is uncertain and is likely to change with new studies.

Very low: One cannot be certain about the effects of the intervention.

Formulation of recommendations

The GDG followed a two-step process to draft the recommendations. In the first step, the evidence was summarized, and quality of evidence assessed for all the questions. Following this, the GDG considered factors like summary and quality of evidence, balance between benefits and harms, values and preferences of policymakers, health care providers and parents, feasibility and resource use, and costs and benefits involved. On the basis of the above considerations, the GDG additionally provided a judgment on the strength of each recommendation, to be categorized as *strong* or *weak*. In some circumstances, recommendations may apply only if specific conditions are met, and had categorized them as context-specific recommendations.

Although the degree of confidence is a continuum, the GRADE system defines two categories: ***strong*** and ***weak***.

- A *strong* recommendation is one for which the panel is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects. This can be either in favor of or against an intervention.
- A *weak* recommendation is one for which the panel concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, but the panel is not confident about these trade-offs. Reasons for not being confident can include:
    - Absence of high-quality evidence
    - Presence of imprecise estimates of benefits or harms
    - Uncertainty or variation in how different individuals value the outcomes
    - Small benefits
    - The benefits may not be worth the costs (including the costs of implementing the recommendation).

Despite the lack of a precise threshold between a strong and a weak recommendation, the presence of important concerns about one or more of the above reasons makes a weak recommendation more likely. In addition, some of the recommendations were *context-specific*, i.e. some recommendations, be strong or weak, might not be applicable in all settings.

Implications of a strong recommendation are as follows:

- For patients: most people in this situation would want the recommended course of action and only a small proportion would not.
- For clinicians: most patients should receive the recommended course of action. Adherence to this recommendation is a reasonable measure for good quality care.
- For policy makers: the recommendation can be adopted as a policy in most situations. Quality initiatives could use this recommendation to measure variations in quality.

Implications of a weak recommendation are as follows:

- For patients: the majority of people in this situation would want the recommended course of action, but many would not.
- For clinicians: be prepared to help patients to make a decision that is consistent with their own values.
- For policy makers: there is a need for substantial debate and involvement of stake-holders.

Questions, Evidence summary and Recommendations

Practice question 1: Does implementation and sustenance of clean birth practices in the delivery room reduce the risk of infection in neonates?

Summary of evidence- Values and benefits

Table 2 enlists the effect size for the available key outcomes for the comparison of interventions:

1. Neonatal mortality: A total of 3 observational studies (2-4) addressed this outcome and the evidence has very low certainty. Serious risk of bias was observed as well as very serious rating for imprecision. Neonatal mortality was 49 fewer per 1000 deliveries where clean birth practices were implemented.
2. Neonatal sepsis: Only one observational study (5) was identified which has assessed this outcome. The evidence has very low certainty. Serious risk of bias was observed as well as very serious rating for imprecision. Neonatal sepsis was 110 fewer per 1000 deliveries where clean birth practices were implemented with a very wide confidence interval.
3. Long-term Neurodevelopmental outcome (18-24 months): None of the studies have assessed this outcome.
4. Need for oxygen by 36 weeks PMA: None of the studies have assessed this outcome.
5. Need for neonatal intensive care admission: None of the studies have assessed this outcome.

While clean birth and immediate care is widely accepted, there is very low certainty evidence for the effect of these interventions especially in low-income settings on neonatal mortality and neonatal sepsis. However, since there is strong biological plausibility and given that clean practices are an accepted standard of care, the GRADE recommendation is strong.

Table 2: Practicing clean birth practices in delivery room compared to not practicing in prevention or reduction of neonatal infections

Patient or population: prevention or reduction of neonatal infections
Setting: Health facility
Intervention: practising clean birth practices in delivery room
Comparison: not practising

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with not practising	**Risk with practising clean birth practices in delivery room**			
Neonatal sepsis	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(0 studies)	-
Invasive infection (any organism)	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(0 studies)	-
Mortality	91 per 1,000	**79 per 1,000** (68 to 94)	**RR 0.87** (0.75 to 1.03)	41133 (3 observational studies)	⊕◯◯◯ VERY LOW [a,b]
Mortality - Low or middle income	475 per 1,000	**389 per 1,000** (328 to 465)	**RR 0.82** (0.69 to 0.98)	535 (0 studies)	-
Long term neurodevelopment outcome (18-24 months) follow up: mean 2 years	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(studies)	-
Need for neonatal intensive care admission	0 per 1,000	**0 per 1,000** (0 to 0)	not estimable	(studies)	-

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

Explanations : a. Multiple interventions and confounding bias b. Statistical heterogeneity

RECOMMENDATION 1

Asepsis should be maintained during the birthing process by following the clean birth practices.

Strong recommendation, Very low certainty of evidence

Practice question 2: Among pregnant women with leaking membranes and are at risk of preterm birth, does administration of antibiotics versus no antibiotics/placebo reduce the risk of neonatal infections and other major outcomes?

Summary of evidence- Values and benefits

Table 3 enlists the effect size for the available key outcomes for the comparison of interventions:

1. Perinatal death / death before discharge: A total of 12 randomized trials (6) addressed this outcome and the evidence has moderate certainty. Serious risk of bias was observed for imprecision. Even though there seemed to be trend in reduction of perinatal death, the effect was not statistically significant.
2. Neonatal infections including pneumonia: A total of 12 randomized trials (6) addressed this outcome. There was a 33%reduction in the risk of neonatal infections including pneumonia with 54 fewer cases of the outcome for every 1000 pregnant women treated with antibiotics.
3. Major cerebral abnormalities on ultrasound before discharge: A total of 12 randomized trials (6) addressed this outcome. There was a 19% reduction in the risk of this outcome, which was statistically significant. There were 18 fewer neonates with major cerebral USG abnormalities for every 1000 pregnant women treated with antibiotics
4. None of the critical rated neonatal outcomes were observed to have a significant impact on administering antibiotics to pregnant women

Table 3: Antibiotics compared to No antibiotics or placebo for pregnant women at risk of preterm birth and with ruptured membranes

Patient or population: pregnant women at risk of preterm birth and with ruptured membranes
Setting: Hospital
Intervention: Antibiotics
Comparison: No antibiotics or placebo

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with No antibiotics or placebo	**Risk with Antibiotics**			
Perinatal death/death before discharge - Any antibiotic versus placebo	69 per 1,000	**65 per 1,000** (53 to 79)	**RR 0.93** (0.76 to 1.14)	6301 (12 RCTs)	⊕⊕⊕◯ MODERATE [a]
Neonatal infection including pneumonia - Any antibiotic versus placebo	165 per 1,000	**110 per 1,000** (86 to 140)	**RR 0.67** (0.52 to 0.85)	1680 (12 RCTs)	⊕⊕⊕⊕ HIGH
Chorioamnionitis	247 per 1,000	**163 per 1,000** (114 to 238)	**RR 0.66** (0.46 to 0.96)	1559 (11 RCTs)	⊕⊕⊕⊕ HIGH

Table 3: Antibiotics compared to No antibiotics or placebo for pregnant women at risk of preterm birth and with ruptured membranes

Patient or population: pregnant women at risk of preterm birth and with ruptured membranes
Setting: Hospital
Intervention: Antibiotics
Comparison: No antibiotics or placebo

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with No antibiotics or placebo	**Risk with Antibiotics**			
Neonatal intensive care	730 per 1,000	**715 per 1,000** (613 to 825)	**RR 0.98** (0.84 to 1.13)	5023 (4 RCTs)	⊕⊕⊕◯ MODERATE [b]
Days in neonatal intensive care unit	The mean days in neonatal intensive care unit was **0**	MD **5.05 lower** (9.77 lower to 0.33 lower)	-	225 (3 RCTs)	⊕⊕◯◯ LOW [c,d]
Positive neonatal blood culture	80 per 1,000	**63 per 1,000** (50 to 79)	**RR 0.79** (0.63 to 0.99)	4961 (3 RCTs)	⊕⊕⊕⊕ HIGH
Perinatal death/death before discharge - Antibiotics versus no antibiotics (all studies)	76 per 1,000	**67 per 1,000** (56 to 82)	**RR 0.89** (0.74 to 1.08)	6872 (18 RCTs)	⊕⊕⊕◯ MODERATE [a]

***The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio; MD: Mean difference

Explanations
a. Wide confidence intervals crossing the line of no-effect
b. Statistical heterogeneity (I2 was > 60%)
c. half the weightage came from a single study which has design limitations
d. Estimate based on small sample size

RECOMMENDATION 2

Pregnant women with preterm premature rupture of membranes should be prescribed antibiotics.

Strong recommendation, High certainty of evidence

Practice question 3 : What is the effect of interventions to improve hand hygiene in Neonatal units on Hand hygiene compliance(HHC) , infection rates and mortality?

Summary of evidence- Values and benefits

Table 4 enlists the effect size for the available key outcomes for the comparison of interventions to improve HHC vs. no interventions to improve HHC.

1. ***Hand hygiene compliance:*** Twenty-one studies (7-20) involving 63,930 observations of hand hygiene reported this outcome. The quality of evidence was graded as *low*. There was a significant increase in the compliance to hand hygiene compliance before and during/after the intervention (RR 1.42; 95% CI 1.40 to 1.44). The number of properly performed hand hygiene events increased by 187 more per 1,000 (from 179 more to 196 more)
2. ***Hospital acquired infections:*** Eight studies (7, 9, 12, 14) reported this outcome. The number of neonates involved is not mentioned, and data was reported as infection rates per 1,000 patient days**.** The quality of evidence was graded as *high*. The risk of having an infection significantly decreased (RR 0.57; 95% CI: 0.45 to 0.71). The infection rates during intervention and post-intervention periods decreased by 11 per 1,000 patient days (95% CI: 7, 14).
3. ***In-hospital mortality:*** Two studies (7, 14) involving 3,028 neonates and 3 neonatal units reported this outcome. The quality of evidence was graded as *high*. There was significant decrease in mortality during/after the interventions (RR: 0.54; 95% CI: 0.48 to 0.61). The neonatal deaths have decreased by 162 per 1,000 neonates (95% CI: 138, 183)

Table 4: Interventions to improve hand hygiene compliance (HHC) compared to no interventions for improving HHC in neonatal units

Patient or population: improving HHC in neonatal units
Setting: Hospital
Intervention: interventions to improve hand hygiene compliance (HHC)
Comparison: no interventions

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with no interventions	**Risk with interventions to improve hand hygiene compliance (HHC)**			
HHC compliance	446 per 1,000	**634 per 1,000** (625 to 643)	**RR 1.42** (1.40 to 1.44)	63930 (21 observational studies)	⊕⊕◯◯ LOW [a,b]
Infection rates per 1,000 patient days (all)	25 per 1,000	**14 per 1,000** (11 to 18)	**RR 0.57** (0.45 to 0.71)	16000 (8 observational studies)	⊕⊕⊕⊕ HIGH
Mortality	353 per 1,000	**190 per 1,000** (169 to 215)	**RR 0.54** (0.48 to 0.61)	3028 (2 observational studies)	⊕⊕⊕⊕ HIGH

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds ratio; **RR:** Risk ratio

Explanations
a. The I2 value is 97% indicating unexplained heterogeneity
b. In the funnel plot, most of the studies are seen outside the funnel region, and studies with small sample size are inappropriately low

RECOMMENDATION 3

Regular system-based and behavioral interventions should be undertaken to improve compliance to hand hygiene.

Strong recommendation , High quality of evidence

Practice question 4 : What is the effect of using hand rub (alcohol based) versus hand wash for hand hygiene in Neonatal units on infection rates and mortality?

Summary of evidence- Values and benefits

Table 5 enlists the effect size for the available key outcomes for the comparison of aseptic non-touch technique with routine care.

1. ***HAI rates:*** One study in NICU (21) has measured infection rates. The infection rates were not different in both the groups, with 9.5 episodes per 1,000 patient days noted in hand washing period compared to 12.1 episodes per 1,000 patient days in hand rub period. The number of neonatal admissions in hand washing period was 1,516 and hand rub period were 1,416.
2. ***CLABSI rates:*** One study in NICU (21) has measured central line associated infection rates. The infection rates were 14.8 episodes per 1,000 central venous catheter days in hand washing period compared to 18.2 episodes per 1,000 central venous catheter days. The number of neonatal admissions in hand washing period was 1,516 and hand rub period were 1,416.
3. ***VAP rates:*** One observational study (21) has shown that ventilator associated pneumonia rates were 1.7 per 1,000 ventilation days in hand washing period and 2.2 per 1,000 patient days in hand rub period. The number of neonatal admissions in hand washing period was 1,516 and hand rub period were 1,416.
4. ***In-hospital mortality:*** None of the studies have reported this outcome
5. ***Duration of hospital stay:*** None of the studies have reported this outcome
6. ***Hand hygiene compliance:*** None of the studies have reported this outcome
7. ***Adverse effects related to hand hygiene:*** One observational study (22) has studied self-reported and observer assessed skin condition. Hand rubs were shown to have better scores in both the ways, indicating lesser adverse effects with hand rubs.
8. ***Bacterial load reduction:*** One observational study (23) has shown that mean bacterial counts (log_{10}) reduced from 3.47 to 3.11 in hand washing period, and from 3.47 to 3.21 in hand rub period. Another study has shown that mean CFU (geometric mean) reduced from 61 (44-85) to 16 (10-25) for palm and from 66 (47-93) to 12 (7-18) for fingertips with hand washing. With hand rub, it reduced from 66 (43-101) to 2 (1-3) for palm and 61 (40-93) to 2 (1-3) for fingertips. The third study has shown 33.3% reduction in median CFU with hand wash and 92% reduction with hand rub. Although the data cannot be pooled, hand rub has higher reduction in bacterial load as compared to hand wash.

Table 5: Hand Rub compared to Hand Wash in in neonates for prevention of infections

Patient or population: in neonates for prevention of infections
Setting: Neonatal units
Intervention: Hand Rub
Comparison: Hand Wash

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with Hand Wash	**Risk with Hand Rub**			
Hospital acquired infections (HAI) assessed with: culture	10 per 1,000	**9 per 1,000** (7 to 12)	**OR 0.98** (0.77 to 1.25)	51760 (1 observational study)	⊕⊕⊕◯ MODERATE [a]
Central line associated blood stream infections (CLABSI) assessed with: culture	15 per 1,000	**15 per 1,000** (11 to 20)	**OR 0.99** (0.77 to 1.33)	17999 (1 observational study)	⊕⊕⊕◯ MODERATE [a]
Ventilator associated pneumonia (VAP) assessed with: culture	2 per 1,000	**3 per 1,000** (1 to 9)	**OR 1.61** (0.55 to 5.44)	8514 (1 observational study)	⊕⊕⊕◯ MODERATE [a]
Bacterial load reduction assessed with: % reduction of CFU	The mean bacterial load reduction was **0**	**0** (0 to 0)	-	125.3 (1 observational study)	⊕⊕⊕◯ MODERATE [b]

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **OR:** Odds ratio

Explanations a. single study with wide CI b. Single Study on CFUs

RECOMMENDATION 4

Hand hygiene should be practiced either by hand washing or by using alcohol-based hand-rub.

Strong recommendation, very low quality evidence

Hand washing should be followed at the time of entry to neonatal intensive care unit / special newborn care unit or when hands are visibly soiled.

Strong recommendation, Moderate quality evidence

Practice question 5: What is the effect of using aseptic non-touch technique (ANTT) in Neonatal units on infection rates and mortality?

Summary of evidence- Values and benefits

Table 6 enlists the effect size for the available key outcomes for the comparison of aseptic non-touch technique with routine care.

1. ***Hospital Acquired Infection rates***: One study in NICU (24) has measured infection rates. The infection rates decreased from 19.9 episodes per 1,000 patient days to 15.3 episodes per 1,000 patient days.
2. ***CLABSI rates***: Two studies (25, 26) reported this outcome- 1 is a randomized controlled trial and another is a retrospective study. These studies were not conducted in neonates, resulting in indirect evidence. The quality of evidence was graded as *low*. The risk of having a CLABSI was shown to be reduced in the RCT- 10.1/1,000 catheter days to 1.9/1,000 catheter days (p=0.026) and not shown to be different in the retrospective study- 0.46/1,000 catheter days to 1.2/1,000 catheter days (p=0.357).
3. ***In-hospital mortality***: None of the studies have reported this outcome.
4. ***Compliance to ANTT procedures***: Two studies (24, 27) reported this outcome, 1 from neonates and another based on pragmatic evaluation using mixed methods approach. These studies provided low-quality evidence that ANTT training improves pre-procedure hand hygiene, key-part protection, and use of non-touch technique; moderate quality evidence that ANTT training does not improve glove use; and high-quality evidence that ANTT training improved cleaning of key-parts.

Table 6: Aseptic non touch technique (ANTT) compared to routine practices for decreasing HAIs

Patient or population: decreasing HAIs
Setting: neonatal units
Intervention: aseptic non touch technique (ANTT)
Comparison: routine practices

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with routine practices	**Risk with aseptic non touch technique (ANTT)**			
pre-procedure hand hygiene	583 per 1,000	**817 per 1,000** (706 to 951)	**RR 1.40** (1.21 to 1.63)	352 (2 observational studies)	⊕⊕◯◯ LOW [a,b]
correct glove use	677 per 1,000	**758 per 1,000** (670 to 860)	**RR 1.12** (0.99 to 1.27)	352 (2 observational studies)	⊕⊕⊕◯ MODERATE [b]
key-part protection	396 per 1,000	**629 per 1,000** (507 to 784)	**RR 1.59** (1.28 to 1.98)	352 (2 observational studies)	⊕⊕◯◯ LOW [b,c]
non touch technique use	613 per 1,000	**790 per 1,000** (686 to 919)	**RR 1.29** (1.12 to 1.50)	320 (2 observational studies)	⊕⊕◯◯ LOW [b,d]
key-part cleaning	0 per 1,000	**0 per 1,000** (0 to 0)	**RR 59.78** (8.14 to 438.97)	146 (2 observational studies)	⊕⊕⊕⊕ HIGH [b]

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

Explanations a. I2 = 95% b. one of these studies was conducted in a non-neonatal population
c. I2 = 89% d. I2 = 90%

RECOMMENDATION 5

Aseptic non touch technique (ANTT) should be followed during invasive procedures like central or peripheral vascular cannulation , intravenous fluid or medication preparation or administration, endotracheal tube insertion or suction.

Strong recommendation, Moderate quality evidence

Practice question 6: Should CLABSI bundle versus routine care be used for reducing CLABSI in neonates admitted to NICU?

Summary of evidence- Values and benefits

Table 7 enlists the pooled effect of Bundle care on the outcome CLABSI.

1. CLABSI rate using Bundle care: 24 observational studies (28) reported this outcome. The quality of evidence is graded as high. Use of bundle approach reduces the rate of central line associated blood stream infections (**RR 0.40:** 0.31 to 0.51). i.e. **6 fewer per 1,000** (from 7 fewer to 5 fewer).

Table 7: CLABSI bundle approach compared to routine care for decreasing incidence of CLABSI

Patient or population: decreasing incidence of CLABSI
Setting: in NICUs
Intervention: CLABSI bundle approach
Comparison: routine care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with routine care	**Risk with CLABSI bundle approach**			
CLABSI rate (CLABSI rate) assessed with: a standard definition	10 per 1,000	**4 per 1,000** (3 to 5)	**RR 0.40** (0.31 to 0.51)	2000 (24 observational studies)	⊕⊕⊕⊕ HIGH [a]

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

Explanations
a. Estimation of risk of bias in the 5 cohort studies by NewCastle Ottawa scale has shown problems with selection of non-exposed cohort and comparability of controls for NICU care and central line days

RECOMMENDATION 6

Neonatal units should implement Central line insertion and care bundle to reduce catheter-related bloodstream infections.

Strong recommendation, High quality evidence

Practice question 7: Should VAP bundle versus routine care be used for reducing ventilation Associated Pneumonia in neonates admitted to NICU?
Summary of evidence- Values and benefits

The Grade table for this question could not be constructed. The summary of evidence is as follows:

1. **Reduction in VAP rate**
   - Dose response effect was not reported in the four studies evaluated.
   - The effect was large in 2 of the 4 studies with p value <0.001 (29, 30)
   - The effect was more significant when applied to infants at lower gestation as in the study by Pepin 2019 and effect was significantly more when applied to units with high VAP rates.

   As 2 of the 3 criteria for upgrading evidence was present from the eligible studies, for reduction in VAP rates, there is moderate quality evidence from observational studies that VAP bundle reduces VAP rates.

2. **Duration of Mechanical ventilation:** Two of the four studies reported reduction in the days of mechanical ventilation. MV days in VAP cases reduced from 47 to 33 days in the QI study by Pipen et al and 21.50 ± 7.6 days in baseline period to 10.36 ± 5.2 days during the QI period in the study by Azeb et al. The effect size appears reasonable and the effect is more when the duration of baseline is more.
3. **Duration or length of hospital stay:** Two of the four studies reported in a reduction of length of hospital or NICU days with the introduction of VAP bundle.
   Azab et al: Reduction days from 23.9 ± 10.3 versus 22.8 ± 9.6 days with introduction of VAP bundle
   Pipen et al: LOS reduced in VAP cases from 136 to 100 days with introduction of VAP bundle approach
   The effect size appears reasonable and the effect is more when the duration of baseline is more.
4. **Mortality:** Only one study reported reduction in the mortality with the introduction of VAP bundle. (Azeb et al…25 % versus 17.3 %)

RECOMMENDATION 7

Neonatal units should implement Ventilator-associated pneumonia (VAP) prevention bundle in neonates on invasive and non-respiratory support.

Strong recommendation, Not graded

Practice question 8: In neonatal ICUs, does education of health care workers and patients result in reduced HAIs?

Summary of evidence- Values and benefits

Table 8 details the following outcomes:

1. ***Hospital acquired Infections:*** Twelve studies (9, 12, 14, 24, 31-38) reported the effect of health education on hospital-acquired infections. Ten studies showed reduction of HAI with use of various health education techniques. However due to variable expression of outcome measures only 4 studies could be considered for GRADE evaluation. The quality of evidence was graded as low. The risk of having infections did not decrease in presently available data with use of intervention (OR-1.05; 95% CI 0.96 to 1.14).
2. ***Mortality:*** One study (14) assessed the impact of health education on mortality of neonates. The quality of evidence was graded low. The risk of mortality decreased significantly from available evidence (OR-0.58; 95% CI 0.40 to 0.83).

Table 8 : Education of healthcare professionals compared to no education in decreasing neonatal sepsis

Patient or population: decreasing neonatal sepsis **Setting**: in NICUs
Intervention: Health education **Comparison**: no education

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with no education	**Risk with Health education**			
Health Care associated Infection (HAI)(Culture positivity)	141 per 1,000	**147 per 1,000** (136 to 157)	**OR 1.05** (0.96 to 1.14)	18532 (4 observational studies)	⊕⊕◯◯ LOW [a,b]
Mortality	145 per 1,000	**90 per 1,000** (64 to 124)	**OR 0.58** (0.40 to 0.83)	1200 (1 observational study)	⊕⊕◯◯ LOW

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

Explanations a. I2 statistic 92%, considerable heterogeneity.b. Wirtschafter and Helder included VLBW only.

RECOMMENDATION 8

Regular educational activities about prevention of healthcare associated infections should be conducted for healthcare professionals

Strong recommendation, Low quality of evidence

Practice question 9 : In neonatal ICUs, does optimizing nurse: patient ratio decrease the incidence of HAI?

Summary of evidence- Values and benefits

Table 9 enlists the pooled effects of estimates.

1. ***Hospital acquired Infections*****:** Grade Table could not be made for the outcome of Hospital acquired Infection. Seven studies reported the effect of optimal nurse patient ratio on hospital-acquired infections. Two out of the seven included studies have shown significant reduction in HAI with higher nursing patient ratio. However due to variable expression of outcome measures, the GRADE table could not be constructed.
   Rogowski et al (39): Odds of nosocomial infection among VLBWs increased significantly with understaffing [OR-1.39 (95% CI, 1.19–1.62; P < .001)]
   Cimiotti et al (40): Higher number of hours of care provided by registered nurses was associated with a decreased risk of bloodstream infection in these infants (hazard ratio, 0.21; 95% confidence interval, 0.06-0.79)
   Beltempo et al (41): Odd of nosocomial infection did not decrease with high ratio of available to recommended nurses. (OR- 1.16; 95% CI, 0.67–1.99)
   Fischer et al (42): No significant reduction of Health care associated infection with Higher nursing patient ratio (3–4 for 18 patients) against low nursing patient Ratio (4-5 per 22 patient) (4.7% vs. 4.8%).
   Tucker et al (43): Non-significant reduction of HAIs with High nursing provision as compared to low nursing provision. [214/6772 (3%) vs166/6562 (3%)]
   Profit et al (44): Non-significant decrease of odds of nosocomial infection with increase patient nurse ratio.
   Lake et al (45): No significant increase in nosocomial infection with understaffing (OR: 1.04 (0.92–1.19))
2. ***Mortality:*** Two studies (43, 46) assessed impact of optimal nurse patient ratio on mortality of neonates. The quality of evidence was graded very low. The risk of mortality decreased non-significantly from available studies (OR-0.95; 95% CI 0.77 to 1.17).

Table 9: Higher nurse: patient ratio compared to standard ratio for preventing infection in preterm infants

Patient or population: preventing infection in preterm infants
Setting: Hospital
Intervention: Higher nurse: patient ratio
Comparison: standard ratio

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with standard ratio	**Risk with Higher nurse: patient ratio**			
Hospital acquired infections (HAI) assessed with: blood culture	32 per 1,000	**25 per 1,000** (21 to 31)	**OR 0.80** (0.65 to 0.98)	13334 (1 observational study)	⊕⊕◯◯ LOW
Mortality (Mortality)	28 per 1,000	**26 per 1,000** (21 to 32)	**OR 0.95** (0.77 to 1.17)	13796 (2 observational studies)	⊕◯◯◯ VERY LOW a,b,c

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **OR:** Odds ratio

Explanations
a. Wide variance in OR across the two studies. I2 statistic – 85%.
b. Callaghan 2002 has included VLBW infants only
c. Wide OR

RECOMMENDATION 9

Optimum nurse-patient ratio should be ensured in neonatal units to prevent healthcare associated infections.

Strong recommendation, Low quality evidence

Practice question 10 : In neonatal units, does adherence to antibiotic stewardship policies result in decreased incidence of HAIs?

Summary of evidence- Values and benefits

Table 10 enlists the effect size for available key outcomes with the use of antibiotic stewardship programs in NICU.

1. ***Hospital acquired Infections:*** 3 studies (47, 48, 49) reported effect of antibiotic stewardship on HAI. The quality of evidence was graded as very low. The risk of having infections decreased (OR-0.80; 95% CI 0.63 to1.03). The infection rates during intervention and post intervention periods decreased by 9 per 1000 patient days (95% CI; 1, 18).
2. ***Antibiotics Usage:*** 6 studies (47-53) assessed the antibiotic usage rate when antibiotic stewardship is used. However data could be pooled only for 2 studies, which showed moderate quality of evidence. The antibiotic usage rate reduced significantly (OR 0.8; 95% CI 0.69 to 0.93). The usage rate during the intervention decreased by 54 per 1000 (from 90 fewer to 17 fewer).
3. ***Mortality:*** None of the studies assessed mortality rate with use of intervention.

Table 10 : Antibiotic stewardship program compared to routine care for decreasing HAIs

Patient or population: decreasing HAIs **Setting**: in NICUs
Intervention: antibiotic stewardship program **Comparison**: routine care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with routine care	**Risk with antibiotic stewardship program**			
Health Care Associated Infection (HAI) (Culture positivity)	49 per 1,000	**40 per 1,000** (32 to 51)	**OR 0.80** (0.63 to 1.03)	7408 (3 observational studies)	⊕◯◯◯ VERY LOW [a]
Antibiotic Usage (Antibiotic prescribed per admission)	622 per 1,000	**569 per 1,000** (532 to 605)	**OR 0.80** (0.69 to 0.93)	2857 (2 observational studies)	⊕⊕⊕◯ MODERATE [b]

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

Explanation a. CI crosses the clinical decision threshold b. I2 statistic – 62%

RECOMMENDATION 10

Regular antibiotic stewardship program should be implemented in neonatal units.

Strong recommendation, Moderate quality of evidence

Practice question 11: In neonatal units, does routine environmental surveillance as compared to no surveillance decreases HAI?

Summary of evidence- Values and benefits

We could not find any eligible studies. Table 11 summarizes the guidelines from Center for Disease Control, USA and the Healthcare Infection Control Practices Advisory Committee.

Table 11: Summary of CDC and HICPAC guidelines about environmental surveillance(54)

S.No.	Recommendation	Category
1	Do not conduct random, undirected microbiologic sampling of air, water, and environmental surfaces in health-care facilities	I B
2	When indicated, conduct microbiologic sampling as part of an epidemiologic investigation or during assessment of hazardous environmental conditions to detect contamination and verify abatement of a hazard.	I B
3	Limit microbiologic sampling for quality assurance purposes to • Biological monitoring of sterilization processes; • Monthly cultures of water and dialysate in hemodialysis units; • Short-term evaluation of the impact of infection-control measures or changes in infection- control protocols.	I B

IB – Strongly recommended for implementation and supported by certain experimental, clinical, or epidemiologic studies and a strong theoretical rationale

Microbiologic sampling of air, water, and inanimate surfaces (i.e., environmental sampling) is an expensive and time-consuming process that is complicated by many variables in protocol, analysis, and interpretation. It is therefore indicated for only four situations:

1. Outbreak investigation
2. Research setting
3. Potentially hazardous environmental condition
4. Quality assurance of a sterile process

RECOMMENDATION 11

Routine environmental surveillance cultures should not be done in neonatal unit. Surveillance cultures should be taken only for (i) outbreak investigation, (ii) specific research question, (iii) potentially hazardous environmental condition, and (iv) quality assurance of a sterile process

Strong Conditional recommendation, Not graded

Practice question 12: In neonatal units, does organism specific surveillance help in reducing HAI?

Summary of evidence- Values and benefits

Table 12 depicts the comparison of organism specific surveillance vs no surveillance.

1. ***Hospital acquired Infections:*** 4 studies (55-58) reported the effect of organism specific surveillance on hospital-acquired infections. The quality of evidence was rated very low. The hospital acquired infections decreased (OR 0.58; 95% CI: 0.45 to 0.75). The HAI decreased by 1 per 1,000 patient days during the surveillance period (from 2 fewer to 1 fewer)
2. ***Blood stream infections:*** Only 1 study (59) reported the effect of organism specific surveillance on rates of BSI. The quality of evidence was rated as very low. There was no effect on rates of BSI (OR 1.28; 95% CI: 0.44 to 3.70).
3. ***Mortality:*** Organism specific surveillance for MSSA and MRSA has shown benefits in reducing HAI (RR: 0.58; 95% CI: 0.45-0.76) and clinical acquisition (colonization during hospital stay) (0.55; 0.43-0.76). It was not able to demonstrate any effects in reducing mortality and BSI rate (59). Studies didn't show any increase in antibiotic resistance pattern due to treatment of colonized infants with topical therapy. The quality of evidence was graded as low.
4. ***Colonization:*** 2 studies (55, 56) reported the effect of organism specific surveillance on colonization rates. The quality of evidence was graded as low. The colonization rates were significantly lower in the surveillance period (OR- 0.54; 95% CI 0.41 to 0.72). The colonization decreased by 8 per 1,000 neonatal admissions (from 10 fewer to 5 fewer).

Organism specific surveillance requires personnel, adequate infrastructure changes in the form of isolation rooms and lab facilities. The surveillance results will guide better cohorting of patients, however it is associated with costs. Implementation of sufficient isolation facilities for colonized neonates is unlikely to be possible in overcrowded facilities.

Table 12: Organism specific surveillance compared to No surveillance for reducing HAI in NICU

Patient or population: decreasing HAIs
Setting: in NICUs
Intervention: Organism specific surveillance
Comparison: routine care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with routine care	**Risk with antibiotic stewardship program**			
Mortality	0 per 1,000	0 per 1,000 (0 to 0)	not estimable	3092 (1 observational study)	⊕⊕◯◯ LOW [a,b]
Colonization rates	17 per 1,000	9 per 1,000 (7 to 13)	**OR 0.54** (0.41 to 0.72)	18823 (2 observational studies)	⊕⊕◯◯ LOW [c,d,e,f]
HAI	3 per 1,000	2 per 1,000 (1 to 2)	**OR 0.58** (0.45 to 0.75)	99518 (4 observational studies)	⊕◯◯◯ VERY LOW [a,g,h,i,j]
BSI	4 per 1,000	5 per 1,000 (2 to 15)	**OR 1.28** (0.44 to 3.70)	3088 (1 observational study)	⊕◯◯◯ VERY LOW [b,l,k]

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **OR:** Odds ratio

Explanations: a. NNT very high b. Only one study included c. Both studies have not compared the profile of patients. Mean patient days were more during intervention periods in Geraci et al. study d. Wide variation in RR intervals though heterogeneity is less. e. Both studies involved other QI strategies to decrease colonization. f. Only 2 studies were included. Other strategies were also used simultaneously. g. In Wisgrill et al. study only VLBW neonates were included. Two studies were done as QI projects, others were pre and post intervention analysis. Difference in profile of patients were not mentioned in Bhardwaj et al, Geraci et al and Popola et al. study. No exclusion criteria were mentioned across studies. h. Wide variation of RRs is seen. Overlapping CIs seen. I2 statistic – 74% i. Wisgrill et al. included only VLBW and screened for MSSA also. Screening areas are different. Outcomes measures are direct only and similar. j. Only 4 studies are included k. Not provided patient days. They only provided number of patients during the period. l. Wide RR interval.

RECOMMENDATION 12

Routine organism- specific surveillance is unlikely to be beneficial in overcrowded and busy facilities. *It may have some utility in set-ups with adequate isolation and lab facilities*.

Weak Conditional recommendation, Low quality of evidence

Abbreviations

ANTT Aseptic non-touch technique	ASP Antibiotic stewardship policy	BAPM British Association of Perinatal Medicine
BPD Bronchopulmonary dysplasia	BSI Blood stream infection	CDC Centre for Disease Control, USA
CI Confidence interval	CLABSI Central line associated blood stream infection	CLD Chronic lung disease
CPAP Continuous positive airway pressure	CPG Clinical practice guidelines	ELBW Extremely low birth weight
EOS Early onset sepsis	ES Effect size	ET Endotracheal tube
GDG Guideline development group	GRADE Grading of Recommendations, Assessment, Development, and Evaluation	HAI Healthcare associated infections
HH Hand Hygiene	HHC Hand hygiene compliance	HICPAC Healthcare Infection Control Practices Advisory Committee
IV Intravenous	LBW Low birth weight	LMIC Low and middle income countries
LOS Late onset sepsis	MD Mean difference	MRSA Methicillin resistant Staphylococcus aureus
MSSA Methicillin sensitive Staphylococcus aureus	NIH National Institute for Health	NOS NewCastle Ottawa scale
OR Odds ratio	PICO Population, intervention, comparison, outcome	PMA Post menstrual age
QALY Quality-adjusted life year	PROM Pre-labour rupture of membranes	PVC Peripheral venous cannula
RR Relative risk	SQUIRE Standards for Quality Improvement Reporting Excellence	VAP ventilator associated pneumonia
VLBW Very low birth weight	WHO World Health Organization	WMD Weighted mean difference

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