Appendix:
Recommendations for Prevention and Control of *Staphylococcus aureus* Infections in Neonatal Intensive Care Unit Patients.

Table of Contents

Tables

Tables

1. Search Strategies and Results

1.A. Guideline Search Strategy

Table 1 Guideline Search of MEDLINE (April 2011)

#	Search History	Results
1	exp Methicillin-Resistant *Staphylococcus aureus*/	1745
2	exp Methicillin Resistance/	8870
3	exp *Staphylococcus aureus*/	38196
4	2 and 3	7359
5	1 or 4	8950
6	limit 5 to ((guideline or practice guideline) and systematic reviews)	17
7	limit 6 to (English language and humans)	11

Table 2 Infection Control Guideline Websites Searched (April 2011)

Organization	Website browsed or keyword(s) used	Results
National Guideline Clearinghouse (NGC)	methicillin-resistant *Staphylococcus aureus*	28
American Academy of Pediatrics (AAP)	http://pediatrics.aappublications.org/site/aappolicy/index.xhtml	10
Association for Professionals in Infection Control and Epidemiology (APIC)	http://www.apic.org	2
Centers for Disease Control and Prevention	https://www.cdc.gov/infectioncontrol/guidelines/index.html	3
Infectious Diseases Society of America (IDSA)	http://www.idsociety.org	0
National Institute for Health and Clinical Excellence (NICE)	http://guidance.nice.org.uk	0
Scottish Intercollegiate Guidelines Network (SIGN)	http://sign.ac.uk/guidelines/index.html	0
Society for Healthcare Epidemiology of America (SHEA)	http://www.shea-online.org	3

1.B. Primary Search Strategies of Databases: Methicillin-sensitive *Staphylococcus aureus*: August 3, 2019

Table 3 Primary Search of MEDLINE

#	Search History	Results
1	exp *Staphylococcus aureus*/	69205
2	exp Intensive Care Units, Neonatal/ or exp Intensive Care, Neonatal/	17158
3	exp Infant, Newborn/	604484
4	2 or 3	605835
5	1 and 4	1809
6	limit 5 to (english language and humans)	1544

Table 4 Primary Search of EMBASE

#	Search History	Results
1	Exp S*taphylococcus aureus*/	124877
2	Exp newborn intensive care/ or exp newborn/	390937
3	1 and 2	2796
4	Limit 3 to exclude medline journals	332
5	Limit 4 to (english language and humans)	243

Table 5 Primary Search of Cochrane Library

#	Search History	Results
1	MeSH descriptor *Staphylococcus aureus* explode all trees	845
2	MeSH descriptor Intensive Care Units, Neonatal explode all trees	602
3	MeSH descriptor Intensive Care, Neonatal explode all trees	314
4	MeSH descriptor Infant, Newborn explode all trees	14862
5	2 or 3 or 4	14906
6	1 and 5	25
7		0

Table 6 Primary Search of CINAHL

#	Search History	Results
1	*Staphylococcus aureus*	31
2	(MH "Infant, Newborn+") or (MH "Intensive Care Units, Neonatal") or (MH "Intensive Care, Neonatal+")	74055
3	1 and 2	4
4	Limit 4 to (english language; exclude MEDLINE records)	1

1.C. Primary Search Strategies of Databases: Methicillin-resistant *Staphylococcus aureus* August 3, 2019

Table 7 Primary Search of MEDLINE

#	Search History	Results
1	exp Methicillin-Resistant *Staphylococcus aureus*/	2342
2	exp Methicillin Resistance/	9013
3	exp *Staphylococcus aureus*/	39584
4	2 and 3	7474
5	1 or 4	9621
6	exp Intensive Care Units, Neonatal/ or exp Intensive Care, Neonatal/	10498
7	exp Infant, Newborn/	440526
8	6 or 7	441265
9	5 and 8	388
10	limit 9 to (english language and humans)	355

Table 8 Primary Search of EMBASE

#	Search History	Results
1	'methicillin resistant *Staphylococcus aureus'*/exp or 'methicillin resistant *Staphylococcus aureus* infection'/exp	17442
2	*'Staphylococcus aureus'*/exp	65872
3	'antibiotic resistance'/exp	89620
4	2 and 3	8464
5	'methicillin'/exp or methicillin and resistance	16163
6	'newborn intensive care'/exp or 'newborn'/exp	435744
7	1 or 4 or 5	29993
8	6 and 7	656
9	Limit 8 to (english language and humans)	485

Table 9 Primary Search of Cochrane Library

#	Search History	Results
1	MeSH descriptor Methicillin-Resistant *Staphylococcus aureus* explode all trees	47
2	MeSH descriptor Methicillin Resistance explode all trees	208
3	MeSH descriptor *Staphylococcus aureus* explode all trees	588
4	2 and 3	157
5	1 or 4	203
6	MeSH descriptor Intensive Care Units, Neonatal explode all trees	401
7	MeSH descriptor Intensive Care, Neonatal explode all trees	253
8	MeSH descriptor Infant, Newborn explode all trees	11220
9	6 or 7 or 8	11252
10	5 and 9	4

Table 10 Primary Search of CINAHL

#	Search History	Results
1	MH "Methicillin-Resistant *Staphylococcus aureus*"	280
2	(MH "Methicillin-Resistant *Staphylococcus aureus*") and (MH "Staphylococcal Infections+")	162
3	1 or 2	280
4	(MH "Infant, Newborn+") or (MH "Intensive Care Units, Neonatal") or (MH "Intensive Care, Neonatal+")	50951
5	3 and 4	9
6	Limit 5 to (english language; exclude MEDLINE records)	0

2. Study Exclusion Criteria

Criteria for excluding studies from the literature review include:

1. Not relevant to key questions
2. Not primary research
3. A meeting abstract only
4. Not available as full text
5. Not in English
6. Not 100% NICU infants or had no NICU subgroup analysis
7. Methods papers on HAI surveillance only (not about *S. aureus,* MRSA, or MSSA interventions to prevent or control colonization, infection, or disease)
8. Studies of only community-acquired or community-onset infections not involving NICU patients. Included studies in which evidence that infections acquired in NICU but strains common in the community were likely acquired from HCP or visitor or new admits to NICU (CA or 300)
9. Studies with N<10 unless study describing transmission from family caregiver to baby
10. Case reports of single site infections (e.g. periorbital cellulitis)
11. Studies only examining treatments for *S. aureus,* MRSA, or MSSA
12. Molecular epidemiology studies of *S. aureus*, MRSA, or MSSA without any clinical patient information
13. Studies examining Japanese neonatal toxic-shock entity (only reported in Japan)
14. Studies with only endocarditis as a reported clinical outcome
15. For Key Question 2.1.A., Studies examining interventions of any kind (single or multi-intervention) unless they provide a clear description of the interventions and statistical analysis comparing time points before and after intervention
16. For Key Question 2.1.B., studies of *S. aureus*, MRSA, or MSSA test performance did not report test characteristics (e.g. SN, SP, PPV, NPV, LRs)
17. For Key Question 2.2.A and 2.2.B., single group studies (i.e. case series) without a comparison group
18. Other

3. Evidence Review

3.A. Summary of Evidence: Interventions to Prevent *S. aureus* Transmission

Key Question 1.A What are effective strategies for preventing *S. aureus* transmission from colonized or infected NICU infants to other patients, and do these strategies differ between MRSA and MSSA or in the setting of an outbreak?

Key Question 1. .B. If active surveillance is conducted, which anatomic sampling sites and laboratory assays most effectively identify *S. aureus* colonization in NICU patients?

3.A.1. Strength of Evidence

3.A.1.a. Multi-Intervention Strategies

Table 11 Strength of Evidence for Implementing Multi-intervention Strategies to Prevent *S. aureus* Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
S. aureus infection*	• 5 observational non-outbreak studies[1-5] reported a reduction in infections after implementing multi-intervention infection prevention and control strategies. Each of these 5 studies implemented decolonization strategies in addition to infection prevention and control measures. ○ One study[1] (N=6283) found a reduction in *S. aureus* infection rate between the beginning and end of the intervention period: 1.42/ 1000 patient days vs. 0.33/1000 patient days; IRR 0.29 (95% CI: 0.166 to 0.512); p<0.0001. ○ One study[2] (N=NR) and saw significant reductions in infection and the eradication of the endemic strain: MRSA incidence density ratio: 0.11 (95% CI: 0.01-0.46) p<0.001. ○ One study[3] (N=NR) found a significant reduction in the trend of MRSA infections: p= 0.04 ○ One study[4] (N=NR) reported a significant reduction in MSSA bacteremia rate/ 1000 admissions between the last 2 years of a 6-year study: 13.63 vs. 6.8; p=0.036 ○ One study[5] (N=1847) reported a significant reduction in *S. aureus* infections: IRR: 0.57 (95% CI 0.40 – 0.80); p=NR. • 2 observational non-outbreak studies[6,7] reported no change in infection incidence or rate. ○ One study[6] (N=722) saw no change in the rate of clinical infections over 3 years: 5.2/1000 patient days vs. 6.5/1000 patient days vs. 4.9/1000 patient-days p=0.48; however, results were confounded by overcrowding and the introduction of a new MRSA strain.	7 OBS[1-7]	Low

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
	○ One study[7] (N=3088) found no difference in the MRSA-related BSI rate between the intervention and control periods: 3.8/1000 patient admissions vs. 5.3/1000 patient admissions; p=0.73 • The combination of interventions for each strategy and the outcome measures were heterogeneous across studies.		
S. aureus colonization	• One observational non-outbreak study[2] (N=NR) reported reductions in *S. aureus* colonization following the implementation of multi-intervention infection prevention and control strategies. • 2 observational non-outbreak studies[6,8] suggested inconsistent reductions in *S. aureus* colonization following the implementation of multiple infection prevention and control strategies. ○ One study[6] (N=722) found a reduction in mean weekly colonization pressure following the introduction of a multi-intervention strategy: Year 1 vs. year 2, p=0.04; however this reduction was not sustained through the introduction of a new strain and a period of overcrowding: Year 1 vs. year 3, p: 0.76; Year 2 vs. year 3, p=0.48 ○ One study[8] (N= 1827) found no change in MRSA new colonization incidence density per 1000 NICU days at risk in NICU I (68.3 vs. 79.3; p=0.54); while NICU II experienced a significant reduction in MRSA (205.8 vs. 0.0; p<.001). However, NICU II also experienced an almost 50% reduction in admissions and both NICUs experienced an increase in hand hygiene compliance during this time. The strategy implemented was a general infection prevention and control strategy and not targeted specifically to *S. aureus* or MRSA.	3 OBS[2,6,8]	Low
S. aureus transmission	• 2 outbreak studies[9,10] reported reductions in MRSA transmission following implementation of multiple infection prevention and control strategies. ○ One outbreak study[9] (N=NR) noted a reduction in the number of MRSA acquisitions/ total days spent by MRSA (+) infants during each month when comparing the 10 months before the intervention with the 5 months after: 0.0729 vs. 0.0241; p=0.013 ○ One outbreak study[10] (N=331) reported a significantly lower risk of MRSA transmission from patients on contact precautions compared with those not on contact precautions: 0.0090/ day vs. 0.140/ day; RR: 15.6 (95% CI 5.3-45.6), p< 0.0001 ▪ Contact precautions were defined as use of gown, gloves, and mask for direct patient contact that was standard of care at the time of the study.	2 OBS[9,10]	Low
Unadjusted length of stay (median)	• One observational non-outbreak study[7] (N=3088) reported no difference in the unadjusted median length of stay between pre and post-intervention time periods: 77 days (26.2-120.0) vs. 62.5 days (39.0-107.5); p=0.94	1 OBS[7] (Kaushik)	Very Low • Imprecise: only 1 study

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
Attributable mortality	• One observational non-outbreak study[7] (N=3088) reported no difference in MRSA-related mortality between pre and post-intervention periods. 0 vs. 1; p>0.999	1 OBS[7] (Kaushik)	Very Low • Imprecise: only 1 study
Mupirocin resistance	• One observational non-outbreak[1] (N=6283) study reported that none of the 19 isolates tested were resistant to mupirocin.	1 OBS (Delaney)	Very Low • Imprecise: only 1 study

Table 12 Strength of Evidence for Implementing Multi-intervention Strategies to Prevent MRSA Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
MRSA infection*	• 2 observational non-outbreak studies[2,3] reported a reduction in MRSA infections implementing multi-intervention strategies to control MRSA. Both studies additionally implemented decolonization strategies when other interventions were unable to reduce MRSA transmission. ○ One study[2] (N=NR) saw significant reductions in infection and the eradication of the endemic strain: MRSA incidence density ratio: 0.11 (95% CI: 0.01-0.46) p<0.001 ○ One study[3] (N=NR) found a significant reduction in the trend of MRSA infections (p=0.04). • 2 observational non-outbreak studies[6,7] reported no change in infection incidence or rate. These studies did not implement decolonization strategies. ○ One study[6] (N=722) saw no change in the rate of infections over 3 years: 5.2/1000 patient-days vs. 6.5/1000 patient-days vs. 4.9/1000 patient-days, p=0.48; however, results were confounded by overcrowding and the introduction of a new MRSA strain. ○ One study[7] (N=3088) found no difference in the MRSA-related BSI rate between the intervention and control periods: 3.8/1000 patient admissions vs. 5.3/1000 patient admissions; p=0.73	4 OBS[2,3,6,7]	Very Low • Inconsistent results across studies.
MRSA colonization	• 2 observational non-outbreak studies[2,11] (N=NR and N=151) reported a reduction in MRSA colonization following the implementation of multi-intervention infection prevention and control strategies. ○ One study[2] (N=NR) noted a reduction in the MRSA monthly colonization rate to almost zero, however it was not noted whether this reduction was statistically significant. ○ One non-outbreak observational study[11] (N=151) found a significant reduction in MRSA colonization in infants whose nares were decolonized compared with decolonization with enhanced cleaning processes: 2.38/1000 patient days vs. 0.92/1000 patient days. • 2 observational non-outbreak studies[6,8] (N= 722 and N=1827), suggested mixed results following the implementation of multiple infection prevention and control strategies.	4 OBS[2,6,8,11]	Low

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
	○ One study[6] (N=722) reported a significant reduction in mean weekly colonization pressure: 19.1±10.7 vs. 13.4±9.6, p=0.04; however, this reduction was not sustained through the introduction of a new strain and a period of overcrowding: Year 1 vs. year 3, p=0.76; Year 2 vs. year 3, p=0.48 ○ One study[8] (N= 1827) found no change in MRSA new colonization incidence density per 1000 NICU days at risk in NICU I (68.3 vs. 79.3; p=0.54); while NICU II experienced a significant reduction in MRSA (205.8 vs. 0.0; p<.001), however, NICU II also experienced an almost 50% reduction in admissions and both NICUs experienced an increase in hand hygiene compliance during this time. The strategy implemented was a general infection prevention and control strategy and not targeted specifically to *S. aureus* or MRSA.		
MRSA transmission	• 2 observational outbreak studies[9,12] reported reductions in MRSA transmission following implementation of multi-intervention infection prevention and control strategies. ○ One outbreak study[9] (N=NR) noted a reduction in the number of MRSA acquisitions/ total days spent by MRSA (+) infants during each month when comparing the 10 months before the intervention with the 5 months after: 0.0729 vs. 0.0241; p=0.013 ○ One outbreak study[10] (N=331) reported a significantly lower risk of MRSA transmission from patients on contact precautions compared with those not on contact precautions: 0.0090/ day vs. 0.140/ day; RR: 15.6 (95% CI 5.3-45.6), p< 0.0001 ▪ Contact precautions were defined as use of gown, gloves, and mask for direct patient contact that was standard of care at the time of the study.	2 OBS[9,10]	Low
Unadjusted length of Stay	• One observational non-outbreak study[7] (N=3088) reported no difference in the unadjusted median length of stay between pre and post-intervention time periods: 77 days (26.2-120.0) vs. 62.5 days (39.0-107.5); p = 0.94	1 OBS[7]	Very Low • Imprecise: only 1 study
Attributable mortality	• One observational non-outbreak study[7] (N=3088) reported no difference in MRSA-related mortality between pre and post-intervention periods. 0 vs. 1; p>0.999	1 OBS[7]	Very Low • Imprecise: only 1 study

Table 13 Strength of Evidence for Implementing Multi-intervention Strategies to Prevent MSSA Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
MSSA infection*	• One observational, non-outbreak study[4] (N=NR) reported a significant reduction in the MSSA bacteremia rate/ 1000 admissions between the last 2 years of a 6-year study: 13.63 vs. 6.8; p=0.036: 13.63/1000 admissions vs. 6.8/ 1000 admissions; p=0.036	1 OBS[4]	Very Low • Imprecise: only 1 study

3.A.1.b. Preemptive Contact Precautions

Table 14 Strength of Evidence for Implementing Preemptive Contact Precautions for Outborn Patients to Prevent MRSA Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
MRSA transmission	• One observational non-outbreak study[13] (N=1646) reported a significant reduction in MRSA transmission in NICU patients: 3.5/1000 patient-days vs. 1.3/1000 patient days; p<0.001. • This reduction is likely confounded by a 25% increase in compliance with hand hygiene.	1 OBS[13]	Very Low • Imprecise: only 1 study

3.A.1.c. New Hand Hygiene Policy

Table 15 Strength of Evidence for Implementing a New Hand Hygiene Policy to Prevent MRSA Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
MRSA infection*	• One observational non-outbreak study[14] (N=377) conducted a subanalysis of MRSA septicemic episodes and reported a significant decrease after the institution of a chlorhexidine hand rub policy: 20/161 (14%) vs. 2/176 (3%); p=0.048	1 OBS[14]	Very Low • Imprecise: only 1 study
Unadjusted length of Stay	• One observational non-outbreak study[14] reported no difference in the mean unadjusted length of stay following the institution of a chlorhexidine hand rub policy: 80 days (39-118) vs. 76 days (48-109); p=NR	1 OBS[14]	Very Low • Imprecise: only 1 study
Attributable mortality	• One observational non-outbreak study[14] reported no difference in the infection-related deaths following the institution of a chlorhexidine hand rub policy: 4/161 (2.5%) vs. 2/176 (1.1%); p=NR	1 OBS[14]	Very Low • Imprecise: only 1 study

3.A.1.d. Implementing Active Surveillance Testing

Table 16 Strength of Evidence for Implementing Active Surveillance Testing to Guide Implementation of any Strategy to Prevent *S. aureus* Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
S. aureus infection*	• 5 observational non-outbreak studies[1,3,5,15,16] reported reductions in *S. aureus* infections after implementing active surveillance strategies. All 5 studies implemented infant decolonization. The population of 2 of these studies overlaps.[5,15] • 2 observational non-outbreak studies[6,7] reported no changes in *S. aureus* infections. ○ The *S. aureus* prevention interventions implemented as a result of active surveillance testing and the outcome measures were heterogeneous across studies.	7 OBS[1,3,5-7,15,16]	Low

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
S. aureus colonization	• One observational non-outbreak study[1] (N=6283) reported reductions in *S. aureus* colonization following the implementation of active surveillance testing programs to guide infection control strategies. • One observational non-outbreak study[6] (N=722) reported a significant reduction in MRSA colonization in the year following the implementation of active surveillance protocol; however, this reduction was not sustained through a period of overcrowding and the introduction of an outbreak strain. • One observational non-outbreak study[8] (N=1827) reported inconsistent results with no change in MRSA colonization in NICU 1 and significant reductions in NICU II; p<.001	3 OBS[1,6,8]	Very Low • Imprecise: inconsistent results across studies
S. aureus transmission	• 2 observational outbreak studies[9,10] reported reductions in MRSA transmission. ○ One outbreak study[9] (N=NR) noted a reduction in the number of MRSA acquisitions/ total days spent by MRSA (+) infants during each month when comparing the 10 months before the intervention with the 5 months after: 0.0729 vs. 0.0241; p=0.013 ○ One outbreak study[10] (N=331) reported a significantly lower risk of MRSA transmission from patients on contact precautions compared with those not on contact precautions: 0.0090/ day vs. 0.140/ day; RR: 15.6 (95% CI: 5.3-45.6), p< 0.0001 ▪ Contact precautions were defined as use of gown, gloves, and mask for direct patient contact that was standard of care at the time of the study.	2 OBS[9,10]	Low

Table 17 Strength of Evidence for Implementing Active Surveillance Testing to Guide Implementation of any Strategy to Prevent MRSA Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
MRSA infection*	• One observational non-outbreak study[3] (N=NR) employed active surveillance to guide implementation of infection prevention and control measures for MRSA and reported reductions in infections. • 2 observational non-outbreak studies[6,7] (N=722 and N=3088) reported no change in MRSA infections while conducting active surveillance to guide implementation of infection prevention and control measures.	3 OBS[3,6,7]	Low
MRSA colonization	• One observational non-outbreak study[6] (N=722) reported a significant reduction in MRSA colonization in the year following the implementation of active surveillance protocol; however, this reduction was not sustained due to the introduction of an outbreak strain.	1 OBS[6]	Very Low • Imprecise: only 1 study

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
MRSA transmission	• 2 observational outbreak studies[9,10] reported reductions in MRSA transmission. ○ One study[9] (N=NR) noted a reduction in the number of MRSA acquisitions/ total days spent by MRSA (+) infants during each month when comparing the 10 months before the intervention with the 5 months after: 0.0729 vs. 0.0241; p=0.013 ○ One study[10] (N=331) reported a significantly lower risk of MRSA transmission from patients on contact precautions compared with those not on contact precautions: 0.0090/ day vs. 0.140/ day; RR: 15.6 (95% CI: 5.3-45.6), p< 0.0001 ▪ Contact precautions were defined as use of gown, gloves, and mask for direct patient contact that was standard of care at the time of the study.	2 OBS[9,10]	Low

Table 18 Strength of Evidence for Implementing Active Surveillance Testing to Guide Implementation of any Strategy to Prevent MSSA Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
MSSA infection*	• 2 observational non-outbreak studies[15,16] employed active surveillance to guide implementation of infection prevention and control measures for MSSA and reported reductions in infections. ○ Both studies implemented active surveillance cultures: one study[15] implemented decolonization for all patients colonized with MSSA, the other implemented decolonization only for colonized very low birthweight infants with IVs.	2 OBS[15,16]	Low

3.A.1.e. Frequency of Active Surveillance Testing

Table 19 Strength of Evidence for Implementing Active Surveillance Testing All Infants on Admission to Guide Implementation of any Strategy to Prevent *S. aureus* Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
S. aureus transmission	• One observational outbreak study[9] (N=NR) reported a decrease in new MRSA acquisitions while conducting admission screening of all infants.	1 OBS[9]	Very low • Imprecise: only one study

Table 20 Strength of Evidence for Implementing Active Surveillance Testing All Infants on Admission and Every Two Weeks Thereafter to Guide Implementation of any Strategy to Prevent *S. aureus* Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
S. aureus infection*	• One observational non-outbreak study[7] (N=3088) reported no change in MRSA BSI	1 OBS[7]	Very low • Imprecise: only one study

Table 21 Strength of Evidence for Implementing Active Surveillance Testing of All Infants on Admission and Weekly Thereafter to Guide Implementation of any Strategy to Prevent *S. aureus* Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
S. aureus infection*	• 2 observational non-outbreak studies[1,17] implemented admission testing for all patients and routine screening and reported reductions in *S. aureus* infections. ○ One study[1] (N=6283) implemented routine screening at a monthly rate, then increased to every 2 weeks, then increased to weekly screening, finally seeing a reduction in infections. ○ One study[17] (N=NR) maintained routine screening at a weekly interval throughout the study.	2 OBS[1,17]	Low

Table 22 Strength of Evidence for Implementing Active Surveillance Testing of All Infants on Admission and Weekly Thereafter to Guide Implementation of any Strategy to Prevent MRSA Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
MRSA infection and colonization*	• One observational non-outbreak study[18] (N=4304) implemented admission testing for *S. aureus* with weekly surveillance tracheal cultures for all patients compared with weekly surveillance tracheal cultures only and reported an increase in MRSA-positive cultures (colonized or invasive): 24.7/1000 NICU admissions vs. 13.7 / 1000 NICU admissions; p=0.010	1 OBS[18]	Very Low • Imprecise: only 1 study

Table 23 Strength of Evidence for Implementing Active Surveillance Testing of All Infants on Admission and Weekly Thereafter to Guide Implementation of any Strategy to Prevent MSSA Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
MSSA infection and colonization*	• One observational non-outbreak study[18] (N=4304) implemented admission testing for *S. aureus* with weekly surveillance tracheal cultures for all patients compared to weekly surveillance tracheal cultures only and reported a decrease in MSSA positive	1 OBS[18]	Very Low • Imprecise: only 1 study

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
	cultures (colonized or invasive). Significant decrease reported: 38.9/1000 NICU admissions vs. 53.6/ 1000 NICU admissions; p=0.044		

Table 24 Strength of Evidence for Implementing Active Surveillance Testing of Outborn Infants on Admission and All Infants Weekly Thereafter to Guide Implementation of any Strategy to Prevent *S. aureus* Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
S. aureus infection*	• 3 observational non-outbreak studies[3,5,15] (N=NR, N= 2717, and N=1847) reported reductions in *S. aureus* infections while conducting admission screening for outborn infants combined with weekly routine screening. The population of 2 of these studies overlaps.[5,15]	3 OBS[3,5,15]	Low

Table 25 Strength of Evidence for Implementing Weekly Active Surveillance Testing of all Infants to Guide Implementation of any Strategy to Prevent S. aureus Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
S. aureus infection*	• One observational non-outbreak study[16] (N=1056) reported a reduction in MSSA infections associated with conducting routine weekly surveillance. • One non-outbreak study[6] (N=722) reported no change in MRSA infection while conducting routine weekly screening of all infants.	2 OBS[6,16]	Very Low • Inconsistent: 2 studies reporting opposite results
S. aureus colonization	• One observational non-outbreak study[6] (N=722) reported a significant reduction in MRSA colonization in the year following the implementation of active surveillance protocol; however, this reduction was not sustained through a period of overcrowding and the introduction of an outbreak strain. • One observational non-outbreak study[16] (N=1056) reported no change in colonization rates while conducting routine weekly screening of all infants for MSSA during the intervention period.	2 OBS[6,16]	Low
S. aureus transmission	• One observational outbreak study[10] reported a reduction in MRSA transmission or acquisition while conducting weekly MRSA screening of all non-colonized infants.	1 OBS[10]	Very Low • Imprecise: only one study

3.A.1.f. Optimal Testing Method

Table 26 Strength of Evidence for Real time PCR testing vs. Culture-based Methods to Screen for *S. aureus* Colonization in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
Sensitivity*	• One study[19] reported higher sensitivity for Real Time PCR (96%) vs. culture (92%) to detect *S. aureus* colonization.	1 DIAG[19] N=299 paired weekly nasal swabs	Moderate • Imprecise: only 1 study
Specificity*	• One study[19] reported identical specificity for Real Time PCR (100%) and culture (100%) to detect *S. aureus* colonization.	1 DIAG[19] N=299 paired weekly nasal swabs	Moderate • Imprecise: only 1 study
Positive predictive value *	• One study[19] reported identical positive predictive values for Real Time PCR (100%) and culture (100%) to detect *S. aureus* colonization.	1 DIAG[19] N=299 paired weekly nasal swabs	Moderate • Imprecise: only 1 study
Negative predictive value*	• One study[19] reported similar negative predictive values for Real Time PCR (99%) and culture (98%) to detect *S. aureus* colonization.	1 DIAG[19] N=299 paired weekly nasal swabs	Moderate • Imprecise: only 1 study

Table 27 Strength of Evidence for Real time PCR testing vs. Culture-based Methods to Screen for MRSA Colonization in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
Sensitivity*	2 studies reported sensitivity of 100% for PCR vs. culture to detect MRSA colonization. • One study[20] (N=696 paired nasal swabs) sensitivity = 100% (95% CI: NR). • One study[21] (N=1873 swabs) sensitivity = 100% (95% CI: 71.5 – 100%).	2 DIAG[20,21] N=1873 swabs, and 696 paired nasal swabs	High • None
Specificity*	2 studies reported specificity values >97% for PCR vs. culture to detect MRSA colonization. • One study[20] (N=696 paired nasal swabs) specificity = 98% (95% CI: 96 – 99%). • One study[21] (N=1873 swabs) specificity = 97.6% (95% CI: 95.7 – 98.9%).	2 DIAG[20,21] N=1873 swabs, and 696 paired nasal swabs	High • None
Positive predictive value*	2 studies[20] reported positive predictive values of 52.4% or 41% for Real Time PCR vs. culture to detect MRSA colonization. • One study[20] (Francis) (N=696 paired nasal swabs) positive predictive value = 41% (95% CI: 15 –72%). This study found 7 samples were MRSA positive for PCR but were negative on culture. 5/7 samples cultured MSSA. • One study[21] (N=1873 swabs) positive predictive value = 52.4% (95% CI: 29.8 – 74.3%).	2 DIAG[20,21] N=1873 swabs, and 696 paired nasal swabs	Moderate • Imprecise: wide confidence intervals

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
Negative predictive value*	2 studies[20,21] reported negative predictive values of 100% for Real Time PCR vs. culture to detect MRSA colonization. • One study[20] (N=696 paired nasal swabs) reported negative predictive value 100% (95% CI: NR). • One study[21] (N=1873 swabs) negative predictive value 100% (95% CI: 99.1-100%).	2 DIAG[20,21] N=1873 swabs, and 696 paired nasal swabs	High • None

Table 28 Strength of Evidence for changing from Culture-based to PCR testing for Active Screening to Prevent MRSA Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
MRSA infection*	• One observational study[22] (N= NR) in an outbreak setting found that changing from culture-based methods to PCR for active screening was associated with decreased incidence of infection: IRR: 2.48 (95% CI: 1.06-5.80), (p=NR).	1 OBS[22]	Very Low • Imprecise: only 1 study
MRSA colonization	• One diagnostic study[23] (N= 4202 swabs) reported diagnostic accuracy and found no difference in MRSA colonization rates between hospitals that routinely use PCR (4.2%) or culture-based (4.3%) MRSA-detection methods.	1 DIAG[23] N=4202 swabs	Moderate • Imprecise: only 1 study

3.A.1.g. Optimal Testing Site

Table 29 Strength of Evidence for Optimal Anatomical Site to Screen for MRSA Colonization in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
Sensitivity*	3 studies[23-25] conducting weekly surveillance cultures reported higher sensitivity for nares specimens (71%, 87%, or 95.8%) than for other anatomic sites to detect MRSA colonization using culture-based methods. • One study[24] (N=1341 swabs) reported results for the sensitivity of nares (71%) and umbilicus (60%) and found nares had higher number of positive MRSA isolates than postauricular areas, axillae, umbilicus, and perineum. • One study[25] (N=558 paired cultures) reported sensitivity for nares (95.8%), rectum (29.2%), axilla (22.2%), and umbilicus (0%). • One study[23] (N= 4202 swabs) reported results for the sensitivity of nares (87%) and umbilicus (55%) and found nares had higher number of positive MRSA isolates than umbilicus using PCR.	3 DIAG[23-25] N=5543 swabs, and 558 paired cultures	Moderate • Inconsistent: inconsistent point estimates
Negative predictive value*	• One study[25] (N=558 paired cultures) reported a higher negative predictive value for nares (99.6%) than rectum (93.6%), axilla (95.7%), and umbilicus (83.1%) to detect MRSA colonization using culture-based methods. • One study[23] (N=4202 cultures) reported a higher negative predictive value for umbilicus (98%) than nares (99.4%) to detect MRSA colonization using PCR.	2 DIAG[23,25] N=4202 cultures and 558 paired cultures	• High

3.A.1.h. Infant Decolonization and Active Surveillance Testing

Table 30 Strength of Evidence for Implementing Decolonization of Colonized Infants (any strategy or combination of strategies) to Prevent *S. aureus* Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
S. aureus infection*	• 5 observational studies[5,15,16,26,27] found a reduction in infections: one study reported a significant reduction in *S. aureus* infections following decolonization of colonized infants. ○ One study[26] (N=525) found a 50% non-significant reduction in MRSA infections in colonized infants whose nares and umbilicus were decolonized compared with colonized infants who were not decolonized using intranasal mupirocin: 7/257 (2.7%) vs. 15/268 (5.6%); p=0.128. However, this study conducted active surveillance for only the first 2 weeks of an infant's stay in the NICU, and 30% of infants in the treatment group did not receive mupirocin. ○ One study[15] (N=2717) found a reduction in MSSA infection incidence rate: 1.07/1000 patient days vs. 0.55/1000 patient days; IRR: 0.83 (95% CI: 0.62-1.12). This study's patient population overlaps with the population analyzed in another study included in this analysis.[5] ○ One study[5] (N=1847) found a 43% reduction in *S. aureus* clinical isolates with the addition of active surveillance for and decolonization of MSSA colonized infants to a comprehensive MRSA prevention strategy: IRR: 0.57 (95% CI: 0.40 – 0.80); p=NR. ○ One study[16] (N=1056) implemented surveillance and targeted decolonization solely for MSSA positive infants with IVs and found a reduction in the incidence rate of MSSA attributable infections: 1.63/1000 patient-days (CI: 1.12–2.31) vs. 0.83/1000 patient-days (CI: 0.47–1.35); p= 0.024 ○ One study[27] (N=1233) found a significant reduction in MRSA infections in infants whose nares and umbilicus were decolonized compared with no decolonization: 5/450 (1.1% vs. 92/783 (12%); OR: 11.85 (95% CI: 4.6-33.3); p<0.001	5 OBS[5,15,16,26,27]	Low
S. aureus colonization	• One non-outbreak observational study[26] (N=525) found no difference in the incidence of MRSA colonization in a group of infants where colonized infants had nares and umbilicus decolonized compared with the control group where colonized infants were not decolonized: 62/257 (24%) vs. 68/268 (25%); p=0.740. However, this study conducted active surveillance for only the first 2 weeks of an infant's stay in the NICU, and 30% of infants in the treatment group did not receive mupirocin. • One non-outbreak observational study[27] (N=1233) found a significant reduction in MRSA colonization in infants whose nares and umbilicus were decolonized compared with no decolonization: 39/450 (8.7% vs. 323/783 (41%); OR: 7.4 (95% CI: 5.1-10.76); p<0.001 • One non-outbreak observational study[11] (N=151) found no difference in MRSA colonization in infants whose nares were decolonized compared to no decolonization: 2.38/1000 patient days vs. 2.00/1000 patient days	3 OBS[11,26,27]	Very Low • Inconsistent results across studies
Mupirocin resistance	• One observational non-outbreak study[26] (N=525) reported all isolates were susceptible to mupirocin. • One observational study[26] found 0/65 MRSA isolates were resistant to mupirocin.	2 OBS[15,26]	Low
Unadjusted length of stay	• One observational non-outbreak study[26] (N=525) reported no difference in the unadjusted length of stay between decolonized infants and those not receiving decolonization.	1 OBS[26]	Very Low • Imprecise: only 1 study

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
Product-related adverse events	• One observational non-outbreak study[26] (N=525) noted that although the authors were not vigilantly monitoring adverse events, no adverse events such as apnea and local irritation were identified. • One study[16] (N=1056) reported no adverse effects from application of the decolonization protocol with mupirocin and octenidin.	2 OBS[16,26]	Low

Table 31 Strength of Evidence for Implementing Decolonization of Colonized Infants (any agent or combination of agents) to Prevent MRSA Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
MRSA infection*	• One non-outbreak study[26] (N=525) found a 50% non-significant reduction in MRSA infections in colonized infants whose nares and umbilicus were decolonized compared with colonized infants who were not decolonized using intranasal mupirocin: 7/257 (2.7%) vs. 15/268 (5.6%) p=0.128. However, this study conducted active surveillance for only the first 2 weeks of an infant's stay in the NICU, and 30% of infants in the treatment group did not receive mupirocin. • One study[27] (N=1233) implemented infection control measures and found a significant reduction in the incidence of MRSA infection when comparing decolonization of nares and umbilical areas vs no decolonization: 5/450 (1.1% vs. 92/783 (12%); OR: 11.85 (95% CI: 4.6-33.3); p<0.001	2 OBS[26,27]	Low
MRSA Colonization	• One observational non-outbreak study[26] (N=525) found no difference in the incidence of MRSA colonization in a group of infants where colonized infants had nares and umbilicus decolonized compared with the control group where colonized infants were not decolonized: 62/257 (24%) vs. 68/268 (25%); p=0.740. However, this study conducted active surveillance for only the first 2 weeks of an infant's stay in the NICU, and 30% of infants in the treatment group did not receive mupirocin. • One study[27] (N=1233) found a significant reduction in MRSA colonization in infants whose nares and umbilicus were decolonized compared with no decolonization: 39/450 (8.7% vs. 323/783 (41%); OR: 7.4 (95% CI: 5.1-10.76); p<0.001 • One observational non-outbreak study[11] (N=151) found a non-significant increase in MRSA colonization in infants whose nares were decolonized compared to no decolonization: 2.38/1000 patient days vs. 2.00/1000 patient days.	3 OBS[11,26,27]	Very Low • Inconsistent results across studies
Mupirocin resistance	• One observational non-outbreak study[26] (N=525) reported all isolates were susceptible to mupirocin.	1 OBS[26]	Very low • Imprecise: only 1 study
Length of stay	• One observational non-outbreak study (N=525) reported no difference in the unadjusted length of stay between decolonized infants and those not receiving decolonization.	1 OBS[26]	Very Low • Imprecise: only 1 study

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
Adverse events	• One observational non-outbreak study[26] (N=525) noted that although the authors were not vigilantly monitoring adverse events, no adverse events such as apnea and local irritation were identified.	1 OBS[26]	Very Low • Imprecise: only 1 study

Table 32 Strength of Evidence for Implementing Decolonization of Colonized Infants (any agent or combination of agents) to Prevent MSSA Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
MSSA infection*	• 2 observational, non-outbreak studies[15,16] reported a significant reduction in MSSA-attributable infections with the implementation of active surveillance and decolonization of the nares and skin of colonized patients. • One study[15] (N=2717) found a reduction in MSSA infection incidence rate after decolonizing colonized infants with intranasal mupirocin and chlorhexidine baths: 1.07/1000 patient days vs. 0.55/1000 patient days; IRR: 0.83 (95% CI: 0.62-1.12) • One study[16] (N=1056) implemented surveillance and targeted decolonization solely for MSSA positive infants with IVs and found a reduction in the incidence rate of MSSA attributable infections: 1.63/1000 patient-days (CI: 1.12–2.31) vs. 0.83/1000 patient-days (CI: 0.47–1.35); p= 0.024	2 OBS[15,16]	Low
Mupirocin Resistance	• One observational study[15] (N=2717) found 0/65 MRSA isolates were resistant to mupirocin.	1 OBS[15]	Very Low • Imprecise: only 1 study
Product-related adverse events	• One study[16] (N=1056) reported no adverse effects from application of the decolonization protocol with mupirocin and octenidin.	1 OBS[16]	Very Low • Imprecise: only 1 study

Table 33 Strength of Evidence for Universal Decolonization of all infants (any strategy or combination of strategies) to Prevent *S. aureus* Transmission in NICU Patients

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
S. aureus infection*	• 2 observational non-outbreak studies[1,17] reported reductions in infections with implementation of universal decolonization. One of the 2 studies[1] implemented universal decolonization in conjunction with other infection prevention and control interventions. • One non-outbreak study[1] (N=6283) reported a significant reduction in *S. aureus* infections implementing a comprehensive *S. aureus* prevention strategy including universal decolonization with mupirocin: 1.42/ 1000 patient days vs. 0.33/1000 patient days; IRR 0.29 (95% CI: 0.166 to 0.512); p<0.0001. • One non-outbreak study[17] (N=NR) reported a 73% reduction in the rate of invasive *S. aureus* infections following the change from targeted to universal intranasal decolonization for	2 OBS[1,17]	Low

Outcome	Findings	Quantity and Type of Evidence and Sample Size	GRADE of Evidence for Outcome and Limitations of the Evidence
	endemic MRSA to a comprehensive infection prevention and control strategy. Decolonization was scheduled every 5 weeks (p=0.03). Of the 86 post-intervention patients who acquired MRSA, 64 (74%) were never treated with mupirocin because they were admitted between scheduled courses of mupirocin.		
S. aureus transmission	• One non-outbreak study[17] (N=NR) reported a significant 45% reduction in the rate of MRSA transmission following the implementation of universal intranasal decolonization.	1 OBS[17]	Very Low • Imprecise: only 1 study
Mupirocin resistance	• One non-outbreak study[1] (N=6283) reported that none of the 19 isolates tested were resistant to mupirocin • One non-outbreak study[17] (N=NR) implementing universal decolonization of MRSA colonized infants found 0/57 MRSA isolates in the pre-intervention period, and 3/112 MRSA isolates in the post-intervention period were resistant to mupirocin. One of the mupirocin resistant isolates was identified as *S. haemolyticus.* The other 2 mupirocin resistant MRSA isolates were unrelated, and one had no prior mupirocin exposure.	2 OBS[1,17]	Low
Product-related adverse events	• One non-outbreak study[17] (N=NR) reported apneic spells temporally associated with mupirocin administration: 1 preterm infant; 1.15 (95% CI: 0.03-6.23)	1 OBS[17]	Very Low • Imprecise: only 1 study

3.A.2. Extracted Evidence

Table 34 Extracted Studies on Interventions to Prevent *S. aureus* Transmission

Study Data	Population and Setting	Intervention	Definitions	Results
Author: Ristagno[17] **Year:** 2018 **Study design:** Interrupted time series **Outbreak:** N **Risk of bias:** Moderate	**Population:** N=NR **Setting:** 1 Level 4 NICU with 101 beds, at 1 university hospital **Location:** USA **Study dates:** Dec 1, 2009 – December 31, 2015 **Inclusion criteria:** All neonates admitted during study dates. **Exclusion criteria:** NR	**Intervention Group: N=NR** **Post-intervention** • All NICU patients received mupirocin to the anterior nares twice daily for 5 days. • Courses were repeated every 5 weeks. • NICU pharmacists prompted attending physician on the designated day to order mupirocin, unless attending identified a contraindication (e.g. nares too small to admit applicator tip). • Infants could receive mupirocin more than once if they were present in the unit for more than 5 weeks. **Device/agent:** Universal mupirocin decolonization **Monitoring (compliance) intervention:** Compliance for 20/22 months: 85% (95% CI: 0.76–0.91)	**Outcome Definitions:** Present on admission (POA): infants with MRSA surveillance cultures positive at admission and those known to be colonized (e.g. tested at another facility). Transmission: positive MRSA surveillance or clinical culture preceded by a negative culture. Invasive *S. aureus* infection: MRSA or MSSA isolated from Blood, joint fluid, or cerebrospinal fluid. Compliance with the mupirocin prophylaxis protocol: retrospectively calculated as the number of unique mupirocin orders placed within 24 hours of the first day of scheduled monthly prophylaxis divided by the	**MRSA Transmission:** (HA) MRSA transmission: n/ 10,000 patient days • Pre-intervention: 23.1 (95% CI, 11.8–41.2) • Post-intervention: 12.7 (95% CI, 6.7–24.9) • P= .009 • 45% reduction. *S. aureus* invasive infection: n/10,000 patient days • Pre-intervention: 3.0 (95% CI, 1.8–7.2) • Post-intervention: 0.8 (95% CI, 0.3–1.5) • p =.030 • 73% reduction. **Topic Specific Outcomes:** • Post-intervention patients who acquired MRSA but were never treated with mupirocin b/c they were admitted between scheduled courses of mupirocin: 64/86 (74%) MRSA transmission: • Pre-intervention vs. post-intervention intercepts of regression lines: −20.39 (95% CI: −4.93 to 34.87);

Study Data	Population and Setting	Intervention	Definitions	Results

		Control/Comparison group:
		Pre-intervention:
		• Comprehensive strategy for preventing MRSA transmission, including admission and weekly surveillance cultures.
		• Colonized infants were cohorted, placed on contact precautions and received topical mupirocin to nares twice daily for 7 days and periodic chlorhexidine baths
		
		Standard preventive measures: NR
			number infants present in the NICU at 23:59 on that day
			
			Adverse events: actively solicited through daily interviews with bedside nurses and medical staff only during the initial unit-wide administration.
			
			Sampling strategy: surveillance cultures at admission and weekly thereafter.
			
			Testing: Culture using chromogenic agar plates and confirmation with matrix-assisted laser desportion ionization-time of flight mass spectrometry. MIC measured using break points of ≤4 µg/mL for susceptible isolates and ≥512 µg/mL for high-level resistance
				p< .001 suggesting a change in rates.
				• Pre-intervention vs. post-intervention change in the slopes of regression lines: −0.84 (95% CI: −1.45 to −0.39) p=.024 suggesting a change in trajectory
				Invasive *S. aureus* infection:
				• Pre-intervention vs. post-intervention intercepts of regression lines −1.2 (95% CI: −1.8 to −0.7); p=.002 suggesting a change in rates
				• Pre-intervention vs. post-intervention change in the slopes of regression lines: −0.12 (95% CI: −0.34 to 0.45); p=.644, suggesting no change in trajectory
				
				Pathogen replacement:
				CLABSI:
				• 2013: 2.35/ 1000 catheter days
				• 2014: 1.26/ 1000 catheter days
				• 2015: 0.96/ 1000 catheter days
				
				Gram negative infections:
				• 2013: 5/7 (71%)
				• 2014: 6/9 (67%)
				• 2015: 3/5 (60%)
				
				Adverse Event:
				Mupirocin resistance:
				• Pre-intervention: 0/57
				• Post-intervention: 3/112 (2.7%)
				  • Identified *as S. haemolyticus* (could not exclude the possibility of a mixed culture)*:* 1/3
				  • Identified as MRSA: both isolates were unrelated.
				  • Identified as MRSA with no prior mupirocin exposure: 1/3
				
				Chlorhexidine resistance: NR
				Product related adverse events:
				  • Apneic spells temporally associated with mupirocin administration: 1 preterm infant; 1.15 (95% CI: 0.03-6.23)
				Mortality n (%): NR
				
				Length of Stay, median (range): NR

Author: Voskertchian [5]	**Number of patients:** N=1847 neonates screened for *S. aureus*	**Intervention group:** • Active surveillance cultures for *S. aureus* (MRSA and MSSA)	**Outcomes:** NICU-attributable: clinical cultures obtained >2 days after unit admission.	***S. aureus* infections:** NICU-attributable *S. aureus* clinical infections • Pre-intervention: 74

Study Data	Population and Setting	Intervention	Definitions	Results

Year: 2018
 	
Study Design: Retrospective Pre-Post
 	
Outbreak: N
 	
Risk of bias: High
	N=116 patients with 142 *S. aureus* infections
	
	Setting: NICU at an academic hospital
	
	Location: USA
	
	Dates: April 1, 2011 – June 30, 2016.
	
	Inclusion Criteria: All neonates admitted to the NICU between April 1, 2011 and June 30, 2016.
	
	Exclusion Criteria: NR
		• Targeted decolonization of *S. aureus* positive NICU patients.
		
		Device/agent: ASC + targeted decolonization
		
		Monitoring (compliance) intervention: Colonized patients treated with mupirocin/ all colonized patients: 243/333 (72.9%)
		
		Control/Comparison group: n= NR
		• Active surveillance cultures for MRSA
		• Targeted decolonization of MRSA positive NICU patients.
		
		Standard preventive measures: NR
			Bloodstream infection (BSI): if a blood culture grew *S. aureus*.
			
			Sampling strategy: NR
			
			Testing: NR
			
			Other notes: none
				• Post-intervention: 68
				Post intervention colonization incidence: 333/1847
				
				S. aureus infections:
				• Overall 43% reduction in incidence rate of *S. aureus* clinical isolates: IRR: 0.57 (95% CI: 0.40 – 0.80).
				S. aureus BSI
				• Pre-intervention: IRR, 1.00; (95% CI: 0.78–1.29).
				• Post-intervention: statistically nonsignificant reductions
				  • Overall incidence rate: IRR, 0.50 (95% CI: 0.18–1.34)
				  • Immediate change in rate IRR: 0.73; (95% CI: 0.20–2.58)
				  • Quarterly incidence rate: IRR: 0.97; (95% CI: 0.92–1.03)
				
				Other infections: NR
				
				Topic-specific outcomes:
				Length of Stay: NR
				Mortality: Length of Stay: NR
				Mortality: NR
				
				Adverse events:
				Mupirocin Resistance: NR
				
				Adverse events: NR

Author: Delaney[1] **Year:** 2013 **Study Design:** Retrospective cohort study **Outbreak:** N **Risk of bias:** High	**Number of patients:** N=6283 **Setting:** Level IIIB NICU at a regional referral hospital **Location:** USA **Dates:** January 2004 – December 2010 **Inclusion Criteria: A**ll infants with positive *S. aureus* cultures from Jan 2004 – Dec 2010 identified via electronic medical records.	**Intervention group:** N = 25 cases (inferred from Fig 1) Cases Dec 2005 – end of study July 2004: • Twice daily application of mupirocin to nares, umbilical stump, and eroded skin and wounds of all infants admitted to NICU. • Infants with positive infection cultures were isolated. • Surveillance screening not otherwise performed beyond infection cultures. Feb 2005: • Prophylactic mupirocin discontinued due to resistance concerns Nov 2005: • Another outbreak occurred Dec 2005:	**Outcomes:** Infection: Based on CDC/ NHSN definitions and based on clinical, laboratory, and radiographic findings when applicable. Mortality: *S. aureus* was considered to have contributed to an infant's mortality when it occurred within 1 week of death and no other reason for death was evident. **Sampling strategy**: Nares were sampled initially monthly, then weekly, then admission screening was added.	***S. aureus* infections:** Infections/ patient: 96/66 • Infection Rate: • Dec 2005: 1.42/ 1000 patient days • December 2010: 0.33/1000 patient days • P<0.0001 • Number needed to treat: 49 • IRR: 0.29 (95% CI: 0.166 – 0.512) **Other infections:** NR **Topic-specific outcomes:** Length of Stay: NR Mortality: Length of Stay: NR Mortality: • Due to *S. aureus* bacteremia: 31% • Overwhelming *S. aureus* sepsis deaths: 8

Study Data	Population and Setting	Intervention	Definitions	Results
	Exclusion Criteria: NR	• Adopted intervention bundle including: • Universal mupirocin • Adoption of the Institute of Healthcare Improvement central line bundle (including renewed emphasis on handwashing technique) • Bundle included standardization of infection control techniques already practiced. • Monthly performance evaluation reviews of infection rates April 2008: • Monthly active surveillance cultures of nares of all infants admitted to NICU • Nov 2008: • Surveillance changed to weekly surveillance cultures • March 2009 • Surveillance on admission added to isolate infants colonized at birth • Once infants were found to be colonized with *S. aureus*, they no longer underwent surveillance screening and remained in isolation with cohorting when applicable throughout hospitalization **Device/agent:** Multimodal intervention **Monitoring (compliance) intervention:** NR **Control/Comparison group:** N = 18 cases (inferred from Fig 1) Patients admitted between April – Dec 2005 who did not receive universal mupirocin **Standard preventive measures:** NR	**Testing:** Culture **Other notes:** Authors note: Overall when comparing the mupirocin prophylactic period, which may have been from a mupirocin resistant strain although this was not tested, a significant reduction in the rate of *S. aureus* infection	**Adverse events:** Mupirocin Resistance: Began Mupirocin resistance testing in May 2010. May 2010 - Dec 2010: Positive infection + colonization *S. aureus* isolates that were resistant to Mupirocin: 0/19 Adverse events: NR
Author: Rana[18] **Year:** 2012 **Study Type:** Cohort study **Outbreak:** N **Risk of bias:**	**Population:** n=4304 **Setting:** Level III NICU **Location:** USA **Study dates:** 2001-2008 **Inclusion criteria:** NR **Exclusion criteria:**	**Intervention Group:** N=NR Period 2: 2006-2008 Surveillance cultures on admission from umbilicus and nares **Device/agent:** Screening for MRSA colonization **Monitoring (compliance) intervention:** NR **Control/Comparison group:** N=NR Period 1: 2001-2005 No policy for MRSA admission screening; SA (+)	**Outcome Definitions:** Cases: any infant with a SA-positive culture Colonized cases: positive culture from skin, anterior nares, umbilicus, or tracheal aspirate without signs or symptoms of active infection or treatment with antibiotics Infected cases: bacteremia, pneumonia, or meningitis	Invasive disease • MRSA: 22/75 (29.3%) • MSSA: 46/198 (23.3%) • p=0.298 Incidence of ALL MRSA colonization and invasive disease per 1000 NICU admissions: • Period 1: 13.7 • Period 2: 24.7 • p=0.010 Incidence of ALL MSSA cultures colonization and

Study Data	Population and Setting	Intervention	Definitions	Results
Low	NR	culture infants identified from electronic medical records **Standard preventive measures:** • Surveillance Screening: Weekly surveillance tracheal cultures obtained on all intubated babies • Cohorting/Contact precautions: Whenever infants with MRSA invasive disease or colonization (surface or tracheal) discovered, all infants in that room were swabbed for SA carriage (umbilical/nasal), placed in cohort with contact precautions and further managed according to infection control procedures • Decolonization: If a second case of MRSA was identified in the same room, then all infants in the room were treated with a regimen of 0.3% triclosan bath once a week (if weight > 1500 g) and intranasal mupirocin ointment. • Screening: If additional case(s) were identified in another room, then all infants in the entire NICU were swabbed (umbilical/nasal) for SA carriage. • Cohorting/ weekly Surveillance cultures: Infants positive for MRSA remained in a cohort and additional surveillance cultures were obtained weekly until two consecutive cultures demonstrated no growth or the infant was discharged or died. • All positive SA cultures reported as MSSA or MRSA • Additional surface cultures done on any infant with MRSA (+) tracheal aspirate, blood, or CSF culture	Bacteremia and meningitis: positive SA blood or cerebrospinal fluid (CSF) cultures, respectively. Pneumonia: Centers for Disease Control/National Healthcare Safety Network (CDC/NNIS) criteria or the attending neonatologist's diagnosis based on clinical findings (including change in respiratory status, need for increased respiratory support, change in or new-onset purulent sputum requiring frequent suctioning, and leukocytosis or leukopenia associated with left shift) and radiographic findings (new or worsening infiltrates or consolidation or cavitations on serial X-rays), a SA-positive tracheal aspirate and/or blood culture and at least 7 days of antistaphylococcal antibiotic treatment. Invasive disease: necrotizing fasciitis, necrotizing pneumonia, osteomyelitis, and other deep tissue infections Total duration of positive cultures: calculated from the first day of positive culture to the day of last positive culture or death/discharge (which ever came first). Total duration of positive tracheal culture/colonization: calculated from the first culture positive aspirate to the last culture-positive day or the day infant was extubated **Sampling strategy**: Umbilical and nasal swabs at admission **Testing:** Cultures PFGE	invasive disease per 1000 NICU admissions: • Period 1: 53.6 • Period 2: 38.9 • p=0.044 Incidence of Invasive MRSA cultures per 1000 NICU admissions: • Period 1: 4.4 • Period 2: 6.40 • p=0.38 Incidence of Invasive MSSA cultures per 1000 NICU admissions: • Period 1: 9.9 • Period 2: 12.2 • p=0.49 MSSA vs MRSA More likely to be culture positive for MSSA than MRSA • Period 1: OR= 3.76 (95% CI: 2.61-5.40); p<0.001 • Period 2: OR = 1.55 (95% CI: 1.03 – 2.33); p=0.041 • p=0.010 **Adverse Events:** Length of Stay, median (range): NR Mupirocin resistance: NR Chlorhexidine resistance: NR Product related adverse events: NR Mortality: NR

Study Data	Population and Setting	Intervention	Definitions	Results
			Methicillin resistance by disk diffusion method Molecular typing by PFGE following DNA extraction on some MRSA isolates **Other notes:** NA	

Table 35 Extracted Studies on Interventions to Prevent MRSA Transmission

Study Data	Population and Setting	Intervention	Definitions	Results

Author: Bozzella[11]
 	
Year: 2019
 	
Study Type: retrospective
 	
Outbreak: N
 	
Risk of bias: Low
	Population: n=151
	
	Setting: Level IV NICU
	
	Location: USA
	
	Study dates: 2013 –2018
	
	Inclusion criteria: Patients admitted to NICU during study period and eligible for decolonization (MRSA positive, weighed > 1000g, >32 weeks gestational age at birth or ≥ 30 days old)
	
	Exclusion criteria: NR
		Intervention Group: N=151
		
		April 2015 – February 2016
		• Decolonization protocol instituted: Twice daily intranasal mupirocin application and daily bathing with CHG impregnated cloths for 5 consecutive days
		• Active screening: continued after decolonization
		• Group classification: based on test results patients classified in 2 groups—
		  • Group 1: successfully decolonized determined by 3 negative MRSA tests in 3 subsequent weeks—if had ≥1 positive MRSA test before unit discharge considered recolonized
		  • Group 2: failed decolonization assessment if ≥ 1 MRSA tests were positive in the 3 weeks following decolonization
		
		March 2016 - June 2018
		• Environmental cleaning: Technician hired in unit to enhance cleaning process of shared medical equipment between patient use (isolettes, warmers, cribs)
		
		Device/agent: multi-intervention
		
		Monitoring (compliance) intervention: NR
		
		Control/Comparison group:
		
		2013-2014
		
		Baseline: MRSA acquisition rates from 2013 and 2014, combined used for baseline comparison
			Outcome Definitions:
			Community acquired (CA) MRSA: if MRSA detected for the first time ≤ 3 days following the admission (with the day of admission as day 1).
			
			Hospital acquired (HA) MRSA: if MRSA detected after ≥ 1 negative screening
			
			MRSA infection: presence of clinical symptoms
			
			MRSA colonization: absence of clinical symptoms but detected from clinical specimen
			
			MRSA acquisition rate: the number of HA-MRSA cases per 1000 patient days
			
			Sampling strategy: nasal swabs at admission and weekly; routine clinical specimens
			
			Testing: NR
			
			Other notes:
			Patients were censored if they were discharged before completing the decolonization or the 3 consecutive MRSA screening tests.
				MRSA Transmission:
				
				MRSA positive, n/N (%):
				• HA-MRSA colonized: 78/151 (51.6%)
				
				MRSA acquisition rate (HA-MRSA / 1000 patient days)
				• Baseline rate (2013-2014): 2.00
				• April 2015-June 2018 rate: 1.27 (decreased 37%)
				• IRR: 0.63 (95%CI: 0.46-0.87)
				• p= NR
				
				• Baseline rate (2013-2014): 2.00
				• Decolonization protocol alone (April 2015-Feb 2016): 2.38
				• IRR: 1.85 (95% CI: 0.80-1.73)
				• p= NR; study states NS
				
				• Decolonization alone (April 2015-Feb 2016): 2.38
				• Decolonization + Cleaning technician (March 2016 – June 2018): 0.92
				• IRR: 0.39 (95%CI: 0.24-0.58)
				• p= NR; study states Significant
				
				Topic specific outcomes
				
				Decolonization protocol, n/N (%)
				Completed decolonization protocol: 49/78 (62.8%)
				
				Remained colonized: 11/49 (22.4%)
				Successfully decolonized: 38/49 (77.6%)
				
				Recolonized before discharge: 13/38 (34.2%)
				Remained decolonized: 25/38 (32.1%)

Study Data	Population and Setting	Intervention	Definitions	Results
		Standard preventive measures: • Active screening: nasal swabs tested at admission and weekly thereafter until positive or discharge • Contact precautions: MRSA patients; staff required to wear isolation gown and gloves upon entry to patient room; parents and visitors NOT required to wear isolation gown and gloves in patient room • Cohorting: nursing staff assigned to care for only MRSA patients throughout shift • Environmental cleaning: frequently; nursing staff cleaned and disinfected work environment at beginning of shift; terminal cleaning done if room has been continuously occupied by same patient for ≥ 3 weeks Hand hygiene: strict adherence by all providers; parents and visitors only required to sanitize hands upon entry and exit from patient room and before holding patient		Average days to recolonization: 23 (range: 18-33) after decolonization Average days stayed in unit and MRSA free: 22 (range: 8-35) **Adverse Event:** Length of Stay, median (range): NR Mupirocin resistance: NR Chlorhexidine resistance: NR Product related adverse events: NR Mortality: NR
Author: Ristagno[17] **Year:** 2018 **Study design:** Interrupted time series **Outbreak:** N **Risk of bias:** Moderate	**Population:** N=NR **Setting:** 1 Level 4 NICU with 101 beds, at 1 university hospital **Location:** USA **Study dates:** Dec 1, 2009 – Dec 31, 2015 **Inclusion criteria:** All neonates admitted during study dates. **Exclusion criteria:** NR	**Intervention Group: N=NR** **Post-intervention** • All NICU patients received mupirocin to the anterior nares twice daily for 5 days. • NICU pharmacists prompted attending physician on the designated day to order mupirocin, unless attending identified a contraindication (e.g. nares too small to admit applicator tip). • Infants could receive mupirocin more than once if they were present in the unit for more than 5 weeks. **Device/agent:** Universal mupirocin decolonization **Monitoring (compliance) intervention:** Compliance for 20/22 months: 85% (95% CI: 0.76–0.91) **Control/Comparison group:** Pre-intervention: • Comprehensive strategy for preventing MRSA transmission, including admission and weekly surveillance cultures.	**Outcome Definitions:** Present on admission (POA): infants with MRSA surveillance cultures positive at admission and those known to be colonized (e.g. tested at another facility). Transmission: positive MRSA surveillance or clinical culture preceded by a negative culture. Invasive *S. aureus* infection: MRSA or MSSA isolated from Blood, joint fluid, or cerebrospinal fluid. Compliance with the mupirocin prophylaxis protocol: retrospectively calculated as the number of unique mupirocin orders placed within 24 hours of the first day of scheduled monthly prophylaxis divided by the number infants present in the NICU at 23:59 on that day	**MRSA Transmission:** (HA) MRSA transmission: n/ 10,000 patient days • Pre-intervention: 23.1 (95% CI, 11.8–41.2) • Post-intervention: 12.7 (95% CI, 6.7–24.9) • p=.009 • 45% reduction. *S. aureus* invasive infection: n/10,000 patient days • Pre-intervention: 3.0 (95% CI, 1.8–7.2) • Post-intervention: 0.8 (95% CI, 0.3–1.5) • p=.030 • 73% reduction. **Topic Specific Outcomes:** • Post-intervention patients who acquired MRSA but were never treated with mupirocin b/c they were admitted between scheduled courses of mupirocin: 64/86 (74%) • MRSA transmission: • Pre-intervention vs. post-intervention intercepts of regression lines: −20.39 (95% CI: −4.93 to 34.87); p< .001 suggesting a change in rates. • Pre-intervention vs. post-intervention change in the slopes of regression lines: −0.84 (95% CI:

Study Data	Population and Setting	Intervention	Definitions	Results

		• Colonized infants were cohorted, placed on contact precautions and received topical mupirocin to nares twice daily for 7 days and periodic chlorhexidine baths
		
		Standard preventive measures: NR
			Adverse events: actively solicited through daily interviews with bedside nurses and medical staff only during the initial unit-wide administration.
			
			Sampling strategy: surveillance cultures at admission and weekly thereafter.
			
			Testing: Culture using chromogenic agar plates and confirmation with matrix-assisted laser desportion ionization-time of flight mass spectrometry. MIC measured using break points of ≤4 µg/mL for susceptible isolates and ≥512 µg/mL for high-level resistance
				−1.45 to −0.39_ P= .024 suggesting a change in trajectory
				Invasive *S. aureus* infection:
				• Pre-intervention vs. post-intervention intercepts of regression lines −1.2 (95% CI, −1.8 to −0.7); p=.002 suggesting a change in rates
				• Pre-intervention vs. post-intervention change in the slopes of regression lines: −0.12 (95% CI: −0.34 to 0.45); p=.644, suggesting no change in trajectory
				
				Pathogen replacement:
				CLABSI:
				• 2013: 2.35/ 1000 catheter days
				• 2014: 1.26/ 1000 catheter days
				• 2015: 0.96/ 1000 catheter days
				
				Gram negative infections:
				• 2013: 5/7 (71%)
				• 2014: 6/9 (67%)
				• 2015: 3/5 (60%)
				
				Adverse Event:
				Mupirocin resistance:
				• Pre-intervention: 0/57
				• Post-intervention: 3/112 (2.7%)
				  • Identified *as S. haemolyticus* (could not exclude the possibility of a mixed culture)*:* 1/3
				  • Identified as MRSA: both isolates were unrelated.
				  • Identified as MRSA with no prior mupirocin exposure: 1/3
				
				Chlorhexidine resistance: NR
				Product related adverse events:
				• Apneic spells temporally associated with mupirocin administration: 1 preterm infant; 1.15 (95% CI: 0.03-6.23)
				Mortality n (%): NR
				
				Length of Stay, median (range): NR

Author: Huang[26] **Year:** 2015	**Number of patients:** N= 525 NICU 1: N= 214/525 NICU 2:	**Intervention group:** N= 257/525 • All infants: Daily disinfectant bath with soap and baby lotion,	**Outcomes:** MRSA colonization and infection **Sampling strategy**: surveillance cultures (nares and umbilicus) were taken within	**MRSA infection:** 22/525 (4.2%) Colonization detected: 15/22 (68%) • N= 2/15 had colonization detected after MRSA infections, and both had MRSA infection at other neonatal units then were transferred to NICU

Study Data	Population and Setting	Intervention	Definitions	Results
Study Design: Prospective cohort study with embedded cross-over design **Outbreak:** N **Risk of bias:** Moderate	N= 311/525 **Setting:** Two Level III NICUs in 1 teaching hospital **Location:** Taiwan **Dates:** Nov 2007–Oct 2008 **Inclusion Criteria:** All neonates admitted from Nov 2007–Oct 2008 **Exclusion Criteria:** NR	• Colonized infants were decolonized with topical mupirocin ointment applied to both nares and umbilicus twice daily for 5 days. Follow-up cultures were obtained one week later and repeated weekly until 2 consecutive cultures were negative. Decolonization was repeated if follow-up cultures were positive. • Decolonization procedures were only used during first 6 months of study period in NICU-1 and only used for second 6 months of study period in NICU-2). **Device/agent:** Bundled decolonization intervention **Monitoring (compliance) intervention:** NR **Control/Comparison group:** N= 268/525 • No decolonization procedures **Standard preventive measures:** • Surveillance cultures (nares and umbilicus) were taken within 24 hrs of admission and weekly cultures for 2 weeks. • Sink available between every 2 isolettes. Alcohol hand rub at each bed.	24 hrs of admission and weekly cultures for 2 weeks. **Testing:** Identification of MRSA was confirmed according to Clinical Laboratory Standards Institutes guidelines; 5% sheep blood agar plate; Cefoxitin test; pulsed-field gel electrophoresis (PFGE) with *Sma*I digestion, staphylococcal chromosomal cassette (SCC*mec*) **Other notes:** • 69/130 (25%) colonized were detected on admission, 43/130 were detected on the 2nd sampling, 16/130 were detected on the 3rd sampling and 2/130 were detected on the 2nd admission (transferred back to NICU). • Infants were assessed for MRSA infection throughout hospital stay, even when transferred to other wards. Once transferred outside NICU, infants did not undergo surveillance cultures or decolonization. • 19/ 62 infants with MRSA colonization in decolonized group were outside NICU when MRSA was identified and were not decolonized • If single infant had > 1 MRSA infection episode, infant was considered distinct for purposes of calculating outcomes if > 2 wks., apart, had received course of effective antibiotics, clinical symptoms had resolved, and > 1 negative culture from the previously infected site.	Intervention Group Infections: 7/257 (2.7%) • Documented previous colonization: 2/7 Rate of MRSA infection following prior colonization in colonized infants: • Intervention: 3.2% • Control: 16%, • p = 0.014 • • Intervention: 3.2% • Infants with no colonization: 2.6%, • p = 0.7804 Incidence rate of MRSA infection: • Prior colonization: 13/128 (10.2%) vs. • No colonization: 9/397 (2.3%), • p < 0.001, OR: 4.77; 95% CI: 1.85–12.44] MRSA infection density: incidence/ 1000 colonized patient days • Intervention: 0.51 • Control: 2.30 • p = 0.047 **MRSA colonization:** 130/525 (25%) • Intervention: 62/257 (24%) • Comparison: 68/268 (25%) • p=0.740 **Topic-specific outcomes:** NR **Adverse events:** Mupirocin Resistance: all isolates in this study were susceptible to mupirocin Mortality: NR Length of NICU stay mean±SD: • Mupirocin treated: 26.74±33.90 • No Mupirocin: 25.57±39.27 • P=0.795 Product related adverse events: although not vigilantly monitoring the adverse effects, no apparent adverse events due to mupirocin treatment, such as apnea and local irritation, in these infants were identified.
Author: Geraci[6]	**Number of patients:** N= 722	**Intervention group:** • Weekly surveillance swabs of nares and rectum.	**Outcomes:** MRSA colonization or infection Colonized: when at least one nasal swab	**MRSA colonization or infection:** **Colonized:** 187/722 (25.9%) • High rates of MRSA colonization were recorded

Study Data	Population and Setting	Intervention	Definitions	Results
Year: 2014 **Study Design:** Prospective pre-post study **Outbreak:** N **Risk of bias:** Moderate	**Setting:** Tertiary NICU associated with the center for genetic diseases and entails an intensive room and intermediate care room in one teaching hospital **Location:** Italy **Dates:** June 16, 2009 - June 15, 2012 **Inclusion Criteria:** All NICU patients admitted between June 16, 2009 and June 15, 2012 who stayed at least 48 hrs and had at least 1 nasal swab **Exclusion Criteria:** NR	• Admission cultures were also obtained for the first 6 months of study but discontinued due to low rate of positive culture. • For colonized infants, contact precautions, • use of dedicated equipment, • periodic HCP training on hand hygiene, and • Intensified sanitation of cot spaces. • Physical separation of colonized and non-colonized infants with the same HCP caring for both groups. • No mupirocin decolonization of colonized infants. • After a high prevalence of MRSA was detected among infants, HCP were screened and decolonized with nasal mupirocin and had follow up cultures of anterior nares to assess decolonization. • Colonized HCP were not furloughed. **Device/agent:** Bundled interventions **Monitoring (compliance) intervention:** NR **Control/Comparison group:** NA **Standard preventive measures:** Policies for appropriate management of devices including removal of central umbilical catheters at 72 hrs and replace central venous catheters after 21 days or if blood stream infection suspected or documented.	tested positive. **Sampling strategy:** Weekly cultures of anterior nares and rectum **Testing:** Brain Hearth Infusion broth, colony screening onto oxacillin agar, cefoxitin disk diffusion test and PCR for detection of *mec*A **Other notes:** None	during the first two quarters of study, but implementation of targeted control strategies (starting June 2009, the 1st quarter of study) resulted in decreased colonization prevalence to 10% by 5th quarter of study. • However, dramatic rise of rates occurred in 8th-10th quarters of with entry of new MRSA strain into NICU and, soon afterwards, with a period of substantial overcrowding. (No statistical analysis) **WCP = MRSA mean weekly colonization pressure (MRSA positive patient-days in each weekx100/ total number of patient days in week)** • Year 1 vs. year 2, p: 0.04 • Year 1 vs. year 3, p: 0.76 • Year 2 vs. year 3, p: 0.48 **WCP directly correlated with the number of MRSA acquisitions in following week:** Correlation Coefficient 0.77; p=0.009 **Annual incidence density of acquisition of MRSA (cases/patient-days):** • Year 1: 20.2/ 1000 • Year 2: 8.8/ 1000 • Year 3: 13.1/ 1000 • p: NR (noted not significant) **Incidence of clinical infections:** • Year 1: 5.2/1000 patient- days • Year 2: 6.5/1000 patient-days • Year 3: 4.9/1000 patient-days • p=0.48 **MRSA patient-days by year (mean ± SD):** • Year 1: 12.4 ± 8.4 • Year 2: 9.3 ± 6.7 • Year 3: 13.8 ± 10.9 • Year 1 vs. year 2, p: 0.23 • Year 1 vs. year 3, p: 0.98 • Year 2 vs. year 3, p: 0.03 **Topic-specific outcomes:** NR **Adverse events:** Length of Stay: Over the study period the median length significantly increased up to • Year 1: 9, IQR 7–22 days,

Study Data	Population and Setting	Intervention	Definitions	Results
				• Year 2: 10, IQR 7.5–18.5 days • Year 3: 14 days, IQR 8–26 days • Year 1 to year 2: p = 0.91 • Year 1 to year 3: p 0.02 • Year 2 to year 3: P = 0.02 Mortality: • Colonized: 5 (2.7%) • Non-colonized: 8 (1.5%) • p=0.30 Mupirocin resistance: NR Adverse events: NR

Author: Kaushik[7]
 	
Year: 2014
 	
Study Design: Prospective and Retrospective non-concurrent cohort study
 	
Outbreak: N
 	
Risk of bias: High
	Number of patients: N= 3088
	
	Setting: Level III NICU in one tertiary hospital
	
	Location: US
	
	Dates: April 1, 2006-March 31, 2010
	
	Period 1: Pre-MRSA surveillance = April 1, 2006-March 31, 2008
	
	Period 2: Post-implementation of MRSA Surveillance period = April 1, 2008-March 31, 2010
	
	Inclusion Criteria: All infants admitted to the NICU between April 1, 2006-March 31, 2010.
	
	Exclusion Criteria: NR
		Intervention group:
		n = 1512
		Period 2: April 1, 2008
		• New surveillance policy implemented that involved testing all infants for MRSA nasal carriage via PCR upon admission and every 2 weeks using MRSA selective agar cultures.
		• Neonates colonized at admission or during hospitalization were cohorted in a designated room throughout hospitalization.
		• HCP observed contact precautions with gloves and gowns throughout hospitalization for infants in cohort room.
		
		Device/agent: Bundled intervention
		
		Monitoring (compliance) intervention:
		NR
		
		Control/Comparison group:
		n = 1576
		Period 1: NR
		
		Standard preventive measures: NR
			Outcomes:
			MRSA colonization and/or MRSA-related BSI
			
			MRSA-related BSI- clinical disease with isolation from blood
			
			Sampling strategy: Nasal swabs on admission and every 2 weeks
			
			Testing: PCR testing and chromogenic agar after admission test
			
			Other notes: None
				MRSA-related BSI:
				• Period 1: 6/1576 (3.8/1000 patient admissions)
				• Period 2: 8/1512 (5.3/1000 patient admissions)
				• p=0.73
				
				MRSA-related BSI in colonized neonates
				Period 2:
				• all MRSA BSI occurred after detection of colonization with MRSA
				  • MRSA-BSI in colonized infants: 15%
				  • MRSA-BSI in non-colonized infants: 0%
				  • p < 0.0001
				
				MRSA colonization:
				Period 2:
				• MRSA Colonized: 54/1512 (35/1000 patient admissions)
				• Colonized at admission: 31/54 (57%)
				• Colonized during hospitalization: 23/54 (43%)
				• Detected at 2 weeks of age: 8/23 (35%)
				• Detected during later surveillance cultures: 15/23 (65%)
				  • p=0.076
				
				Topic-specific outcomes:
				Period 2: Compliance rates with the surveillance policy measures were a 100%
				
				Adverse events:
				Length of Stay, days, median (IQR):
				• Period 1: 77 (26.2-120.0)
				• Period 2: 62.5 (39.0-107.5)
				• P = 0.94
				Mortality: MRSA associated deaths, n
				• Period 1: 0

Study Data	Population and Setting	Intervention	Definitions	Results
				• Period 2: 1 (This patient was the smallest and sickest in the P2 cohort, born at 24 weeks, known to be colonized at DOL 11 and received clindamycin and gentamicin as initial empiric therapy.) • P>0.999 Mupirocin resistance: NR Adverse events: NR
Author: Morioka[13] **Year:** 2013 **Study Design:** Prospective non-concurrent cohort study **Outbreak:** N **Risk of bias:** High	**Number of patients:** N = 1646 **Setting:** Level III intensive care and level II transition care in one hospital **Location:** Japan **Dates:** Jan 2007 – Dec 2010. • January 2007-August 2008: pre-introduction of preemptive contact precautions • September 2008-December 2010: post-introduction of preemptive contact precautions **Inclusion Criteria:** All neonates admitted to the NICU from January 2007 – December 2010 **Exclusion Criteria:** None	**Intervention group:** Post-intervention period: 956/1646 September 2008 • NICU added preemptive contact precautions for up to 72 hours for all outborn infants while awaiting results from active surveillance cultures taken upon admission. **Device/agent:** Preemptive contact precautions on admission for outborn infants transferred from other hospitals or clinics **Monitoring (compliance) intervention:** compliance with HH calculated as: Compliance (%) = (# of performed actions with accurate timing/ Number of opportunities) x 100 **Control/Comparison group:** Pre-intervention period: 690/1646 **Standard preventive measures:** • Active surveillance on admission and weekly. • HCP washed hands with soap and water when visibly soiled and used ABHR for routine decontamination of hands. Plastic gloves were worn when in contact with any infant body fluids, non-intact skin, and mucous membranes. Clinical staff educated at least four time per year. • Cohorting and contact precautions were applied for infants with MRSA and other MDROs. • All clinical staff were required to wear a disposable vinyl gown and plastic gloves for all actions that may involve contact with the patient or potentially contaminated areas in patient's environment.	**Outcomes:** MRSA transmission includes colonization and apparent infection HA- MRSA transmission: Patients whose weekly surveillance or clinical cultures became positive for MRSA >48 h after admission to the NICU Outborn infants: neonates with unknown colonization transferred from other hospitals or clinics **Sampling strategy:** Active surveillance cultures for all on NICU admission (pharynx and acoustic meatus for all patients plus and umbilical cord swab for outborn patients). Weekly cultures of MRSA by nasal swab during were performed during NICU stay. **Testing:** NR **Other notes:** None	**MRSA colonization or infection on admission:** Incidence of MRSA (+) outborn: • Pre-introduction: 5/154 (3.2%) • Post-introduction: 8/209 (3.8%) • p= 0.77 Incidence of MRSA (+) inborn: none in either period **HA-MRSA colonization or infection incidence:** • Pre-introduction: 47/690 • Post-introduction: 27/956 **HA-MRSA infection incidence:** • Pre-introduction: 10/690 • Post-introduction: 1/956 • p=NR **Total HA-MRSA transmission (colonization and infection):** • Pre-introduction: 3.5 cases/1000 patient days • Post-introduction: 1.3 cases/1000 patient days • p<0.0001 **HA-MRSA infection transmission:** • Pre-introduction: 0.7 cases/1000 patient days • Post-introduction: 0.05 cases/1000 patient days • p= NR **Topic-specific outcomes:** Hand hygiene compliance for clinical staff: • Pre-introduction: 50% • Post-introduction: 75% **Adverse events:** Length of Stay, days median (range): • Pre-introduction: 8 (1-477) • Post-introduction: 9 (1-345) • P=0.92

Study Data	Population and Setting	Intervention	Definitions	Results
		• No use of preemptive contact precautions for outborn infants.		Mortality: NR Adverse events: NR
Author: Rana[18] **Year:** 2012 **Study Type:** Cohort study **Outbreak:** N **Risk of bias:** Low	**Population:** n=4304 **Setting:** Level III NICU **Location:** USA **Study dates:** 2001-2008 **Inclusion criteria:** NR **Exclusion criteria:** NR	**Intervention Group:** N=NR Period 2: 2006-2008 Surveillance cultures on admission from umbilicus and nares **Device/agent:** Screening for MRSA colonization **Monitoring (compliance) intervention:** NR **Control/Comparison group:** N=NR Period 1: 2001-2005 No policy for MRSA admission screening; SA (+) culture infants identified from electronic medical records **Standard preventive measures:** • Surveillance Screening: Weekly surveillance tracheal cultures obtained on all intubated babies • Cohorting/Contact precautions: Whenever infants with MRSA invasive disease or colonization (surface or tracheal) discovered, all infants in that room were swabbed for SA carriage (umbilical/nasal), placed in cohort with contact precautions and further managed according to infection control procedures • Decolonization: If a second case of MRSA was identified in the same room, then all infants in the room were treated with a regimen of 0.3% triclosan bath once a week (if weight > 1500 g) and intranasal mupirocin ointment. • Screening: If additional case(s) were identified in another room, then all the infants in the entire NICU were swabbed (umbilical/nasal) for SA carriage. • Cohorting/ weekly Surveillance cultures: Infants' positive for MRSA remained in a cohort and additional surveillance cultures were obtained weekly until two consecutive cultures demonstrated no growth or the infant was discharged or died.	**Outcome Definitions:** Cases: any infant with a SA-positive culture Colonized cases: positive culture from skin, anterior nares, umbilicus, or tracheal aspirate without signs or symptoms of active infection or treatment with antibiotics Infected cases: bacteremia, pneumonia, or meningitis Bacteremia and meningitis: positive SA blood or cerebrospinal fluid (CSF) cultures, respectively. Pneumonia: Centers for Disease Control/National Healthcare Safety Network (CDC/NNIS) criteria or the attending neonatologist's diagnosis based on clinical findings (including change in respiratory status, need for increased respiratory support, change in or new-onset purulent sputum requiring frequent suctioning, and leukocytosis or leukopenia associated with left shift) and radiographic findings (new or worsening infiltrates or consolidation or cavitations on serial X-rays), a SA-positive tracheal aspirate and/or blood culture and at least 7 days of antistaphylococcal antibiotic treatment. Invasive disease: necrotizing fasciitis, necrotizing pneumonia, osteomyelitis, and other deep tissue infections Total duration of positive cultures: calculated from the first day of positive culture to the day of last positive	Invasive disease • MRSA: 22/75 (29.3%) • MSSA: 46/198 (23.3%) • p=0.298 Incidence of ALL MRSA colonization and invasive disease per 1000 NICU admissions: • Period 1: 13.7 • Period 2: 24.7 • p=0.010 Incidence of ALL MSSA cultures colonization and invasive disease per 1000 NICU admissions: • Period 1: 53.6 • Period 2: 38.9 • p=0.044 Incidence of Invasive MRSA cultures per 1000 NICU admissions: • Period 1: 4.4 • Period 2: 6.40 • p=0.38 Incidence of Invasive MSSA cultures per 1000 NICU admissions: • Period 1: 9.9 • Period 2: 12.2 • p=0.49 MSSA vs MRSA More likely to be culture positive for MSSA than MRSA • Period 1: OR= 3.76 (95% CI: 2.61-5.40); p<0.001 • Period 2: OR = 1.55 (95% CI: 1.03 – 2.33); p=0.041 • p=0.010 **Adverse events:** Length of Stay, median (range): NR Mupirocin resistance: NR Chlorhexidine resistance: NR Product related adverse events: NR Mortality: NR

Study Data	Population and Setting	Intervention	Definitions	Results
		• All positive SA cultures reported as MSSA or MRSA • Additional surface cultures done on any infant with MRSA (+) tracheal aspirate, blood, or CSF culture	culture or death/discharge (which ever came first). Total duration of positive tracheal culture/colonization: calculated from the first culture positive aspirate to the last culture-positive day or the day infant was extubated **Sampling strategy**: Umbilical and nasal swabs at admission **Testing:** Cultures PFGE Methicillin resistance by disk diffusion method Molecular typing by PFGE following DNA extraction on some MRSA isolates **Other notes:** NR	
Author: Huang[27] **Year:** 2011 **Study Type:** Retrospectiv e Pre-Post **Outbreak:** N **Risk of bias:** Low	**Population:** N=1233 **Setting:** 1 hospital with 3 NICUs, Levels 1-3 **Location:** Taiwan **Study dates:** 1997 - 2007 **Inclusion criteria:** NR **Exclusion criteria:** NR	**Intervention Group (mupirocin treatment)** • Dates: 8/2005 – 7/2006 • n= 450 Aug 2005 – July 2006 • Screening: cultures collected within 24 hours of admission, or weekly for two weeks (3 times in total) • Cohorting: placed the colonized infants in a segregated area and cohorted care • Decolonization: Decolonization procedures with topical mupirocin ointment application to nares and umbilical area were administered twice daily for 5 consecutive days if stayed in NICU August 2006 –October 2007 • Screening: No active surveillance for MRSA conducted due to lack of funding **Device/agent:** Bundled interventions; Targeted mupirocin decolonization **Monitoring (compliance) intervention:**	**Outcome Definitions:** Infection: any infant with clinical isolates of MRSA who was receiving antimicrobial therapy HAI: from 1999-2007 standard CDC definition used **Sampling strategy**: Neonates: Pre-intervention: March 2003- Feb 2004: specimens from nares, postauricular areas, axillae, ad umbilicus obtained weekly and tested for MRSA Post-intervention: August 2005- July 2006: only specimens from both nares and umbilicus obtained within 24 hrs of admission and then weekly for 2 weeks (3 times total) HCWs: surveillance cultures if worked in both units	**No. of MRSA infections**, n/N (%): • No mupirocin (pre-intervention): 92/783 (12%) • Mupirocin (post-intervention): 5/450 (1.1%) • p<0.001 • OR: 11.85 (95%CI: 4.6-33.3) **No. of MRSA colonized**, n/N (%): • No Mupirocin: 323/783 (41%) • Mupirocin: 39/450 (8.7%) • p<0.001 • OR: 7.4 (95%CI: 5.1-10.76) **No. of colonized w/ infection**, n/N (%): • No Mupirocin: 84/783 (10.7%) • Mupirocin: 1/450 (0.22%) • p<0.001 • OR: 53.96 (8.1-1048) **No. of non-colonized**, n/N (%): • No Mupirocin: 460/783 (59%) • Mupirocin: 410/450 (91%) • p<0.001 • OR: 0.14 (0.1-0.2) **No. of non-colonized w/ infection**, n/N (%):

Study Data	Population and Setting	Intervention	Definitions	Results

		26/39 colonized infants received treatment;
		2/18 positive follow-up cultures—failure decolonize
		1/2 MRSA sepsis
		2/2 MRSA eradicated with second course of treatment
		
		Control/Comparison group (No mupirocin treatment)
		• Dates: 3/2003 – 2/2004
		• n= 783
		
		March 2003- Feb 2004
		• Surveillance screening: Surveillance culture for MRSA carriage
		• Cohorting: cohort care of neonates
		• Isolation: MRSA colonized infants separated from non-colonized infants—isolated
		
		Standard preventive measures:
		HCWs
		Screening: Surveillance cultures performed during surveillance periods—taken from nares of HCWs working in both units—MRSA colonized HCWs treated with intranasal mupirocin
		
		Jan 2000
		• Hand hygiene education and audits: Augmenting hand washing before and after contact with patients by Increasing infection control education of HAIs, increasing infection control practitioner's audits of HAIs, and feedback of HAIs data to the HCWs working in NICU
		July 2001
		• PICC care:
		  • Revision of standardized operation procedures for the insertion and continuous care of PICC
		  • 10% povidone-iodine containing alcohol (75%) was applied to the insertion site, normal saline used to decolorize, and the area was covered by a transparent dressing. Nurses checked the insertion site
			Surveillance culture specimens were obtained with cotton swab, placed in transport medium, and processed in lab within 4 hours.
			
			Testing:
			Culture
			Confirmation according to National Committee for Clinical Laboratory Standard guidelines
			
			Other Notes: confounded data; analysis does not align with intervention implementation
			
			April 2003
			Institution of alcohol-based hand rubs implemented due to the outbreak of severe acute respiratory syndrome (SARS) occurred in Taiwan
				• No Mupirocin: 8/783 (1.02%)
				• Mupirocin: 4/450 (0.89%)
				• p=0.819
				• OR: 1.15 (0.31-4.56)
				
				Topic Specific Outcomes:
				Patient days
				• 1999: 29,609
				• 2006: 24,199
				• 2007: 25,284
				
				HCW colonized, n/N (%):
				• No Mupirocin: 6/123 (4.9%)
				• Mupirocin: 5/85 (5.9%)
				• p=0.764
				• OR: 0.82 (0.21-3.23)
				
				Adverse Event:
				Mupirocin resistance: NR
				Chlorhexidine resistance: NR
				Product related adverse events:
				Mortality n (%): NR
				Length of Stay, median (range): NR

Study Data	Population and Setting	Intervention	Definitions	Results
		frequently and changed the dressing every 3 days. • The PICC lines were not impregnated with antibacterial or antiseptic agents and antibiotic lock prophylaxis was not used. **April 2003** Institution of alcohol-based hand rubs		
Author: Milstone[3] **Year:** 2010 **Study Design:** Retrospective cohort study **Outbreak:** N **Risk of bias:** High	**Number of patients:** N= 60 with *S. aureus* infection **Setting:** Level IV NICU in one hospital **Location:** US **Dates:** Jan 1, 2002-June 30, 2009 **Inclusion Criteria:** All infants in NICU between Jan 1, 2002 to June 30, 2009. **Exclusion Criteria:** NR	**Intervention group:** April 2007 • admission surveillance cultures were obtained from all infants transferred from outside hospitals and weekly cultures from all patients, • cohorting and isolating MRSA-colonized patients, • reinforcing hand hygiene, environmental surface cleaning, and • implementing strict contact precautions. June 2007 • MRSA colonized infants were decolonized using intranasal mupirocin and topical chlorhexidine baths for infants of 36 weeks gestational age or over 4 weeks chronological age. July 2007: • Healthcare personnel screened and carriers decolonized. **Device/agent:** Bundled intervention **Monitoring (compliance) intervention:** NR **Control/Comparison group:** NA **Standard preventive measures:** NR	**Outcomes:** MSSA or MRSA infection incidence over time **Sampling strategy**: Admission and weekly **Testing:** NR **Other notes:** Rates or IRR in post-intervention period not reported. Cluster of cases that occurred in April 2007 prompted change in IPC practices.	**MRSA infection:** N (%) = 17/60 (28%) **MSSA infection (control):** N (%) = 43/60 (72%) Pre-intervention (2002-2007): • MRSA infections: increased trend: IRR: 1.54 (95% CI 1.04-2.29) • MSSA infections: no increased trend: IRR=1.04 (95% CI 0.84-1.29) Post intervention (2007-2009): • MRSA infections: significant reduction in trend: p=.04 • MSSA infections: no reduction in trend: p= .82 **Topic-specific outcomes:** NR **Adverse events:** Length of Stay: NR Mortality: NR Mupirocin Resistance: NR Adverse events: NR
Author: Song[22] **Year:** 2010 **Study Design:** Retrospective non-concurrent cohort study	**Number of patients:** N= 218 colonized or infected with MRSA **Setting:** Levels II/III NICU outborn unit in one hospital **Location:** US	**Intervention group:** April 2007: implemented intervention Bundle II that included: • same measures as Bundle I • used real-time PCR for active surveillance screening. **Device/agent:** Bundled intervention **Monitoring (compliance) intervention:** monitoring details NR	**Outcomes:** MRSA transmission or infection MRSA colonization- recovery of MRSA from specimens collected during active surveillance or from nasal specimens MRSA infection- patients with positive MRSA cultures from normally sterile sites like blood, wound, or cerebrospinal fluid	**MRSA transmission rate**: • Bundle I: 2.95/1000 patient-days; • Bundle II: 2.13/1000 patient-days • Incidence rate ratio: 1.38 (95% CI 0.85-2.22) **MRSA infection rate:** • Bundle I: 1.3/1000 patient-days; • Bundle II: 0.5/1000 patient-days • Incidence rate ratio: 2.48 (95% CI 1.06-5.80) **Topic-specific outcomes:**

Study Data	Population and Setting	Intervention	Definitions	Results
Outbreak: Y **Risk of bias:** High	**Dates:** September 2004-March 31, 2009 Bundle I: July 2006-March 2007 Bundle II: April 2007-March 2009 **Inclusion Criteria:** infants admitted to the NICU from September 2004 through March 31, 2009 **Exclusion Criteria:** NR	**Control/Comparison group:** July 2006: implemented intervention Bundle I that included preemptive contact precautions for up to 72 hours for all new admissions without documented MRSA infection/colonization, culture-based active surveillance of nares specimens upon admission and weekly thereafter, cohorting the assignments of direct caregivers **Standard preventive measures:** Mid-September 2004; 1st outbreak • Initiated nasal surveillance cultures at admission and weekly thereafter. September 2004 – September 2005: 2nd outbreak added • Contact precautions • Cohorting patients with MRSA • Enhanced education • Improved hand hygiene compliance • Infection control professionals and NICU leadership met weekly to evaluate MRSA transmission and prevalence rate to revise infection control strategies. October 2004 – Dec 2004: added • Nasal decolonization with mupirocin (or polysporin) and umbilical stump and skin decolonization with chlorhexidine for infants >34 weeks gestation applied to MRSA patients only. November 2004: added • partial unit closure to new admissions • Screening HCP for MRSA carriage, with decolonization if positive. December 2004: • screening environment for MRSA contamination, • continued MRSA screening and decolonization of HCP Dec 2004 – Mar 2005 • Blanket decolonization with mupirocin in nasal passages applied to all patients (blanket decolonization) • cohorting assignments of direct care providers by infant MRSA status	MRSA transmission- negative for MRSA at admission and then became colonized or infected during their hospitalization **Sampling strategy**: Nares at least on admission. Subsequent sampling frequency varied throughout study. **Testing:** Rep Repetitive extragenic palindromic (Rep-PCR) **Other notes:** Investigators note PCR (in 2nd set of interventions) is more sensitive than culture and likely detected MRSA in patients missed by culture and accelerated control of MRSA but notes higher cost of PCR.	Compliance rates: • hand hygiene: range: 65% -80% • contact precautions: range 61% to 78% **Adverse events:** Length of Stay: NR Mortality: NR Mupirocin Resistance: NR Adverse events: NR

Study Data	Population and Setting	Intervention	Definitions	Results
		• increased frequency of [patient] screening to twice weekly, • Implemented unit-wide contact isolation Dec 2004 – April 2005: • Improving staff compliance with contact precautions (wearing gowns and gloves) and hand hygiene. March 2005 – Sept 2005 • reduced frequency of active screening to once weekly March 2005 – Sept 2005 • ended "blanket decolonization," • contact precautions for MRSA patients • Preemptive contact precautions applied to newly admitted patients with pending MRSA screening results.		
Author: Gill[8] **Year:** 2009 **Study Design:** Prospective non-concurrent cohort study **Outbreak**: N **Risk of bias:** High	**Number of patients:** N= 1827 NICU 1: N= 925 NICU 2: N= 903 **Setting:** Two level III NICUs in two hospitals **Location:** Philippines **Dates:** May 2003-July 2004 **Inclusion Criteria:** All infants admitted to the NICUs between May 2003 to July 2004 **Exclusion Criteria:** NR	**Intervention group:** NICU 1: 597; NICU 2: 305 Phase II: • installation of ethanol hand rub at each basinet; • staff education on hand hygiene and infection control; • Introduction of daily and monthly infection-control checklists. • Infant anterior nares and umbilical were swabbed for MRSA within 16 hours of admission, and on days 2, 7, and every 7 days thereafter until discharge. **Device/agent:** Bundled intervention **Monitoring (compliance) intervention:** No effort was made to blind NICU staff to the purpose of the observations. One-hour observations were performed intermittently during the day or night shift at a 2:1 ratio. A neonate was chosen, and then all hygiene encounters for that patient and the adjacent 2 neonates were monitored (3 neonates per observer period) **Control/Comparison group:** NICU 1: 328; NICU 2: 597 Phase I: • hand hygiene compliance surveys;	**Outcomes:** MRSA colonization **Sampling strategy**: perianal swab and/or stool sample **Testing:** Culture using Mueller-Hinton agar plates, Kirby-Bauer disk diffusion, **Other notes:** Investigators describe as "before-and-after quasi-experimental design, but CDC classified as non-concurrent cohort because infants in Phase 1 (early-late 2003) likely differed from patients in Phase II ((late 2003-2004) so cannot be regarded as a single, "open cohort" and before-after analysis. Investigators note: • Interventions were associated with increased rates of hand hygiene compliance in general and of alcohol-based hand rub in particular. • Due to lack of statistically significant declines in colonization incidence density and bacteremia due to pathogens other than MRSA, "We were unable to conclude definitively	**MRSA colonization incidence:** NICU 1: • Phase I: 41/328 (12.5%) • Phase II: 111/597 (18.6%) NICU 2: • Phase I: 263/597 (44.1%) • Phase II: 1/305 (0.3%) **Incidence density of new colonization per 1000 NICU patient days at risk:** NICU 1: • Phase I: 68.3 • Phase II: 79.3 • p=0.54 NICU 2: • Phase I: 205.8 • Phase II: 0 • p<0.001 **Topic-specific outcomes:** NR The likelihood of pre-contact hand-hygiene compliance improved at both units: • NICU 1: RR, 1.3 (95% CI 1.15–1.49) • NICU 2: RR, 1.61 (95% CI, 1.40–1.86) **Adverse events:** Length of Stay: NR Mortality: all deaths/1000 admissions NICU 1:

Study Data	Population and Setting	Intervention	Definitions	Results
		• serial surveillance cultures for all neonates; • documentation of blood culture results **Standard preventive measures:** NR	that our interventions were effective."	• Phase I: 290 • Phase II: 144 • Absolute risk reduction: 15% (19 – 20%) NICU 2: • Phase I: 598 • Phase II: 481 • Absolute risk reduction: 12% (6-18%) Mupirocin resistance: NR Adverse events: NR
Author: Ng[14] **Year:** 2004 **Study Design:** Retrospective non-concurrent cohort study **Outbreak:** N **Risk of bias:** High	**Number of patients:** N= 337 **Setting:** NICU with intensive and special care in one hospital **Location:** Hong Kong, China **Dates:** December 1993-November 1999 **Inclusion Criteria:** VLBW infants admitted to NICU between December 1993-November 1999 **Exclusion Criteria:** Infants with lethal congenital malformations or chromosomal abnormalities	**Intervention group:** n=176 Period 2: December 1996- Nov 1999: • HCP used hand rub containing 1% chlorhexidine in isopropyl alcohol and ethyl alcohol. • New protocol required wearing disposable, clean but non-sterile gloves for routine, non-invasive procedures and repeating hand rubbing on gloves before entering incubators. • Hand hygiene protocol for parents remained the same. (not defined) **Device/agent:** Improved HCP HH **Monitoring (compliance) intervention:** NR **Control/Comparison group:** n=161 Period 1: Dec 1993 - Dec 1996: • The unit utilized chlorhexidine gluconate 4% cleansing agent for handwashing and used the standard handwashing technique defined in the 1985 CDC [handwashing] guidelines. • Infection control team provided monthly lectures on hand hygiene and contact precautions. **Standard preventive measures:** NR	**Outcomes:** Late onset septicemia • Late-onset sepsis: positive blood culture and clinical features of sepsis that were detected after 72+ hrs of postnatal age. **Sampling strategy**: Sepsis screen included cerebrospinal fluid, blood, stool, urine, and endotracheal aspirate (infants on mechanical ventilation) cultures for bacteria and fungi. Central line tips and surgical specimens such as peritoneal fluid, pus, and biopsy specimens were also sent for culture. **Testing:** NR microbiology results extracted from hospital computer system. **Other notes:** • Study noted: "The reason for disproportional decrease in MRSA sepsis has not been fully elucidated….There was no concurrent reduction of MRSA sepsis in the hospital during the study period. The results also suggest that significantly more VLBW infants in NICU were discharged home without ever being infected, and few infants had multiple (2 or 3) episodes of systematic infection after switching to the HR regimen."	**Septicemic MRSA episodes (some infants had >1 episode/ patient):** • Period 1: 20/161 (14%) • Period 2: 2/176 (3%) • p=0.048 **Topic-specific outcomes:** NR **Adverse events:** NR Length of Stay**:** Hospital stay (days) median (IQR): • Period 1: 80 (39-118) • Period 2: 76 (48-109) P=NR (not noted as significant) Mortality: Infection related deaths n (%): • Period 1: 4/161 (2.5%) • Period 2: 2/176 (1.1%) • P=NR (not reported as significant) Chlorhexidine resistance: NR Adverse events: NR

Study Data	Population and Setting	Intervention	Definitions	Results
Author: Jernigan[10] **Year:** 1996 **Study Design:** TBA **Outbreak:** N **Risk of Bias:**	**Number of patients:** N= 331 **Setting:** NICU in one hospital **Location:** US **Dates:** July 18, 1991-January 30, 1992 **Inclusion Criteria:** Infants admitted to NICU during 7-month outbreak period: July 18, 1991 – January 30, 1992. **Exclusion Criteria:** NR	**Intervention group:** • Weekly surveillance cultures for all NICU patients not previously known to be colonized or infected with MRSA • Staff compliance with control measures including diligent hand washing with chlorhexidine soap was repeatedly encouraged through discussions with unit personnel and memoranda. • Attempted eradication for selected patients using regimens selected by patient's physician followed by monitoring. Eradication defined by three consecutive daily cultures of nares, axilla, groin, wound, and any previously known colonized sites); • Culture surveillance of previously colonized patients continued until discharge via 4 consecutive weekly cultures followed by monthly cultures. • Surveillance cultures of nares and any visible skin lesions of HCP who had contact with new cases of colonization during the 2 weeks that preceded first identification of colonization. **Device/agent:** Bundled intervention **Monitoring (compliance) intervention:** monitoring HH compliance NR. **Control/Comparison group:** NA **Standard preventive measures:** • Twice weekly prospective infection surveillance using Kardex method and daily monitoring for MRSA isolates from any site. • Surveillance cultures were obtained from nares, axilla, groin and sites of percutaneous devices or skin wounds. • All colonized or infected patients were placed in contact isolation until discharge or eradication of colonization had been documented. This consisted of masks within 5 ft of patient, gown for direct contact with patient, and gloves for manual contact with patient or potentially contaminated surfaces.	**Outcomes:** MRSA colonization or infection **Sampling strategy**: cultures of nares, groin, axilla, and wounds (if present) **Testing:** culture, and resistance determination by disk diffusion testing and oxacillin salt agar screening **Other notes:** Five months after the final transmission of the outbreak and 6 weeks after discharge of the final patient reservoir from the NICU, two new cases of MRSA colonization with the outbreak strain were identified in adjacent beds within the unit. Two nurses were found to be colonized with MRSA. One of these nurses (Nurse A) was epidemiologically linked to the new cases. Nurse A had worked with the last colonized infant in the isolation room of the unit. The other nurse (Nurse B), who had not worked with any of the previous MRSA cases, worked with the two new cases after Nurse A and prior to their being isolated The nurses' colonization was eradicated. No further cases of MRSA colonization or infection were observed in the ensuing 44 months. Sub-analysis is classified as prospective cohort (instead of a cross-sectional analysis of risk factors) b/c exposure classification aimed to assess exposure to isolated or un-isolated patients prior to MRSA detection.	**MRSA colonization or infection:** MRSA(+) infants: 16/331 (4.8%) • Colonized: 13/16 (81%) • Infected: 3/16 (19%) • Incidence of MRSA transmission from NICU patients: • isolated: 5 • not on isolation: 10 • Rate of MRSA transmission from NICU patients: • Isolated:0.0090/ day • Not on isolation: 0.140/ day • RR of transmission: 15.6 (95% CI 5.3-45.6), p< 0.0001 **Topic-specific outcomes:** NR During outbreak: • MRSA positive HCP: 0/144 cultures Post-outbreak: • MRSA colonized HCP: 2/181 (1.1%) **Adverse events:** Length of Stay: NR Mortality: NR Mupirocin resistance: NR Adverse events: NR

Study Data	Population and Setting	Intervention	Definitions	Results
		• Roommates and other nearby patients considered at risk were cultured for MRSA. When positive results were found, area of surveillance was widened to assure that additional undetected cases were not present.		

Author: Haley[2]
 	
Year: 1995
 	
Study Design: Prospective cohort study
 	
Outbreak: N
 	
Risk of bias: Moderate
	Number of patients: NR
	
	Setting: NICU with an intensive care (ICU), intermediate care (ITU), and long-term care (LTU) area in one hospital
	
	Location: US
	
	Dates: January 1, 1988-May 31, 1993
	
	Period 1: January 1, 1988-August 24, 1988
	
	Period 2: August 25, 1988-June 25, 1990
	
	Period 3: June 26, 1990-April 30, 1991
	
	Period 4: May 1, 1991-March 31, 1992
	
	Period 5: April 1, 1992-May 31, 1993
	
	Inclusion Criteria: infants admitted to NICU between January 1, 1988 – May 31, 1993
	
	Exclusion Criteria: Excluding [cultures] infants previously identified as colonized or infected with MRSA
		Intervention group:
		Period 2: August 225,1988 – June 25, 1990:
		• Triple dye topical antimicrobial prophylaxis use was instituted in the intermediate care area. On admission, a single application of dye was painted on the umbilical stump and surrounding 2.5 cm of skin of infants.
		• Understaffing was episodic and of mild to moderate degree
		Period 3: June 26, 1990 – April 30, 1991:
		• Triple dye used in intermediate care area
		• Understaffing became severe in immediate care area
		• March 1991: New policy designated a staff nurse as a full-time admission/ resuscitation nurse whom performed all routine admission procedures, cared for newborns in first 4 hours of life, and assisted in delivery room resuscitations. Policy was implemented intermittently for the first two months and consistently thereafter.
		Period 4 May 1, 1991 – March 31, 1992:
		• Triple dye was applied to the umbilicus and periumbilical area of all infants in ICU immediately following umbilical vessel catheterization (usually w/ in 12 hr. of birth), in addition to intermediate care babies.
		• Admission/ resuscitation nurse designated on each shift
		• New IPC nurse assigned to NICU and instituted a new campaign:
		  • visited NICU 3x/ week,
		  • ensured incubators with MRSA-positive infants were labeled with MRSA signs,
		  • conducted in-service education classes;
		  • put up signs and posters to encourage handwashing between infant contacts
		  • organized cohorts of MRSA infected/ colonized infants, and
			Outcomes:
			MRSA infection
			MRSA sepsis: required a positive blood culture accompanied w/in 24 h by clinical signs of sepsis, supporting laboratory findings and clinical response to treatment with antimicrobial agents found to be active against the isolate(s).
			MRSA colonization rate: the percentage of surveyed infants from whom MRSA was isolated.
			Incidence density: time and intensity of care adjusted incidence density:
			
			Sampling strategy: Monthly cultures of both anterior nares, both axillae, and other sites likely to be colonized
			
			Testing: Culture, Enrichment broth and incubated at 370C for 24 h before being streaked onto solid medium. Clinical specimens or broth from surveillance cultures were streaked onto mannitol-salt agar containing 6 Mg/mL oxacillin
			
			Other notes: none
				Overall MRSA infection:
				Jan 88 – March 1992: 85 infections in 76 infants
				
				Periods 1 vs. 2:
				MRSA decreased significantly in the intermediate-care area, coincident with the institution of triple dye applications (P= .01), but did not change significantly in the intensive-care area, where triple dye was not used (P= 0.5)
				
				Intermediate Care Unit (ITU) Incidence Density (infections/ 1000 patient days):
				• Period 1: Before use of triple dye 0.62 infections/1000 patient care hours
				• Period 2: After use of triple dye 0.21 infections/1000 patient care hours
				• Ratio: 0.35 (95% CI: 0.14 – 0.87); p = 0.01
				Intensive Care Unit (ICU) Incidence Density (infections/ 1000 patient days)
				• Period 1: 0.73
				• Period 2: 0.67
				• Ratio: 0.92 (95% CI: 0.41 – 2.24); p = 0.48
				
				Period 2 vs. 3:
				Intermediate care unit (ITU) Incidence Density:
				• MRSA incidence density in ITU (where daily workload-to-staffing ratio increased to 17% above maximum recommended level):
				• Increase in infections began within a month after increase in infant census and worsening staffing ratios in ITU.
				• Ratio of the intensity-adjusted incidence densities: 1.9 (95% CI: 0.7 – 4.7)
				
				MRSA ICU Incidence density (where staffing ratio did not change):
				• Ratio of the intensity-adjusted incidence densities: 1.6 (95% CI: 0.8 – 3.2)

Study Data	Population and Setting	Intervention	Definitions	Results
		• Enforced aseptic contact by all workers who entered the NICU from other hospital areas. • Period 5: April 1, 1992 – May 31, 1993: Follow up period to determine whether endemic strain was eradicated **Device/agent:** Bundled intervention **Monitoring (compliance) intervention:** NR **Control/Comparison group:** Period 1: Jan 1988 – August 1988 (no consistent new interventions applied): 2 months in 1988, admission MRSA surveillance cultures were conducted. (when NR) **Standard preventive measures:** • Emphasizing handwashing (incl in-service training on handwashing, personal reminders from IC staff, and poster campaigns to gain compliance) • Wearing gown and gloves, • Isolating colonized and infected infants, • treating colonized personnel, were begun in • Routine hand-washing procedures included an initial 3-min scrub with either 2% chlorhexidine or P-I on entrance to the NICU and 2% chlorhexidine for handwashing between infant contacts • Prospective surveillance for all nosocomial infections occurring beyond 72h of age. • During first week of each month (except July and August of 1988), cultures obtained from all infants in all areas who had not been previously identified as colonized or infected. • HCP screening of nares for all NICU personnel (incl physicians, nurses, aides, clerks, and volunteers) on 3 occasions since 1998 (when NR) • 16 focused environmental cultures (when NR)		**Period 3 (where dye was used in ITU and understaffing occurred in ITU and ICU) vs. Period 4 (where staffing ratios improved, and dye was used in ITU and ICU):** **MRSA ITU Incidence Density (infections/ 1000 patient days):** • Period 3: 0.4 • Period 4: 0.04 • Ratio of incidence densities: 0.09 (95% CI: 0.00 – 0.66); p = 0.004 **MRSA ICU incidence density (infections/ 1000 patient days):** • Period 3: 1.09 • Period 4: 0.12 • Ratio of incidence densities: 0.11 (95% CI: 0.01 – 0.46); p < 0.001 **Topic-specific outcomes:** Asymptomatic HCP carriers: 20/488 (5%) Successfully decolonized: 20/20 Confirmed by f/u cultures at 1 and 14 days after completion of regimen **Adverse events:** Length of Stay: NR Mortality: NR Skin decolonization agent resistance: NR Adverse events: NR
Author: Farrington[9] **Year:** 1990	**Number of patients:** NR **Setting:** special care baby unit (SCBU) and burn unit (BU) in one hospital	**Intervention group:** Sept 1985 – Jan 1986 July 1985: • Environment was screened July – December 1985.	**Outcomes:** MRSA colonization **Sampling strategy**: On the SCBU the nose, throat, umbilicus, ear and rectum were screened on admission.	**MRSA colonization:** N= 50 cases **Corrected acquisition Rate:** New MRSA acquisitions/ total days spent by MRSA(+) babies during each month:

Study Data	Population and Setting	Intervention	Definitions	Results

Study Design: Retrospective non-concurrent cohort study
 	
Outbreak: Y
 	
Risk of bias: High
	Location: Hong Kong, China
	
	Dates: September 1984-December 1985
	
	Inclusion Criteria: All infants in the SCBU with 104 in two wards with extensive sharing of staff and equipment from September 1984 – December 1985
	
	Exclusion Criteria: NR
		• staff were screened four times (anterior nares and hands of nurses and medical staff)
		July 1985
		• Screening revealed 3 nurses with persistent carriage and 1 with transient carriage.
		  • 1/3 offered decolonization but eft hospital before treatment
		  • 2/3 offered decolonization but moved to different department before post-treatment screening completed
		  • 1/1 transient carriage resolved
		August 1985: added:
		• staff hand hygiene education,
		• access to pump dispensers of chlorhexidine hand lotion, and
		• Regular visits from infection control nurses.
		• Due to staff shortage, no cohorting of colonized staff or patients.
		
		Device/agent: Bundled intervention
		
		Monitoring (compliance) intervention: NR
		
		Control/Comparison group:
		Sept 1984 – July 1985
		Standard preventive measures:
		• Control measures followed those of the Joint Hospital Infection Society and British Society of Antimicrobial Chemotherapy (full compliance was impossible because of limited isolation facilities and inadequate funding.)
		• Patient screening on admission. Cultures taken of nose, throat, umbilicus, ear, and rectum
			Testing: Bijoux bottles containing 2 ml broth containing 5% sodium chloride and 10 mg/1 methicillin
			
			Other notes:
			• Classified as non-concurrent cohort because infants evaluated before additional interventions added (late '84-Jul 85) likely differed from infants evaluated after interventions added (after Aug 85) so cannot be regarded as a single, "open cohort" with before- after design.
			• Authors note new hospital had cramped wards, no areas with controlled ventilation and no dedicated isolation unit.
			• Author notes "encouragement of optimal hand hygiene and removal from work of members of staff with only long-term colonization were highly effective at reducing transmission. [On p 222, they note work restrictions of HCP carrier]) This occurred despite the presence of long-stay MRSA-positive neonates, and without therapy or cohorting of staff with transient nasal colonization, and in the face of increasing numbers of admissions.
			• Eradication was not achieved, and isolations continued throughout 1986 and 1987 …. at a similar relatively low rate…."
				• Intervention: 0.0241
				• Control: 0.0729
				• P=0.013
				
				Topic-specific outcomes:
				July 1985
				• Screening revealed 3 nurses with persistent carriage and 1 with transient carriage.
				  • 1/3 offered decolonization but eft hospital before treatment transient carriage resolved
				  • 2/3 offered decolonization but (1 left hospital, the other moved to different department both of these before post-treatment screening completed)
				  • 1/1 transient carriage resolved
				Staff with dermatitis on hands: 5/108
				MRSA colonized Hand Lesions: 4/5
				
				Adverse events:
				Length of Stay: NR
				Mortality: NR
				Mupirocin resistance: NR
				Adverse events: NR

Table 36 Extracted Studies with Interventions for Preventing MSSA Transmission

Study Data	Population and Setting	Intervention	Definitions	Results
Author: Wisgrill[16] **Year:** 2017 **Study Design:** Retrospecti	**Number of patients:** N= 1056 N= 552 pre-intervention N= 504 post-intervention **Setting:** Two Level IV NICUs and two intermediate care	**Intervention group:** Post-intervention (2014-2016): N = 504 January 2014, • MSSA screening and decolonization protocol was introduced. • Screening: VLBWI that were admitted were screened for MSSA once/ week.	**Outcomes:** Primary outcome: MSSA-attributable infections (BSI and Pneumonia using NHSN definitions). Secondary outcome: Rates of MSSA-positive surveillance cultures	**Incidence rate of MSSA-attributable infections:** Pre-intervention = 1.63/1000 patient-days (CI 1.12–2.31) Post-intervention = 0.83/1000 patient-days (CI 0.47–1.35) p= 0.024 **Incidence of MSSA attributable infection:**

Study Data	Population and Setting	Intervention	Definitions	Results
ve cohort study **Outbreak:** N **Risk of bias:** High	wards in on tertiary-care academic center **Location:** Austria **Dates:** January 2011-December 2016 Pre-intervention: 2011-2013 Post-intervention: 2014-2016 **Inclusion Criteria:** Very low birth weight infants admitted during January 2011-December 2016 **Exclusion Criteria:** NR	• Decolonization: all MSSA colonized infants with central and/or peripheral lines were decolonized with the daily application of nasal mupirocin gel 3 times/ day and daily skin washing with 0.1% octenidin solution for a total of 5 days. Protocol was repeated if the infant had a positive surveillance culture after decolonization with a central and/or peripheral line in place. Infants without central/ peripheral lines in situ did not receive decolonization treatment when the surveillance culture was MSSA-positive. **Device/agent:** Bundled intervention **Monitoring (compliance) intervention:** NR **Control/ Comparison group:** Pre-Intervention: 2011-2013: N= 552 **Standard preventive measures:** • A care bundle to reduce the incidence of central-line-associated blood stream infections in premature infants (elements NR) High hygiene standards (hygiene training of NICU staff and parents) and the same antibiotic regimens were maintained in both the study periods investigated.	**Sampling strategy**: Swabs from the nares and skin **Testing:** Specimens were cultured on *S. aureus* agar in an aerobic atmosphere at 35 ± 2 ° C for 48 h. **Other notes:** Infants with MSSA-positive nasal and/or skin swabs were considered to be colonized. MSSA infection- (1) an MSSA-positive blood culture or tracheal aspirate and (2) fulfilling the modified criteria for bloodstream infection (BSI) and pneumonia of the National Healthcare Safety Network	2011-2016 = 48/1056 Pre-intervention: 32 /522 Post-intervention: 16 /504 - 2/16 received decolonization - 14/16 had negative culture prior to infection **Incidence of *S. aureus* colonization:** Post-intervention: Positive cultures: 159 (31.5%) • Colonized patients with IV lines: 121/159 (76%) Post intervention *S. aureus* colonization by year: N (%) 2014: 73/186 (39.2%) 2016: 48/177 (27.1%) p= 0.056 *S. aureus* number of patients by year (estimated from Fig 1a): 2014: N= ~75 colonized N= ~180 non-colonized 2015: N= ~30 colonized N= ~140 non-colonized 2016: N= ~45 colonized N= ~175 non-colonized **Other infections:** NR **Topic-specific outcomes:** Length of Stay: NR Mortality: NR Decolonization: N=121 decolonized infants Infants with at least 1 surveillance culture that displayed 6 negative results before discharge or transfer = 9/121 (66.6%) Negative surveillance cultures until discharge = 39/112 (34.8%) Patient-days (Mean ± SD): • Pre-Intervention: 35.5 ± 21.5 • Post-Intervention: 38.2 ± 21.3 • P=0.03 **Adverse events:** Mupirocin Resistance: noted, but not analyzed.

Study Data	Population and Setting	Intervention	Definitions	Results
				Octenidin resistance: NR Adverse events: No adverse effects were observed from application of the decolonization protocol with mupirocin and octenidin.
Author: Popoola[15] **Year:** 2016 **Study Design:** Retrospective cohort **Outbreak:** N **Risk of Bias:** High	**Number of patients:** N = 2717 neonates admitted to NICU **Setting:** Level IV NICU in a tertiary care academic medical center **Location:** USA **Dates:** April 1, 2011 – September 30, 2014 **Inclusion Criteria:** neonates admitted to the NICU from April 1, 2011 – September 30, 2014 **Exclusion Criteria:** NR	**Intervention group:** N = 1193 neonates admitted to NICU; 899 screened for MSSA; 89 grew MSSA and were decolonized April 1, 2013 • ASC program expanded to identify and decolonize for MSSA-colonized neonates • Decolonization: Mupirocin applied to nares 2x/d for 5d and baths with 2% chlorhexidine gluconate-impregnated cloths administered 48h apart for infants >2 months chronological age **Device/agent:** ACS and decolonization (nares and chlorhexidine washcloths) **Monitoring (compliance) intervention:** NR **Control/Comparison group:** **N**= 1524 Active surveillance cultures and decolonization of MRSA-colonized neonates **Standard preventive measures:** NR	**Outcomes:** NICU-attributable MSSA: 1. MSSA Clinical Culture: any clinical culture sent as a part of clinical care that grew MSSA 2. MSSA infection: any clinical culture that grew MSSA and Met NHSN surveillance definition for that HAI 3. To distinguish infection from colonization, NHSN definitions for HAIs were applied by a trained observer consistently over the study period. 4. Present on admission: collected < 3 days after admission to NICU 5. NICU-attributable: obtained ≥3 days after admission to NICU **Sampling strategy:** Nares swabs sampled weekly and at time of admission for neonates transferred from other hospitals and admitted from home. **Testing:** Culture **Other notes:** None	**MSSA:** MSSA Infections: • Pre-intervention: 31 • Post-intervention: 12 • MSSA infection incidence rate: • Pre-intervention: 1.07/1000 patient days • Post-intervention: 0.55/1000 patient days • IRR: 0.51 (95% CI: 0.14-1.82) • Immediately following the intervention, incidence rate of MSSA infections decreased by an estimated 73% • IRR: 0.27 (95% CI: 0.10 – 0.79) • But this was not sustained: IRR: 0.83 (95% CI:0.62-1.12) MSSA(+) clinical cultures: • Pre-intervention: 106 MSSA(+) clinical cultures • Post-intervention: 36 • IRR: 0.45 (95% CI: 0.22 – 0.92) • Reduction sustained during post intervention period with an estimated quarterly decrease of 21% Sensitivity analysis: a statistically significant immediate drop in level of MSSA clinical culture rates occurred only at the actual start date (p=NR) **Other infections:** NR **Topic-specific outcomes:** **Length of Stay:** median, days • Pre-intervention: 7.2 days • Post-intervention: 6.5 days • P=0.20 **Mortality:** NR **Mupirocin Resistance:** 65 isolates available for mupirocin susceptibility testing from the first 85 neonates with surveillance or clinical culture growing MRSA: 0/65 resistant to mupirocin. **Adverse events: NR**

Study Data	Population and Setting	Intervention	Definitions	Results
Author: O'Connell[4] **Year:** 2012 **Study Design:** Retrospective case series of MSSA bacteremia cases **Outbreak:** N **Risk of Bias:** Moderate	**Number of patients:** N= 54 **Setting:** Neonatal unit in tertiary referral center in one university-affiliated hospital **Location:** Ireland **Dates:** January 1, 2004-December 31, 2010 **Inclusion Criteria:** Neonates with positive blood cultures from January 1, 2004–December 31, 2010 for whom clinical data was available **Exclusion Criteria:** NR	**Intervention group:** Throughout study period: Intensification of general infection control measures including: • increased frequency of hand hygiene audits in addition to education sessions, • introduced alcohol hand sanitizer containers to all incubators, • "date of cleaning" stickers to equipment, and • "wipe-clean" covers to unit's computer keyboard. • Increase in frequency of environmental cleaning; 2008: • Parent waiting area converted into 3-bed clinical area to increase unit size to 39 cots (reduce overcrowding). Early 2010: • Introduced root cause analysis for every bacteremia episode; • Once off screening of all HCP and infants. • Cohorting and decolonization of colonized infants (decolonized using mupirocin, Octenidine hydrochloride washes and chlorhexidine powder to umbilical stump and diaper area. • Decolonization of HCP • Introduction of line insertion checklists of PVCs and CVCs, and intravascular line care bundles. **Device/agent:** Bundled intervention **Monitoring (compliance) intervention:** NR **Control/Comparison group:** N= NR **Standard preventive measures:** NR	**Outcomes:** MSSA bacteremia: Definitions for calculating the number of catheter-related infections were taken from CDC. **Sampling strategy**: Blood cultures **Testing:** characterization of strains was undertaken by both *spa* typing and multi-locus sequence typing (MLST). **Other notes:** Study noted: • "While the cause of reduction [2005] is not clear, two potential factors contributing to this reduction may be that the number of babies born weighing less than 1500 g was the lowest in 2005 out of all the years studied and also, the heightened attention to infection control practices amongst staff in 2005 following a complicated MSSA bacteremia in December 2004. Staffing levels throughout the study period were an issue with only 13 staff rostered per shift (nurse; baby ratio of 1:3)." • It is not known if reduction in prevalence in 2010 was due to intravascular line care bundles, screening for MSSA carriage with decolonization of carriers, or intensification of practices already in place such as existing hand hygiene and environmental cleaning practices or a combination of these factors • Authors notes that reduction of rate from 2009 (13.63/1000 admissions) to rate in 2010 (6.8) was statistically significant and that root cause analysis for every bacteremia episode starting in early 2010 found that line care was inadequately documented and this was fed back to NICU. However, it does not present analysis	**MSSA bacteremia:** Incidence: 55 episodes/ 55 infants Rate (incidence/ 1000 admissions): 7.3 **Bacteremia: incidence/ 1000 admissions, by year:** • 2004: 6.9 • 2005: 0 • 2006: 7 • 2007: 7.35 • 2008: 9.2 • 2009: 13.63 • 2010: 6.8 • The reduction in the number of infections in 2010 was found to be statistically significant (p= 0.036). **Other infections:** NR **Topic-specific outcomes:** Length of Stay: NR Mortality: NR **Adverse events:** Chlorhexidine or Mupirocin Resistance: NR Adverse events: Year reported: NR Complications: 10/54 (19%) • Osteomyletis: 3/10 • concurrent osteomyelitis and meningitis: 1/10 • Abscess formation: 5/10 • Death: 1/10 (in an extremely premature neonate) • Intravascular catheter-related infections: 7/10(70%) neonates with complications.

Study Data	Population and Setting	Intervention	Definitions	Results
			of association between line care and rates. • Statistical test not reported	
Author: Rana[18] **Year:** 2012 **Study Type:** Cohort study **Outbreak:** N **Risk of bias:** Low	**Population:** n=4304 **Setting:** Level III NICU **Location:** USA **Study dates:** 2001-2008 **Inclusion criteria:** NR **Exclusion criteria:** NR	**Intervention Group:** N=NR Period 2: 2006-2008 Surveillance cultures on admission from umbilicus and nares **Device/agent:** Screening for MRSA colonization **Monitoring (compliance) intervention:** NR **Control/Comparison group:** N=NR Period 1: 2001-2005 No policy for MRSA admission screening; SA (+) culture infants identified from electronic medical records **Standard preventive measures:** • Surveillance Screening: Weekly surveillance tracheal cultures obtained on all intubated babies • Cohorting/Contact precautions: Whenever infants with MRSA invasive disease or colonization (surface or tracheal) discovered, all infants in that room were swabbed for SA carriage (umbilical/nasal), placed in cohort with contact precautions and further managed according to infection control procedures • Decolonization: If a second case of MRSA was identified in the same room, then all infants in the room were treated with a regimen of 0.3% triclosan bath once a week (if weight > 1500 g) and intranasal mupirocin ointment. • Screening: If additional case(s) were identified in another room, then all the infants in the entire NICU were swabbed (umbilical/nasal) for SA carriage. • Cohorting/ weekly Surveillance cultures: Infants' positive for MRSA remained in a cohort and additional surveillance cultures were obtained weekly until two consecutive cultures demonstrated no growth or the infant was discharged or died.	**Outcome Definitions:** Cases: any infant with a SA-positive culture Colonized cases: positive culture from skin, anterior nares, umbilicus, or tracheal aspirate without signs or symptoms of active infection or treatment with antibiotics Infected cases: bacteremia, pneumonia, or meningitis Bacteremia and meningitis: positive SA blood or cerebrospinal fluid (CSF) cultures, respectively. Pneumonia: Centers for Disease Control/National Healthcare Safety Network (CDC/NNIS) criteria or the attending neonatologist's diagnosis based on clinical findings (including change in respiratory status, need for increased respiratory support, change in or new-onset purulent sputum requiring frequent suctioning, and leukocytosis or leukopenia associated with left shift) and radiographic findings (new or worsening infiltrates or consolidation or cavitations on serial X-rays), a SA-positive tracheal aspirate and/or blood culture and at least 7 days of antistaphylococcal antibiotic treatment. Invasive disease: necrotizing fasciitis, necrotizing pneumonia, osteomyelitis, and other deep tissue infections Total duration of positive cultures: calculated from the first day of positive culture to the day of last positive	Invasive disease • MRSA: 22/75 (29.3%) • MSSA: 46/198 (23.3%) • p=0.298 Incidence of ALL MRSA colonization and invasive disease per 1000 NICU admissions: • Period 1: 13.7 • Period 2: 24.7 • p=0.010 Incidence of ALL MSSA cultures colonization and invasive disease per 1000 NICU admissions: • Period 1: 53.6 • Period 2: 38.9 • p=0.044 Incidence of Invasive MRSA cultures per 1000 NICU admissions: • Period 1: 4.4 • Period 2: 6.40 • p=0.38 Incidence of Invasive MSSA cultures per 1000 NICU admissions: • Period 1: 9.9 • Period 2: 12.2 • p=0.49 MSSA vs MRSA More likely to be culture positive for MSSA than MRSA • Period 1: OR= 3.76 (95% CI: 2.61-5.40); p<0.001 • Period 2: OR = 1.55 (95% CI: 1.03 – 2.33); p=0.041 • p=0.010 **Adverse Event:** Length of Stay, median (range): NR Mupirocin resistance: NR Chlorhexidine resistance: NR Product related adverse events: NR Mortality: NR

Study Data	Population and Setting	Intervention	Definitions	Results
		• All positive SA cultures reported as MSSA or MRSA • Additional surface cultures done on any infant with MRSA (+) tracheal aspirate, blood, or CSF culture	culture or death/discharge (which ever came first). Total duration of positive tracheal culture/colonization: calculated from the first culture positive aspirate to the last culture-positive day or the day infant was extubated **Sampling strategy**: Umbilical and nasal swabs at admission **Testing:** Cultures PFGE Methicillin resistance by disk diffusion method Molecular typing by PFGE following DNA extraction on some MRSA isolates **Other notes:** NR	

Table 37 Extracted Studies Addressing Laboratory Assays and Anatomic Sampling Sites to Screen for *S. aureus* Colonization

Study Data	Setting and Location	Population and Specimens	Testing Methodology	Outcomes	Performance of Lab Test
Author: Paule[19] **Year:** 2004 **Study Design:** Diagnostic **Outbreak**: N **Risk of bias:** Low	**Setting:** 1 hospital, Level III infant special care unit **Location:** USA	**Number of patients**: N=NR **Specimens in analysis**: N=299 paired samples **Specimens per patient:** Paired nasal swabs **Inclusion criteria:** Neonates admitted from December 2002 to March 2003. **Exclusion criteria**: NR	**Sampling site/assay:** nares/ real-time PCR **Comparator site/ assay**: nares/ culture **Sampling strategy:** Weekly screening of neonates was part of routine infection control. Paired nasal samples were taken with pre-moistened, double-headed rayon tipped swabs. Both swabs were inserted into each nostril, which yielded paired swabs. The first swab was used for culture analysis and the second for real-time PCR. **Culture:** Culture swabs plated to Columbia colistin-nalidixic agar (CNA) with 5% sheep blood and incubated in 5% CO_2 at 35°C for 24–48 hrs. *S. aureus* was identified by colony morphology and a latex agglutination test. Oxacillin susceptibility testing using oxacillin disk diffusion and oxacillin agar screen was done according to guidelines from the National Committee for Clinical Laboratory Standards.	**Reported outcome:** detected presence of *S. aureus* colonization **Diagnostic accuracy:** • Colonized: 45/299 (15.1%) • Culture and PCR positive: 39/299 (13%) • Culture positive: 2/299 (0.7%) • Review of samples found only 1 and 2 colonies of *S. aureus* present on each culture plate, indicating very low-density colonization • PCR positive: 4/299 (1.3%) • Routine culture processing of samples revealed final culture results at 48h as negative for *S. aureus*; however, extended culture recovered *S. aureus* in all cases.	**Culture** (n=299): • sensitivity: 92% • specificity:100% • PPV+:100% • PPV-: 98% **PCR** (n=299): • sensitivity: 96% • specificity:100% • PPV+:100% • PPV-: 99%

Study Data	Setting and Location	Population and Specimens	Testing Methodology	Outcomes	Performance of Lab Test
			Susceptibility results were read and interpreted after 24 hrs of incubation at 35°C. **PCR:** Second swab was analyzed with primers that were designed to amplify a unique conserved region of the *femA* gene in *S. aureus* only. Tests took 2h. Controls for each run included a blank (water), *S. epidermidis* (negative), and methicillin-resistant *S. aureus* (positive). Culture considered the criterion standard		

Table 38 Extracted Studies Addressing Laboratory Assays and Anatomic Sampling sites to screen for MRSA colonization

Study Data	Setting and Location	Population and Specimens	Testing Methodology	Outcomes	Performance of Lab Test
Author: Lyles[23] **Year:** 2016 **Study Type:** Diagnostic **Outbreak**: N **Risk of Bias:** Moderate	**Setting**: multi-unit & multi-center; 10 hospitals: 10 NICUs **Location:** USA	**Number of patients**: N= 2101 **Specimens in analysis:** N= N/A Specimens per patient: 2 **Inclusion criteria:** All patients present in NICU at time of surveillance visit; f bedside verbal parental consent **Exclusion criteria:** NR	**Sampling site/ assay:** Nares, Umbilicus / PCR **Comparator** site/ assay: nares, Umbilicus/ Culture **Sampling Strategy:** Local hospital staff (infection preventionists or ICU nurses) and 1 investigator collected the specimens using sterile dry rayon swabs, one swab placed in nostril, rotated 3 times. A second swab obtained from umbilical region of each NICU patient to detect MRSA. **Lab testing:** All specimens tested by both PCR and culture. Nasal and umbilical swab specimens each were cultured with broth enrichment (tryptic soy broth with 6.5% sodium chloride) in separate tubes of and inoculated onto chromogenic agar plates. *S. aureus* was then confirmed by colonial morphology and standard biochemical techniques. Susceptibility to oxacillin was determined by using the cefoxitin disk diffusion method and mupirocin susceptibility was determined by using the E-test method. All MRSA isolates were subtyped by pulsed-field gel electrophoresis	**Reported outcome:** detected presence of MRSA colonization MRSA colonization, n (%): 89/2101 (4.2%); (95% CI: 3.4%-5.1%) MRSA colonization year-over-year relative risk: 0.93 (95% CI: 0.78-1.12) p=0.45 **Diagnostic accuracy**: • PCR + MRSA rate: 4.2% • Culture + MRSA rate: 4.3% • p=0.99 **Topic Specific Outcomes:** Compliance with the state law, %: NICUs: 95% of patients receiving active surveillance testing for MRSA	**PCR** Sensitivity • Nose only: 87% (95% CI: 77–94) • Umbilicus only: 55% (95% CI: 43–67) Negative predictive value: • Nose only: 99.4% (95% CI: 99-100) • Umbilicus only: 98% (95% CI: 97–99)

Study Data	Setting and Location	Population and Specimens	Testing Methodology	Outcomes	Performance of Lab Test
			Culture considered the criterion standard: "a positive culture result for MRSA was always considered true positive"		

Author: Francis[20]
 	
Year: 2010
 	
Study type: Diagnostic
 	
Outbreak: N
 	
Risk of bias: Moderate
	Setting: 1 hospital, tertiary neonatal ward
	
	Location: UK
		Number of Patients N=410
		
		Specimens in analysis: N=696 paired swabs
		
		Specimens per patient: Range 1–15
		
		Inclusion criteria: All patients admitted between September 2007 and September 2008
		
		Exclusion criteria: NR
			Sampling site/ assay: Nares/ Real time PCR
			
			Comparator site/ assay: Nares/ Culture
			
			Sampling strategy: Standard paired nasal swabs from neonates collected upon admission to unit and weekly thereafter.
			
			Lab testing: Swabs for culture and PCR collected at the same time. Results from PCR compared with culture results. Suspect colonies from the cultures confirmed by tube coagulase test and sensitivity testing with cefoxitime. The sensitivity and specificity of the PCR calculated in comparison with the traditional culture methods using a standard 2 x 2 table.
			
			Culture considered the criterion standard.
				Reported outcome: detection of MRSA and MSSA colonization
				
				Diagnostic accuracy:
				• MRSA colonized (positive culture or positive PCR): 12/410 (2.9%)
				• 3/12 colonized on admission
				• PCR Positive MRSA: 12/12
				• Culture Positive MRSA: 5/12
				• Culture Negative MRSA: 7/12
				  • MSSA Positive: 5/7 MSSA
				  • Outborn and receiving abx at screening: 2/7
					PCR
					• Sensitivity: 100%
					• Specificity: 98% (95% CI: 96–99%)
					• Positive predictive value: 41% (95% CI: 15–72%)
					• Negative predictive value: 100%

Author: Sarda[21]
 	
Year: 2009
 	
Study Type: Diagnostic
 	
Outbreak: Y
 	
Risk of Bias: Moderate
	Setting: 1 hospital Level III neonatal intensive care unit
	
	Location: USA
		Number of patients: N= 435
		
		Specimens in analysis: N= 1873
		
		Specimens per patient: 2, median (IQR 1 – 6)
		
		Inclusion criteria: All patients admitted to NICU from March 2007 to November 2007
		
		Exclusion criteria: NR
			Sampling site/ assay: Nares/ Real time PCR
			
			Comparator site/ assay: Nares/ Culture
			
			Sampling Strategy: Standard nasal swabs collected on a weekly basis. Specimens collected by staff after cleaning hands, swabs from the anterior nares taken using a dry swab rolled 5 times, and swabs were placed in transport container.
			
			Lab testing: All specimens tested by both PCR and culture. Swabs were cultured using Columbia colistin-nalidixic acid blood agar plates and agar plates that incorporated cefoxitin to detect MRSA. Swab specimens placed in tube of sample buffer for real-time PCR assay. Colonies identified, and presumptive *S. aureus* colonies identified via slide agglutination. Colonies sub-cultured, and antimicrobial susceptibility testing performed, and MRSA strain typing performed on all isolates obtained by culture. Culture plates with no presumptive MRSA colonies after 24 hrs incubated another 24 hrs. Then real-time PCR performed.
			
			Culture considered the criterion standard.
				Reported outcome: detected presence of MRSA colonization
				
				Diagnostic accuracy:
				• N colonized (positive culture or positive PCR): 21/435 (4.8%)
				• PCR Positive MRSA: 21/21 (100%)
				• Culture Positive MRSA: 11/21 (52.4%)
				  • Second(+) PCR: 8/11
				  • Culture (+) and PCR (+) and discharged before 2nd PCR test: 1/11
				  • Only patients with positive culture results developed frank infections.
				• Negative culture results: 10/21 (47.6%)
				  • (+) after delivery but then PCR (-)retest: 3/10
				  • Converted from PCR (-) to (+): 7/10 (after 19 days [mean]).
				  • Culture (-) and PCR (+) on at least one retest: 2/10
					PCR
					• Sensitivity: 100% (95% CI: 71.5–100%)
					• Specificity: 97.6% (95% CI: 95.7–98.9%)
					• Positive predictive value: 52.4% (95% CI: 29.8–74.3%)
					• Negative predictive value: 100% (95% CI: 99.1–100%)

Study Data	Setting and Location	Population and Specimens	Testing Methodology	Outcomes	Performance of Lab Test
Author: Huang[24] **Year:** 2006 **Study type:** Diagnostic **Outbreak:** N **Risk of bias**: Moderate	**Setting:** 1 hospital, 2 Level III NICUs **Location:** Taiwan	**Number of patients:** 783 **Specimens in analysis**:1925 **Specimens per patients:** range 1–27 specimens **Inclusion criteria:** infants admitted to either NICU from March 2003 through February 2004 **Exclusion criteria:** NR	**Sampling site/assay:** nares, postauricular areas, axillae, umbilicus, and perineum **Comparator site/ assay:** site results were compared with each other **Sampling Strategy:** Specimens from the nares, postauricular areas, axillae, umbilicus, and perineum were obtained weekly. Specimens from the perineum were discontinued after 1 month due to low yield rate. Specimens were obtained via cotton swabs and placed in transport medium and processed within 4 hrs. **Lab testing:** Identification of MRSA was confirmed according to Clinical Laboratory Standards Institutes guidelines (not further described). MRSA isolates underwent further molecular characterization.	**Reported outcome:** detected presence of MRSA colonization **Diagnostic accuracy:** • N colonized (positive culture or positive PCR): 323/783 (41.3%) infants • 1341/1925 specimens (69.7%) • ≥2 sites of colonization: 202/323 (63%) • Nares colonized: 227/323 (70%) • Umbilicus colonized: 195/323 (60%) • Nares or umbilicus colonized: 279/323 (86%) • Postauricular area colonized: 145/323 (45%) • Axillae colonized: 125/323 (30%) • 12 infants colonized in perineum before screening at this anatomic site ceased.	**Sites:** Sensitivity of sites: • Nares: 71% • Umbilicus: 60% • Nares and umbilicus were two sites most likely to yield positive culture or PCR. When sampling both sites, sensitivity of screening "could reach 90%" • Postauricular Area: NR • Axillae: NR • Perineum: NR

Author: Singh[25]
 	
Year: 2003
 	
Study Type: Diagnostic
 	
Outbreak: Y
 	
Risk of bias: Moderate
	Setting: 2 hospitals,
	• Hospital 1 — teaching hospital NICU.
	• Hospital 2 — tertiary referral center NICU.
	
	Location: USA
		Number of patients: N=38
		
		Specimens in analysis: N=558 paired cultures (373 nasal/rectal cultures, 185 nasal/axillary cultures (53/185 included umbilical cultures)
		
		Specimens per patient: NR weekly nares and rectum swabs)
		
		Inclusion criteria: Infants that were colonized or infected during the outbreak period (starting in July 2001 for hospital 1 and starting in October
			Sampling site: anterior nares and rectum
			
			Comparator site: site results were compared with each other
			
			Sampling Strategy:
			• Hospital 1 — specimens obtained weekly with sterile rayon-tip swabs.
			• Hospital 2 — specimens obtained weekly from anterior nares and rectum starting October 2001. Beginning December 2001, rectum swabbing discontinued in favor of obtaining axillary cultures instead. Umbilical stump swabs also collected in some infants.
			
			Lab testing:
			• Samples plated on mannitol salt agar and incubated at 35°C for 48 hrs. Mannitol-fermenting colonies sub-cultured onto 5% sheep blood agar plates and *S. aureus* identified using latex agglutination test. MRSA was defined as isolates which the oxacillin MIC was ≥4 µg/mL by agar technique
			• Hospital 2: All cultures were plated directly onto Colombia-colistin-nalidixic acid-5% sheep blood agar
				Reported outcome: detected presence of MRSA colonization
				
				Diagnostic accuracy:
				• N colonized (positive culture): 33/38
				• N infected: 5/38
				
				• 373 nasal/rectal pairs:
				  • (+) Nasal culture: 23/24 infants
				  • (+) Rectal culture: 7/24 infants
				  • (+) Nasal and rectal cultures: 6/24 infants
				185 nasal/axilla pairs:
				  • (+) Nasal culture: 9/9 infants
				  • (+) Axilla culture: 2/9
				  • (+) Nasal and axilla cultures: 2/9 infants
				
				53 nasal/umbilicus pairs:
				• (+) Nasal culture: 9/9 infants
				• (+) Umbilicus culture: 0/9 infants
					Sites:
					Nares
					• Sensitivity: 95.8%;
					• Negative predictive value: 99.6%
					
					Rectum
					• Sensitivity: 29.2%;
					• Negative predictive value: 93.6%
					
					Axilla
					• Sensitivity: 22.2%;
					• Negative predictive value: 95.7%
					
					Umbilicus
					• Sensitivity: 0%;
					• Negative predictive value: 83.1%
					
					% (+) culture by site:
					• Nares: 97% positive
					• Rectum: 32% positive
					• Axilla: 22% positive

Study Data	Setting and Location	Population and Specimens	Testing Methodology	Outcomes	Performance of Lab Test
		2001 for hospital 2). No end date given. **Exclusion criteria:** NR	plates and incubated at 35°C for 48 hrs. Isolates that were catalase- and coagulase-positive and demonstrated growth on 6% µg/mL oxacillin salt agar were identified as MRSA.		

3.A.3. Risk of Bias

Table 39 Risk of Bias of Observational Studies on Interventions to Prevent *S. aureus* Transmission

Author Year	All study groups derived from similar source/ reference populations	Attrition not significantly different across study groups	Measure of exposure is valid	Measure of outcome is valid	Investigator blinded to endpoint assessment or outcomes are objective	Potential confounders identified	Statistical adjustment for potential confounders done	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Bozzella 2019[11]	✓	✓	✓	✓	✓			✓	Low
Voskertchian 2017[5]	✓	✓	✓	✓	✓				Moderate
Wisgrill 2017[16]	✓		✓	✓	✓	✓		✓	Low
Popoola 2016[15]	✓		✓	✓	✓				Moderate
Ristagno 2016[17]	✓	✓	✓	✓	✓			✓	Low
Huang 2015[26]	✓		✓	✓	✓			✓	Moderate
Kaushik 2015[7]	✓		✓	✓	✓				Moderate
Geraci 2014[6]	✓		✓	✓	✓	✓		✓	Low
Delaney 2013[1]	✓		✓	✓	✓	✓		✓	Low
Morioka 2013[13]	✓		✓	✓	✓	✓			Moderate
O'Connell 2012[4]	✓		✓	✓	✓				Moderate
Huang 2011[27]	✓	✓	✓	✓	✓	✓	✓	✓	Low
Milstone 2010[3]	✓		✓		✓				High

Author Year	All study groups derived from similar source/ reference populations	Attrition not significantly different across study groups	Measure of exposure is valid	Measure of outcome is valid	Investigator blinded to endpoint assessment or outcomes are objective	Potential confounders identified	Statistical adjustment for potential confounders done	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Song 2010[22]	✓	✓	✓	✓	✓				Moderate
Gill 2009[8]			✓	✓	✓			✓	Moderate
Ng 2004[14]	✓		✓	✓	✓				Moderate
Jernigan 1996[10]	✓		✓	✓	✓			✓	Moderate
Haley 1995[2]	✓		✓	✓	✓	✓	✓		Low
Farrington 1990[9]	✓		✓		✓				High

Table 40 Risk of Bias of Individual Single-Group Descriptive Studies on Interventions to Prevent *S. aureus* Transmission

Author Year	Did the study enroll all suitable patients or consecutive suitable patients within a time period?	Was the study prospectively planned?	Were independent or blinded assessors used to assess subjective outcomes, or were the outcomes objective?	Was the funding for this study derived from a source that would not benefit financially from results in a particular direction?	Risk of Bias
Rana 2012[18]	✓	✓	✓	✓	Low

Table 41 Risk of Bias of Diagnostic Studies on Laboratory Assays and Anatomic Sites to Screen NICU Patients for *S. aureus* Colonization

Author Year	Did the study avoid using a case-control design?	Did the study enroll all suitable patients or consecutive suitable patients within a time period?	Were readers of the diagnostic test of interest blinded to the results of the reference standard?	Were patients assessed by a reference standard regardless of the test's results?	Was the funding for this study derived from a source that would not benefit financially from results in a particular direction?	Risk of Bias
Lyles 2016[23]	✓	✓		✓	✓	Moderate
Francis 2010[20]	✓	✓		✓		Moderate
Sarda 2009[21]	✓	✓		✓		Moderate
Huang 2006[24]	✓			✓	✓	Moderate

Author Year	Did the study avoid using a case-control design?	Did the study enroll all suitable patients or consecutive suitable patients within a time period?	Were readers of the diagnostic test of interest blinded to the results of the reference standard?	Were patients assessed by a reference standard regardless of the test's results?	Was the funding for this study derived from a source that would not benefit financially from results in a particular direction?	Risk of Bias
Paule 2004[19]	✓	✓	✓	✓	✓	Low
Singh 2003[25]	✓	✓		✓		Moderate

3.B. Summary of Evidence: Potential Risk Factors and Risk Indicators for *S. aureus*

Key Question 2.A. What are the risk factors and risk indicators for *S. aureus* infection in NICU patients, and do they differ between MRSA and MSSA or in the setting of an outbreak?

Key Question 2.B. What are the risk factors and risk indicators for *S. aureus* colonization in NICU patients, and do they differ between MRSA and MSSA or the setting of an outbreak?

3.B.1. Strength of Evidence

3.B.1.a. *S. aureus* Infection

Table 42 Non-modifiable infant characteristics examined for association with *S. aureus* infection

Characteristic	Resultsa
Age at admission	Younger age at admission was not associated in 1 study: - MRSA infection: 1 study[28]
Age at time of bacteremia	MRSA vs. MSSA infection: - Age at time of bacteremia was not different in infants with MRSA and MSSA infections: 1 study[29]
Age at first positive culture/ diagnosis of infection	MRSA vs. MSSA infection - There was a higher incidence of MSSA infections in older infants (whose first positive culture was at >28 days or median 32 days): 2 studies[30,31]
Birthweight	Lower birthweight was associated in 5 studies: - *S. aureus* infection: 1 study[1] - MRSA Infection: 4 studies[28,32-34] Lower birthweight was not associated in 1 study: - MRSA infection in 1 study[35] MRSA vs MSSA infection: - Birthweight was not different in infants with MRSA and MSSA infections: 1 study[29]
Delivery method (cesarean vs. vaginal)	Cesarean delivery was not associated in 1 study: - MRSA infection: 1 study[34] MRSA vs. MSSA: - Delivery method was not different for MRSA vs. MSSA infection: 1 study[31]

Characteristic	Resultsa
Gestational age	Younger gestational age was associated in 3 studies: - *S. aureus* infection: 1 study[1] - MRSA infection: 2 studies[32,33] Gestational age was not associated in 2 studies: - MRSA infection: 2 studies[34,35] MRSA vs. MSSA infection: - Gestational age was not different in infants with MRSA and MSSA infections: 3 studies[29-31]
Multiple gestation	Multiple gestation was associated in 1 study: - MRSA Infection: 1 study[32] Multiple gestation was not associated in 1 study: - MRSA infection: 1 study[33]
Race	Black race was associated in 1 study: - MRSA infection: 1 study[33] Race was not associated in 1 study: - MRSA infection: 1 study[28] MRSA vs. MSSA infection - Black race was associated with MRSA infection: 1 study[31]
Sex	Sex was not associated in 2 studies: - *S. aureus* infection: 1 study[1] - MRSA infection: 3 studies[28,34,35] MRSA vs. MSSA infection - Sex not associated: 2 studies[29,31]

Table 43 Non-modifiable maternal characteristics examined for association with *S. aureus* infection

Characteristic	Results
Maternal age	Maternal age was not associated in 1 study: - MRSA infection: 1 study[34]
Maternal antibiotic therapy during pregnancy	Maternal antibiotic therapy during pregnancy was not associated: - MRSA infection: 1 study[32]

Table 44 Non-modifiable clinical characteristics examined for association with *S. aureus* infection

Characteristic	Results
Apgar score at 1 minute	Apgar score at 1 minute was associated in 1 study - MRSA infection: 1 study[34] MRSA vs. MSSA infection: - Apgar score at 1 minute was not associated: 1 study[29]
Apgar score at 5 minutes	Apgar score was not associated: 1 study - MRSA infection: 1 study[34] MRSA vs. MSSA infection: - Apgar score not associated: 2 studies[29,31]
MRSA colonization	MRSA colonization was associated in 1 study:

Characteristic	Results
	- MRSA infection: 1 study[34]
Pneumonia	Pneumonia was not associated - MRSA infection: 2 studies[35,36]
Prior colonization	Prior colonization was associated: - *S. aureus* infection: 1 study[1] - MRSA infection: 1 study[26]
Respiratory distress syndrome	Respiratory distress syndrome was not associated in 1 study: - MRSA infection: 1 study[35]
Skin and soft tissue infection, prior	Prior skin and soft tissue infection was associated in 1 study: - MRSA infection: 1 study[35]
Surgical procedure	Surgical procedure was not associated in 1 study: - MRSA infection: 1 study[35]

Table 45 Potentially modifiable clinical characteristics examined for association with *S. aureus* infection

Characteristic	Results
Antimicrobial therapy within 24 hours after birth	Antimicrobial therapy (ampicillin, cefotaxime, gentamicin, cefazolin, or amikacin) within 24 hours of birth was not associated in 1 study: - MRSA infection: 1 study[34]
Hyperalimentation/ parenteral nutrition	Hyperalimentation or parenteral nutrition was not associated in 1 study: - MRSA infection: 1 study[35]
Incubator	Incubator stay was not associated in 1 study: - MRSA infection: 1 study[35]

3.B.1.b. *S. aureus* Colonization

Table 46 Non-modifiable infant characteristics examined for association with MRSA colonization

Characteristic	Results
Birthweight	Lower birthweight was associated in 9 studies: - MRSA colonization in 9 studies[22,24,26,28,32,33,37-39] Lower birthweight was not associated in 6 studies: - MRSA colonization in 6 studies[6,36,40-43]
Age	Older mean age was not associated in 1 study - MRSA colonization: 1 study[36]
Age at NICU admission	Older age at NICU admission was associated with MRSA in 2 studies. - MRSA colonization: 2 studies[6,44] Age at NICU admission was not associated with MRSA in 5 studies. - MRSA colonization: 5 studies[24,26,28,37,42] - One of these studies[37] conducted a subanalysis of acquired colonization and age at NICU admission was not associated with acquired colonization.
Delivery method (cesarean vs. vaginal)	Cesarean delivery was associated in 4 studies: - MRSA colonization: 3 studies[33,39,40] - Acquired MRSA colonization: 1 study[37]

Characteristic	Results
	Vaginal delivery was not associated in 1 study: - MRSA colonization: 1 study[43] Delivery method was not associated in 5 studies: - MRSA colonization: 5 studies[6,36,40,42,45]
Gestational age	Younger gestational age was associated in 8 studies: - MRSA colonization: 8 studies[24,26,32,33,37,39,44,46] - Acquired MRSA colonization: 1 study[37] Gestational age was not associated in 6 studies: - MRSA colonization: 6 studies[6,36,40,42,43,45]
Inborn Status	Inborn status was associated in 6 studies: MRSA colonization: 6 studies[6,26,33,37,39,46] Inborn status was not associated in 5 studies: - MRSA colonization: 3 studies[24,36,45,47] - Acquired MRSA colonization: subanalysis of 1 study[37]
Multiple gestation	Multiple gestation was associated in 3 studies: - MRSA colonization: 2 studies[32,33] - Acquired MRSA colonization: subanalysis of 1 study[37] Multiple gestation was not associated in 3 studies: - MRSA colonization: 3 studies[39,42,43]
Race	Black race was associated in 1 study: - MRSA colonization: 1 study[33] White race was associated as a protective factor in 1 study: - MRSA colonization: 1 study[39] Race was not associated in 6 studies: - MRSA colonization 6 studies[28,38,40,42,46,48]
Sex	Male sex was negatively associated in 2 studies: - MRSA colonization: 1 study[6] - Acquired MRSA colonization: subanalysis of 1 study[37] Sex was not associated in 15 studies: - MRSA colonization: 15 studies[24,26,28,33,36,38-40,42-46,48,49]

Table 47 Non-modifiable maternal characteristics examined for association with MRSA colonization

Characteristic	Results
Maternal age	Maternal age was not associated in 2 studies: - MRSA colonization: 2 studies[40,42]
Maternal antibiotic therapy during pregnancy	Maternal antibiotic therapy during pregnancy was not associated: - MRSA colonization: 1 study[32]
Maternal education	Maternal formal education was associated in 1 study: - MRSA colonization: 1 study[43]
Maternal hospitalization	Maternal hospitalization greater than 1 month before delivery was not associated in 1 study: - MRSA colonization: 1 study[43]

Table 48 Non-modifiable facility characteristics examined for association with MRSA colonization

Characteristic	Results
Prior admission to NICU	Prior admission to NICU was associated in 1 study - MRSA colonization: 1 study[44]
Additional unknown MRSA (+) infant on ward	An additional unknown MRSA (+) infant was associated in 1 study: - MRSA colonization: 1 study[45]
Contact with a colonized HCW	Contact with a colonized HCW was associated in 1 study: - MRSA Colonization: 1 study[45]

Table 49 Non-modifiable clinical characteristics examined for association with MRSA colonization

Characteristic	Results
Apgar score at 1 minute	Apgar score ≤3 was not associated in 1 study - MRSA colonization: 1 study[43] Apgar score <6 was not associated in 1 study - MRSA colonization: 1 study[43]
Apgar score at 5 minutes	Apgar score <8 was associated in 1 study: - Acquired MRSA colonization: 1 study[37] Apgar score was not associated: 3 studies - MRSA colonization: 2 studies[6,40] Apgar score <8 was negatively associated: - MRSA colonization: 1 study[37]
Broncho-pulmonary dysplasia	Broncho-pulmonary dysplasia was associated in 1 study: - MRSA colonization: 1 study[36]
Congenital heart disease	Congenital heart disease was not associated: - MRSA colonization: 1 study[36]
Gastrointestinal disease (admitting diagnosis)	Admitting diagnosis of GI disease was associated with a decreased risk: - MRSA colonization: 1 study[44]
Length of stay, at risk	At risk length of stay was associated: - Acquired MRSA colonization: 1 study[37] Length of Stay was not associated: - MRSA colonization: 2 studies[36,48]
Malformation	Malformation was not associated: - MRSA colonization: 2 studies[6,37]
MRSA infection (any), prior	Prior MRSA infection was associated: - MRSA colonization: 1 study[36]
Necrotizing enterocolitis	Necrotizing enterocolitis was not associated: - MRSA colonization: 1 study[36]
Retinopathy of prematurity	Retinopathy of prematurity was associated : 1 study - MRSA colonization: 1 study[44] Retinopathy of prematurity was not associated: 1 study - MRSA colonization: 1 study[42]

Characteristic	Results
Skin and soft tissue infection, prior	Prior skin and soft tissue infection was associated in 1 study: - MRSA colonization: 1 study[36]
Surgical Procedure	Occurrence of a surgical procedure was not associated in 3 studies: - MRSA colonization: 2 studies[36,42,43]
Transferred from nursery	Transfer from nursery was associated: - MRSA colonization: 1 study[37] - Acquired MRSA colonization: subanalysis of 1 study[37]

Table 50 Potentially modifiable infant characteristics examined for association with MRSA colonization

Characteristic	Results
Feeding (formula vs. Breast fed)	Feeding of formula or breast milk were not associated: - MRSA colonization: 1 study[37]

Table 51 Potentially modifiable clinical characteristics examined for association with MRSA colonization

Characteristic	Results
Antibiotic therapy (systemic)	Systemic antibacterial therapy, per day increase, was associated: - MRSA colonization: 1 study[36] - Acquired MRSA colonization: subanalysis of 1 study[37]
Antibiotic therapy, duration	Mean duration of antibiotic therapy was not associated in 1 study: - MRSA colonization: 1 study[42]
Catheterization (any)	Any catheterization was not associated: - MRSA colonization: 1 study[36]
Blood transfusion	Blood transfusion was not associated in 1 study: - MRSA colonization: 1 study[43]
Central venous line, incidence	Central venous catheter was not associated in 3 studies: - MRSA colonization: 3 studies[35,36,42,43]
Endotracheal intubation	Intubation was not associated: 2 studies - MRSA colonization: 2 studies[36,42]
Nasogastric tube	Nasogastric tube was not associated: - MRSA colonization: 1 study[36]
Foley catheter	Foley catheter was not associated: - MRSA colonization: 1 study[36]

Table 52 Potentially modifiable facility characteristics examined for association with MRSA colonization

Characteristic	Results
Days of exposure to untreated carrier	Days of exposure to an untreated carrier was associated: - MRSA colonization: 1 study[48]
HCP hand hygiene compliance	Hand hygiene compliance upon room entry and exit significantly associated when controlling for room layout (single bed vs. open): - MRSA colonization: 1 study[12] Hand Hygiene compliance was not associated: - MRSA colonization: 1 study[42]

MRSA colonization pressure	MRSA colonization pressure was associated per unit increase: - Acquired MRSA colonization: subanalysis of 1 study[37] MRSA colonization pressure was not associated: - MRSA colonization: 1 study[42]
Staff/Nurse-to-patient ratio	Increase of infant-to-staff ratio by 1 unit was associated in 1 study: - MRSA colonization: 1 study[45]
Housed in single bed room	Housing infants in a single bed unit was negatively associated: - MRSA colonization: 1 study[42]

3.B.1.c. MSSA Colonization

Table 53 Non-modifiable infant characteristics examined for association with MSSA colonization

Characteristic	Results
Birthweight	Birthweight <1000g was a significant risk factor in 1 study: - MSSA colonization: 1 study[50] Birthweight was not associated in 2 studies - MSSA colonization: 2 studies[42,51]
Mean age	Higher mean age was a significant risk factor in 1 study - MSSA colonization: 1 study[50]
Age at admission	Age at admission was not associated: - NSSA colonization: 1 study[42]
Gestational age	Younger gestational age was not associated in 3 studies: - MSSA colonization: 3 studies[42,50,51] - There was a higher incidence of MSSA colonization in the case groups of 2 studies,[50,51] but it did not reach statistical significance
Multiple gestation	Multiple gestation was not associated: - MSSA Colonization: 1 study[42,50]
Delivery method (cesarean vs. vaginal)	Delivery method not associated: - MSSA colonization: 2 studies[42,50]
Race	Race was not associated in 1 study: - MSSA colonization: 1 study[42]
Ethnicity	Ethnicity was not associated in 1 study: - MSSA colonization: 1 study[42]
Sex	Sex was not associated in 2 studies: - MSSA colonization: 2 studies[42,51]

Table 54 Non-modifiable maternal characteristics examined for association with MSSA colonization

Characteristic	Results
Maternal age	Maternal age was not associated - MSSA colonization: 1 study[42]

Table 55 Non-modifiable facility characteristics examined for association with MSSA colonization

Characteristic	Results
Length of stay, pre-colonization	Significant association: - MSSA colonization: 1 study[50]

Table 56 Non-modifiable clinical characteristics examined for association with MSSA colonization

Characteristic	Results
Apgar score at 5 minutes	Low Apgar score was a significant risk factor: 1 study - MSSA colonization: 1 study[50] Apgar score not associated: 1 study - MSSA colonization: 1 study[51]
Retinopathy of Maturity (ROM)	ROM was not associated: - MSSA colonization: 1 study[42]
Surgical Procedure	Occurrence of a surgical procedure was not associated: - MSSA colonization: 2 studies[42,50]

Table 57 Potentially modifiable facility characteristics examined for association with MSSA colonization

Characteristic	Results
Housed in single bed room	Housing infants in a single bed unit was negatively associated: - MSSA colonization: 1 study[42]
Hand hygiene compliance	Hand hygiene compliance was not associated: - MSSA colonization: 2 studies[42,50]
MSSA colonization pressure	MSSA colonization pressure was not associated: - MSSA colonization: 1 study[42]

Table 58 Potentially modifiable clinical characteristics examined for association with MSSA colonization

Characteristic	Results
Respiratory support	Respiratory support was not associated (either ETT or NCPAP): 1 study - MSSA colonization: 1 study[50]
Intubation	Intubation was not associated: - MSSA colonization: 1 study[42]
Central venous catheter	Central venous catheter was not associated: - MSSA colonization: 2 studies[42,50]
Peripheral intravenous catheter	Peripheral intravenous catheters were negatively associated: 1 study - MSSA colonization: 1 study[50]
Nasogastric/ gastric tube	Nasogastric tube was not associated: - MSSA colonization: 1 study[50]
Antibiotic therapy duration	Duration of antibiotic therapy was not associated : - MSSA colonization: 1 study[42]
Antibiotic therapy (all agents)	Administration of antibiotics was not associated : - MSSA colonization: 1 study[50]
Anti-staphylococcal antibiotics	Administration of anti-staphylococcal antibiotics was not associated : - MSSA colonization: 1 study[50]

Characteristic	Results
Gentamicin	Administration of gentamicin was negatively associated: - MSSA colonization: 1 study[50]
H2 blockers	H2 blocker administration was a significant risk factor: - MSSA colonization: 1 study[50]

3.B.2. Extracted Evidence

3.B.2.a. Study Summaries

Table 59 Extracted Studies Examining Potential Risk Factors and Risk Indicators for *S. aureus* Infection or Colonization

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with *S. aureus* infection or colonization
Author: Ericson[31] **Year:** 2015 **Study design:** Retrospective cohort **Outbreak:** N **Risk of bias:** High	**Setting:** 348 NICUs in 34 states **Bed configuration:** NR **Nurse/patient ratio:** NR **Population:** 3888 infants with 3978 infections (2868 MSSA; 1110 MRSA) **Inborn:** 2236 MSSA; 783 MRSA **Inclusion criteria:** All infants with invasive *S. aureus* infection who were discharged from calendar year 1997 through calendar year 2012 from 348 NICUs. **Exclusion criteria:** Excluded surveillance and noninvasive cultures from analysis. Infections in which all positive cultures were obtained from trachea, urine, conjunctiva, or a wound were considered to be noninvasive. Excluded cultures for which the	**Routine practices:** NR **Sampling strategy:** NR **Additional practices during study:** NR **Lab testing:** culture	**Outcomes definitions:** Invasive infection: Infections in which any positive culture was obtained from cerebrospinal fluid, blood, sterile fluid, or an abscess Single infection: positive *S. aureus* cultures obtained within 21 days of each other **Reported outcomes:** N infection: 3888/887,910 (0.4%) infants Prevalence of infection 3978 invasive *S. aureus* infections. Infections were caused more commonly by MSSA (2868 of 3978 (72.1%)) than MRSA (1110 of 3978 (27.9%)). Incidence of *S. aureus*: 44.8 infections per 10,000 infants N colonized = NA Prevalence of colonization: NA	**Associated with MSSA or MRSA infection:** • Infant characteristics: race/ethnicity, infant born at hospital where infection occurred, age at first positive culture • Clinical characteristics: oxygen support **Not associated with MSSA or MRSA infection:** • Infant characteristics: gestational age, birthweight, Apgar score, male sex, born by cesarean section, small-for-gestational age • Clinical characteristics: congenital anomaly, previous surgical procedure, inotropic support, ventilator support, antibiotic use, anti-MRSA antibiotic use

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with *S. aureus* infection or colonization
	specimen type was "unknown" or "other."			
Author: Delaney[1] **Year:** 2013 **Study design**: Retrospective cohort **Outbreak**: N **Risk of bias:** Low	**Setting**: Level 3B NICU in a tertiary care hospital **Location:** USA **Bed configuration**: NR **Nurse/patient ratio**: NR **Population:** N = 6283 neonates **Inborn:** NR **Inclusion criteria**: All neonates admitted from 2004 to 2010 identified via the hospital database. **Exclusion criteria**: NR	**Routine practices:** Isolation and cohorting for all infants found to be infected or colonized with *S. aureus*; universal decolonization of nares and umbilicus with mupirocin for all neonates on admission and throughout hospitalization. **Sampling strategy:** 2004-April 2008, no surveillance cultures, Infection surveillance cultures only. April 2008 – November 2008, bi-monthly surveillance cultures of nares of all infants, Nov 2008, frequency was changed to weekly, then admission screening was added in March 2009. **Additional practices during study:** adopted central line bundle in December 2005 **Lab testing:** Culture	**Outcome definitions:** Infection: CDC NHSN definitions Colonization: positive surveillance cultures of nares **Reported outcomes:** Characteristics associated with *S. aureus* colonization or infection N infected or colonized: • *S. aureus* infection incidence rate: 3.61/1000 patient-days • *S. aureus* infection: 66/6283 (1.1%) • *S. aureus* colonization: 77/2558 (3.0%)	**Associated with *S. aureus* infection** (multivariate): • Infant characteristics: birthweight, gestational age **Associated with *S. aureus* infection** (univariate): • Infant characteristics: birthweight, gestational age **Not associated with *S. aureus* infection**: • Infant characteristics: sex **Associated with *S. aureus* colonization** (univariate): • Infant characteristics: outborn, birthweight, gestational age • Clinical characteristics: *S. aureus* infection **Not associated with *S. aureus* colonization**: • Infant characteristics: sex
Author: Carey[30] **Year:** 2010 **Study design:** Retrospective cohort **Outbreak:** Y **Risk of bias:** High	**Setting:** Level III NICU of a university-affiliated children's hospital **Bed configuration:** 62 beds **Nurse/patient ratio:** NR **Population:** 172 **Inborn:** NR **Inclusion criteria:** Data were obtained from hospital's computerized information system to identify infants hospitalized in the NICU with positive cultures for either MSSA or MRSA from January 1, 2000 to December 31, 2007. Infection confirmation	**Routine practices:** NR **Sampling strategy:** NR **Additional practices during study:** NR **Lab testing:** Culture testing with species identification and antimicrobial susceptibility testing	**Outcomes definitions: p**atients were considered to have invasive SSTIs if there was documentation of treatment with parenteral antibiotics, and they fulfilled the following criteria: (1) purulent drainage from central line insertion site; (2) drainage or dehiscence from a surgical wound; (3) cellulitis; or (4) abscess. **Reported outcomes:** During the study period, the rate of MSSA and MRSA infections ranged from 15 to 30 infections per 1000 patient admissions. **Prevalence of infection:** MSSA n = 123 MRSA n = 49 **N colonized =** NA **Prevalence of colonization:** NA	**Associated with MSSA infection:** • Infant characteristics: age at diagnosis of infection **Not associated with MSSA infection:** • Infant characteristics: gestational age • Clinical characteristics: duration of hospitalization, clinical presentations **Not associated with MRSA infection:** • Infant characteristics: gestational age, age at diagnosis of infection • Clinical characteristics: duration of hospitalization, clinical presentations MRSA outbreaks occurred in 2002, 2005, and 2007, and an MSSA outbreak occurred in 2004

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with *S. aureus* infection or colonization
	defined as positive cultures of sterile body sites (BSI) or invasive skin and soft tissue infections (SSTIs) **Exclusion criteria:** Positive cultures from skin lesions or the conjunctiva treated with topical antibiotics, or surveillance cultures of the anterior nares were not included in the analysis.			
Author: Sakaki[34] **Year:** 2009 **Study design:** Prospective cohort **Outbreak:** N **Risk of bias:** Low	**Setting:** 1 Level 2/3 NICU with 17 beds (6 intensive care and 11 intermediate care beds) at a 350-bed teaching hospital **Location:** Japan **Bed configuration:** NR **Nurse/patient ratio:** NR **Population:** N = 923 patients **Inborn:** 25/28 (89.3%) MRSA (+) infants **Inclusion criteria:** All neonates admitted during the study period who did not require surgical intervention **Exclusion criteria:** neonates who developed MRSA < 48 hours after admission, had unidentified gestational age, discharged from NICU ≤ 48hrs after admission, hospitalized for periods > 1 year	**Routine practices:** NR **Sampling strategy:** Admitted patients to the NICU underwent a surveillance culture of an anterior nares specimen the day of admission and once a week. **Additional practices during study period:** After surveillance culture, patients colonized or infected with MRSA were isolated from non-colonized patients, and contact precautions were implemented. **MRSA lab testing:** NR	**Outcome definitions:** Hospital-acquired MRSA: the first isolation of MRSA from patients 48 hours after admission to the NICU. MRSA infection: defined according to the Centers for Disease Control and Prevention standard definition for specific infections Colonization: a case from which MRSA was isolated from any body site without infection. MRSA colonization rate: average rate of patients with MRSA colonization in all patients was calculated daily; an average during hospitalization until the day before the patient developed a MRSA infection or was discharged **Reported outcomes:** N newborns with incident or prevalent colonization = 193/923 (21%) N newborns with MRSA infection = 28/923 (2.9%)	**Associated with MRSA infection (multivariate analysis):** • Infant characteristics: birthweight • Facility characteristic: MRSA colonization rate **Not associated with MRSA infection (multivariate analysis):** • Infant characteristics: gestational age, Apgar score at 1 or 5 min, twin, cesarean section, sex, inborn, • Maternal characteristics: maternal age • Facility/ Unit characteristic: average nurse-to-patient ratio, MRSA colonization **Associated with MRSA infection (univariate analysis):** • Infant characteristics: birthweight, gestational age, Apgar score at 1 min, twin, cesarean section • Clinical characteristics: ampicillin within 24h after birth • Facility/ Unit characteristics: average MRSA colonization rate **Not associated with MRSA infection (univariate analysis):** • Infant characteristics: sex, Apgar score at 5 min, breast milk feeds, inborn, cefotaxime, gentamicin, amikacin within 24h after birth • Maternal characteristics: maternal age • Facility characteristic: average nurse-to-patient ratio

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with *S. aureus* infection or colonization
Author: Cohen-Wolkowiez[29] **Year:** 2007 **Study design:** Cohort study **Outbreak:** N **Risk of bias:** Low	**Setting:** 1 NICU at a university medical center **Location:** USA **Bed configuration:** NR **Nurse/patient ratio:** NR **Population:** N = 53 **Inborn:** NR **Inclusion criteria:** Infants < 121 days of age admitted to NICU from July 1, 1996 – June 30, 2006 who had at least 1 blood culture positive for *S. aureus.* **Exclusion criteria:** NR	**Routine practices:** NR **Sampling strategy:** Blood cultures **Additional practices during study period:** NR **Lab testing:** Blood culture samples processed using blood culture automated systems; all isolates were identified by standard microbiological methods	**Outcome definitions:** Persistence of *S. aureus* bacteremia: presence of a blood culture positive for *S. aureus* within 4 days with the same susceptibility pattern of the initial positive blood culture **Reported outcomes:** N with *S. aureus* infection = 53 N with MRSA infection = 21/53 (40%) N with MSSA infection = 32/53 (40%)	**Associated with MRSA or MSSA infection (univariate analysis):** None **Not associated with MRSA or MSSA infection (univariate analysis):** • Infant characteristics: sex, birthweight, gestation age at birth-weeks, Apgar score, age at time of bacteremia • Clinical characteristics, , ampicillin, gentamicin, tobramycin, daptomycin, antibiotics used 72 h before positive culture
Author: Huang[35] **Year:** 2005 **Study design:** Case-control study **Outbreak:** N **Risk of bias:** Low	**Setting:** 1 NICU in 1 children's hospital **Location:** Taiwan **Bed configuration:** NR **Nurse/patient ratio:** NR **Population:** N= 42 **Inborn:** NR **Inclusion criteria:** infants with nosocomial MRSA bacteremia hospitalized at study hospital during study period; controls were infants hospitalized in same NICU during same time and matched on sex, gestational age, and birthweight	**Routine practices:** standard practices **Sampling strategy:** Blood cultures **Additional practices during study period:** NR **MRSA lab testing:** Two genotyping methods, pulsed-field gel electrophoresis (PFGE) and infrequent-restriction-site PCR (IRS-PCR) were used	**Outcome definitions:** MRSA bacteremia: blood cultures obtained peripherally positive for MRSA with clinical symptoms and signs of infection such as fever, hypothermia, apnea, cyanosis, and desaturation MRSA: identified according to standard methods **Reported outcomes:** N infants with nosocomial MRSA bacteremia = 21	**Associated with MRSA infection (multivariate analysis):** • Clinical characteristics: presence of skin infection at onset; prior duration of indwelling CVC **Not associated with MRSA infection (univariate analysis):** • Prior duration of antibiotics, prior duration of hyperalimentation, prior duration of stay in incubator, prior duration of mechanical ventilation, prior duration of phototherapy, presence of CVC at onset. **Associated with MRSA infection (univariate analysis):** • Clinical characteristics: duration of indwelling CVC, presence of skin infection at onset, length of hospital stay **Not associated with MRSA infection (univariate analysis):** • Infant characteristics: sex, gestational age, birthweight, • Clinical characteristics: prior antibiotic therapy, hyperalimentation, stay in incubator, mechanical ventilation, phototherapy, presence of CVC at onset, pneumonia, respiratory distress syndrome, perinatal asphyxia, patent ductus arteriosus, intraventricular hemorrhage, surgery

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	Exclusion criteria: infants without complete medical records available for review or without the isolates available for genotyping analysis were excluded			

Table 60 Extracted Studies Examining Potential Risk Factors and Risk Indicators for MRSA Infection or Colonization

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
Author: Washam[42] **Year:** 2018 **Study design:** Retrospective case-control **Outbreak: N** **Risk of bias:** Low	**Setting:** 1 Level 4 NICU with 45 beds, at 1 university teaching hospital **Location:** USA **Bed configuration:** During 2007–2011: open and private bays; During 2012–2014: only private bays (in new facility) **Nurse/patient ratio:** NR	**Routine practices:** NR **Sampling strategy:** Nasal swabs were obtained weekly and on admission for neonates admitted from home and other hospitals. **Additional practices during study period:** Active surveillance culture (ASC) involving weekly nasal swabs for all infants and admission nasal swabs for all outborn infants. Intranasal mupirocin (twice daily for 5 days) applied to colonized infants. Infants > 36 wks. of gestational age or > 4 wks. chronological age were eligible for washing with 2% chlorhexidine gluconate (CHG) impregnated cloths twice, 48 hrs apart. Infants aged > 2 mo. were eligible for daily CHG washing for 5 days. All colonized infants were placed on contact isolation (i.e., gown and gloves for HCP and visitors) until discharge. In 2012, NICU moved to new facility consisting only of private bays. MRSA-colonized infants were placed in private rooms. Infants who became recolonized were retreated with mupirocin. **MRSA lab testing:** NR (referred to other publications that describe	**Outcome definitions:** Incident colonization: laboratory identification of the first MRSA-positive nasal surveillance culture from computerized surveillance system among infants who had 1) at least one surveillance culture at day 3 or later of their NICU stay and 2) no previous MRSA-positive clinical or surveillance cultures. Prevalent colonization: laboratory identification of MRSA-positive nasal surveillance culture from computerized surveillance system among infants cultured within 2 days of admission **Reported outcomes:** N with incident or prevalent colonization = 101/4296 (2.4%) of screened infants N with incident colonization = 87/3783 (2.4%) of screened infants at risk for incident MRSA acquisition after NICU admission Risk of incident colonization at baseline: 5.5/1000 infants (95% CI: 3.87–7.72)	**Associated with MRSA acquisition (adjusted for confounding):** • Hospital characteristics: Housed in single bed (protective factor) **Not associated with MRSA acquisition (adjusted for confounding):** • Infant characteristics: birthweight, gestational age, multiple gestation • Clinical characteristics: Operation performed, type of operation • Hospital characteristics: Infants with bed transfers, colonization pressure, hand hygiene compliance • Maternal characteristics: maternal age **Associated with MRSA acquisition (univariate analysis):** • Clinical characteristics: central venous access, **Not associated with MRSA acquisition (univariate analysis):** • Infant characteristics: sex (male), race, ethnicity, birth weight, gestational age, age at admission, multiple gestation, birth via cesarean, prolonged ROM, mortality, • Clinical characteristics: Operation performed, type of operation, antibiotic exposure, • Hospital characteristics: Infants with bed transfers, infants housed in single bed, colonization pressure, hand hygiene compliance • Maternal characteristics: maternal age

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
		plating on selective and differential media (MRSA plates) before 2008 and agar from 2008 and confirmation of suspicious colonies by Gram stain and slide coagulase testing.		
Author: Azarian[52] **Year:** 2016 **Study design:** Retrospective cohort **Outbreak:** N **Risk of bias:** Moderate	**Setting:** 1 level 3 NICU with 48 open-beds\ at 1 hospital **Location:** USA **Bed configuration:** Open beds **Nurse/patient ratio:** NR **Population:** N = 1940 infants **Inborn:** 137/177 (77.4%) colonized infants **Inclusion criteria:** NR **Exclusion criteria:** NR	**Routine practices:** Since 2004: Weekly MRSA screening of nares until detection of colonization using standardized protocol. **Sampling strategy:** Nasal swabs were obtained weekly until detection of colonization using standardized protocol or discharge. **Additional practices during study period:** Infection prevention and treatment practices followed current guidelines – colonized infants placed on contact precautions, cohorted, and assigned dedicated clinical staff; decolonization was attempted using nasal mupirocin, though infants were not rescreened to determine success; hand hygiene and contact precaution adherence was monitored through infection prevention surveillance and compliance remained high during the study period. Visitors were educated on hand hygiene and contact precautions. **MRSA lab testing:** NR	**Outcome definitions:** Colonization: positive surveillance culture Infection: MRSA isolation from clinical specimen collected during routine clinical care **Reported outcomes:** N with incident or prevalent colonization = 177/1940 (9.1%) of hospitalized infants N with infection = 33/177 (18.6%) of screened colonized infants after MRSA screening Risk of incident colonization at baseline: NR	**Associated with MRSA acquisition (univariate analysis):** • Infant characteristics: birthweight, born off-site, sex, gestational age, white race, birth by caesarean section • Clinical characteristics: **Not associated with MRSA acquisition (univariate analysis):** • Infant characteristics: multiple births, sex
Author: Pierce[48] **Year:** 2016 **Study design:** Retrospective cohort study	**Setting:** 1 Level 4 NICU with 45 beds, at 1 university teaching hospital **Location:** USA **Bed configuration:** During 2007–2011: open and private bays; During 2012–2014: only private bays (in new facility)	**Routine practices:** NR **Sampling strategy:** Nasal swabs were obtained weekly and on admission for neonates admitted from home and other hospitals. **Additional practices during study period:** Active surveillance culture (ASC) involving weekly nasal swabs for all infants and admission nasal swabs for all outborn infants. Intranasal	**Outcome definitions:** Incident colonization: laboratory identification of the first MRSA-positive nasal surveillance culture from computerized surveillance system among infants who had 1) at least one surveillance culture at day 3 or later of their NICU stay and 2) no previous MRSA-positive clinical or surveillance cultures.	**Associated with MRSA colonization (adjusted for confounding):** • Clinical characteristics: longer exposure to untreated carrier **Not associated with MRSA colonization (adjusted for confounding):** • Infant characteristics: inborn status • Clinical characteristics: length of NICU stay; longer exposure to treated carrier • Hospital characteristics: year of admission, unit census, monthly unit hand hygiene compliance **Associated with MRSA colonization (univariate analysis):** • Infant characteristics: outborn • Clinical characteristics: longer length of NICU stay

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
Outbreak: N **Risk of bias:** High	**Nurse/patient ratio:** NR **Population:** N=4296 Analysis: 3783 at-risk neonates **Inborn:** 2540/3783 (67%) – numerator and denominator reported, percentage calculated **Occupancy rate:** NR **Infant transfer between sections:** Accepts outborn infants **Inclusion criteria:** All neonates admitted from April 1, 2007-December 31, 2014 **Exclusion criteria:** NR	mupirocin (twice daily for 5 days) applied to colonized infants. Infants > 36 wks. of gestational age or > 4 wks. chronological age were eligible for washing with 2% chlorhexidine gluconate (CHG) impregnated cloths twice, 48 hrs apart. Infants aged > 2 mo. were eligible for daily CHG washing for 5 days. All colonized infants were placed on contact isolation (i.e., gown and gloves for HCP and visitors) until discharge. In 2012, NICU moved to new facility consisting only of private bays. MRSA-colonized infants were placed in private rooms. Infants who became recolonized were retreated with mupirocin. **MRSA lab testing:** NR (referred to other publications that describe plating on selective and differential media (MRSA plates) before 2008 and agar from 2008 and confirmation of suspicious colonies by Gram stain and slide coagulase testing.	Prevalent colonization: laboratory identification of MRSA-positive nasal surveillance culture from computerized surveillance system among infants cultured within 2 days of admission **Reported outcomes:** N with incident or prevalent colonization = 101/4296 (2.4%) of screened infants N with incident colonization = 87/3783 (2.4%) of screened infants at risk for incident MRSA acquisition after NICU admission Risk of incident colonization at baseline: 5.5/1000 infants (95% CI: 3.87–7.72)	• Hospital characteristics: lower unit hand hygiene compliance **Not associated with MRSA colonization (univariate analysis):** • Infant characteristics: sex, race, ethnicity
Author: Huang[26] **Year**: 2015 **Study design:** Prospective cohort study with embedded cross-over design, 2007–2008 **Outbreak:** N	**Setting**: Two level III NICUs at teaching hospital **Bed configuration**: 17 beds in NICU-1 20 beds in NICU-2 Both NICUs have 1 single-bed room, 1 two-bed room and open unit beds in which isolettes are 2 m apart; sink located between isolettes **Nurse/patient ratio:** 1:2 **Population:** N = 525; 385 (73%) admitted to NICU within 24 hrs of birth; treatment group =	**Routine practices**: Alcohol-based hand rub available for each bed **Sampling strategy:** Nares and umbilicus sampling within 24 hrs of admission then weekly for 2 weeks **Additional practices during study**: NICU-1 colonized infants given topical mupirocin to nares and umbilicus for 5 days during 1st six months; NICU-2 colonized infants received 5-day mupirocin during 2nd six months of study. All study infants given once daily disinfectant bath with soap Follow-up cultures obtained after 1 week and repeated once weekly. Sampling discontinued after 2	**Outcome definitions**: Colonization: Based on CLSI guidelines using surveillance cultures of nares and umbilicus Infection: Infants with clinical isolates of MRSA detected within 48 hrs of admission who had compatible clinical manifestations and received in vitro susceptible antimicrobial therapy **Reported outcomes:** Infected: 22/525 (4%) Colonized: 130/525 (25%); treatment group (24%) vs. control group (25%) 69/130 [53%] of colonized infants detected on admission, 43 on second	**Associated with MRSA infection**: • Infant characteristics: prior MRSA colonization **Associated with MRSA colonization** (detected at time of admission, during NICU stay, and/or readmission): • Infant characteristics: inborn, premature birth (gestational age > 28–32 weeks), low birthweight (<1000g) • Clinical diagnosis: MRSA infection (at time of positive culture in 2 readmitted infants) • Clinical interventions: longer duration of NICU stay, longer duration of hospital stay • Hospital characteristics: higher MRSA infection density **Not associated with MRSA colonization:** • Infant characteristics: age at admission, sex

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
Risk of bias: Moderate	257/525 control group = 268/525 **Inborn**: 326/525 (62%) **Location**: Taiwan **Inclusion criteria**: All neonates admitted between November 2007 and October 2008 **Exclusion criteria**: NR	consecutive negative cultures. Decolonization repeated if follow-up cultures were positive **MRSA lab testing**: Surveillance specimens placed in transport medium and processed within 4 hrs. MRSA confirmed according to Clinical Laboratory Standards Institute (CLSI) guidelines, including specimen incubation at 37°C overnight with 5% sheep blood agar. Suspected colonies of *S. aureus* were further incubated with 5% sheep blood agar at 37°C overnight. Coagulase testing performed using rabbit plasma and then cefoxitin testing to distinguish MRSA from MSSA	sampling, 16 on third sampling and 2 on readmission	
Author: Julian[12] **Year:** 2015 **Study design:** Retrospective cohort study, 2009–2011 **Outbreak**: N **Risk of bias:** Moderate	**Setting:** NICU at tertiary referral hospital **Bed configuration**: 36 single patient beds 9–14 beds in 3 open-unit areas; flexible beds organized in an 8-bed open-unit model **Nurse/patient ratio:** 1:1–3 **Population:** N = 1796 neonates **Inborn:** 0/1796 (0%) **Location:** US **Inclusion criteria:** All infants in NICU from July 2009 through November 2011 **Exclusion criteria:** Infants transferred between single-patient and open-unit bed configuration	**Routine practices:** Standard precautions used for all patients. Use of alcohol foam or hand washing stations on room entry and exit is standard. All patients in a nursing assignment are in the same bed configuration. No visitor restrictions regardless of colonization status **Sampling strategy:** Screening of anterior nares on admission and weekly thereafter **Additional practices during study:** Colonized infants placed in contact isolation; applied to staff, relatives and visitors. All providers observed for hygiene compliance **MRSA lab testing:** NR	**Outcome definitions:** Colonization: NR Infection: Confirmed late-onset sepsis (CLOS) defined as having culture positive bacterial infection of the blood or CSF on or after 72 hrs of life needing 5 or more days of antibiotic treatment **Reported outcomes:** CLOS: 3.9% of 912 infants in single-patient bed configuration vs. 4.1% of 884 infants in open unit bed configuration ($\chi^2 p = 0.89$) Colonized: 2.1% of 912 infants in single-patient bed configuration vs.3.3% of 884 infants in open-unit bed configuration ($\chi^2 p = 0.11$)	**Associated with colonization** (bivariate analysis that included bed configuration variable): • Hospital characteristics: HCP hand hygiene compliance (on room entry), HCP hand hygiene compliance (on room exit) in analysis of all infants, each additional patient increase in average unit census during their hospitalization (in analysis of subset of infants in single-patient bed configuration) **Not associated with MRSA colonization** (bivariate analysis that included bed configuration variable): • Infant characteristics: sex, ethnicity, birthweight, gestational age, Clinical Risk Index for Babies score, 5-minute Apgar score, maximum acuity score throughout stay • Maternal characteristics: type of insurance coverage • Hospital characteristics: average census (at infant's bedside), average census (in entire unit) (for infants in either bed configuration), mean MRSA colonization pressure (at patient bedside), mean MRSA colonization pressure (in entire unit), bed configuration (single patient- vs. open-unit)

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
Author: Garcia[43] **Year:** 2014 **Study design:** Prospective cohort **Outbreak:** N **Risk of bias:** Low	**Setting:** 1 NICU and nursey with 65 beds at 1 level 3 public university hospital **Location:** Brazil **Bed configuration:** Open beds **Nurse/patient ratio:** NR **Population:** N = 403 newborns and their 382 mothers **Inborn:** NR **Inclusion criteria:** all newborns born-alive **Exclusion criteria:** none	**Routine practices:** The staff in all the sectors remained the same but each HCW worked in only 1 sector during each work shift **Sampling strategy:** • Infants: Swabs of the anterior nares, oropharynx, perineum and umbilical stump were collected from newborn within 6 hours of delivery and immediately before discharge (60–72 hours of life); if remained hospitalized, surveillance cultures were collected on days 7, 14, 21 and 28 of life, unless discharge or death occurred before. • Mothers: Swabs of anterior nares, oropharynx, anus and perineum were collected from the mothers during labor; if remained hospitalized or returned to visit or breastfeed the newborn, cultures were cultured on days 3, 7, 14, 21 and 28, from their anterior nares and oropharynx. **Additional practices during study period:** Hand hygiene was performed with alcohol hand rubs, hand washing with plain soap and chlorhexidine, all of which were available in unit. **MRSA lab testing:** Sterile swabs used to culture body sites were transported in medium and added to brain heart infusion medium, incubated at 35° C for 24 hours for sample enrichment then plated in mannitol salt agar and then incubated at 35° C for 48 hours. After incubation, the characteristic colonies were plated and isolated in sheep blood agar 5% and incubated at 35° C for 24 hours. Colonies suspected to be *S. aureus* were identified by phenotypic	**Outcome definitions:** NR **Reported outcomes:** N newborns with colonization of MRSA = 59/403 (15%) newborns N mothers with colonization of MRSA = 18/382 (4.7%) mothers Risk of incident colonization at baseline: NR	**Associated with MRSA acquisition (multivariate analysis of all newborns):** • Maternal characteristics: mother with <4 years of formal education **Not associated with MRSA acquisition (multivariate analysis all newborns):** • Maternal characteristics: maternal hospitalization >1 month before delivery **Not associated with MRSA acquisition (multivariate analysis of newborns hospitalized >72 hours) (n=80):** • Infant characteristics: male sex • Mother characteristics: maternal hospitalization > month before delivery **Associated with MRSA acquisition (bivariate analysis):** • Maternal characteristics: mother with <4 years of formal education **Not associated with MRSA acquisition (bivariate analysis):** • Infant characteristics: male sex, twinning, birthweight <2000g, gestational age at birth < 37 weeks, Apgar 1st minute ≤ 3 points, Apgar 5th minute < 6 points, breastfeeding, vaginal delivery • Maternal characteristics: maternal hospitalization > month before delivery

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
		Tests, tested for virulence factors, susceptibility and submitted to molecular typing via multiplex PCR.		
Author: Geraci[6] **Year:** 2014 **Study design**: Prospective cohort study, 2009–2012 **Outbreak:** N **Risk of bias:** Moderate	**Setting**: Teaching hospital tertiary-level NICU with intensive and intermediate care sections; hospital associated with regional reference center for genetic diseases **Bed configuration**: 8 cot spaces in intensive care room 8 cots spaces in intermediate care room **Nurse/patient ratio:** 1:3 in intensive care room 1:4 in intermediate care room **Population:** N = 722 neonates **Inborn**: 428/722 (59.3%) **Location**: Italy **Inclusion criteria:** All NICU patients admitted between June 2009 and June 2012 who stayed at least 48 hrs and had at least 1 nasal swab **Exclusion criteria**: NR	**Routine practices**: Invasive device protocol included removal of central umbilical catheter at 72 hrs and substitution of any further central venous line within 21 days (maximum) in cases of suspected/documented BSI **Sampling strategy:** Anterior nasal and rectal swabs obtained weekly as part of study period surveillance protocol. Note: colonized infants were not treated with mupirocin; however, 380 infants received antibiotics in the course of NICU stay **Additional practices during study:** Contact precautions (physical separation of colonized and noncolonized neonates with the same HCP caring for both groups), use of dedicated equipment, periodic training sessions on hand hygiene and intensified sanitation of surfaces around colonized/infected infant cot spaces. Overcrowding and understaffing avoided, and length of stay minimized During 1st six months of study, surveillance cultures from HCP showed carriage of 8%; HCP decolonized (confirmed with anterior nares culture) but not furloughed to avoid understaffing **MRSA lab testing:** Surveillance specimens from the anterior nares of infants were processed within 2 hrs. Swabs were incubated overnight in Brain Hearth Infusion broth and plated onto mannitol salt agar, incubated in	**Outcome definitions:** Colonization: Infants were categorized as colonized by MRSA when at least one nasal swab tested positive Infection: NR **Reported outcomes:** Characteristics associated with MRSA colonization Outcomes: Colonized: 187/722 (30%) Not colonized: 535/722 (74%) Mean weekly colonization pressure (mean number of MRSA patient-days in week/total number of patient-days in same week by year [expressed as percentage of patient days per week]): 19.1 ± 10.7 year 1 13.4 ± 9.6 year 2 16.8 ± 13.7 year 3 Incidence of clinical infections varied over study period: 5.2/1000 year 1 6.5/1000 patient-days year 2 4.9/1000 patient-days year 3	**Associated with MRSA colonization**: • Infant characteristics: sex, inborn, admission to NICU < 24hrs after birth • Clinical interventions: length of stay, lower frequency of insertion of CVC, incidence of systemic antibacterial therapy, incidence of ampicillin-sulbactam plus gentamicin **Not associated with MRSA colonization:** • Infant characteristics: birthweight, gestational age, vaginal birth, twin birth, 5-minute Apgar score of 8+, formula feeding, breast milk feeding, malformation • Clinical interventions: endotracheal tube, nasogastric tube, nCPAP, parenteral nutrition, surgical procedure, duration of systemic antibacterial therapy, duration of ampicillin-sulbactam plus gentamicin treatment

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
		air at 35°C, and examined at both 24 and 48 hrs. Presumptive *S. aureus* isolates were identified using standard methods. MRSA colonies were searched for by colony screening onto oxacillin agar and confirmed using the cefoxitin disk diffusion test and PCR for detection of *mec*A.		
Author: Giuffre[37] **Year:** 2013 **Study design**: Prospective cohort study, 2009–2013 **Outbreak:** N **Risk of bias:** High	**Setting**: Level III NICU with intensive care and immediate care rooms at regional reference center teaching hospital **Bed configuration**: 8 cot spaces in intensive care room 8 cot spaces in intermediate care room **Nurse/patient ratio:** 1:2.7 for intensive care room and 1:2.0 in intermediate care room year-round; changes during summer to 2.0 and 1.5, respectively **Population:** N = 949 neonates; 832/949 infants with negative first culture (collected within 0–7 days after NICU admission) **Inborn**: 595/949 (62.7%) **Location:** Italy **Inclusion criteria:** Admitted to NICU between June 16, 2009 and June 15, 2013, hospitalized for at least 48 hrs, and at least 1 nasal swab collected **Exclusion criteria**: NR	**Routine practices:** NR **Sampling strategy:** Weekly nares cultures. Note: no mupirocin treatment **Additional practices during study:** Contact isolation and cohorting of MRSA infants, minimized length of stay, use of dedicated equipment, cyclic HCP training sessions and overcrowding and understaffing avoided. Also, intensified environmental sanitation with all cots cleaned post-discharge in NICU disinfection room **MRSA lab testing:** Surveillance specimens taken from anterior nares were incubated overnight in brain-heart infusion broth and then plated on mannitol salt agar. *S. aureus* isolates identified via standard methods and MRSA isolates via colony screening on oxacillin agar and confirmed by disk diffusion test and PCR for detection of *mec*A.	**Outcome definitions:** Colonization: MRSA colonization of swabs of anterior nares within the first 7 days after NICU admission (a mean of 4 days after admission) and lack of signs of infection (defined by CDC NHSN criteria for postnatally acquired infections) Infection: Centers for Disease Control and Prevention National Healthcare Safety Network criteria Acquisition: MRSA colonization of anterior nares occurring among the subset of infants whose first anterior nares cultures (collected from 0–7 days after NICU admission) were negative **Reported outcomes:** Characteristics associated with MRSA acquisition among infants whose first swab was negative Characteristics associated with colonization among all infants whose first swab was positive Outcomes: N colonized: 217/949 (22.9%) N colonized at time of first culture after NICU admission: 117/217 (53.9%) N colonized at time of later cultures during NICU admission: 100/217 (46.1%) Mean quarterly colonization incidence density was 6.84 cases/1000 patient days (95% CI: 5.62–8.31) during study period, but varied by quarter	**Associated with MRSA acquisition** (multivariate analysis*): • Infant characteristics: female sex, lower birthweight • Clinical interventions: duration of systemic antibacterial therapy, length of stay • Hospital characteristics: colonization pressure **Not associated with MRSA acquisition** (multivariate analysis*): • Infant characteristics: malformation **Associated with risk of MRSA acquisition** (univariate analysis*): • Infant characteristics: female sex, twin birth, cesarean section, lower 5-minute Apgar score, lower gestational age, lower birthweight, higher diagnosis-related group weight • Clinical diagnosis: malformation • Clinical interventions: use of central venous access device, endotracheal tube, nasogastric tube, nCPAP, length of stay, systemic antibacterial therapy • Hospital characteristics: higher colonization pressure **Not associated with MRSA acquisition** (univariate analysis*): • Infant characteristics: inborn, age at NICU admission under 24 hrs, transferred from hospital nursery, breast fed, formula fed • Clinical interventions: use of parenteral nutrition, surgical procedure • Hospital characteristics: bed occupancy rate, infant-to-nurse ratio *Analysis restricted to 832 infants (100 colonized and 732 noncolonized) whose first culture (collected 0–7 days after NICU admission) was negative **Associated with MRSA colonization within first week of NICU admission** (univariate analysis):** • Infant characteristics: inborn, higher birthweight (>2500 grams), lower gestational age, 5 min Apgar score of 8+ **Not associated with MRSA colonization within first week of NICU admission** (univariate analysis):** • Infant characteristics: sex, twin birth, cesarean delivery, younger age at admission (< 24 hrs old) • Clinical diagnosis: malformation

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
			During study period, colonization incidence declined by about half except during one transient increase after importation of new MRSA strain and period of overcrowding	
Author: Kuo[36] **Year:** 2013 **Study design**: Cross-sectional prevalence study **Outbreak:** N **Risk of bias:** Low	**Setting:** Level III NICUs across 7 hospitals **Bed configuration**: NR **Nurse/patient ratio:** NR **Population:** N = 251 **Inborn:** 198/251 (79%) **Location:** Taiwan **Inclusion criteria**: NICU patients across the 7 facilities who were cultured on October 11 or December 12, 2011 **Exclusion criteria**: Infants in these NICUs who were not cultured on these dates	**Routine practices**: NR **Sampling strategy:** Nares and umbilicus specimens (one each) from each patient **Additional practices during study**: NR **MRSA lab testing:** Swab samples were inoculated via streak plate method onto Trypticase soy agar with 5% sheep blood plates and incubated at 37° C overnight. *S. aureus* colonies identified via morphologic evaluation, Gram staining, and coagulase tests of strains grown on agar plates. MRSA identified via cefoxitin disks using the disk diffusion method per Clinical and Laboratory Standards Institutes recommendations	**Outcome definitions:** NR **Reported outcomes:** Characteristics associated with MRSA colonization Outcomes: N colonized among infants across all 7 NICUs: 11/251 (4.4%)	**Associated with MRSA colonization** (multivariate analysis): • Clinical diagnosis: prior skin and soft tissue infection **Not associated with MRSA colonization** (multivariate analysis): • Infant characteristics: age • Clinical diagnoses: bronchopulmonary dysplasia, prior MRSA infection • Clinical interventions: antimicrobial use at time of sampling **Associated with MRSA colonization** (univariate analysis): • Infant characteristics: older age • Clinical diagnoses: bronchopulmonary dysplasia, prior skin and soft tissue infection, prior MRSA infection • Clinical interventions: antibiotic use at time of sampling **Not associated with MRSA colonization** (univariate analysis): • Infant characteristics: sex, inborn, gestational age, birthweight, birth location (specific ICU) • Clinical diagnoses: pneumonia, respiratory distress syndrome, congenital heart disease, necrotizing enterocolitis • Clinical interventions: any catheterization (endotracheal tube, central venous or arterial catheter, urinary catheter, chest tube, other drainage tube.), central venous catheter, intubation, nasogastric tube, Foley urine catheter, length of stay in NICU, surgical procedures
Author: Macnow[44] **Year:** 2013 **Study design**: Retrospective cohort study **Outbreak:** NICU 1 had MRSA outbreak	**Setting:** Two Level III NICUs at 2 academic medical centers **Bed configuration**: NR **Nurse/patient ratio:** NR **Population**: N = 1725 **Inborn**: In this facility (but not necessarily during study period) NICU 1: ~ 75% NICU 2: ~ 85%	**Routine practices**: Neither NICU performed routine surveillance for AROs in inborn infants nor ongoing surveillance of transferred patients following admission cultures, except during periods of an ARO outbreak **Sampling strategy:** NICU 1: Before 2006, only infants admitted at age ≥ 3 days had surveillance cultures. From 2006–2010, at admission, all outborn infants had surveillance cultures of nares for MRSA, VRE and AR-GNR. Before fourth quarter of 2007, only anterior nares cultured for MRSA.	**Outcome definitions**: Colonization: Patients were defined as colonized if surveillance cultures were positive for MRSA. Positive MRSA culture from swabs collected at 3+ days of age (during period before 2006) or from swabs collected when transferred to NICU (during period 2006–2010). Infection: NR **Reported outcomes:** Characteristics associated with MRSA colonization. Outcomes: N colonized: 52/1725 (3%)	**Associated with MRSA colonization at admission** (univariate analysis): • Infant characteristics: older age at admission, younger gestational age, lower birthweight, previous admission to study NICUs • Clinical diagnosis: admitting diagnosis of retinopathy of prematurity **Not associated with MRSA colonization at admission** (univariate analysis): • Infant characteristics: sex • Clinical diagnosis: GI disease

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
in 2005 and 2007 NICU 2 had no outbreaks during study period **Risk of bias:** High	**Location:** US **Inclusion criteria**: admitted or readmitted to study NICUs from study hospitals or other hospitals between June 2004 and December 2010 (NICU 1) or June 2007 and December 2010 (NICU 2) and had 1+ surveillance culture obtained within 1st day after admission **Exclusion criteria:** admitted or readmitted from home or surveillance cultures not obtained 2+ days after admission to study NICUs	Starting in fourth quarter of 2007, surveillance cultures included nares, groin, axilla, and umbilical regions NICU 2: Surveillance cultures from all transferred infants regardless of age throughout study period **Additional practices during study**: Colonized infants >1500 g were decolonized. All transferred infants placed on contact precautions at admission; was continued throughout hospitalization if surveillance culture(s) were positive but discontinued once negative. During ARO outbreaks, surveillance cultures were continued after NICU admission. **MRSA lab testing:** In NICU 1, multisite swabs were inoculated onto colistin nalidixic acid agar and/or MRSA. Presumptive staphylococcal colonies were identified using catalase, latex agglutination and combination ID/AST panel. In NICU 2, swabs were inoculated onto colistin nalidixic acid and mannitol salt agar until August 2008. From September 2008–August 2009, BBL MRSA plates were used. From September 2009–2010, MRSA plates were used before final negative results could be reported after 24 hrs incubation. An Assay was used on suspicious colonies to identify MRSA isolates		
Author: Nübel[45] **Year:** 2013 **Study design**: Retrospec	**Setting:** Neonatology unit in a tertiary care hospital **Bed configuration:** NR **Nurse/patient ratio:** NR **Population:** N = 60 **Inborn**: 53/60 (88.3%)	**Routine practices**: NR **Sampling strategy**: Screening of all admitted infants by nasopharyngeal and perianal swabbing for MRSA culture once a week from February 8th, 2010, and twice weekly from July 21st, 2010 until the end of study	**Outcome definitions**: Cases: NICU patient in whom colonization or infection with MRSA *spa* type *t032* was detected during the study period. Colonization and infection were not further defined Exposure period**:** Presumptive exposure period for MRSA transmission was from birth or one day before the last	**Associated with MRSA colonization or infection** (being a case): • Hospital characteristics: each additional unknown MRSA-positive infant on ward, increased infant to-staff ratio by 1 unit, contact with colonized healthcare worker **Not associated with MRSA colonization or infection** (being a case): • Infant characteristics: male sex, multiple gestation, mean gestational age, cesarean section birth, inborn • Clinical diagnosis: bradycardia

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
tive matched case-control study **Outbreak:** N **Risk of bias:** High	**Location:** Germany **Inclusion criteria**: Infants in the NICU from February 8, 2010 through August 31, 2010. Controls were matched for birthweight (±100 g); when > 2 eligible controls were identified. Two controls were randomly selected. **Exclusion criteria:** NR	**Additional practices during study**: Staff members (166) were also screened by nasopharyngeal swabbing in both February and August 2010 **MRSA lab testing**: NR	negative swab to one day before the first positive swab **Reported outcomes**: Characteristics associated with colonization or infection with MRSA **Outcomes:** N colonized = 18 N infected = 5	• Clinical interventions: peripheral venous line, kangaroo care (skin-to-skin), blood transfusion, x-ray treatments, gastric tube, sonographies, mechanical ventilation with intubation, parenteral nutrition, antibiotic therapy during exposure, oral medications, central venous line, physiotherapy, length of stay • Hospital characteristics: additional unknown MRSA-positive infant in room, known MRSA-positive infant on ward • The presumptive exposure period for MRSA transmission was from birth or one day before the last negative swab to one day before the first positive swab. In addition to basic data like mode of delivery, etc. authors compared a wide range of exposures in the presumed exposure period of each case and in the corresponding days of life of the controls.
Author: Lazenby[40] **Year:** 2012 **Study design**: Prospective cohort study **Outbreak:** N **Risk of bias**: High	**Setting:** Level III NICU at academic medical center **Bed configuration**: NR **Nurse/patient ratio**: NR **Population:** N = 212 (Risk factor analysis based on 205 infants) **Inborn:** 212/212 (100%) **Location:** US **Inclusion criteria:** Neonates delivered by women admitted for preterm labor, preterm premature rupture of membranes, and/or an indicated iatrogenic preterm delivery and screened for MRSA, January 2009 through March 2010 **Exclusion criteria**: Outborn infants not admitted to the NICU	**Routine infection prevention practices:** NR **Sampling strategy:** Nares, axilla, and diaper area cultures on admission then repeated twice weekly for as long as the neonate remained MRSA negative **Additional practices during the study:** NR **MRSA lab testing**: Specimens collected in BD Culture-Swabs with liquid transport media. Swabs were inoculated on MRSA plates and incubated for 24 hrs at 35°C. Green colonies consistent with MRSA were then identified using conventional microbiologic techniques	**Outcome definitions**: NR **Reported outcomes**: Characteristics associated with colonization with MRSA **Outcomes**: N colonized = 13/212 (6.3%); 4/13 (30.8%) were colonized within 7 days of admission N infected = 3/212 (1.4%)	**Associated with MRSA colonization** (multivariate analysis) : • Infant characteristics: cesarean delivery **Associated with MRSA colonization** (univariate analysis): • Infant characteristics: cesarean delivery • Clinical diagnosis: **Not associated with MRSA colonization** (univariate analysis): • Infant characteristics: black ethnicity, mean birthweight, mean gestational age, low 5 min APGAR (<6 points), male sex • Maternal characteristics: maternal age > 35 years
Author: Maraqa[33] **Year:** 2011	**Setting:** Level III NICU **Bed configuration**: NR **Nurse/patient ratio:** NR	**Routine practices**: NR **Sampling strategy:** Nasal MRSA surveillance cultures on admission to NICU. Sampling protocol changed 18	**Outcome definitions:** Colonization: Isolation of MRSA from anterior nares without evidence of infection.	**Associated with MRSA infection** (multivariate analysis, timing of detection unknown): • Infant characteristics: lower gestational age • Clinical diagnosis: MRSA colonization • Clinical interventions: longer length of stay

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
Study design: Retrospective cohort study **Outbreak:** N **Risk of bias**: High	**Population:** N = 2048 **Inborn:** 1616/2048 (79%) **Location:** US **Inclusion criteria:** All neonates admitted to NICU from January 2004 through December 2006 **Exclusion criteria:** NR	weeks into study (when no infants were positive) to culture of inborn neonates at first weekly surveillance after birth **Additional practices during study**: MRSA colonized, or infected neonates kept in contact isolation and cohorted until weekly surveillance results available and received nasal mupirocin ointment for 5 days Weekly surveillance cultures of infants not MRSA colonized or infected Staff in-service provided education on hand hygiene and control of MRSA spread. Visitors limited to parents and grandparents **MRSA lab testing**: Swabs were streaked onto differential media, MRSA plates, and incubated aerobically at 35–37°C for 24hrs ± 4 hrs. Plates examined for mauve-colored colonies consistent with MRSA. If negative, plates were incubated for another 24 hrs. If mauve colonies detected, specimen was reported as positive for MRSA	Infection: Isolation of MRSA from normally sterile sites (e.g., blood, urine, or CSF) or from nonsterile sites (e.g., skin, eye, or umbilical stump) in the presence of clinical signs of infection using the National Healthcare Safety Network criteria for nosocomial infection. LBW infants: ≤ 2500 g Low gestational age: infants born at 32 weeks or earlier **Reported outcomes**: Characteristics associated with colonization or infection with MRSA **Outcomes:** N colonized = 138/2048 (6.74%) N infected = 41/2048 (2%) Prevalence of colonization: 3.356/1000 patient-days (95% CI: 3.043–4.205) Prevalence of infection: 0.997/1000 patient-days (95% CI: 0.692–1.302)	**Associated with MRSA infection** (univariate analysis): • Infant characteristics: lower birthweight, lower gestational age, black race • Clinical diagnosis: MRSA colonization • Clinical interventions: longer length of stay **Associated with MRSA infection among subset of infants with prior MRSA colonization**: • Clinical interventions: longer length of stay **Not associated with MRSA infection among subset of infants with prior MRSA colonization:** • Infant characteristics: mean birthweight, mean gestational age, black race, mode of delivery, multiple gestation status **Associated with MRSA colonization** (univariate analysis): • Infant characteristics: inborn, black race, cesarean delivery, lower birthweight, lower gestational age, multiple gestation • Hospital characteristics: inborn • Clinical interventions: longer length of stay **Not associated with MRSA colonization** (univariate analysis): • Infant characteristics: sex
Author: Carey[30] **Year:** 2010 **Study design:** Retrospective cohort **Outbreak:** Y **Risk of bias:** High	**Setting:** Level III NICU of a university-affiliated children's hospital **Bed configuration:** 62 beds **Nurse/patient ratio:** NR **Population:** 172 **Inborn:** NR **Inclusion criteria:** Data were obtained from hospital's computerized information system to identify infants hospitalized in the NICU with positive cultures for	**Routine practices:** NR **Sampling strategy:** NR **Additional practices during study:** NR **Lab testing:** Culture testing with species identification and antimicrobial susceptibility testing	**Outcomes definitions:** patients were considered to have invasive SSTIs if there was documentation of treatment with parenteral antibiotics, and they fulfilled the following criteria: (1) purulent drainage from central line insertion site; (2) drainage or dehiscence from a surgical wound; (3) cellulitis; or (4) abscess. **Reported outcomes:** During the study period, the rate of MSSA and MRSA infections ranged from 15 to 30 infections per 1000 patient admissions. Prevalence of infection: MSSA n = 123	**Associated with MSSA infection:** • Infant characteristics: age at diagnosis of infection **Not associated with MSSA infection:** • Infant characteristics: gestational age • Clinical characteristics: duration of hospitalization, clinical presentations MRSA outbreaks occurred in 2002, 2005, and 2007, and an MSSA outbreak occurred in 2004 **Not associated with MRSA infection:** • Infant characteristics: gestational age, age at diagnosis of infection • Clinical characteristics: duration of hospitalization, clinical presentations

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
	either MSSA or MRSA from January 1, 2000 to December 31, 2007. Infection confirmation defined as positive cultures of sterile body sites (BSI) or invasive skin and soft tissue infections (SSTIs) **Exclusion criteria:** Positive cultures from skin lesions or the conjunctiva treated with topical antibiotics, or surveillance cultures of the anterior nares were not included in the analysis.		MRSA n = 49 N colonized = NA Prevalence of colonization: NA	
Author: Song[22] **Year:** 2010 **Study design**: Retrospective case control study **Outbreak:** N **Risk of bias**: High	**Setting:** Level III–IV NICU that provides tertiary care to neonates with complicated conditions such as preterm birth, very low birthweight, genetic disorder, or organ failure **Bed configuration**: NR **Nurse/patient ratio:** NR **Population:** N = 2280 **Inborn:** NR **Location**: US **Inclusion criteria**: All newborns and infants admitted to NICU from September 2004 through March 2008 (readmissions during study period analyzed for first visit only) **Exclusion criteria**: NR	**Routine practices**: Active screening since 2004; nasal swab samples of patients upon admission and weekly thereafter throughout their stay. Screening compliance was over 95% **Sampling strategy:** Nasal swab samples taken on admission and weekly thereafter during NICU stay **Additional practices during study**: NR **MRSA lab testing:** Two methods used. 1) A traditional culture method was used from September 2004 to April 2007. After April 2007, real-time rapid PCR employed. 2) Specimens (e.g., skin, soft tissue, blood) tested using 5% sheep blood agar, chocolate agar, and colistin-nalidixic acid agar. For specific lab requests to rule out MRSA, mannitol salt agar was added to the inoculation media to detect MRSA	**Outcome definitions**: Colonization: Patient who had one or more specimens collected for MRSA screening that grew MRSA Infection: Patient who presented with clinical symptoms followed by the recovery of MRSA from one or more non-nasopharyngeal specimens **Reported outcomes**: Characteristics associated with colonization or infection with MRSA Outcomes: N infected = 63 (2.76%) N colonized = 128 (5.61%) N infected or colonized (on admission) = 60 N infected or colonized (during stay) = 131	**Associated with MRSA infection or colonization** (univariate analysis): • Infant characteristics: lower birthweight (≤1000 g) • Clinical interventions: use of extracorporeal membrane oxygenation procedure, use of central line, respiratory support • Clinical diagnosis: necrotizing enterocolitis **Not associated with MRSA infection or colonization** (univariate analysis): • Infant characteristics: ethnicity, sex, age at admission
Author: Song[28]	**Setting:** Level I–III NICU outborn unit	**Routine practices**: NR	**Outcome definitions**:	**Associated with MRSA colonization or infection** (being a case) [multivariate analysis]:

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
Year: 2010 **Study design:** Retrospective matched case-control study **Outbreak:** Y **Risk of bias**: High	**Bed configuration**: Open floor design of 6 bays for 42 isolates **Nurse/patient** ratio: NR **Population:** N = 136 **Inborn:** 0/136 **Location:** US **Inclusion criteria**: Infants who stayed in the NICU between September 2004 and March 2009; risk factor analysis with matched controls conducted September 2004–September 2005 **Exclusion criteria**: NR	**Sampling strategy**: Active surveillance on admission and weekly thereafter **Additional practices during study:** Infection control professionals and NICU leadership met weekly to evaluate MRSA transmission and prevalence rate and to review management plan as needed. Basic infection control measures included contact precautions, isolation or cohorting of patients, and improving HCP hand hygiene compliance November 2004: After rise in MRSA nasal decolonization implemented with mupirocin or polysporin and chlorhexidine gluconate body washes for infants older than 30 days or greater than 36 weeks gestation. At onset protocol only for known colonized or infection infants December 2004: protocol expanded to all infants as was contact precautions and part of NICU closed to new admissions Direct care providers were cohorted such that nursing staff cared either for MRSA patients or non-MRSA patients during a given shift; 227 HCP providing care to NICU patients screened and decolonized if positive July 2006: another increase in MRSA colonization prompted use of bundles; Bundle-I included preemptive contact precautions for up to 72 hrs for all new admissions with no documented history of colonization or infection, active surveillance of nasal specimens on admission and weekly thereafter, and cohorting of direct care givers April 2007: Bundle-2 included preemptive contact precautions, cohorting staff assignments, and use	Colonization: Recovery of MRSA from specimens collected during active surveillance or from nasal specimens obtained during routine medical care from patients without clinical indications of infection Infection: Patients with positive MRSA cultures from normally sterile sites (blood, wound, CSF) Very low birthweight: 751–1000 g Extremely low birth weight infants: less than 750 g **Reported outcomes**: Characteristics associated with colonization or infection with MRSA Outcomes: N colonized/infected: 68	• Infant characteristics: lower birthweight • Clinical interventions: prolonged ventilator use **Associated with MRSA colonization or infection** (univariate analysis): • Infant characteristics: lower birthweight • Clinical interventions: respiratory support, prolonged use of a central line **Not associated with MRSA colonization or infection** (multivariate analysis): • Clinical interventions: use of central line, number of clinical consultations **Not associated with MRSA colonization or infection** (univariate analysis): • Clinical interventions: mupirocin use

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
		of real time PCR of nasal specimens collected on admission **MRSA lab testing:** specimens were cultured using standard method of detection and isolates were characterized using Repetitive extragenic palindromic-Polymerase Chain Reaction technique		
Author: Sakaki[34] **Year:** 2009 **Study design:** Prospective cohort **Outbreak:** N **Risk of bias:** Low	**Setting:** 1 Level 2/3 NICU with 17 beds (6 intensive care and 11 intermediate care beds) at a 350-bed teaching hospital **Location:** Japan **Bed configuration:** NR **Nurse/patient ratio:** NR **Population:** N = 923 patients **Inborn:** 25/28 (89.3%) MRSA (+) infants **Inclusion criteria:** All neonates admitted during the study period who did not require surgical intervention **Exclusion criteria:** neonates who developed MRSA < 48 hours after admission, had unidentified gestational age, discharged from NICU ≤ 48hrs after admission, hospitalized for periods > 1 year	**Routine practices:** NR **Sampling strategy:** Admitted patients to the NICU underwent a surveillance culture of an anterior nares specimen the day of admission and once a week. **Additional practices during study period:** After surveillance culture, patients colonized or infected with MRSA were isolated from non-colonized patients, and contact precautions were implemented. **MRSA lab testing:** NR	**Outcome definitions:** Hospital-acquired MRSA: the first isolation of MRSA from patients 48 hours after admission to the NICU. MRSA infection: defined according to the Centers for Disease Control and Prevention standard definition for specific infections Colonization: a case from which MRSA was isolated from any body site without infection. MRSA colonization rate: average rate of patients with MRSA colonization in all patients was calculated daily; an average during hospitalization until the day before the patient developed a MRSA infection or was discharged **Reported outcomes:** N newborns with incident or prevalent colonization = 193/923 (21%) N newborns with MRSA infection = 28/923 (2.9%)	**Associated with MRSA infection (multivariate analysis):** • Infant characteristics: birthweight • Facility characteristic: MRSA colonization rate **Not associated with MRSA infection (multivariate analysis):** • Infant characteristics: gestational age, Apgar score at 1 or 5 min, twin, cesarean section, sex, inborn • Maternal characteristics: maternal age • Facility/ Unit characteristic: average nurse-to-patient ratio, MRSA colonization **Associated with MRSA infection (univariate analysis):** • Infant characteristics: birthweight, gestational age, Apgar score at 1 min, twin, cesarean section • Clinical characteristics: ampicillin within 24h after birth • Facility/ Unit characteristics: average MRSA colonization rate **Not associated with MRSA infection (univariate analysis):** • Infant characteristics: sex, Apgar score at 5 min, breast milk feeds, inborn, cefotaxime, gentamicin, amikacin within 24h after birth • Maternal characteristics: maternal age • Facility characteristic: average nurse-to-patient ratio
Author: Cohen-Wolkowiez[29] **Year:** 2007	**Setting:** 1 NICU at a university medical center **Location:** USA **Bed configuration:** NR	**Routine practices:** NR **Sampling strategy:** Blood cultures **Additional practices during study period:** NR	**Outcome definitions:** Persistence of *S. aureus* bacteremia: presence of a blood culture positive for *S. aureus* within 4 days with the same susceptibility pattern of the initial positive blood culture	**Associated with MRSA vs. MSSA infection (univariate analysis):** None **Not associated with MRSA vs. MSSA infection (univariate analysis):** • Infant characteristics: sex, birthweight, gestation age at birth-weeks, Apgar score, age at time of bacteremia • Clinical characteristics, ampicillin, gentamicin, tobramycin, daptomycin, antibiotics used 72 h before positive culture

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
Study design: Cohort study **Outbreak:** N **Risk of bias:** Low	**Nurse/patient ratio:** NR **Population:** N = 53 **Inborn:** NR **Inclusion criteria:** Infants < 121 days of age admitted to NICU from July 1, 1996 – June 30, 2006 who had at least 1 blood culture positive for *S. aureus.* **Exclusion criteria:** NR	**Lab testing:** Blood culture samples processed using blood culture automated systems; all isolates were identified by standard microbiological methods	**Reported outcomes:** N with *S. aureus* infection = 53 N with MRSA infection = 21/53 (40%) N with MSSA infection = 32/53 (40%)	
Author: Schultz[46] **Year:** 2009 **Study design:** Prospective cohort **Outbreak:** N **Risk of bias:** Low	**Setting:** 1 NICU with 49 beds at 1 university medical center **Location:** USA **Bed configuration:** NR **Nurse/patient ratio:** NR **Population:** N = 1760 **Inborn:** 1269/1760 **Inclusion criteria:** all neonates admitted to medial center during study period **Exclusion criteria:** neonates who died during hospitalization	**Routine practices:** Weekly MRSA surveillance on all NICU patients during study period (June 2004-December 2006) using PCR or culture (before May 2006) nasopharyngeal swab samples Contact isolation/ cohorting: Patients identified as colonized with MRSA were placed on contact isolation and cohorted both by location and by healthcare providers **Sampling strategy:** Weekly PCR or culture (before May 2006) nasopharyngeal swab samples **Additional practices during study period:** NR **MRSA lab testing:** NR	**Outcome definitions:** NR **Other definitions:** NR **Reported outcomes:** N newborns with incident or prevalent colonization = 59/1760 (3.35%)	**Associated with MRSA acquisition (univariate analysis):** • Infant characteristics: gestational age, inborn birth, **Not associated with MRSA acquisition (univariate analysis):** • Infant characteristics: male sex, race
Author: Huang[24] **Year:** 2006 **Study design:**	**Setting:** 2 (of 3) level III NICUs on separate floors at single teaching hospital **Bed configuration**: NR **Nurse/patient ratio**: NR	**Routine practices**: NR **Sampling strategy**: All infants admitted or transferred to NICU routinely screened on weekly basis (i.e., 0-7 days after admission). Weekly MRSA surveillance cultures from nares, postauricular area, axillae,	**Outcome definitions**: Colonization: Isolation of MRSA from weekly surveillance cultures Infection: Colonized infant in whom MRSA was isolated from clinical isolates of infants who were receiving antimicrobial therapy	**Associated with MRSA infection**: • Infant characteristics: MRSA colonization * **Associated with MRSA infection with colonization (vs. colonization alone):** • Infant characteristics: premature birth (< 28 weeks), birthweight < 1000 g) **Associated with MRSA colonization:**

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
Prospective cohort study **Outbreak:** N **Risk of bias**: Moderate	**Population**: N = 783 **Inborn:** 399/783 (51%) **Location**: Taiwan **Inclusion criteria**: Infants admitted to either NICU from March 2003 through February 2004 **Exclusion criteria**: NR	umbilicus, and perineum (perineum cultures discontinued after first month due to low yield rate) **Additional practices during study period:** Colonized infants separated from noncolonized infants and cared for by designated cohort of nurses. Surveillance cultures (nares) obtained from HCP at 3 points during study. MRSA-colonized HCP were administered nasal mupirocin treatment **MRSA lab testing**: Specimens placed in transport medium and processed within 4 hrs. Identification of MRSA was confirmed according to National Committee for Clinical Laboratory Standards guidelines. MRSA isolates underwent further molecular characterization	Episodes of infection considered distinct if > 2 weeks apart, a course of effective antibiotics had been administered, the symptoms had resolved, and infant had documentation of 1+ negative culture from the site that was originally infected site **Reported outcomes**: Characteristics associated with colonization and infection Outcomes: N colonized: 323/783 (41.3%) 89% of colonized infants were detected by the first 2 surveillance cultures	• Infant characteristics: premature birth (< 28 weeks), low birthweight (1100– 1500 g) **Not associated with MRSA colonization**: • Infant characteristics: sex, inborn status, age at admission * >80% of these infected infants had previous or concurrent colonization and MRSA strain in clinical isolates were indistinguishable from strains in surveillance cultures in > 90% of episode)
Author: Huang[35] **Year:** 2005 **Study design:** Case-control study **Outbreak:** N **Risk of bias:** Low	**Setting:** 1 NICU in 1 children's hospital **Location:** Taiwan **Bed configuration:** NR **Nurse/patient ratio:** NR **Population:** N= 43 **Inborn:** NR **Inclusion criteria:** infants with nosocomial MRSA bacteremia hospitalized at study hospital during study period; controls were infants hospitalized in same NICU during same time and matched on sex, gestational age, and birthweight	**Routine practices:** standard practices **Sampling strategy:** Blood cultures **Additional practices during study period:** NR **MRSA lab testing:** Two genotyping methods, pulsed-field gel electrophoresis (PFGE) and infrequent-restriction-site PCR (IRS-PCR) were used	**Outcome definitions:** MRSA bacteremia: blood cultures obtained peripherally positive for MRSA with clinical symptoms and signs of infection such as fever, hypothermia, apnea, cyanosis, and desaturation MRSA: identified according to standard methods **Reported outcomes:** N infants with nosocomial MRSA bacteremia = 21	**Associated with MRSA infection (multivariate analysis):** • Clinical characteristics: presence of skin infection at onset; prior duration of indwelling CVC **Not associated with MRSA infection (univariate analysis):** • Prior duration of antibiotics, prior duration of hyperalimentation, prior duration of stay in incubator, prior duration of mechanical ventilation, prior duration of phototherapy, presence of CVC at onset. **Associated with MRSA infection (univariate analysis):** • Clinical characteristics: duration of indwelling CVC, presence of skin infection at onset, length of hospital stay **Not associated with MRSA infection (univariate analysis):** • Clinical characteristics: duration of the following: prior antibiotic therapy, hyperalimentation, stay in incubator, mechanical ventilation, phototherapy, presence of CVC at onset, pneumonia, respiratory distress syndrome, perinatal asphyxia, patent ductus arteriosus, intraventricular hemorrhage, surgery

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
	Exclusion criteria: infants without complete medical records available for review or without the isolates available for genotyping analysis were excluded (n=22)			
Author: Khoury[32] **Year:** 2005 **Study design** Retrospective nested case-control study **Outbreak:** Y **Risk of Bias:** Moderate	**Setting:** Level III–IV community hospital NICU used for routine admissions **Bed configuration**: 18-bed NICU divided into two large rooms with five sections; 2–5 beds per section; room 1 has additional section for 3 isolation beds **Nurse/patient ratio**: NR **Population:** N = 80 **Inborn:** 0/80 **Location:** US **Inclusion criteria:** All colonized and infected NICU patients present in the NICU on October 14, 2001 and all admitted from January 2001 through January 2002 **Exclusion criteria**: NR	**Routine practices:** Routine surveillance of all clinical cultures to monitor incidence of nosocomial MRSA infections **Sampling strategy:** Routine surveillance identified cluster of 6 cases in the NICU prompting active culture surveillance. Samples from periumbilical and perirectal areas **Additional practices during outbreak**: Infected/colonized patients were placed in contact isolation and cohorted geographically. Colonized patients received mupirocin ointment BID to anterior nares and umbilical area for 7 days Visible signs were placed on beds of infected patients to remind staff and patients' families about compliance with contact isolation (including gloves, gowns, and sometimes face masks for all direct contact), and hand hygiene One-time screening cultures of HCP in NICU from anterior nares. Colonized HCP were decolonized and underwent 3 repeat weekly nasal cultures to assess clearance and identify persistent carriage. Positive HCP (6/110 [5.5%]) took a hexachlorophene shower daily and received oral antibiotics (BID for one week) and mupirocin ointment for the anterior nares Infection control nurses directly observed HCP and educated them about proper contact isolation	**Outcome definitions:** Cases: Were defined as infants in the NICU during January 1, 2001 to January 31, 2002 who had a positive culture for MRSA Controls: Prior to October 14, 2001, controls were defined as infants who had negative culture for MRSA and were in the NICU during the same time period as a case. After October 14, 2001, controls were randomly selected from infants with negative MRSA surveillance screening cultures **Reported outcomes:** characteristics associated with MRSA colonization or infection Outcomes: N cases:12 N controls: 68	**Associated with MRSA infection**: • Infant characteristics: low birthweight, lower gestational age, multiple gestation • Clinical interventions: longer length of stay, gavage feeding, endotracheal intubation **Associated with MRSA colonization**: • Infant characteristics: low birthweight, low gestational age, multiple gestation **Not associated with MRSA infection or colonization**: • Maternal characteristics: maternal antibiotic therapy during pregnancy **Not associated with MRSA colonization:** • Clinical interventions: gavage feedings, use of endotracheal tube

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
		techniques and the importance of hand hygiene before and after every patient contact Unit-wide cleaning with quaternary ammonium disinfectants at the beginning of outbreak, but no environmental cultures performed **MRSA lab testing:** Identification of MRSA from screening cultures was performed using oxacillin salt agar plates according to methods recommended by the National Committee for Clinical Laboratory Standards. All MRSA isolates (NICU and HCP) were then saved for molecular typing and analysis of the SCC*mec* cassette and Panton-Valentine leukocidin		
Author: Uehara[41] **Year:** 2001 **Study design:** Retrospective cohort study **Outbreak:** N **Risk of bias:** High	**Setting:** Referral NICU divided into an intensive care area and intermediate care area at regional children's hospital **Bed configuration**: 26 bassinets or incubators across the two NICU areas of 207 m^2 total floor space (meets AAP standards, but at times less room than recommended) **Nurse/patient ratio:** NR **Population:** N = 415; of these 103 included in risk factor analysis **Inborn:** 0/415 **Location:** Japan **Inclusion criteria**: All NICU patients in unit from April 1995 to May 1997 **Exclusion criteria**: NR	**Routine practices:** Prospective surveillance of newborns, staff, and environment. Nasal colonized infants who were not intubated were treated with methylrosanilinium chloride ointment until September 1996 or mupirocin during and after September 1996. HCP performed one 3-minute scrub with povidone-iodine or 2% chlorhexidine at entry to NICU, washed hands with 2% chlorhexidine between contact with newborns, wore gowns, and changed shoes **Sampling strategy:** At admission, infants had surveillance cultures of feces, and oral and nasal cavities (when < 24 hrs of age) and weekly thereafter of oral and nasal cavities throughout hospitalization and the day prior to discharge **Additional practices during study**: In the latter half of the study period, mupirocin applied to nares of 37 infants BID per day for 5 days. Infants with intubation or mild disease status	**Outcome definitions:** Colonization: NR Infection: NR **Reported outcomes**: characteristics associated with colonization with MRSA Outcomes: Colonized: 46/103 (11.1%) Not colonized: 57/103 (55.3%) Average rate of colonization was as high as 46.5% for nares and 49.9% for oral cavities during study period Rate of colonization for newborns hospitalized: • <11 days: 17.3% • >61 days: >90% • >43 days, MRSA colonization rate increased rapidly, and newborns discharged without MRSA colonization decreased significantly • ≥43 days, a negative correlation between duration of hospitalization and number of newborns discharged without MRSA colonization became significant	**Not associated with MRSA colonization**: • Infant characteristics: birthweight, breast feeding, combined breast and formula feeding, delivery method • Clinical diagnoses: asphyxia neonatorum, patent ductus arteriosus, respiratory distress syndrome • Clinical interventions: antibiotic therapy >3 days, antibiotic therapy ≥ 11 days of life, blood culture-proven sepsis, intubation

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
		expected to be discharged within 2–3 weeks of admission did not receive mupirocin; 92 colonized infants did not receive any treatment (mupirocin and methylrosanilinium chloride) **MRSA lab testing**: Swabs were inoculated onto plates with 5% sheep blood agar, chocolate agar, modified Drigarsky agar, and OPA *Staphylococcus* agar then incubated for 24 hrs at 37°C in 5% CO_2 in air. Bacterial identification and antibiotic susceptibility testing were performed. MRSA was defined as *S. aureus* for which the MIC of oxacillin was >4 µg/ml		
Author: Reboli[38] **Year:** 1989 **Study design:** Non-concurrent cohort study **Outbreak:** Y **Risk of bias**: High	**Setting:** Level III NICU with intensive care and intermediate care modules **Bed configuration**: 4 incubators each in three intensive care modules and 9 incubators each in two intermediate care modules; 10 sinks located throughout and separate room for HCP gowning at entrance of unit **Nurse/patient ratio:** 1:2 in intensive care unit and 1:4 in intermediate care unit **Population:** N = 656 **Inborn:** NR **Location:** US **Inclusion criteria**: Patients admitted to the NICU from October 1985 to August 1986	**Routine practices:** Standard antibiotic therapy for suspected sepsis is ampicillin and gentamicin. **Sampling strategy:** Cultures of nares, pharynx, or endotracheal tubes weekly. During the last few months, weekly cultures also taken of the umbilicus **Additional practices during study**: Colonized/infected infants placed on contact precautions and cohorted into one intensive care module when potential. Surveillance screening (nares) of nursing staff, physicians, and respiratory therapists on 5 separate occasions. Staff cohorted and assigned to either MRSA-positive or MRSA-negative infants. HCP in-service training of strict handwashing with chlorhexidine soap between handling patients and advised to wash hands and forearms up to elbows on NICU entry, before, and after infant handling beginning in July 1985 **MRSA lab testing: MRSA lab testing**: *S. aureus* isolates identified as methicillin resistant by oxacillin disks,	**Outcome definitions:** Colonization: NR Infection: Presence of MRSA with clinical symptoms and signs, or a positive culture from a normally sterile body fluid **Reported outcomes**: Characteristics associated with infection and colonization with MRSA Outcomes: Colonization=15/656 (2.3%) Infection=11/656 (1.7%)	**Associated with MRSA infection or colonization**: • Infant characteristics: lower birthweight • Clinical interventions: longer length of stay, use of ventilator **Not associated with MRSA infection or colonization:** • Infant characteristics: race, sex • Clinical diagnosis or interventions: leukopenia

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MRSA infection or colonization
	Exclusion criteria: NR	reconfirmed by Gram's staining, slide coagulase testing, catalase test, and deoxyribonuclease production. Strains were confirmed as MRSA when produced bright orange colonies on *Staphylococcus* 110 agar containing 15 µg of methicillin. Further antibiotic susceptibility testing was performed by the disk-diffusion method and specimens were incubated at 30° C for 24 hrs		

Table 61 Extracted Studies with Potential Risk Factors and Risk Indicators for MSSA Infection or Colonization

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MSSA infection or colonization
Author: Washam[42] **Year:** 2018 **Study design:** Retrospective case-control **Outbreak: N** **Risk of bias:** Low	**Setting:** 1 Level 4 NICU with 45 beds, at 1 university teaching hospital, USA **Bed configuration:** During 2007–2011: open and private bays; During 2012–2014: only private bays (in new facility) **Nurse/patient ratio:** NR **Population:** N=4296 Analysis: 3783 at-risk neonates **Inborn:** 2540/3783 (67%) – numerator and denominator reported, percentage calculated **Occupancy rate:** NR **Infant transfer between sections:** Accepts outborn infants **Inclusion criteria:** All neonates admitted from	**Routine practices:** NR **Sampling strategy:** Nasal swabs were obtained weekly and on admission for neonates admitted from home and other hospitals. **Additional practices during study period:** Active surveillance culture (ASC) involving weekly nasal swabs for all infants and admission nasal swabs for all outborn infants. Intranasal mupirocin (twice daily for 5 days) applied to colonized infants. Infants > 36 wks. of gestational age or > 4 wks. chronological age were eligible for washing with 2% chlorhexidine gluconate (CHG) impregnated cloths twice, 48 hrs apart. Infants aged > 2 mo. were eligible for daily CHG washing for 5 days. All colonized infants were placed on contact isolation (i.e., gown and gloves for HCP and visitors) until discharge. In 2012, NICU moved to new facility consisting only of private bays. MRSA-colonized infants were placed in private rooms. Infants who became recolonized were retreated with mupirocin.	**Outcome definitions:** Incident colonization: laboratory identification of the first MRSA-positive nasal surveillance culture from computerized surveillance system among infants who had 1) at least one surveillance culture at day 3 or later of their NICU stay and 2) no previous MRSA-positive clinical or surveillance cultures. Prevalent colonization: laboratory identification of MRSA-positive nasal surveillance culture from computerized surveillance system among infants cultured within 2 days of admission **Reported outcomes:** N with incident or prevalent colonization = 101/4296 (2.4%) of screened infants N with incident colonization = 87/3783 (2.4%) of screened infants at risk for incident MRSA acquisition after NICU admission Risk of incident colonization at baseline: 5.5/1000 infants (95% CI: 3.87–7.72)	**Associated with MSSA acquisition (adjusted for confounding):** • Hospital characteristics: Housed in single bed (protective factor) **Not associated with MSSA acquisition (adjusted for confounding):** • Infant characteristics: birthweight, gestational age, multiple gestation • Clinical characteristics: Operation performed, type of operation • Hospital characteristics: Infants with bed transfers, colonization pressure, hand hygiene compliance • Maternal characteristics: maternal age **Associated with MSSA acquisition (univariate analysis):** • Hospital characteristics: Infants with bed transfers, infants housed in single bed **Not associated with MSSA acquisition (univariate analysis):** • Infant characteristics: sex (male), race, ethnicity, birth weight, gestational age, age at admission, multiple gestation, birth via cesarean, prolonged ROM, mortality, • Clinical characteristics: Operation performed, type of operation, antibiotic exposure, central venous access • Hospital characteristics: colonization pressure, hand hygiene compliance • Maternal characteristics: maternal age

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MSSA infection or colonization
	April 1, 2007-December 31, 2014 **Exclusion criteria:** NR	**MRSA lab testing:** NR (referred to other publications that describe plating on selective and differential media (MRSA plates) before 2008 and agar from 2008 and confirmation of suspicious colonies by Gram stain and slide coagulase testing.		
Author: Azarian[52] **Year:** 2016 **Study design:** Retrospective cohort **Outbreak:** N **Risk of bias:** Moderate	**Setting:** 1 level 3 NICU with 48 open-beds at 1 hospital **Location:** USA **Bed configuration:** Open beds **Nurse/patient ratio:** NR **Population:** N = 1940 infants **Inborn:** 137/177 (77.4%) colonized infants **Inclusion criteria:** NR **Exclusion criteria:** NR	**Routine practices:** Since 2004: Weekly MRSA screening of nares until detection of colonization using standardized protocol. **Sampling strategy:** Nasal swabs were obtained weekly until detection of colonization using standardized protocol or discharge. **Additional practices during study period:** Infection prevention and treatment practices followed current guidelines – colonized infants placed on contact precautions, cohorted, and assigned dedicated clinical staff; decolonization was attempted using nasal mupirocin, though infants were not rescreened to determine success; hand hygiene and contact precaution adherence was monitored through infection prevention surveillance and compliance remained high during the study period. Visitors were educated on hand hygiene and contact precautions. **MRSA lab testing:** NR	**Outcome definitions:** Colonization: positive surveillance culture Infection: MRSA isolation from clinical specimen collected during routine clinical care **Reported outcomes:** N with incident or prevalent colonization = 177/1940 (9.1%) of hospitalized infants N with infection = 33/177 (18.6%) of screened colonized infants after MRSA screening Risk of incident colonization at baseline: NR	**Associated with MRSA acquisition (univariate analysis):** • Infant characteristics: birthweight, born off-site, sex, gestational age, black race, birth by caesarean section **Not associated with MRSA acquisition (univariate analysis):** • Infant characteristics: multiple births, sex
Author: Garcia[43] **Year:** 2014 **Study design:**	**Setting:** 1 NICU and nursey with 65 beds at 1 level 3 public university hospital **Location:** Brazil **Bed configuration:** Open beds	**Routine practices:** The staff in all the sectors remained the same but each HCW worked in only 1 sector during each work shift **Sampling strategy:** • Infants: Swabs of the anterior nares, oropharynx, perineum and umbilical stump were collected from newborn	**Outcome definitions:** NR **Reported outcomes:** N newborns with colonization of MRSA = 59/403 (15%) newborns N mothers with colonization of MRSA = 18/382 (4.7%) mothers	**Associated with MRSA acquisition (multivariate analysis of all newborns):** • Maternal characteristics: mother with <4 years of formal education **Not associated with MRSA acquisition (multivariate analysis all newborns):** • Maternal characteristics: maternal hospitalization >1 month before delivery

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MSSA infection or colonization
Prospective cohort **Outbreak:** N **Risk of bias:** Low	**Nurse/patient ratio:** NR **Population:** N = 403 newborns and their 382 mothers **Inborn:** NR **Inclusion criteria:** all newborns born-alive **Exclusion criteria:** none	within 6 hours of delivery and immediately before discharge (60–72 hours of life); if remained hospitalized, surveillance cultures were collected on days 7, 14, 21 and 28 of life, unless discharge or death occurred before. • Mothers: Swabs of anterior nares, oropharynx, anus and perineum were collected from the mothers during labor; if remained hospitalized or returned to visit or breastfeed the newborn, cultures were cultured on days 3, 7, 14, 21 and 28, from their anterior nares and oropharynx. **Additional practices during study period:** Hand hygiene was performed with alcohol hand rubs, hand washing with plain soap and chlorhexidine, all of which were available in unit. **MRSA lab testing:** Sterile swabs used to culture body sites were transported in medium and added to brain heart infusion medium, incubated at 35° C for 24 hours for sample enrichment then plated in mannitol salt agar and then incubated at 35° C for 48 hours. After incubation, the characteristic colonies were plated and isolated in sheep blood agar 5% and incubated at 35° C for 24 hours. Colonies suspected to be S. aureus were identified by phenotypic tests, tested for virulence factors, susceptibility and submitted to molecular typing via multiplex PCR.	Risk of incident colonization at baseline: NR	**Not associated with MRSA acquisition (multivariate analysis of newborns hospitalized >72 hours) (n=80):** • Infant characteristics: male sex • Mother characteristics: maternal hospitalization > 1 month before delivery **Associated with MRSA acquisition (bivariate analysis):** • Maternal characteristics: mother with <4 years of formal education **Not associated with MRSA acquisition (bivariate analysis):** • Infant characteristics: male sex, twinning, birthweight <2000g, gestational age at birth < 37 weeks, Apgar 1st minute ≤ 3 points, Apgar 5th minute < 6 points, breastfeeding, vaginal delivery • Maternal characteristics: maternal hospitalization > month before delivery
Author: Carey[30] **Year:** 2010	**Setting:** Level III NICU of a university-affiliated children's hospital **Bed configuration:** 62 beds	**Routine practices:** NR **Sampling strategy:** NR **Additional practices during study:** NR	**Outcomes definitions:** patients were considered to have invasive SSTIs if there was documentation of treatment with parenteral antibiotics, and they fulfilled the following criteria: (1) purulent drainage from central	**Associated with MSSA infection:** • Infant characteristics: age at diagnosis of infection **Not associated with MSSA infection:** • Infant characteristics: gestational age

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MSSA infection or colonization
Study design: Retrospective cohort **Outbreak:** Y **Risk of bias:** High	**Nurse/patient ratio:** NR **Population:** 172 **Inborn:** NR **Inclusion criteria:** Data were obtained from hospital's computerized information system to identify infants hospitalized in the NICU with positive cultures for either MSSA or MRSA from January 1, 2000 to December 31, 2007. Infection confirmation defined as positive cultures of sterile body sites (BSI) or invasive skin and soft tissue infections (SSTIs) **Exclusion criteria:** Positive cultures from skin lesions or the conjunctiva treated with topical antibiotics, or surveillance cultures of the anterior nares were not included in the analysis.	**Lab testing:** Culture testing with species identification and antimicrobial susceptibility testing	line insertion site; (2) drainage or dehiscence from a surgical wound; (3) cellulitis; or (4) abscess. **Reported outcomes:** During the study period, the rate of MSSA and MRSA infections ranged from 15 to 30 infections per 1000 patient admissions. Prevalence of infection: MSSA n = 123 MRSA n = 49 N colonized = NA Prevalence of colonization: NA	• Clinical characteristics: duration of hospitalization, clinical presentations **Not associated with MRSA infection:** • Infant characteristics: gestational age, age at diagnosis of infection • Clinical characteristics: duration of hospitalization, clinical presentations MRSA outbreaks occurred in 2002, 2005, and 2007, and an MSSA outbreak occurred in 2004
Author: Schultz[46] **Year:** 2009 **Study design:** Prospective cohort **Outbreak:** N **Risk of bias:** Low	**Setting:** 1 NICU with 49 beds at 1 university medical center **Location:** USA **Bed configuration:** NR **Nurse/patient ratio:** NR **Population:** N = 1760 **Inborn:** 1269/1760 **Inclusion criteria:** all neonates admitted to	**Routine practices:** Weekly MRSA surveillance on all NICU patients during study period (June 2004-December 2006) using PCR or culture (before May 2006) nasopharyngeal swab samples Contact isolation/ cohorting: Patients identified as colonized with MRSA were placed on contact isolation and cohorted both by location and by healthcare providers **Sampling strategy:** Weekly PCR or culture (before May 2006) nasopharyngeal swab samples	**Outcome definitions:** NR **Other definitions:** NR **Reported outcomes:** N newborns with incident or prevalent colonization = 59/1760 (3.35%)	**Associated with MRSA acquisition (univariate analysis):** • Infant characteristics: gestational age, inborn birth, **Not associated with MRSA acquisition (univariate analysis):** • Infant characteristics: male sex, race

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MSSA infection or colonization
	medial center during study period **Exclusion criteria:** neonates who died during hospitalization	**Additional practices during study period:** NR **MRSA lab testing:** NR		

Author: Silva[51]
 	
Year: 2009
 	
Study design: Case-control study
 	
Outbreak: N
Risk of bias: Low
	Setting: Level 3 NICU in a university teaching hospital
	
	Bed configuration: NR
	
	Nurse/patient ratio: 1:2
	
	Population: N = 405 neonates
	
	Inborn: NR
	
	Inclusion criteria: All neonates admitted from January 1, 2004 to June 30, 2005 staying > 24h
	
	Exclusion criteria: NR
		Routine practices: NR
		
		Sampling strategy: Monthly active surveillance of *S. aureus* colonization; samples taken from anterior nares and anus; and clinical cultures
		
		Additional practices during study: Cultures of clinical specimens (blood, skin, eye secretions) from infants with clinical symptoms
		
		Lab testing: Culture. Susceptibility test performed by agar disc diffusion test technique according to the Clinical and Laboratory Standards Institute. Molecular Typing: PFGE following DNA extraction.
			Outcome definitions:
			Infection: MSSA isolated from normally sterile site (blood) or cultures obtained for clinical purposes specimen (e.g. skin or eyes).
			Colonization: positive surveillance cultures of nares and/or anus
			Reported outcomes: Characteristics associated with MSSA colonization or infection
			N infected or colonized:
			• *S. aureus* infection incidence rate: 3.61/1000 patient-days
			• *S. aureus* (+): 32 neonates
			  • MSSA infection: 9/30 (30%)
			  • MSSA Colonization: 15/30 (50%)
			  • MSSA colonization followed by infection: 6/30 (20%)
			  • MRSA infection: 2/32 (19%)
				Associated with MSSA colonization or infection (multivariate):
				• Clinical interventions: polystyrene CVC insertion by dissection (phlebotomy)
				
				Associated with MSSA colonization or infection (univariate):
				• Clinical interventions: antibiotic use, any CVC use polystyrene CVC insertion by dissection (phlebotomy)
				
				Not associated with MSSA colonization or infection:
				• Infant characteristics: birthweight, sex, gestational age
				• Clinical characteristics: Apgar score at 5 min
				• Clinical interventions: mechanical ventilation, gastric tube, parenteral nutrition, Peripheral VC, umbilical CVC, PICC

Author: Graham[50] **Year:** 2002 **Study design**: Retrospective cohort study **Outbreak**: Y **Risk of bias:** Low	**Setting:** Level III-IV NICU in university-affiliated children's hospital **Bed configuration**: NR **Nurse/patient ratio**: NR **Population:** N = 83 **Inborn:** NR **Inclusion criteria**: Infants hospitalized in the NICU from December 21, 1999 to January 19, 2000. **Exclusion criteria**: NR	**Routine practices:** NR **Sampling strategy:** Routine active surveillance at irregular intervals and review of clinical microbiology laboratory reports; Sampling of anterior nares of all infants in NICU during study period; **Additional practices during study**: Cohorting and contact precautions for colonized or infected infants, universal glove use for all staff and patient contacts. The ban on staff wearing artificial nails was reemphasized. Case infants were maintained on contact isolation until hospital discharge. Repeat surveillance cultures of the anterior nares cultures after mupirocin treatment assessed the efficacy	**Outcome definitions:** Incident cases**:** Infants with a positive clinical or surveillance culture for MSSA Epidemic Case infants: Infants in the cohort with the epidemic MSSA clone "B" recovered from clinical or surveillance culture Epidemic Non-case infant: Infant in the cohort with negative surveillance culture or a positive culture for non-clone "B" MSSA strain Non-Epidemic Case infants: Infants in the cohort with any MSSA recovered from clinical or surveillance culture Non-Epidemic Non-case infant: Infant in the cohort with negative surveillance culture or a positive culture for any MSSA strain	**Associated with Epidemic MSSA colonization or infection** (multivariate analysis): • Clinical interventions: LOS, use of H2 blockers **Associated with All MSSA colonization or infection** (multivariate analysis): • Infant characteristics: birthweight (≤ 1500 g); **Associated with Epidemic MSSA colonization or infection** (univariate analysis): • Infant characteristics: extremely low birthweight (≤ 1000 g) • Clinical characteristics: Apgar score <7 • Clinical interventions: H_2 blockers **Not associated with Epidemic MSSA colonization or infection** (univariate analysis): • Clinical interventions: LOS, intubation, CVC, hyperalimentation, intralipids

Study Data	Setting and Population	Interventions	Outcomes	Characteristics assessed for association with MSSA infection or colonization
		of these infection control strategies. Topical mupirocin applied to anterior nares of all NICU infants BID for 5 days and hexachlorophene bath for all hospitalized infants ≥ 1500 g **MSSA lab testing:** Culture. Specimens inoculated onto 5% sheep blood agar and incubated aerobically at 37°C for 24 hrs. MSSA identified via Staphaurex.	Colonization: MSSA cultured from the anterior nares during surveillance efforts. Infection: Infants considered infected if MSSA was isolated from either a normally sterile site (e.g., blood) or clinical cultures (e.g., skin or eyes) Incidence: Number of infected or colonized infants per 1000 patient-days per month Length of stay (LOS): Duration of hospitalization until the last negative surveillance culture (case infants); duration of hospitalization until the last negative surveillance culture (non-case infants) **Reported outcomes:** Characteristics associated with MSSA colonization or infection MSSA colonization or infection: 6.4 to 13.5 cases per 1000 patient days per month 77 infants with positive MSSA cultures; 58% clinically indicated and 42% detected by surveillance	

3.B.2.b. Study Findings

Table 62 Characteristics Examined for Association with S. aureus or MSSA Infection or Colonization
Infant Characteristics

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Findings	Results	Author Year	Comments
Age, mean, weeks*	MSSA colonization or infection vs. no colonization or infection	Student's *t*-test	Yes, Univariate No, Multivariate	**Univariate analysis:** • 53 vs. 23; p = 0.003	Graham 2002[50]	

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Findings	Results	Author Year	Comments
Birthweight, n/N (%)	MSSA colonization or infection vs. no colonization or infection	Chi-squared or Fisher's exact test and odds ratios	No	**Univariate analysis:** • <1000 g: 5/30 (16.6%) vs. 30/310 (9.7%); p=0.21 • 1000-1500 g: 4/30, 13.3% vs. 64/310 (20.6%); p=0.47 • >1501 g: 21/30 (70.1%) vs. 216/310 (69.7%); p=0.86	Silva 2009[51]	
Birthweight, n/N (%)*	*S. aureus* infection vs. no infection	Student's *t* test or multivariate logistic regression	Yes, Univariate Yes, Multivariate	**Univariate analysis:** • ≤1000 g: 29/364 (8.0%); OR: 17.58 (95% CI: 8.49 – 36.41); p < 0.0001 • 1001 to 1500 g: 16/577 (2.8%); OR: 5.79 (95% CI: 2.61 – 12.48); p < 0.0001 • 1501 to 2500 g: 11/2175 (0.5%); OR: 1.03 (95% CI: 0.44 – 2.44); p = 0.9420 • > 2500 g: 10/2041 (0.5%) **Multivariate analysis:** • Results remained highly significant even after adjusting for time to infection.	Delaney 2013[1]	
Birthweight, n/N (%)*	*S. aureus* colonization vs. no colonization	Student's *t* test or multivariate logistic regression	Yes, Univariate	**Univariate analysis:** • ≤1000 g: 16/152 (10.5%); OR: 2.93 (95% CI: 1.56 – 5.52); p = 0.0009 • 1001 to 1500 g: 14/220 (6.4%); OR: 1.69 (95% CI: 0.88 – 3.25); p = 0.1143 • 1501 to 2500 g: 17/948 (1.8%); OR: 0.46 (95% CI: 0.25 – 0.83); p = 0.0104 • >2500 g: 30/777 (3.9%) **Multivariate analysis:** • Results remained highly significant even after adjusting for time to infection.	Delaney 2013[1]	
Birthweight, n/N (%)*	MSSA colonization or infection vs. no colonization or infection	Student's *t* test or multivariate logistic regression	Yes, Univariate No, Multivariate	**Univariate analysis:** • ≤1000 g: 6/11 (55%) vs. 14/72 (19%); OR: 6.43 (95% CI: 1.19 - 38.25); p=0.016 • 1001 to 1500 g: 2/11 (18%) vs. 13/72 (18%); OR: 2.31 (95% CI: 0.24 - 19.99); p=0.585 • >1500 g: 3/11 (27%) vs. 45/72 (63%)	Graham 2002[50]	
Birthweight, n/N (%)	MSSA colonization or infection vs. no colonization or infection	Multivariate logistic regression	Yes	**Multivariate analysis:** Birth weight ≤1500 g: OR: 37.19 (95% CI: 1.68 - 825.54); p=.03	Graham 2002[50]	
Sex, male, n/N (%)	*S. aureus* infection vs. no infection	Chi-squared test and logistic regression	No	**Univariate analysis:** • 45/3622 (1.2%) • OR =1.58 (95% CI: 0.94–2.66); p = 0.0845	Delaney 2013[1]	

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Findings	Results	Author Year	Comments
Sex, male, n/N (%)	*S. aureus* colonization vs. no colonization	Chi-squared test and logistic regression	No	**Univariate analysis:** • 40/1474 (2.7%) • OR =0.79 (95% CI: 0.50–1.24); p = 0.3072	Delaney 2013[1]	
Sex, male, n/N (%)	MSSA colonization or infection vs. no colonization or infection	Chi-squared or Fisher's exact test and odds ratios	No	**Univariate analysis:** • 12/30 (40.0%) vs. 176/310 (56.7%) • OR =0.51 (95% CI: 0.22–1.15); p = 0.115	Silva 2009[51]	
Gestational age, n/N (%)*	*S. aureus* infection vs. no infection	Student's *t* test or multivariate logistic regression	Yes, Univariate Yes, Multivariate	**Univariate analysis:** • ≤ 25 wks.: 15/172 (8.7%); OR: 25.10 (95% CI: 9.60 – 65.60); p < 0.0001 • 26-30 wks.: 30/650 (4.6%); OR: 12.71 (95% CI: 5.26 – 30.69); p < 0.0001 • 31 – 36 wks.: 15/2748 (0.6%); OR: 1.44 (95% CI: 0.56 – 3.72); p = 0.4499 • > 36 wks.: 6/1582 (0.4%) **Multivariate analysis:** • Results remained highly significant even after adjusting for time to infection.	Delaney 2013[1]	
Gestational age, n/N (%)*	*S. aureus* colonization vs. no colonization	Student's *t* test or multivariate logistic regression	Yes, Univariate	**Univariate analysis:** • ≤ 25 wks.: 7/60 (11.7%); OR: 3.28 (95% CI: 1.35 – 8.00); p 0 0.0090 • 26-30 wks.: 18/271 (6.6%); OR: 1.77 (95% CI: 0.94 – 3.33 30.69); p = 0788 • 31 – 36 wks.: 29/1170 (2.5%); OR: 0.63 (95% CI: 0.36 – 1.10); p = 0.1048 • > 36 wks.: 23/594 (3.9%) **Multivariate analysis:** • Results remained highly significant even after adjusting for time to infection.	Delaney 2013[1]	
Gestational age <26 weeks, n/N (%)	MSSA colonization or infection vs. no colonization or infection	Chi-squared or Fisher's exact test and odds ratios	No	**Univariate analysis:** • 1/30 (3.3%) vs. 20/310 (6.4%) • OR = 0.50 (95% CI: 0.02–3.74); p = 1.00	Silva 2009[51]	
Gestational age, mean, weeks*	MSSA colonization or infection vs. no colonization or infection	Chi-squared or Fisher's exact test and odds ratios	No, Univariate No, Multivariate	**Univariate analysis:** • 30 vs. 33; p = 0.059	Graham 2002[50]	

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Findings	Results	Author Year	Comments
Delivery method, cesarean, n/N (%)*	MSSA colonization or infection vs. no colonization or infection	Student's *t* test or multivariate logistic regression	No, Univariate No, Multivariate	**Univariate analysis:** • 6/11 (55%) vs. 39/72 (54%); OR: 1.02 (95% CI: 0.24 – 4.3); p = 0.763	Graham 2002[50]	

Table 62 Characteristics Examined for Association with S. aureus or MSSA Infection or Colonization
Clinical Characteristics

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Findings	Results	Author Year	Comments
Apgar at 5 min < 7, n/N (%)	MSSA colonization or infection vs. no colonization or infection	Chi-squared or Fisher's exact test and odds ratios	No	**Univariate analysis:** • 2/30 (6.6%) vs. 36/310 (11.6%) • OR = 0.54 (95% CI: 0.09–2.49); p = 0.55	Silva 2009[51]	
Apgar at 5 min < 7, n/N (%)*	MSSA colonization or infection vs. no colonization or infection	Student's *t* test or multivariate logistic regression	Yes, Univariate No, Multivariate	**Univariate analysis:** • 3/11 (27%) vs. 4/72 (6%); • OR: 6.28 (95% CI: 0.67 – 43.6); p = 0.047	Graham 2002[50]	
Length of stay, days*	MSSA colonization or infection vs. no colonization or infection	Chi-squared or Fisher's exact test and odds ratios	Yes, Univariate Yes, Multivariate	**Univariate analysis:** • 51 vs. 18; p < 0.001 **Multivariate analysis:** • OR: 1.035 (per day) (95% CI: 1.008 - 1.062); p = 0.010	Graham 2002[50]	
Outborn, n/N (%)	*S. aureus* colonization vs. no colonization	Chi-squared test and logistic regression	Yes	**Univariate analysis:** • 18/278 (6.5%) • OR =2.64 (95% CI :1.54–4.55); p = 0.0003	Delaney 2013[1]	
S. aureus colonization, n/N (%)	*S. aureus* infection vs. no infection	Chi-squared test and logistic regression	Yes	**Univariate analysis:** • 11/77 (14.3%) vs. 5/2481 (0.2%) • OR: 82.53 (95% CI: 27.89–244.26); p < 0.0001 • Colonized infants were 82 times more likely to become infected with *S. aureus* than non-colonized infants.	Delaney 2013[1]	

Table 62 Characteristics Examined for Association with S. aureus or MSSA Infection or Colonization
Clinical Interventions

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Findings	Results	Author Year	Comments
Antibiotic use, n/N (%) (mainly ampicillin & gentamycin)	MSSA colonization or infection vs. no colonization or infection	Chi-squared or Fisher's exact test and odds ratios	Yes	**Univariate analysis:** • 25/30 (83.3%) vs. 182/310 (58.7%) • OR = 3.52 (95% CI: 1.24–10.78); p = 0.01	Silva 2009[51]	
Antibacterial agents, all, n/N (%)*	MSSA colonization or infection vs. no colonization or infection	Student's *t* test or multivariate logistic regression	No, Univariate No, Multivariate	**Univariate analysis:** • 6/11 (55%) vs. 57/72 (79%); • OR: 0.32 (95% CI: 0.07 – 1.32); p = 0.096	Graham 2002[50]	
Anti-Staphylococcal antibiotics, all, n/N (%)*	MSSA colonization or infection vs. no colonization or infection	Student's *t* test or multivariate logistic regression	No, Univariate No, Multivariate	**Univariate analysis:** • 6/11 (55%) vs. 54/72 (61%); • OR: 4.0 (95% CI: 0.09 – 1.75); p = 0.168	Graham 2002[50]	
Ophthalmic antibiotics, all, n/N (%)*	MSSA colonization or infection vs. no colonization or infection	Student's *t* test or multivariate logistic regression	No, Univariate No, Multivariate	**Univariate analysis:** • 6/11 (55%) vs. 44/72 (75%); • OR: 0.76 (95% CI: 0.18 – 3.24); p = 0.746	Graham 2002[50]	
Penicillin, all, n/N (%)*	MSSA colonization or infection vs. no colonization or infection	Student's *t* test or multivariate logistic regression	No, Univariate No, Multivariate	**Univariate analysis:** • 4/11 (36%) vs. 47/72 (65%); • OR: 0.30 (95% CI: 0.07 – 1.32); p = 0.096	Graham 2002[50]	
Gentamicin, n/N (%)*	MSSA colonization or infection vs. no colonization or infection	Student's *t* test or multivariate logistic regression	Yes, Univariate No, Multivariate	**Univariate analysis:** • 3/11 (27%) vs. 46/72 (64%); • OR: 0.62 (95% CI: 0.08 – 3.54); p = 0.044	Graham 2002[50]	
Cephalosporins, n/N (%)*	MSSA colonization or infection vs. no colonization or infection	Student's *t* test or multivariate logistic regression	No, Univariate No, Multivariate	**Univariate analysis:** • 2/11 (18%) vs. 19/72 (26%); • OR: 0.62 (95% CI: 0.08 – 3.54); p = 0.721	Graham 2002[50]	
Vancomycin, n/N (%)*	MSSA colonization or infection vs. no colonization or infection	Student's *t* test or multivariate logistic regression	No, Univariate No, Multivariate	**Univariate analysis:** • 2/11 (18%) vs. 15/72 (21%); • OR: 0.84 (95% CI: 0.11 – 4.95); p = 1.0	Graham 2002[50]	

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Findings	Results	Author Year	Comments
H_2-blockers, n/N (%)*	MSSA colonization or infection vs. no colonization or infection	Student's *t* test or multivariate logistic regression	Yes, Univariate Yes, Multivariate	**Univariate analysis:** • 4/11 (36%) vs. 5/72 (7%); • OR: 7.66 (95% CI: 1.32 – 45.71); p = 0.016 **Univariate analysis:** • OR: 20.44 (95% CI: 2.48 – 168.26); p = 0.005	Graham 2002[50]	
Central venous catheter, any, n/N (%)	MSSA colonization or infection vs. no colonization or infection	Chi-squared or Fisher's exact test and odds ratios	Yes	**Univariate analysis**: • 21/30, 70.0% vs. 152/310, 49.0% • OR = 2.43 (95% CI:1.02–5.92); p = 0.045	Silva 2009[51]	
Central venous catheter, n/N (%)*	MSSA colonization or infection vs. no colonization or infection	Student's *t* test or multivariate logistic regression	No, Univariate No, Multivariate	**Univariate analysis:** • 5/11 (45%) vs. 41/72 (57%); • OR: 0.63 (95% CI: 0.15 – 2.63); p = 0.528	Graham 2002[50]	
Central Venous Catheter, umbilical, n/N (%)	MSSA colonization or infection vs. no colonization or infection	Chi-squared or Fisher's exact test and odds ratio	No	**Univariate analysis:** • 3/30 (10.0%) vs. 35/310 (11.3%) • OR = 0.87 (95% CI:0.20–3.24); p = 1.00	Silva 2009[51]	
Central Venous Catheter, Peripherally inserted central catheter (PICC), n/N (%)	MSSA colonization or infection vs. no colonization or infection	Chi-squared or Fisher's exact test and odds ratio	No	**Univariate analysis:** • 9/30 (30.0%) vs. 88/310 (28.3%) • OR= 1.08 (95% CI:0.44–2.60)p = 0.98	Silva 2009[51]	
Central Venous Catheter, inserted by phlebotomy, n/N (%)	MSSA colonization or infection vs. no colonization or infection	Chi-squared or Fisher's exact test and odds ratio	Yes, Multivariate Yes, Univariate	**Multivariate analysis:** • Associated with MSSA colonization or infection (p value, OR, or adjustment factors NR) **Univariate analysis:** • 9/30 (30.0%) vs. 29/310 (9.4%) • OR = 4.15 (95% CI: 1.59–10.67), p = 0.002	Silva 2009[51]	
Peripheral venous catheter (PVC), n/N (%)	MSSA colonization or infection vs. no colonization or infection	Chi-squared or Fisher's exact test and odds ratio	No	**Univariate analysis:** • 21/30 (70.0%) vs. 240/310 (77.4%) • OR = 0.68 (95% CI: 0.28–1.69); p = 0.48	Silva 2009[51]	
Peripheral venous catheter, n/N (%)*	MSSA colonization or infection vs. no colonization or infection	Student's *t* test or multivariate logistic regression	Yes, Univariate Yes, Multivariate	**Univariate analysis:** • 6/11 (55%) vs. 64/72 (89%); • OR: 0.15 (95% CI: 0.03 – 0.74); p = 0.004 **Multivariate analysis:** • OR: 0.06 (95% CI: 0.01 – 0.43); p = 0.005	Graham 2002[50]	

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Findings	Results	Author Year	Comments
Mechanical ventilation, n/N (%)	MSSA colonization or infection vs. no colonization or infection	Chi-squared or Fisher's exact test and odds ratios	No	**Univariate analysis:** • 18/30 (60.0%) vs. 129/310 (41.6%) • OR = 2.10 (95% CI: 0.91–4.84); p = 0.08	Silva 2009[51]	
Respiratory support, ETT, n/N (%)*	MSSA colonization or infection vs. no colonization or infection	Student's *t* test or multivariate logistic regression	No, Univariate No, Multivariate	**Univariate analysis:** • 4/11 (36%) vs. 24/72 (33%); • OR: 1.14 (95% CI: 0.25 – 4.98); p = 1.0	Graham 2002[50]	
Respiratory Support, NCPAP, n/N (%)*	MSSA colonization or infection vs. no colonization or infection	Student's *t* test or multivariate logistic regression	No, Univariate No, Multivariate	**Univariate analysis:** • 9/11 (82%) vs. 57/72 (79%); • OR: 1.18 (95% CI: 0.20 – 8.89); p = 1.0	Graham 2002[50]	
Nasogastric tube, n/N (%)	MSSA colonization or infection vs. no colonization or infection	Chi-squared or Fisher's exact test and odds ratios	No	**Univariate analysis:** • 29/30, (96.6%) vs. 262/310 (84.5%) • OR = 5.31 (95% CI: 0.75–107.28); p = 0.09	Silva 2009[51]	
Orogastric/ nasogastric tube, n/N (%)*	MSSA colonization or infection vs. no colonization or infection	Student's *t* test or multivariate logistic regression	No, Univariate No, Multivariate	**Univariate analysis:** • 10/11 (91%) vs. 55/72 (76%); • OR: 3.09 (95% CI: 0.36 – 69.13); p = 0.442	Graham 2002[50]	
Parenteral nutrition, n/N (%)	MSSA colonization or infection vs. no colonization or infection	Chi-squared or Fisher's exact test and odds ratios	No	**Univariate analysis:** • 19/30, 63.3% vs. 140/310 (45.1%) • OR = 2.1 (95% CI: 0.91–4.84); p = 0.08	Silva 2009[51]	
Surgical Procedures, n/N (%)*	MSSA colonization or infection vs. no colonization or infection	Student's *t* test or multivariate logistic regression	No, Univariate No, Multivariate	**Univariate analysis:** • 7/11 (64%) vs. 32/72 (44%); • OR: 2.19 (95% CI: 0.51 – 9.9); p = 0.388	Graham 2002[50]	

Abbreviations: CI = confidence interval, MRSA = methicillin-resistant *Staphylococcus aureus*, MSSA = methicillin-susceptible S*taphylococcus aureus*, OR = odds ratio

Table 63 Characteristics Examined for Association with MRSA vs. MSSA Infection or Colonization
Infant Characteristics

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	Results	Author Year	Comments
Gestational age, wks., n/N (%)	MSSA infection vs. MRSA infection	Wilcox rank sum tests	No	• ≤25 wks.: 723/2821 (25.6%) vs. 270/1063 (25.4%) • 26–28 wks.: 966/2821 (34.2%) vs. 345/1063 (32.5%) • 29–32 wks.: 660/2821 (23.4%) vs. 259/1063 (24.4%) • 33–36: 253/2821 (9.0%) vs. 107/1063 (10.1%) • ≥37: 219/2821 (7.8%) vs. 82/1063 (7.7%) • p=0.73	Ericson 2015[31]	MSSA: N = 2821/2825* *Patient counts for particular characteristics may not equal total patient counts because some patients have missing values for some data. Denominators for all percentages are the number of patients with data for that characteristic.
Gestational age, wks., median (IQR)	MSSA infection vs. MRSA infection	Permutation test	No	• 27/123 (25, 34) vs. 28/49 (25, 37) • p = 0.20	Carey 2010[30]	Gestational age missing for 1 infant and outcome data missing for 3 infants.
Birthweight, g, n/N (%)	MSSA infection vs. MRSA infection	Wilcox rank sum tests	No	• <1000 g: 1480/2823 (52.4%) vs. 528/1063 (49.7%) • 1000–1499 g: 689/2823 (24.4%) vs. 284/1063 (26.7%) • 1500–2499 g: 387/2823 (13.7%) vs. 145/1063 (13.6%) • 2500-3499 g: 194/2823 (6.9%) vs. 82/1063 (7.7%) • ≥3500 g: 73/2823 (2.6%) vs. 24/1063 (2.3%) • p=0.42	Ericson 2015[31]	MSSA: N = 2823/2825* *Patient counts for particular characteristics may not equal total patient counts because some patients have missing values for some data. Denominators for all percentages are the number of patients with data for that characteristic.
Weight, g, n/N (%)	MSSA colonization vs. MRSA colonization	OR (CI)	Yes	• <1500 g: 10/40 (25%) vs. 16/30 (53%) • p=0.029 • OR (CI): 3.43 (1.11–10.78)	Silva 2003[51]	
Apgar score, n/N (%)	MSSA infection vs. MRSA infection	χ^2 tests	No	• 0–3: 147/2746 (5.4%) vs. 49/1026 (4.8%) • 4-6: 512/2746 (18.6%) vs. 215/1026 (21.0%) • 7-10: 2087/2746 (76.0%) vs. 762/1026 (74.3%) • p = 0.24	Ericson 2015[31]	MSSA: N = 2746/2825* MRSA N= 1026/1063* *Patient counts for particular characteristics may not equal total patient counts because some patients have missing values for some data. Denominators for all percentages are the number

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	Results	Author Year	Comments
						of patients with data for that characteristic.
Apgar score	MSSA colonization vs. MRSA colonization	OR (CI)	No	• 0–4: 1/40 (2.5%) vs. 4/30 (13%) • p = 0.203 • OR (CI): 6.00 (0.57–149.37) • 5–7: 30/40 (75%) vs. 21/30 (70%) • p = 0.846 • OR (CI): 0.78 (0.24–2.55) • 8–10: 9/40 (22%) vs. 5/30 (17%) • p = 0.762 • OR (CI): 0.69 (0.17–2.66)	Silva 2003[51]	
Apgar score, 5 minutes (range)	MRSA infection vs MSSA infection	nonparametric testing, Mann-Whitney test, or Fisher exact test	No	**Univariate analysis:** • 5 (2-9) vs. 7 (2-9) • p= 0.17	Cohen-Wolkowiez 2007[29]	
Race/ethnicity, n/N (%)	MSSA infection vs. MRSA infection	Chi-squared tests	Yes	• White: 1329/2725 (48.8%) vs. 467/1035 (45.1%) • African American: 681/2725 (25%) vs. 330/1035 (31.9%) • Hispanic: 564/2725 (20.7%) vs. 201/1035 (19.4%) • Other: 151/2725 (5.5%) vs. 37/1035 (3.6%) • p = <0.001	Ericson 2015[31]	MSSA: N = 2725/2825* MRSA N= 1035/1063* *Patient counts for particular characteristics may not equal total patient counts because some patients have missing values for some data. Denominators for all percentages are the number of patients with data for that characteristic.
Male sex, n/N (%)	MSSA infection vs. MRSA infection	Chi-squared tests	No	• 1555/2825 (55.1%) vs. 575/1063 (54.2%) • p = 0.60	Ericson 2015[31]	
Male sex, n/N (%)	MSSA colonization vs. MRSA colonization	OR (CI)	No	• 28/40 (70%) vs. 16/30 (53%) • p = 0.238 • OR (CI): .49(0.16–1.47)	Silva 2003[51]	
Male sex, n/N (%)	MRSA infection vs MSSA infection	nonparametric testing, Mann-Whitney test, or Fisher exact test	No	**Univariate analysis:** • 12/21 (57%) vs. 15/32 (47%) • p=0.57	Cohen-Wolkowiez 2007[29]	
Infant born at hospital where infection occurred, n/N (%)	MSSA infection vs. MRSA infection	Chi-squared tests	Yes	• 2236/2825 (80.0%) vs. 783/1063 (74.2%) • p = < 0.001	Ericson 2015[31]	

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	Results	Author Year	Comments
Born by cesarean section, n/N (%)	MSSA infection vs. MRSA infection	Chi-squared tests	No	• 2033/2825 (72.9%) vs. 741/1063 (70.6%) • p = 0.16	Ericson 2015[31]	
Small-for-gestational age status, n/N (%)	MSSA infection vs. MRSA infection	Chi-squared tests	No	• 541/2825 (19.2%) vs. 207/1063 (19.5%) • p = 0.84	Ericson 2015[31]	
Gestational age at birth, weeks (range)	MRSA infection vs MSSA infection	nonparametric testing, Mann-Whitney test, or Fisher exact test	No	**Univariate analysis:** • 26 weeks (23-29) vs. 26.5 weeks (22-36) • p=0.63	Cohen-Wolkowiez 2007[29]	
Birthweight, g (range)	MRSA infection vs MSSA infection	nonparametric testing, Mann-Whitney test, or Fisher exact test	No	**Univariate analysis:** • 810g (500-3230) vs. 830g (580-3000) • p=0.80	Cohen-Wolkowiez 2007[29]	
Congenital anomaly, n/N (%)	MSSA infection vs. MRSA infection	Chi-squared tests	No	• 363/2825 (12.9%) vs. 150/1063 (14.1%) • p = 0.30	Ericson 2015[31]	None
Age at first positive culture, d, n/N (%)	MSSA infection vs. MRSA infection	Wilcox rank sum tests	Yes	• <7 days: 324/2825 (11.5%) vs. 123/1063 (11.6%) • 7–14 days: 659/2825 (23.3%) vs. 292/1063 (27.5%) • 15–28 days: 905/2825 (32.0%) vs. 348/1063 (32.7%) • >28 days: 937/2825 (33.2%) vs. 300/1063 (28.2%) • p = 0.01	Ericson 2015[31]	
Age at diagnosis of infection, days, median (IQR)	MSSA infection vs. MRSA infection	Permutation test	No	• 32 (15, 57.5) vs. 23 (12, 35) • p = 0.03	Carey 2010[30]	
Age at time of bacteremia, days (range)	MRSA infection vs MSSA infection	nonparametric testing, Mann-Whitney test, or Fisher exact test	No	**Univariate analysis:** • 26 days (0-71) vs. 38.5 days (0-94) • p= 0.06	Cohen-Wolkowiez 2007[29]	
Previous surgical procedure, n/N (%)	MSSA infection vs. MRSA infection	Chi-squared tests	No	• 476/2825 (16.8%) vs. 186/1063 (17.5%) • p = 0.63	Ericson 2015[31]	
Inotropic support, median days (25–75th percentiles)	MSSA infection vs. MRSA infection	Wilcox rank sum tests	No	• 0 (0–2) vs. 0 (0–2) • p = 0.53	Ericson 2015[31]	The median (25th–75th percentiles) values represent the number of days with exposure before the first invasive *S. aureus* infection.
Treated with inotropes, n/N (%)	MRSA infection vs MSSA infection	nonparametric testing, Mann-Whitney test, or Fisher exact test	No	**Univariate analysis:** • 3/21 (15%) vs. 2/32 (6%) • p=0.45	Cohen-Wolkowiez 2007[29]	
Oxygen support, median d (25–75th percentiles)	MSSA infection vs. MRSA infection	Wilcox rank sum tests	Yes	• 8 (1–20) vs. 5 (1–15) • p < 0.001	Ericson 2015[31]	The median (25th–75th percentiles) values represent the number of days with exposure before the first invasive *S. aureus* infection.

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	Results	Author Year	Comments
Ventilator support, median d (25–75th percentiles)	MSSA infection vs. MRSA infection	Wilcox rank sum tests	No	• 5 (0–16) vs. 5 (1–13) • p = 0.05	Ericson 2015[31]	The median (25th-75th percentiles) values represent the number of days with exposure before the first invasive *S. aureus* infection.
Mechanical ventilation, n/N (%)	MSSA colonization vs. MRSA colonization	OR (CI)	No	• 7/40 (17%) vs. 4/30 (13%) • p = 0.886 • OR(CI): .73(.16–3.20)	Silva 2003[51]	
Invasive devices, n/N (%)	MSSA colonization vs. MRSA colonization	OR (CI)	No	• 16/40 (40%) vs. 19/30 (63%) • p = 0.090 • OR(CI): 2.59 (0.88–7.76)	Silva 2003[51]	
Antibiotic use, median days (25-75th percentiles)	MSSA infection vs. MRSA infection	Wilcox rank sum tests	No	• 4 (1–11) vs. 4 (1–10) • p = 0.56	Ericson 2015[31]	The median (25th–75th percentiles) values represent the number of days with exposure before the first invasive *S. aureus* infection.
Anti-MRSA antibiotic use, median d (25–75th percentiles)	MSSA infection vs. MRSA infection	Wilcox rank sum tests	No	• 0 (0–4) vs. 0 (0–3) • p = 0.53	Ericson 2015[31]	The median (25th–75th percentiles) values represent the number of days with exposure before the first invasive *S. aureus* infection.
Antibiotic use, n/N (%)	MSSA colonization vs. MRSA colonization	OR (CI)	Yes	• 8/40 (20%) vs. 14/30 (46%) • p = 0.034 • OR(CI): 3.50 (1.08–11.58)	Silva 2003[51]	
Duration of hospitalization, days, median (IQR)	MSSA infection vs. MRSA infection	Permutation test	No	• 64/123 (40, 113) vs. 64/49 (35, 109) • p = 0.80	Carey 2010[30]	
Length of hospitalization, n/N (%)	MSSA colonization vs. MRSA colonization	OR (CI)	No	• ≥7 days: 30/40 (75%) vs. 27/30 (90%) • p = 0.198 • OR (CI): 0.33 (0.06–1.52)	Silva 2003[51]	
Clinical presentations, n/N (%)	MSSA infection vs. MRSA infection	Fisher's exact test	No	• Bacteremia: 43/123 (35%) vs. 19/49 (39%) • Skin and soft tissue, including post-operative wound: 41/123 (33%) vs. 12/49 (24%) • Bacteremia + skin and soft tissue: 18/123 (15%) vs. 7/49 (14%) • Endocarditis: 8/123 (7%) vs. 3/49 (6%) • Bacteremia + other site of infection: 5/123 (4%) vs. 2/49 (4%) • Other: 8/123 (7%) vs. 6/49 (12%) • p = 0.76	Carey 2010[30]	Bacteremia + other site of infection: Other included tracheitis, osteomyelitis, meningitis, or mediastinitis

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	Results	Author Year	Comments
Incubator care, n/N (%)	MSSA colonization vs. MRSA colonization	OR (CI)	No	• 15/40 (37%) vs. 15/30 (50%) • p = 0.442 • OR (CI): 1.67 (0.57–4.88)	Silva 2003[51]	

Abbreviations: CI = confidence interval, MRSA = methicillin-resistant *Staphylococcus aureus*, MSSA = methicillin-susceptible S*taphylococcus aureus*, OR = odds ratio

Table 64 Characteristics Examined for Association with MRSA Infection or Colonization

Infant Characteristics

Risk Factor	Outcome	Analytical Statistics	Significant Finding	Results	Author Year	Comments
Age, mean, days	MRSA colonization vs. no colonization	Mann-Whitney test Multivariate logistic regression	Yes (univariate) No (multivariate)	• 39.3 days vs. 29.4 days • p = 0.043 OR = NR	Kuo 2013[36]	• Specimens obtained from nares and umbilicus on two dates: Oct 11, and Dec 12, 2011
Age at NICU admission, mean, days	MRSA infection vs. colonization vs. no MRSA detected	NR	No	• Infected: 1 day • Colonized: 3 days • No MRSA detected: 2 days • p > 0.05	Song 2010[28] (262)	• Active screening for MRSA on admission and weekly thereafter
Age at admission, days, n (%)	MRSA colonization vs. no colonization	Continuity-adjusted chi-squared test and odds ratio	No	• <1 day: 220/323 (68%) vs. 289/460 (63%); p = 0.13 • 1–7 days: 63/323 (20%) vs. 82/460 (18%); p = 0.55 • >7–30 days: 23/323 (7%) vs. 54/460 (12%); p<0.05 • >30 days: 17/323 (5%) vs. 35/460 (7%); • p = 0.19	Huang 2006[24]	• Weekly screening of nares, postauricular areas, axilla, and umbilicus
Age at NICU admission, days, n (%)	MRSA colonization vs. no colonization	Continuity-adjusted chi- squared test	No	• < 1 day: 96/130 (74%) vs. 288/395 (73.0%) • 1–7 day: 20/130 (15%) vs. 73/395 (18%) • > 7–30 days: 8/130 (6%) vs. 15/395 (4%) • > 30 days: 6/130 (5%) vs. 19/395 (5%) • p = 0.617	Huang 2015[26]	• Active screening: specimens obtained within 24 hrs of admission, and repeated weekly for 2 weeks (from nares and umbilicus)
Age at NICU admission, hrs, n (%)	Colonization vs. no colonization	Pearson's chi-squared test, chi-squared test for linear trend, or Fisher's exact test	No (all infants) No (subset)	First nasal swab: • < 24 hrs: 100/117 (85.5%) vs. 628/832 (75.5%) • 24–48 hrs: 8/117 (6.8%) vs. 106/832(12.7%) • > 48 hrs: 9/117 (7.7%) vs. 96/832 (11.5%) • p = 0.059 Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • < 24 hrs: 83/100 (83.0%) vs. 545/732 (74.5%) • p = 0.07	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after NICU admission (median 4 days [range: 1–6])
Age at NICU admission, ≥24 hrs, n (%)	Colonization vs. no colonization	Chi-squared test or Fisher's exact test	Yes	• ≥ 24 hrs: 16/187 (8.6%) vs. 92/535 (17.2%) • p = 0.001	Geraci 2014[6]	• Weekly nasal and rectal swabs obtained. For the 1st 6 months universal admission screening was performed
Age at NICU admission, days	Colonization vs. no colonization	Student's t- test or Wilcoxon rank sum test	Yes	• Infants colonized with MRSA were significantly older when transferred to NICU (p=NR)	Macnow 2013[44]	• Multi-NICU study: • NICU 1: First 2 years of study, surveillance cultures

Risk Factor	Outcome	Analytical Statistics	Significant Finding	Results	Author Year	Comments
						obtained from infants transferred at ≥ 3 days of age. Last 4 years of study, surveillance cultures obtained from all transferred infants. Routine surveillance only during outbreak (2 outbreaks occurred) • NICU 2: Surveillance cultures obtained from all transferred patients, no routine cultures. • Study reports no MRSA-specific quantitative data
Birthweight, mean, g	Infection vs. no infection	2-sample t-test (all infants) NR (subanalysis)	Yes (all infants) No (subanalysis)	All infants: • 1720g vs. 2480g; 95% CI: 0.46–1.06 • p < 0.0001 Subanalysis of 138 colonized infants: • Not significant, p=NR	Maraqa 2011[33]	• Admission cultures of all neonates; weekly surveillance cultures included patients who were not MRSA colonized or infected during NICU stay.
Birthweight, mean, g	Infection vs. no infection	Two-tailed t-test	Yes	• 1347g vs. 2445g • p < 0.001	Khoury 2005[32]	• Single screening of patients on Oct 14, 2001; newly admitted patients were screened through January 2002. Periumbilical and perirectal sites were screened
[a]Birthweight, mean, g	Colonization or infection vs. no MRSA	Two-sample t-test	Yes	• 1317g vs. 2367g • p < 0.000001	Reboli 1989[38]	• Weekly culture of nares, pharynx, or endotracheal tubes
[a]Birthweight, median (range)	Colonization or infection vs. no colonization or infection	Chi-squared test	No	• <1500 g: 17/ 68 (25%) • All new admissions: 34/745 (4%) RR: 17 (95% CI: 8.1 – 35.5)	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites
Birthweight, mean (SD), g	Colonization vs. no colonization	One-way ANOVA or Kruskal-Wallis test	No	• 2568g (867) vs. 2673g (760) • p = 0.12	Geraci 2014[6]	• Weekly nasal and rectal swabs obtained. For the 1st 6 months universal admission screening was performed
Birthweight, mean, g, mean (SD)	Colonization vs. no colonization	NR	No	• 1554g (± 673.4) vs. 1432.2g (± 657) • p = 0.59	Lazenby 2012[40]	• Admission screening of nares, axilla, and diaper area on admission and twice weekly as long as neonate was MRSA negative
Birthweight, mean, g	Colonization vs. no colonization	Two-sample t-test	Yes	• 1710g vs. 2520g • p < 0.0001	Maraqa 2011[33]	• Admission cultures of all neonates; weekly surveillance cultures

Risk Factor	Outcome	Analytical Statistics	Significant Finding	Results	Author Year	Comments
						included patients who were not MRSA colonized or infected during NICU stay
Birthweight, mean, g	Colonization vs. no colonization	Two-tailed t-test	Yes	• 1522g vs. 2445g • p < 0.001	Khoury 2005[32]	• Single screening of patients on Oct 14, 2001; newly admitted patients were screened through January 2002. Periumbilical and perirectal sites were screened
Birthweight, mean (SD), g	Colonization vs. no colonization	Paired student's T-test	No	• 2482g ± 756 vs. 2740g ± 721 • Study states no statistical significance (p=NR)	Uehara 2001[41]	• Screened on admission (at < 24 hrs of age), weekly on Monday, and 1 day before discharge. Additional cultures performed according to clinical requirements.
Birthweight, n (%)	Colonization or infection vs. no MRSA detected	NR	Yes	≤1000g: • Colonized: 35/128 (27%) • Infected: 24/63 (38%) • No MRSA detected: 301/2089 (14%) 1001–1500g: • Colonized: 20/128 (16%) • Infected: 10/63 (16%) • No MRSA detected: 153/2089 (7%) 1501–2500g: • Colonized: 18/128 (14%) • Infected: 7/63 (11%) • No MRSA detected: 382/2089 (18%) ≥2501g: • Colonized: 40/128 (32%) • Infected: 17/63 (27%) • No MRSA detected: 1115/2089 (53%) Unknown birthweight: • Colonized: 15/128 (11%) • Infected: 5/63 (8%) • No MRSA detected: 138/2089 (7%) • p < 0.001	Song 2010[28]	• Active screening for MRSA on admission and weekly thereafter • Study provided only one p value for all categories
[a]Birthweight, OR (95% CI)	Colonization or infection vs. no MRSA	Poisson regression	Yes (univariate) Yes (multivariate)	• Univariate analysis: Colonization or infection associated with significantly lower birthweight: OR = 0.86 (0.80–0.93), p=NR • • Multivariate analysis: Colonization or infection associated with low birthweight: OR = 0.84 (0.75–0.93), p=NR	Song 2010[22]	• Nasal swabs collected on admission and weekly thereafter • Very low birthweight infants = 751–1000 g and extremely low birthweight infants = < 750 g during study period

Risk Factor	Outcome	Analytical Statistics	Significant Finding	Results	Author Year	Comments
						• Variables included in the multivariate analysis NR
Birthweight, g, OR (95% CI)	Infection with colonization vs. colonization	Odds ratio	Yes	• MRSA infection with colonization was associated with low birthweight (< 1000 g), compared with MRSA colonization only: OR = 3.79 (1.69–8.51), • p < 0.0005	Huang 2006[24]	• Weekly screening of nares, postauricular areas, axilla, and umbilicus
Birthweight, g, n (%); OR (95% CI); p	Colonization vs. no colonization	Student's t tests	Yes	• ≤1000g: 32/323 (10%) vs. 17/460 (4%); OR = 2.87 (1.51-5.49); p < 0.005 • 1001–1500g: 58/323 (18%) vs. 50/460 (11%); OR = 1.79 (1.17–2.76); p < 0.005 • 1501–2500g: 123/323 (38%) vs. 172/460 (37%); OR = 1.03 (0.76–1.40); p < 0.8447 • >2500g: 110/323 (34%) vs. 221/460 (48%); OR = 0.56 (0.41–0.76); p < 0.0001	Huang 2006[24]	• Weekly screening of nares, postauricular areas, axilla, and umbilicus
Birthweight, g, n (%) Subset: birthweight, g, median, (IQR)	Colonization vs. no colonization	Student's t test or Mann-Whitney-Wilcoxon test Odds ratio Pearson's chi-squared test, chi-squared test for linear trend, or Fisher's exact test	Yes (all infants) Yes (subset for univariate and multivariate analyses)	First nasal swab: • ≤ 1000 g: 0/117 (0%) vs 28/832 (3.4%) • 1001–1500g: 2/117 (1.7%) vs 51/832 (6.1%) • 1501–2000 g: 13/117 (11.1%) vs. 99/832 (11.9%) • 2001–2500 g: 21/117 (18.0%) vs. 150/832 (18.0%) • >2500 g: 80/117 (68.4%) vs. 500/832 (60.1%) • p = 0.008 Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • Univariate analysis: o 2170 g (I,420–2770) vs. 2775 g (2190–3265) o p < 0.001 • Multivariate analysis: o Odds of colonization was negatively associated with each additional 100 g of birthweight: OR = 0.96 (0.93–0.99), p = 0.047	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4 days [range: 1–6])
Birthweight, n (%)	Colonization vs. no colonization	Chi-squared or Fisher's exact test	No	• < 1000 g: 3/11 (27%) vs. 86/240 (36%); • 1000–1500 g: 6/11 (55%) vs. 76/240 (31%) • 1501–2500 g: 0/11 (0%) vs. 49/240 (20%) • ≥2500 g: 2/11 (18%) vs. 30/240 (13%) • p = 0.174	Kuo 2013[36]	• Specimens obtained from nares and umbilicus on two dates: Oct 11, and Dec 12, 2011
Birthweight, g	Colonization vs. no colonization	Continuity adjusted chi-squared test	Yes, for birthweight <1000g	• < 1000 g: 29/130 (22%) vs. 54/395 (14%) (Colonization significantly associated with low birthweight (< 1000 g), p < 0.05) • 1001–1500 g: 36/130 (28%) vs. 77/395 (20%) • 1501-2500 g: 34/130 (26%) vs. 120/395 (31%) • >2500 g: 31/130 (24%) vs. 141/395 (36%) • p < 0.006 = overall	Huang 2015[26]	• • Active screening: specimens obtained within 24 hrs of admission, and repeated weekly for 2 weeks (from nares and umbilicus)

Risk Factor	Outcome	Analytical Statistics	Significant Finding	Results	Author Year	Comments
Birthweight, g	Single patient room MRSA colonization vs. open unit MRSA colonization	Bivariate Cox proportional hazards model	No	• No difference in MRSA colonization rates between bed configurations when controlling for birthweight: p = 0.79	Julian 2015[12]	• Anterior nares swabbed on admission and weekly thereafter
Birthweight, g	Colonization vs. no colonization	Student's t test or Wilcoxon rank sum test	Yes	• Infants colonized with MRSA were of significantly lower birthweight when transferred to NICU (p=NR)	Macnow 2013[44]	• Multi-NICU study: • NICU 1: First 2 years of study, surveillance cultures obtained from infants transferred at ≥ 3 days of age. Last 4 years of study, surveillance cultures obtained from all transferred infants. Routine surveillance only during outbreak (2 outbreaks occurred) • NICU 2: Surveillance cultures obtained from all transferred patients, no routine cultures. • Study reports no MRSA-specific quantitative data
Birthweight, kilograms, median (range)	MRSA colonization vs. no colonization	Kruskal-Wallis and Chi-squared tests	Yes	**Univariate analysis:** • 1.59kg (0.46-4.38kg) vs. 2.42kg (0.35-5.28kg) p<0.001	Azarian 2016[52]	
Birthweight, <2000g, n/N (%)	MRSA colonization vs. no colonization	Chi-squared, Fisher test	No	**Bivariate analysis:** • 3/59g (5%) vs. 22/344g (6%); RR = 0.81; 95%CI: 0.27-2.41 p=1.00	Garcia 2014[43]	
Birthweight, grams, n/N (%)	MRSA infection vs no infection	Chi-squared or Fisher's exact test	No	**Univariate analysis:** • ≤1000g: 4/21 (19%) vs. 4/21 (19%) • 1001g-1500g: 6/21 (29%) vs. 5/21 (25%) • 1501g-2000g: 3/21 (14%) vs. 4/21 (19%) • 2001g-2500g: 0/21 (0%) vs. 0/21 (0%) • >2500g: 8/21 (38%) vs. 8/21 (38%) p=NR but no significant difference between both groups	Huang 2005[35]	
Birthweight, grams, mean ± SD (median, range)	MRSA infection vs. no infection	Student t test Logistic regression	Yes, univariate Yes, multivariate	**Univariate analysis:** • 1758±601g (1567, 972-3314) vs. 2657±334g (2548, 662-4420) • p=0.001 **Multivariate analysis:** • OR= 0.91; 95%CI: 0.93-0.99 • p=0.040	Sakaki 2009[34]	

Risk Factor	Outcome	Analytical Statistics	Significant Finding	Results	Author Year	Comments
Breast fed, n (%)	Colonization vs. no colonization	Chi- squared test	No	• 0/46 (0%) vs. 0/57 (0%) • Denominator and percentages reported, numerator calculated • Study states no statistical significance (p=NR)	Uehara 2001[41]	• Screened on admission (at <24h of age), weekly on Monday, and 1 day before discharge. Additional cultures performed according to clinical requirements
Breast milk and formula fed, n (%)	Colonization vs. no colonization	Chi- squared test	No	• 46/46 (100%) vs. 57/57 (100%) • Denominator and percentages reported, numerator calculated • Study states no statistical significance (p=NR)	Uehara 2001[41]	• Screened on admission (at <24hrs of age), weekly on Monday, and 1 day before discharge. Additional cultures performed according to clinical requirements. • Feeding of >90% of infants receiving breast milk was simultaneously supplemented with formula
Breast milk fed, n (%)	Colonization vs. no colonization	Pearson's chi-squared test, chi-squared test for linear trend, or Fisher's exact test	No	Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • 57/100 (57%) vs. 383/732 (52.3%) • p = 0.95	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4 days [range: 1–6]).
Formula fed, n (%)	Colonization vs. no colonization	Pearson's chi-squared test, chi-squared test for linear trend, or Fisher's exact test	No	Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • 98/100 (98%) vs. 683/732 (93.3%) • p = 0.13	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4 days [range: 1–6]).
Breast milk fed, n (%)	Colonization vs. no colonization	Chi-squared test or Fisher's exact test	No	• 97/187 (51.9%) vs. 275/535 (51.4%) • p = 0.46	Geraci 2014[6]	• Weekly nasal and rectal swabs obtained. For the 1st 6 months, universal admission screening was performed.
Formula fed, n (%)	Colonization vs. no colonization	Chi-squared test or Fisher's exact test	No	• 181/187 (96.8%) 496/535 (92.7%) • p = 0.07	Geraci 2014[6]	• Weekly nasal and rectal swabs obtained. For the 1st 6 months, universal admission screening was performed
Delivery method, cesarean	Infection vs. no infection	NR	No	Subanalysis of 138 colonized infants: • Study states not significant (p=NR)	Maraqa 2011[33]	• Admission cultures of all neonates; weekly surveillance cultures included patients who were not MRSA colonized or infected during NICU stay

Risk Factor	Outcome	Analytical Statistics	Significant Finding	Results	Author Year	Comments
Delivery method, cesarean, n (%)	Colonization or infection vs. no colonization or infection	Chi-squared test	No	• 19/23 (83%) vs. 29/36 (81%) • p = 0.84	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites
Delivery method, cesarean, n (%)	Colonization vs. no colonization	Pearson's chi-square test, chi-square test for linear trend, or Fisher's exact test	No (all infants) Yes (subset)	First nasal swab: • 74/117 (63.3%) vs. 549/832 (66.0%) • p = 0.53 Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • 80/100 (80.0%) vs. 469/732 (64.1%) • p = 0.003	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4 days [range: 1-6])
Delivery method, vaginal, n (%)	Colonization vs. no colonization	Chi-squared test or Fisher's exact test	No	• 52/187 (27.8%) vs. 158/535 (29.5%) • p = 0.29	Geraci 2014[6]	• Weekly nasal and rectal swabs obtained. For the first 6 months, universal admission screening was performed
Delivery method, cesarean, n (%)	Colonization vs. no colonization	Chi-squared or Fisher's exact test (not clarified) (univariate) NR (multivariate)	Yes (univariate and multivariate)	• 8/13 (61.5%) vs. 94/192 (49%) • OR = 13.2 (1.7–102.5); p = 0.16 Multivariate analysis • OR = 12.5 (1.5–97.2), p=NR (cesarean deliveries independently associated with MRSA colonization)	Lazenby 2012[40]	• Admission screening of nares, axilla, and diaper area on admission and twice weekly as long as neonate was MRSA negative. •
Delivery method, cesarean, rate/100 births	Colonization vs. no colonization	Chi-squared test	Yes	• 8.11 vs. 4.72 • p = 0.0026	Maraqa 2011[33]	• Admission cultures of all neonates; weekly surveillance cultures included patients who were not MRSA colonized or infected during NICU stay
Delivery method, abdominal, n (%)	Colonization vs. no colonization	Chi-squared test	No	• 15/46 (33%) vs. 9/57 (16%) • Denominator and percentages reported, numerator calculated • Study states no statistical significance (p=NR)	Uehara 2001[41]	• Screened on admission (at <24hrs of age), weekly on Monday, and 1 day before discharge. Additional cultures performed according to clinical requirements.
Delivery method, cesarean, n/N (%)	MRSA colonization vs. no colonization	Kruskal-Wallis and Chi-squared tests	Yes	**Univariate analysis:** • 130/177 (73.4%) vs. 1090/1763 (61.8%) • p=0.003	Azarian 2016[52]	
Delivery method, cesarean, n/N (%)	MRSA infection vs. no infection	Fisher exact test	Yes	**Univariate analysis:** • 21/28 (75.0%) vs. 373/895 (41.7%) • p<0.001	Sakaki 2009[34]	
Delivery method, vaginal, n/N (%)	MRSA colonization vs. no colonization	Chi-squared, Fisher test	No	**Bivariate analysis:** • 12/59 (20%) vs. 87/344 (25%); RR = 0.76; 95%CI: 0.42-1.38 • p=0.36	Garcia 2014[43]	

Risk Factor	Outcome	Analytical Statistics	Significant Finding	Results	Author Year	Comments
[a]Race, white, n (%)	Colonization or infection vs. no MRSA	Chi-squared test	No	• White: 13/26 (50%) vs. 274/593 (46%) • Non-white: 13/26 (50%) vs. 319/593 (54%) • p = 0.7	Reboli 1989[38]	• Weekly culture of nares, pharynx, or endotracheal tubes
Ethnicity	Single patient room MRSA colonization vs. open unit MRSA colonization	Bivariate Cox proportional hazards model	No	• No difference in MRSA colonization rates between bed configurations when controlling for ethnicity: p = 0.90	Julian 2015[12]	• Anterior nares swabbed on admission and weekly thereafter. • Ethnicity: not defined
Race, n (%)	Colonization vs. no colonization	Fisher's exact test	No	• Asian: 0/87 (0%) vs. 108/3696 (3%) • Black or African American: 46/87 (53%) vs. 1665/3696 (45%) • White: 33/87 (38%) vs. 1499/3696 (41%) • Other/ unknown: 8/87 (9%) vs. 424/3696 (11%) • p = 0.26	Pierce 2016[48]	• Nasal swabs were obtained weekly for all infants and on admission for neonates admitted from home and other hospitals.
Ethnicity, black, n (%)	Colonization vs. no colonization	Chi-squared or Fisher's exact test (not clarified)	No	• 6/13 (6%) vs. 90/192 (46.9%) • p = 0.73	Lazenby 2012[40]	• Admission screening of nares, axilla, and diaper area on admission and twice weekly as long as neonate was MRSA negative
Race, infection rate/100 births	Infection in blacks vs. infection in non-blacks	Chi-squared test (all infants) NR (subanalysis)	Yes (all infants) No (subanalysis)	All infants • Infection in blacks 3.18 vs. infections in non-blacks: 1.65 • p = 0.036 • RR = 1.96 (1.03–3.61) Subanalysis of colonized infants • Study states not significant (p=NR)	Maraqa 2011[33]	• Admission cultures of all neonates; weekly surveillance cultures included patients who were not MRSA colonized or infected during NICU stay
Race, n (%)	Colonization or infection vs. no MRSA detected	NR	No	Black: • Colonized: 56/128 (44%) • Infected: 23/63 (37%) • No MRSA detected: 633/2089 (30%) White: • Colonized: 18/128 (14%) • Infected: 8/63 (13%) • No MRSA detected: 364/2089 (17%) Other: • Colonized: 54/128 (41%) • Infected: 32/63 (51%) • No MRSA detected: 1092/2089 (52%) • p = 0.07	Song 2010[28]	• Active screening for MRSA on admission and weekly thereafter • Study provided only one p value for all categories
Race, white, n/N (%)	MRSA colonization vs. no colonization	Kruskal-Wallis and Chi-squared tests	Yes	**Univariate analysis:** • 102/177 (57.6%) vs. 1229/1763 (69.7%) • p=0.004	Azarian 2016[52]	
Race, n/N (%)	MRSA colonization vs. no colonization	Chi-squared	No	**Univariate analysis:** • White: 27/59 (46%) vs. 693/1701 (41%) • African American: 26/59 (44%) vs. 720/1701 (42%)	Schultz 2009[46]	

Risk Factor	Outcome	Analytical Statistics	Significant Finding	Results	Author Year	Comments
				• Hispanic: 3/59 (5%) vs. 219/1701 (13%) • Other: 3/59 (5%) vs. 69/1701 (4%) • p=0.35		
Race, colonization rate/ 100 births	Colonization in blacks vs. colonization in non-blacks	Chi-squared test	Yes	• 8.92 vs. 6.09 • p = 0.0316	Maraqa 2011[33]	• Admission cultures of all neonates; weekly surveillance cultures included patients who were not MRSA colonized or infected during NICU stay
Ethnicity, n (%)	Colonization vs. no colonization	Fisher's exact test	No	• Hispanic: 5/87 (6%) vs. 184/3696 (5%) • Non-Hispanic: 79/87 (91%) vs. 3312/3696 (90%) • Unknown: 3/87 (3%) vs. 200/3696 (5%) • p = 0.76	Pierce 2016[48]	• Nasal swabs were obtained weekly for all infants and on admission for neonates admitted from home and other hospitals
[a]Sex	Colonization or infection vs. no MRSA	Chi-squared test	No	• Male: 17/26 (65%) vs. 320/593 (53.9%) • Female: 9/26 (34.6%) 273/593 (46%) • p = 0.25	Reboli 1989[38]	• Weekly culture of nares, pharynx, or endotracheal tubes
Sex, male, n (%)	Colonization or infection vs. no MRSA detected	NR	No	• Colonized: 63/128 (50%) • Infected: 42/63 (67%) • No MRSA detected: 1158/2089 (55%) • p > 0.05	Song 2010[22]	• Active screening for MRSA on admission and weekly thereafter
Sex, female, n (%)	Colonization vs. no colonization	Fisher's exact test	No	• 39/87 (45%) vs. 1647/3696 (45%) • p = 1.00	Pierce 2016[48]	• Nasal swabs were obtained weekly and on admission for neonates admitted from home and other hospitals
Sex, male, n (%)	Colonization vs. no colonization	Pearson's chi-squared test, chi-squared test for linear trend, or Fisher's exact test Odds ratio	No (all infants) Yes (univariate and multivariate analyses of subset)	First nasal swab: • 63/117 (53.9%) vs. 484/832 (58.2%) • p = 0.37 Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • Univariate analysis: ○ 42/100 (42%) vs. 442/732 (60.4%) ○ p <0.001 • Multivariate analysis: ○ MRSA acquisition negatively associated with male sex: OR = 0.60 (0.37–0.97); p = 0.038	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4d [range:1-6])
Sex, male, n (%)	Colonization vs. no colonization	Continuity-adjusted chi- squared test	No	• 76/130 (58%) vs.234/395 (59%) • p = 0.876	Huang 2015[26]	• Active screening: specimens obtained within 24hrs of admission, and repeated weekly for 2 weeks (from nares and umbilicus).
Sex	Single patient room MRSA colonization vs.	Bivariate Cox proportional hazards model	No	• No difference in MRSA colonization rates between bed configurations when controlling for sex: p = 0.08	Julian 2015[12]	• Anterior nares swabbed on admission and weekly thereafter.

Risk Factor	Outcome	Analytical Statistics	Significant Finding	Results	Author Year	Comments
	open unit MRSA colonization					
Sex, male, n (%)	Colonization vs. no colonization	Chi-squared test	Yes	• 88/187 (47.1%) vs. 321/535 (60.0%) • p = 0.001	Geraci 2014[6]	• Weekly nasal and rectal swabs obtained. For the first 6 months, universal admission screening was performed.
Sex, male, n (%)	Colonization vs. no colonization	Chi-squared or Fisher's exact test	No	• 7/11 (64%) vs. 124/240 (52%) • p = 0.437	Kuo 2013[36]	Specimens obtained from nares and umbilicus on two dates: Oct 11, and Dec 12, 2011
Sex, male	Colonization vs. no colonization	Student's t test or Wilcoxon rank sum test	No	• Sex was not associated with MRSA colonization status at transfer to NICU	Macnow 2013[44]	• Multi-NICU study: • NICU 1: First 2 years of study, surveillance cultures obtained from infants transferred at ≥ 3 days of age. Last 4 years of study, surveillance cultures obtained from all transferred infants. Routine surveillance only during outbreak (2 outbreaks occurred). • NICU 2: Surveillance cultures obtained from all transferred patients, no routine cultures. • Study reports no MRSA-specific quantitative data.
Sex, male, n (%)	Colonization or infection vs. no MRSA	Chi-squared test	No	• 12/23 (52%) vs. 15/37 (41%) • p = 0.38	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites
Sex, male, n (%)	Colonization vs. no colonization	Chi square or Fisher's exact test (not clarified)	No	• 7/13 (53.8%) vs. 105/192 (54.7%) • p = 0.74	Lazenby 2012[40]	• Admission screening of nares, axilla, and diaper area on admission and twice weekly as long as neonate was MRSA negative.
Sex, rate/ 100 births	Colonization in males vs. colonization in females	Chi-squared test	No	• 6.15 vs. 7.49 • p = 0.2296	Maraqa 2011[33]	• Admission cultures of all neonates; weekly surveillance cultures included patients who were not MRSA colonized or infected during NICU stay
Sex, male, n (%)	Colonization vs. no colonization	Continuity-adjusted chi- squared test and odds ratio	No	• 170/323 (53%) vs. 272/460 (59%); • OR = 0.77 (0.57–1.03); • p = 0.071	Huang 2006[24]	• Weekly screening of nares, postauricular areas, axilla, and umbilicus

Risk Factor	Outcome	Analytical Statistics	Significant Finding	Results	Author Year	Comments
Sex, male, n/N (%)	MRSA colonization vs. no colonization	Kruskal-Wallis and Chi-squared tests	No	**Univariate analysis:** • 96/177 (54.2%) vs. 1006/1763 (57.1%); • p=0.52	Azarian 2016[52]	
Sex, male, n/N (%)	MRSA colonization vs. no colonization	Chi-squared, Fisher test Multiple logistic regression	No, univariate No, multivariate	**Bivariate analysis:** • 33/59 (56%) vs. 167/344 (49%); RR = 1.29; 95%CI: 0.80-2.07 • p=0.30 **Multivariate analysis of newborns hospitalized >72 hours (n=80):** • OR: 4.75; 95%CI: 0.84-26.80 • p=0.08	Garcia 2014[43]	
Sex, male, n/N (%)	MRSA infection vs no infection	Chi-squared or Fisher's exact test	No	**Univariate analysis:** • 18/21 (86%) vs. 17/21 (81%) • p=NR but no significant difference between both groups	Huang 2005[35]	
Sex, n/N (%)	MRSA infection vs. no infection	Fisher exact test	No	**Univariate analysis:** • Male: 17/28 (60.7%) vs. 511/895 (57.1%) • Female: 11/28 (39.3%) vs. 384/895 (42.9%) • p=0.847	Sakaki 2009[34]	
Sex, male, n/N (%)	MRSA colonization vs. no colonization	Chi-squared	No	**Univariate analysis:** • 38/59 (64%) vs. 951/1701 (56%) • p=0.23	Schultz 2009[46]	
Gestational age, mean, weeks	Infection vs. no infection	2-sample T-test (univariate) Multiple logistic regression analysis (multivariate) NR (subanalysis)	Yes (univariate) Yes (multivariate) No (subanalysis)	All infants – univariate analysis • 31.59 weeks vs. 34.68 weeks • 95% CI: 34.51–34.87 • p < 0.0001 All infants – multivariate analysis • Combined with colonization: p = 0.031 • Combined with length of stay: p = 0.0064 • Subanalysis of 138 colonized infants • Not significant (p=NR)	Maraqa 2011[33]	• Admission cultures of all neonates; weekly surveillance cultures included patients who were not MRSA colonized or infected during NICU stay
Gestational age, mean, weeks	Infection vs. no infection	Two-tailed t-test	Yes	• 28.51 weeks vs. 34.41 weeks • p = 0.0002	Khoury 2005[32]	• Single screening of patients on Oct 14, 2001; newly admitted patients were screened through January 2002. Periumbilical and perirectal sites were screened
Gestational age, median (range), weeks	Infection or colonization vs. no infection or colonization	Kruskal-Wallis test	No	• 29 weeks (23–42) vs. 32 weeks (24–41) • p = 0.43	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites

Risk Factor	Outcome	Analytical Statistics	Significant Finding	Results	Author Year	Comments
Gestational age < 28 weeks, OR (95% CI)	Infection with colonization vs. colonization only	Odds ratio	Yes	• MRSA colonization with infection was associated significantly with premature birth (gestational age of < 28 weeks) compared with MRSA colonization alone: OR = 3.33 (1.66–6.70), p < 0.0005	Huang 2006[24]	• Weekly screening of nares, postauricular areas, axilla, and umbilicus
Gestational age, weeks, n (%) Gestational age, weeks, median (IQR) for acquisition analysis	Colonization vs. no colonization	Mann-Whitney-Wilcoxon test or Student t test Pearson's chi-squared, chi-squared for linear trend, or Fisher's exact test	Yes (all infants) Yes (subset)	First nasal swab: • < 30 weeks: 1/117 (0.85%) vs. 42/832 (5.1%) • 30–36 weeks: 29/117 (24.8%) vs. 283/832 (34.0%) • > 36 weeks: 86/117(73.5 %) 666/832 (80.1%) • p = 0.008 Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • 35.5 weeks (32–38) vs. 37 weeks (35–39) • p <0.001	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4 days [range: 1–6])
Gestational age, weeks, n (%)	Colonization vs. no colonization	Continuity adjusted chi-squared test	Yes	• ≤ 28 wks.: 26/130 (20%) vs. 67/395 (17%) • >28–32 wks.: 40/130 (31%) vs. 81/395 (21%); p <0.05 • >32–37 wks.: 29/130 (22%) vs. 101/395 (26%) • > 37 wks.: 35/130 (27%) vs. 144/395 (37%) • p = 0.046	Huang 2015[26]	• Active screening: specimens obtained within 24 hrs of admission, and repeated weekly for 2 weeks (from nares and umbilicus)
Gestational age, weeks	Single Patient Room MRSA colonization vs. Open Unit MRSA colonization	Bivariate Cox proportional hazards model	No	• No difference in MRSA colonization rates between bed configurations when controlling for gestational age: p = 0.75	Julian 2015[12]	• Anterior nares were swabbed on admission and weekly thereafter
Gestational age, mean (SD), wks.	Colonization vs. no colonization	One-way ANOVA or Kruskal-Wallis test	No	• 36.4 wks. (3.5) vs. 36.7 wks. (3.3) • p = 0.23	Geraci 2014[6]	• Weekly nasal and rectal swabs obtained. For the first 6 months, universal admission screening was performed.
Gestational age, n (%)	Colonization vs. no colonization	Chi-squared or Fisher's exact test	No	• <28 weeks: 5/11 (45%) vs. 85/240 (35%); • p = 0.530 • 28-<32 weeks: 4/11 (36%) vs. 77/240 (32%); p = 0.750 • 32-<37 weeks: 0/11 (0%) vs. 53/240 (22%); p = 0.127 • ≥37 weeks: 2/11 (18%) vs. 25/240 (10%); • p = 335 • p = 0.231	Kuo 2013[36]	• Specimens obtained from nares and umbilicus on two dates: Oct 11, and Dec 12, 2011
Gestational age, mean, weeks	Colonization vs. no colonization	Student's t test or Wilcoxon rank sum test	Yes	• Infants colonized with MRSA were of significantly lower gestational age when transferred to NICU (p=NR)	Macnow 2013[44]	• Multi-NICU study: • NICU 1: First 2 years of study, surveillance cultures

Risk Factor	Outcome	Analytical Statistics	Significant Finding	Results	Author Year	Comments
						obtained from infants transferred at ≥ 3 days of age. Last 4 years of study, surveillance cultures obtained from all transferred infants. Routine surveillance only during outbreak (2 outbreaks occurred). • NICU 2: Surveillance cultures obtained from all transferred patients, no routine cultures. • Study reports no MRSA-specific quantitative data.
Gestational age, mean (SD), weeks	Colonization vs. no colonization	NR	No	• 30.3 weeks (±3.9) vs. 29.7 weeks (±3.1) • p = 0.64	Lazenby 2012[40]	• Admission screening of nares, axilla, and diaper area on admission and twice weekly as long as neonate was MRSA negative.
Gestational age, mean, weeks	Colonization vs. no colonization	Two-sample t-test	Yes	• 31.29 weeks vs. 34.87 weeks • p < 0.0001	Maraqa 2011[33]	• Admission cultures of all neonates; weekly surveillance cultures included patients who were not MRSA colonized or infected during NICU stay
Gestational age, weeks, n (%), OR (95% CI); p	Colonization vs. no colonization	Continuity-adjusted chi- squared test	Yes	• < 28 weeks: 45/323 (14%) vs. 23/460 (5%); OR = 3.08 (1.77–5.37); p <0.0001 • >28–32 weeks: 68/323 (21%) vs. 74/460 (16%); OR = 1.39 (0.95–2.04); p = 0.759 • 32–37 weeks: 101/323 (31%) vs. 157/460 (34%); OR = 0.88 (0.64–1.20); p = 0.4018 • > 37 weeks: 109/323 (34%) vs. 206/460 (45%); OR = 0.63 (0.46–0.85); p < 0.005	Huang 2006[24]	• Weekly screening of nares, postauricular areas, axilla, and umbilicus
Gestational age, mean, weeks	Colonization vs. no colonization	Two-tailed t-test	Yes	• 29.83 weeks vs. 34.41 weeks • p = 0.0002	Khoury 2005[32]	• Single screening of patients on Oct 14, 2001; newly admitted patients were screened through January 2002. Periumbilical and perirectal sites were screened
Gestational age, weeks, median (range)	MRSA colonization vs. no colonization	Kruskal-Wallis and Chi-squared tests	Yes	**Univariate analysis:** • 31 weeks (23-42 weeks) vs. 35 weeks (22-42 weeks) • p<0.001	Azarian 2016[52]	

Risk Factor	Outcome	Analytical Statistics	Significant Finding	Results	Author Year	Comments
Gestational age at birth <37 weeks, n/N (%)	MRSA colonization vs. no colonization	Chi-squared, Fisher test	No	**Bivariate analysis:** • 12/59 (20%) vs. 74/344 (22%); RR = 0.94; 95%CI: 0.52-1.69 • p=0.84	Garcia 2014[43]	
Gestational age, weeks, n/N (%)	MRSA infection vs no infection	Chi-squared or Fisher's exact test	No	**Univariate analysis:** • 25-30 weeks: 8/21 (38%) vs. 6/21 (29%) • 31-36 weeks: 7/21 (33%) vs. 8/21 (38%) • ≥37 weeks: 6/21 (29%) vs. 7/21 (33%) • p=NR but no significant difference between both groups	Huang 2005[35]	
Gestational age, weeks, mean ± SD (median, range)	MRSA infection vs. no infection	Student t test	Yes	**Univariate analysis:** • 33.6±3.8 weeks (33.1, 27.3-42.3) vs. 37.2±2.8 weeks (37.6, 24.6-43.4) • p<0.001	Sakaki 2009[34]	
Gestational age, weeks, n/N (%)	MRSA colonization vs. no colonization	Chi-squared	Yes	**Univariate analysis:** • <28 weeks: 26/59 (44%) vs. 226/1701 (13%) • 28-31 weeks: 19/59 (32%) vs. 249/1701 (15%) • > 31 weeks: 14/59 (24%) vs. 1226/1701 (72%) • p<0.001	Schultz 2009[46]	
Multiple births, n/N (%)	MRSA colonization vs. no colonization	Kruskal-Wallis and Chi-squared tests	No	**Univariate analysis:** • 43/177 (24.3%) vs. 355/1763 (20.1%) p=0.23	Azarian 2016[52]	
Multiple births, twinning, n/N (%)	MRSA colonization vs. no colonization	Chi-squared, Fisher test	No	**Bivariate analysis:** • 5/59 (8%) vs. 38/344 (11%); RR = 0.78; 95%CI: 0.33-1.83 p=0.55	Garcia 2014[43]	
Multiple births, twin, n/N (%)	MRSA infection vs. no infection	Fisher exact test	Yes	**Univariate analysis:** • 11/28 (36.3%) vs. 134/895 (15.0%) p=0.002	Sakaki 2009[34]	
Multiple gestation	Infection vs. no infection	NR	No	Subanalysis of 138 colonized infants • Not significant (p=NR)	Maraqa 2011[33]	• Admission cultures of all neonates; weekly surveillance cultures included patients who were not MRSA colonized or infected during NICU stay
Multiple gestation, multiples, n (%)	Infection vs. no infection	Chi-squared test	Yes	• 5/12 (42%) vs 8/68 (12%) • The odds of infection were associated with multiple gestation: OR = 5.36 (1.37–20.96)	Khoury 2005[32]	• Single screening of patients on Oct 14, 2001; newly admitted patients were screened through January 2002. Periumbilical and perirectal sites were screened
Multiple gestation, multiples, n, (%)	MRSA infection or colonization vs. no MRSA	Chi-squared test	No	• 12/23 (52%) vs. 13/37 (35%) • p = 0.15	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites

Risk Factor	Outcome	Analytical Statistics	Significant Finding	Results	Author Year	Comments
Multiple gestation, twin birth, n (%)	Colonization vs. no colonization	Pearson's chi-squared test, chi-squared test for linear trend, or Fisher's exact test	No (all infants) Yes (subset)	First nasal swab: • 12/117 (10.3%) vs. 111/832 (13.3%) • p = 0.34 Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • 22/100 (22%) vs. 89/732 (12.2%) • p = 0.005	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4d [range: 1-6])
Multiple gestation, twins, n (%)	Colonization vs. no colonization	Chi-squared test or Fisher's exact test	No	• 31/187 (16.6%) vs. 73/535 (13.6%) • p = 0.15	Geraci 2014[6]	• Weekly nasal and rectal swabs obtained. For the first 6 months, universal admission screening was performed
Multiple gestation, rate/ 100 births	Colonization vs. no colonization	Chi-squared test	Yes	• 26.08 vs. 17.07 • p = 0.0204	Maraqa 2011[33]	• Admission cultures of all neonates; weekly surveillance cultures included patients who were not MRSA colonized or infected during NICU stay
Multiple gestation, multiple, n (%)	Colonization vs. no colonization	Chi-squared test	Yes	• 5/6 (83%) vs. 8/68 (12%) • Colonization associated with multiple gestation: OR = 37.5 (05% CI, 3.9–363.1)	Khoury 2005[32]	• Single screening of patients on Oct 14, 2001; newly admitted patients were screened through January 2002. Periumbilical and perirectal sites were screened

Table 64 Characteristics Examined for Association with MRSA Infection or Colonization
Maternal Characteristics

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	• Results	Author Year	Comments
Maternal age, advanced, years	MRSA colonization vs. no colonization	Chi-squared or Fisher's exact test	No	• > 35 years: 3/13 (25%) vs. 25/192 (13%) • p = 0.22	Lazenby 2012[40]	• Admission screening of nares, axilla, and diaper area on admission and twice weekly as long as neonate was MRSA negative.
Maternal age, mean ± SD (median, range)	MRSA infection vs. no infection	Student *t* test	No	**Univariate analysis:** • 39.5 years ±4.1 (30, 22-38) vs. 30.1 years ±4.9 (30, 17-46) • p=0.412	Sakaki 2009[34]	
Maternal antibiotic therapy during pregnancy	Infection vs. no infection	Chi-squared test	No	• Maternal antibiotic therapy during pregnancy did not increase the risk of infection in newborns (OR and p=NR)	Khoury 2005[32]	• Single screening of patients on Oct 14, 2001; newly admitted patients were screened through January 2002. Periumbilical and perirectal sites were screened

Maternal antibiotic therapy during pregnancy	Colonization vs. no colonization	Chi-squared test	No	• Maternal antibiotic therapy during pregnancy did not increase the risk of colonization in newborns (OR and p=NR)	Khoury 2005[32]	• Single screening of patients on Oct 14, 2001; newly admitted patients were screened through January 2002. Periumbilical and perirectal sites were screened
Maternal formal education ≤ 4, n/N (%)	MRSA colonization vs. no colonization	Chi-squared, Fischer test Multiple logistic regression	Yes, univariate Yes, multivariate	**Bivariate analysis:** • 7/59 (12%) vs. 14/344 (4%); RR = 2.45; 95%CI: 1.27-4.72 • p=0.02 **Multivariate analysis of all newborns:** • OR= 2.99; 95%CI: 1.10-8.07 • p=0.03	Garcia 2014[43]	
Maternal hospitalization >1 month before delivery, n/N (%)	MRSA colonization vs. no colonization	Chi-squared, Fisher test Multiple logistic regression	No, univariate No, multivariate	**Bivariate analysis:** • 3/59 (5%) vs. 4/344 (1%); RR = 2.97; 95%CI: 1.22-7.23 • p=0.07 **Multivariate analysis of all newborns:** • OR= 4.05; 95%CI: 0.82-20.05 • p=0.09 **Multivariate analysis of newborns hospitalized >72 hours (n=80):** • OR: 8.49; 95%CI: 0.44-165.72 • p=0.16	Garcia 2014[43]	

Table 64 Characteristics Examined for Association with MRSA Infection or Colonization
Unit Characteristics

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	Results	Author Year	Comments
Bed configuration in NICU	MRSA colonization vs. no colonization	Pearson's chi- squared test Bivariate Cox proportional hazards model	No (in univariate analysis) No (bivariate analysis)	• Open unit: 3.3% vs. 96.7% • Single patient: 2.1% vs. 97.9% • p = 0.11 • No difference in MRSA colonization rates between bed configuration in univariate analysis or bivariate analysis (that controlled for birthweight, gestational age, sex, race, maternal health insurance type, CRIB-II score, 5–minute Apgar score, maximum acuity score, averaged daily patient census of unit, MRSA colonization pressure, and hand hygiene compliance.)	Julian 2015[12]	• Anterior nares were swabbed on admission and weekly thereafter. • Not defined if hand hygiene compliance assessed before and/or after colonization detected. Included compliance of all caregivers, not just those who cared for colonized infants.
Colonized healthcare worker contact	Infection or colonization vs. no MRSA	Univariate logistic regression	Yes	• Colonization or infection associated with contact with a colonized healthcare worker: OR = 9.3 (1.24–inf); p = 0.03	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites

Daily bed occupancy rate, %, median (IQR)	Colonization vs. no colonization	Student t test or Mann-Whitney-Wilcoxon test	No	Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • 81.2% (68.7%–87.5%) vs. 75% (62.5–81.2) • p = 0.61	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4 days [range: 1-6]).
Daily census (average during entire infant admission)	Single patient room MRSA colonization vs. open unit MRSA colonization	Bivariate Cox proportional hazards model	Yes (patients in single patient room) No (all patients)	• For single patient rooms, each additional one patient in the average census during their hospitalization was associated with a 31% greater colonization rate: 1.31 (1.02–1.68), p = 0.039 • No difference in MRSA colonization rates between bed configurations when controlling for average daily census in the bivariate model either at the patient's side of the unit (p = 0.90) or the entire unit (p = 0.84)	Julian 2015[12]	• Anterior nares swabbed on admission and weekly thereafter. • Census was assessed during infant's entire admission, not just before colonization detected
Inborn, n (%)	Infection or colonization vs. no infection or colonization	Chi-squared test	No	• 21/23 (91%) vs. 32/33 (97%) • p = 0.35	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites
Birth location, born off-site, n/N (%)	MRSA colonization vs. no colonization	Kruskal-Wallis and Chi-squared tests	Yes	**Univariate analysis:** • 40/177 (22.6%) vs. 581/1763 (33.0%) p=0.006	Azarian 2016[52]	
Birth location, inborn, n/N (%)	MRSA infection vs. no infection	Fisher exact test	No	**Univariate analysis:** • 25/28 (89.3%) vs. 753/895 (84.1%) p=0.604	Sakaki 2009[34]	
Birth location, inborn birth, n/N (%)	MRSA colonization vs. no colonization	Chi-squared	Yes	**Univariate analysis:** • 50/59 (85%) vs. 1219/1701 (72%) p=0.03	Schultz 2009[46]	
Race, n (%)	Colonization vs. no colonization	Fisher's exact test	Yes	• 43/87 (49%) vs. 2497/3696 (68%) • p <0.001	Pierce 2016[48]	• Nasal swabs were obtained weekly for all infants and on admission for neonates admitted from home and other hospitals.
Inborn, n (%)	Colonization vs. no colonization	Pearson's chi-squared test, chi-squared test for linear trend, or Fisher's exact test	Yes (all infants) No (subset)	First nasal swab • 96/117 (82.1%) vs. 499/832(60.0%) • p <0.001 Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • 65/100 (65%) vs. 434/732 (59.3%) • p = 0.27	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4 days [range: 1–6]).
Inborn, n (%)	Colonization vs. no colonization	Continuity-adjusted chi-squared test	Yes	• Inborn: 94/130 (72%) vs. 232/395 (59%) • p = 0.006	Huang 2015[26]	• Active screening: specimens obtained within 24 hrs of admission, and repeated weekly for 2 weeks (from nares and umbilicus).
Inborn, n (%)	Colonization vs. no colonization	Chi-squared test or Fisher's exact test	Yes	• 135/187 (72.2%) vs. 293/535 (54.8%) • p <0.001	Geraci 2014[6]	• Weekly nasal and rectal swabs obtained. For the first 6 months, universal admission screening was performed.

Inborn, n (%)	Colonization vs. no colonization	Chi-squared or Fisher's exact test	No	• 10/11 (91%) vs. 188/240 (78%) • p = 0.466	Kuo 2013[36]	• Specimens obtained from nares and umbilicus on two dates: Oct 11, and Dec 12, 2011
Inborn, rate/100 births	Colonized vs. no colonization	Chi-squared test	Yes	• 7.36 vs. 4.4 • p = 0.0289	Maraqa 2011[33]	• Admission cultures of all neonates; weekly surveillance cultures included patients who were not MRSA colonized or infected during NICU stay
Inborn, n (%)	Colonization vs. no colonization	Continuity-adjusted chi square Odds ratios	No	• 170/323 (53%) vs. 229/460 (50%); • OR = 1.12 (0.83-1.51), p = 0.4324	Huang 2006[24]	• Weekly screening of nares, postauricular areas, axilla, and umbilicus
Transferred from nursery, n (%)	Colonization vs. no colonization	Pearson's chi-squared test, chi-squared test for linear trend, or Fisher's exact test	Yes (all infants) No (subset)	First nasal swab • 59/117 (50.4%) vs. 166/832 (20.0%) • p <0.001 Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • 16/100 (16%) vs. 150/732 (20.5%) • p = 0.29	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4 days [range: 1–6]).
Infant-to-nurse ratio, median (IQR)	Colonization vs. no colonization	Mann-Whitney-Wilcoxon test or Student t test	No	Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • 3.4 (2.6-3.8) vs. 3.1 (IQR: 2.2-3.7) • p = 0.63	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4 days [range:1–6])
Infant-to-staff ratio (increase by 1 unit)	Infection or colonization vs. no infection or colonization	Univariate logistic regression	Yes	• Colonization or infection associated with a 1-unit increase in the infant-to-staff ratio: OR = 2.8 (1.06–9.34); p = 0.04	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites
Average nurse-to-patient ratio, mean ± SD (median, range)	MRSA infection vs. no infection	Wilcoxon rank-sum test	No	**Univariate analysis:** • Daytime: 0.39±0.09 (0.38, 0.30-0.69) vs. 0.41±0.11 (0.38, 0.22-0.91); p=0.576 • Night: 0.18± 0.04 (0.17, 0.13-0.34) vs. 0.18±0.52 (0.17, 0.11-0.80), p=0.788 • Midnight: 0.15±0.01 (0.14, 0.09-0.34) vs. 0.17±0.06 (0.15, 0.08-0.39), p=0.193 • 1 Day: 0.72±0.18 (0.70, 0.52-1.37) vs. 0.76±0.21 (0.71, 0.24-1.66), p=0.502	Sakaki 2009[34]	
HCP hand hygiene compliance	Colonization or infection	Univariate logistic regression	Yes	• MRSA acquisition associated with contact with colonized HCP: • OR = 9.3 (1.24–Inf); p = 0.3	Nübel 2013[45]	• Staff members (n = 166) screened by nasopharyngeal swabbing in February and August 2010, which identified two colonized HCP (A and B); contact with HCP A resulted in MRSA acquisition
MRSA colonization rate	MRSA infection vs. no infection	Wilcoxon rank-sum test Logistic regression	Yes, univariate Yes, multivariate	**Univariate analysis:** • 0.42±0.18 (0.41, 0.12-0.73) vs. 0.32±0.19 (0.28, 0-0.85) • p=0.004	Sakaki 2009[34]	

				Multivariate analysis: • OR= 11.12; 95%CI: 1.32-93.89 p=0.027		
MRSA colonization pressure, %, median (IQR)	Colonization vs. no colonization	Mann-Whitney-Wilcoxon test or Student t-test Odds ratio	Yes (univariate) Yes (multivariate)	Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • 18% (9.5–26) vs. 12% (8–19) • p <0.001 • Multivariate analysis: Odds of MRSA acquisition was significantly associated with per unit increase of colonization pressure: OR = 1.05 (1.02–1.07), p <0.001	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4 days [range: 1-6]). • Colonization pressure defined as % of total patient days in which MRSA-positive patient was present.
MRSA colonization pressure	Single patient room MRSA colonization vs. open unit MRSA colonization	Bivariate Cox proportional hazards model	No	• No difference in MRSA colonization rates between bed configurations when controlling for mean colonization pressure on the patient's side (p = 0.13) or the entire unit (p = 0.15)	Julian 2015[12]	• Anterior nares swabbed on admission and weekly thereafter. • Note: Mean colonization pressure was significantly higher in open-unit (3.6%, IQR 1.2%-6.9%) than in single-patient (2.7%, IQR 0%-3.7%); p<0.001
MRSA-positive infant in room (unknown additional)	Infection or colonization vs. no infection or colonization	Univariate logistic regression	No	• Colonization or infection was not associated with an unknown MRSA-positive infant in the room: OR = 4.2 (0.98–197); p = 0.06	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites
MRSA-positive infant on ward (known)	Infection or colonization vs. no infection or colonization	Univariate logistic regression	No	• Colonization or infection was not associated with a known MRSA-positive infant on the ward: OR = 1.0 (0.97–1.13); p= 0.24	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites
MRSA-positive infant on ward (unknown additional)	Infection or colonization vs. no infection or colonization	Univariate logistic regression	Yes	• Colonization or infection was associated with an unknown MRSA-positive infant on the ward: OR = 2.5 (1.26–7.99); p = 0.003	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites
Readmission to study NICU	Colonization vs. no colonization	Student's t test or Wilcoxon rank sum test	Yes	• Prior admission to study NICU was significantly associated with MRSA colonization at admission to NICU (p=NR)	Macnow 2013[44]	• Multi-NICU study: • NICU 1: First 2 years of study, surveillance cultures obtained from infants transferred at ≥ 3 days of age. Last 4 years of study, surveillance cultures obtained from all transferred infants. Routine surveillance only during outbreak (2 outbreaks occurred). • NICU 2: Surveillance cultures obtained from all transferred patients, no routine cultures. • Study reports no MRSA-specific quantitative data.

Table 64 Characteristics Examined for Association with MRSA Infection or Colonization
Clinical Characteristics

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	Results	Author Year	Comments
Apgar score at 5 minutes <8, n (%)	Colonization vs. no colonization	Pearson's chi-squared test, chi-squared test for linear trend, or Fisher's exact test	Yes (all infants) Yes (subset)	First nasal swab: • 5/117 (4.3%) vs. 92/832 (11.1%) • p = 0.02 Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • 18/100 (18%) vs. 74/732 (10.1%) • p = 0.03	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4 days [range: 1-6]).
Apgar score at 5 minutes	Single patient room MRSA colonization vs. open unit MRSA colonization	Bivariate Cox proportional hazards model	No	• No difference in MRSA colonization rates between bed configurations when controlling for Apgar score at 5 min • p = 0.21	Julian 2015[12]	• Anterior nares swabbed on admission and weekly thereafter.
Apgar score at 5 minutes ≥8, n (%)	Colonization vs. no colonization	Chi-squared test or Fisher's exact test	No	• 163/187 (87.2%) vs. 461/535 (86.2%) • p = 0.43	Geraci 2014[6]	• Weekly nasal and rectal swabs obtained. For the first 6 months, universal admission screening was performed.
Apgar score at 5 minutes, <6, n (%)	Colonization vs. no colonization	Chi-squared or Fisher's exact test (not clarified)	No	• 0/28 (0%) vs, 28/192 (14.6%) • p = 0.38	Lazenby 2012[40]	• Admission screening of nares, axilla, and diaper area on admission and twice weekly as long as neonate was MRSA negative.
Apgar score, 1st minute ≤ 3 points, n/N (%)	MRSA colonization vs. no colonization	Chi-squared, Fisher test	No	**Bivariate analysis:** • 0/59 (0%) vs. 6/344 (2%) • p=0.60	Garcia 2014[43]	
Apgar score, 1st minute < 6 points, n/N (%)	MRSA colonization vs. no colonization	Chi-squared, Fisher test	No	**Bivariate analysis:** • 0/59 (0%) vs. 4/344 (1%) • p=1.00	Garcia 2014[43]	
Apgar score at 1 min, mean ± SD (median, range)	MRSA infection vs. no infection	Wilcoxon rank-sum test	Yes	**Univariate analysis:** • 7.1±1.3 (7, 4-9) vs. 7.6±1.8 (8, 0-10) • p=0.012	Sakaki 2009[34]	
Apgar score at 5 min, mean ± SD (median, range)	MRSA infection vs. no infection	Wilcoxon rank-sum test	No	**Univariate analysis:** • 8.7±0.7 (9, 7-10) vs. 8.8±1.2 (9, 0-10) • p=0.064	Sakaki 2009[34]	
Maximum acuity score	Single patient room MRSA colonization vs. open unit MRSA colonization	Bivariate Cox proportional hazards model	No	• No difference in MRSA colonization rates between bed configurations when controlling for acuity score: p = 0.87	Julian 2015[12]	• Anterior nares swabbed on admission and weekly thereafter. • Score was maximum for entire stay, not just before colonization detected

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	Results	Author Year	Comments
Broncho-pulmonary dysplasia, n (%)	Colonization vs. no colonization	Chi-squared or Fisher's exact test Logistic regression	Yes (univariate) No (multivariate)	Univariate analysis: • 5/11 (45%) vs. 23/240 (9.6%) • p = 0.004 Multivariate analysis: • OR=NR	Kuo 2013[36]	• Specimens obtained from nares and umbilicus on two dates: Oct 11, and Dec 12, 2011 • Multivariate analysis included mean age, bronchopulmonary dysplasia, previous skin/soft tissue infection, previous MRSA infection, and antimicrobial use at time of sampling
Clinical risk index for babies (CRIB-II) score	Single patient room MRSA colonization vs. open unit MRSA colonization	Cox proportional hazards model	No	• No difference in MRSA colonization rates between bed configurations when controlling for CRIB-II Score: p = 0.55	Julian 2015[12]	• Anterior nares swabbed on admission and weekly thereafter.
Malformation, n (%)	Colonization vs. no colonization	Chi-squared test or Fisher's exact test	No	• 40/187 (21.4%) vs. 98/535 (18.3%) • p = 0.18	Geraci 2014[12]	• Weekly nasal and rectal swabs obtained. For the first 6 months, universal admission screening was performed.
Malformation, n (%)	Colonization vs. no colonization	Pearson's chi-squared test, chi-squared test for linear trend, or Fisher's exact test Odds ratios	No (all infants) Yes (univariate analysis of subset) No (multivariate analysis of subset)	First nasal swab: • Infants with malformation who were colonized: 15/117 (12.8%) vs. 158/832 (19.0%) • p = 0.09 Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • 30/100 (30%) vs. 128/732 (17.5%) • p = 0.003 • Multivariate analysis: Odds of acquiring colonization was not significantly associated with malformation: OR = 1.77 (0.98–3.19), p = 0.062	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4 days [range: 1-6]).
Congenital heart disease, n, (%)	Colonization vs. no colonization	Chi-squared test or Fisher's exact test	No	• 4/11 (36%) vs. 110/240 (46%) • p = 0.759	Kuo 2013[36]	• Specimens obtained from nares and umbilicus on two dates: Oct 11, and Dec 12, 2011
Diagnosis-related group weight, median (IQR)	Colonization vs. no colonization	Mann-Whitney-Wilcoxon test or Student's t test	Yes	Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • 1.58 (0.70–5.6) vs. 0.76 (0.72–3.25) • p = 0.0065	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4 days [range: 1-6]).
Gastrointestinal disease (admitting diagnosis)	Colonization vs. no colonization	Student's t test or Wilcoxon rank sum test	Yes	• Diagnosis of GI disease was significantly associated with a decreased risk of MRSA colonization (p=NR)	Macnow 2013[44]	• Multi-NICU study: • NICU 1: First 2 years of study, surveillance cultures obtained from infants transferred at ≥ 3 days of age. Last 4 years of study, surveillance cultures obtained from all transferred infants.

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	Results	Author Year	Comments
						Routine surveillance only during outbreak (2 outbreaks occurred). • NICU 2: Surveillance cultures obtained from all transferred patients, no routine cultures. • Study reports no MRSA-specific quantitative data.
Length of stay, mean, days	Infection vs. no infection	Two-sample t-test (all infants, univariate) Multiple logistic regression analysis (all infants, multivariate) NR (subanalysis)	Yes (univariate) Yes (multivariate) No (subanalysis)	All infants – univariate • 69 days vs. 20 days • 95% CI: 30.6- 67.2 • p < 0.0001 All infants – multivariate • Infection associated with length of stay • p = 0.0279 Subanalysis of 138 colonized infants (30 of whom were infected) • 78 days vs. 43 days • p < 0.0055	Maraqa 2011[33]	• Admission cultures of all neonates; weekly surveillance cultures included patients who were not MRSA colonized or infected during NICU stay
Length of stay, mean, days	Infection vs. no infection	Two-tailed t-test	Yes	• 51.83 days vs. 21.46 days • p = 0.003	Khoury 2005[32]	• Single screening of patients on Oct 14, 2001; newly admitted patients were screened through January 2002. Periumbilical and perirectal sites were screened
[a]Length of stay, mean, days	Infection or colonization vs. no MRSA	Two-tailed t-test	Yes	• 84.9 days vs. 19.3 days • p < 0.0001	Reboli 1989[38]	• Weekly culture of nares, pharynx, or endotracheal tubes
Length of stay, days, median (range)	Infection or colonization vs. no infection or colonization	Kruskal-Wallis test	No	• 47 days (6–103) vs. 38 days (7–116) • p = 0.61	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites
Length of stay, days, median (IQR)	Colonization vs. no colonization	Mann-Whitney-Wilcoxon test or Student t test Odds ratio	Yes (univariate analysis) Yes (multivariate analysis)	Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • 15 days (9–26) vs. 10 (7–19) • p < 0.001 Multivariate analysis: • Odds of acquiring colonization increased with every additional day of stay: OR = 1.04 (1.02–1.05), p <0.001	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4 days [range: 1–6]).
Length of stay, mean (SD), days	Colonization vs. no colonization	One-way ANOVA or Kruskal-Wallis test	Yes	• 25.3 days (30.9) vs. 16.6 days (16.7) • p = 0.02	Geraci 2014[6]	• Weekly nasal and rectal swabs obtained. For the first 6 months universal admission screening was performed.
Length of NICU stay (days),	Colonization vs. no colonization	Wilcoxon rank-sum test	Yes	• 19 (10-43) vs. 15 (8-30) • p= 0.04	Pierce 2016[48]	• Nasal swabs were obtained weekly for all infants and on

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	Results	Author Year	Comments
median (IQR)						admission for neonates admitted from home and other hospitals. • Length of NICU stay includes only pre-colonization length of stay for incident cases.
Length of NICU stay, days (median or mean = NR)	Colonization vs. no colonization	Mann-Whitney test	No	• 38.7 vs. 28.7 days • p = 0.068	Kuo 2013[36]	• Specimens obtained from nares and umbilicus on two dates: Oct 11, and Dec 12, 2011.
Length of stay, mean, days	MRSA Colonization vs. no colonization	T-test	Yes	• 50.65 days vs. 18.96 days • p < 0.0001	Maraqa 2011[33]	• Admission cultures of all neonates; weekly surveillance cultures included patients who were not MRSA colonized or infected during NICU stay
Length of hospital stay, days, mean ± SD	MRSA infection vs no infection	Student's t test	Yes	**Univariate analysis:** • 82.7 days ±48.7 vs. 42 days ±39.2 • p=0.001	Huang 2005[35]	
MRSA colonization	MRSA Infection vs. no infection	Multiple logistic regression analysis (multivariate)	Yes	• Infection was significantly associated with colonization • p = 0.0249	Maraqa 2011[33]	• Admission cultures of all neonates; weekly surveillance cultures included patients who were not MRSA colonized or infected during NICU stay
MRSA infection, n (%)	MRSA Colonization vs. no colonization	Chi-squared or Fisher's exact test (not clarified)	Yes	• 3/13 (23.1%) vs. 0/192 (0%) • p < 0.0002	Lazenby 2012[40]	• Admission screening of nares, axilla, and diaper area on admission and twice weekly as long as neonate was MRSA negative.
MRSA infection, %, RR (95% CI); p	MRSA colonization vs. no colonization	Continuity-adjusted chi square test and odds ratio	No	• 26% vs. 2%; • RR = 2.64% (2.34–2.98); p <0.00001 • MRSA infection significantly associated with MRSA colonization: OR = 19.86 (9.11–45.07); p <0.00000005	Huang 2006[24]	• Weekly screening of nares, postauricular areas, axilla, and umbilicus
Prior MRSA colonization, n (%)	MRSA infection vs. no infection	Continuity-adjusted chi-squared, odds ratio	Yes	• Prior MRSA colonization: 13/128 (10.2%) • No prior colonization: 9/397 (2.3%) • OR = 4.77 (1.85–12.44); p < 0.001	Huang 2015[26]	• Active screening: specimens obtained within 24 hrs of admission and repeated weekly for 2 weeks (from nares and umbilicus). • Data as reported in Results (p 242).
MRSA infection, previous, n (%)	MRSA Colonization vs. no colonization	Chi-squared or Fisher's exact test Multivariate logistic regression	Yes (in univariate analysis) No (in multivariate	Univariate analysis: • 2/11 (18%) vs. 1/240 (0.4%) • p = 0.005 Multivariate analysis: • OR = NR	Kuo 2013[36]	• Specimens obtained from nares and umbilicus on two dates: Oct 11, and Dec 12, 2011 • Multivariate analysis included mean age, bronchopulmonary dysplasia, previous skin/soft

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	Results	Author Year	Comments
			analysis)			tissue infection, previous MRSA infection, and antimicrobial use at time of sampling
Necrotizing enterocolitis, n (%)	Colonization vs. no colonization	Chi-squared or Fisher's exact test	No	• 1/11 (9%) vs. 18/240 (8%) • p = 0.587	Kuo 2013[36]	• Specimens obtained from nares and umbilicus on two dates: Oct 11, and Dec 12, 2011
Necrotizing enterocolitis, n (%)	Colonization or infection vs. no MRSA detected	NR	No	Necrotizing enterocolitis + medical treatment: • Colonized: 6/128 (5%) • Infected: 7/63 (11%) • No MRSA detected: 99/2089 (5%) Necrotizing enterocolitis + surgical treatment: • Colonized: 2/128 (2%) • Infected: 0/63 (0%) • No MRSA detected: 10/2089 (0.5%) None: • Colonized: 120/128 (94%) • Infected: 56/63 (89%) • No MRSA detected: 1980/2089 (95%) • p = 0.08	Song 2010[28]	• Active screening for MRSA on admission and weekly thereafter • Study provided only one p value for all categories • Study compared colonized/infected to those with no MRSA detected • Presence of characteristic may have occurred before or after sampling that determined MRSA status • Intervention could have occurred before or after colonization/ infection
Patent ductus arteriosus, n (%)	Colonization vs. no colonization	Chi-squared	No	• 13/46 (28%) vs.10/57 (17%) • Denominator and percentages reported, numerator calculated • Study states no statistical significance (p=NR)	Uehara 2001[41]	• Screened on admission (at <24 hrs of age), weekly on Monday, and 1 day before discharge. Additional cultures performed according to clinical requirements
Patent ductus arteriosus, n/N (%)	MRSA infection vs no infection	Chi-squared or Fisher's exact test	No	**Univariate analysis:** • 2/21 (9%) vs. 4/21 (19%) • p=NR but no significant difference between both groups	Huang 2005[35]	
Perinatal asphyxia, n/N (%)	MRSA infection vs no infection	Chi-squared or Fisher's exact test	No	**Univariate analysis:** • 12/21 (52%) vs. 6/21 (26%) • p=NR but no significant difference between both groups	Huang 2005[35]	
Phototherapy, days, mean ± SD	MRSA infection vs no infection	Student's t test	No	**Univariate analysis:** • 3.76 days ±3.71 vs. 2.86 days ±2.48 • p=0.358	Huang 2005[35]	
Pneumonia, n (%)	Colonization vs. no colonization	Chi-squared or Fisher's exact test	No	• 3/11 (27%) vs. 42/240 (18%) • p = 0.424	Kuo 2013[36]	Specimens obtained from nares and umbilicus on two dates: Oct 11, and Dec 12, 2011
Pneumonia, n/N (%)	MRSA infection vs no infection	Chi-squared or Fisher's exact test	No	**Univariate analysis:** • 5/21 (22%) vs. 3/21 (13%) • p=NR but no significant difference between both groups	Huang 2005[35]	

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	Results	Author Year	Comments
Respiratory distress syndrome, n (%)	Colonization vs. no colonization	Chi-squared or Fisher's exact test	No	• 7/11 (64%) vs. 177/240 (74%) • p = 0.484	Kuo 2013[36]	• Specimens obtained from nares and umbilicus on two dates: Oct 11, and Dec 12, 2011
Respiratory distress syndrome, n (%)	Colonization vs. no colonization	Chi-squared test	No	• 10/46 (22%) vs.10/57 (17%) • Denominator and percentages reported, numerator calculated • Study states no statistical significance (p=NR)	Uehara 2001[41]	• Screened on admission (at <24 hrs of age), weekly on Monday, and 1 day before discharge. Additional cultures performed according to clinical requirements. • Timing of whether occurred before or after colonization unknown
Respiratory distress syndrome, n/N (%)	MRSA infection vs no infection	Chi-squared or Fisher's exact test	No	**Univariate analysis:** • 9/21 (39%) vs. 8/21 (35%) • p=NR but no significant difference between both groups	Huang 2005[35]	
Prior soft tissue and skin infections, n (%)	Colonization vs. no colonization	Chi-squared or Fisher's exact test Multivariate logistic regression	Yes (in univariate analysis) Yes (in multivariate analysis)	Univariate analysis: • 3/11 (27%) vs. 3/240 (1%) • p = 0.001 Multivariate analysis: • OR = 40.36 (2.32–702.64), p = 0.011	Kuo 2013[36]	• Specimens obtained from nares and umbilicus on two dates: Oct 11, and Dec 12, 2011 • Multivariate analysis included mean age, bronchopulmonary dysplasia, previous skin/soft tissue infection, previous MRSA infection, and antimicrobial use at time of sampling
Skin infection at onset (presence of), n/N (%)	MRSA infection vs no infection	Chi-squared or Fisher's exact test Multiple logistic regression	Yes, univariate Yes, multivariate	**Univariate analysis:** • 10/21 (47.6%) vs. 2/21 (9.5%) • p=0.015 **Multivariate analysis:** • Adjusted OR= 20.8; 95%CI: 2.95-145.4 • p=0.002	Huang 2005[35]	
Antibiotic therapy (during exposure)	Infection or colonization vs. no infection or colonization	Univariate logistic regression	No	• Colonization or infection was not associated with antibiotic therapy: OR = 0.7 (0.13–3.31); p = 0.82	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites
[a]Antibiotic use, mupirocin, OR (95% CI)	Colonization or infection vs. no colonization or infection	Poisson regression	No (univariate or multivariate NR)	• Mupirocin treatment was not associated with a lower risk of MRSA acquisition: OR = 1.17 (0.54–2.55), p=NR	Song 2010[22]	• Nasal swabs collected on admission and weekly thereafter.
Antibacterial therapy (systemic), n (%)	Colonization vs. no colonization	Pearson's chi-squared test, chi-squared test for linear trend, or Fisher's exact test	Yes (univariate analysis)	Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • >7 days: 49/100 (49.0%) vs. 220/732 (30.1%) • 1-7 days: 15/100 (15.0%) vs. 213/732 (29.1%)	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days (median 4 days [range: 1-6]) after admission to NICU.

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	Results	Author Year	Comments
		Odds ratios	Yes (multivariate analysis)	• No systemic antibacterial therapy: 36/100 (36.0%) vs/ 297/732 (40.6%) • p = 0.001 • Multivariate analysis: ○ MRSA acquisition was negatively associated with systemic antibacterial therapy: OR = 0.97 (0.95–0.99), p = 0.026		
Antibiotic therapy (systemic), n (%) or mean (SD)	Colonization vs. no colonization	Chi-squared test or Fisher's exact testing Or One-way ANOVA or Kruskal-Wallis test	Yes (incidence) No (duration)	• 83/187 (44.4%) vs.297/535 (55.5%) • p = 0.004 Mean (SD) duration of systemic antibiotic therapy (days): • Colonized: 7.1 (14.2) days vs. 5.8 (9.1) days • p = 0.07	Geraci 2014[6]	• Weekly nasal and rectal swabs obtained. For the 1st 6 months, universal admission screening was performed.
Antibiotic therapy (ampicillin-sulbactam plus gentamycin), n (%) or mean (SD)	Colonization vs. no colonization	Chi-squared test or Fisher's exact testing Or One-way ANOVA or Kruskal-Wallis test	Yes (incidence) No (duration)	• 73/187 (39.0%) vs. 266/535 (49.7%) • p = 0.005 Mean (SD) duration of antibiotic therapy (days): • 4.8 (7.3) days vs. 5.0 (6.3) days • p = 0.36	Geraci 2014[6]	• Weekly nasal and rectal swabs obtained. For the 1st 6 months, universal admission screening was performed
Antibiotic use at time of sampling, n (%)	Colonization vs. no colonization	Chi-squared or Fisher's exact test Multivariate logistic regression	Yes (univariate analysis) No (multivariate analysis)	Univariate analysis: • 2/11 (18%) vs. 131/240 (55%) • p = 0.017 Multivariate analysis: • OR=NR	Kuo 2013[36]	• Specimens obtained from nares and umbilicus on two dates: Oct 11, and Dec 12, 2011 • Multivariate analysis included mean age, bronchopulmonary dysplasia, previous skin/soft tissue infection, previous MRSA infection, and antimicrobial use at time of sampling
Antibiotic therapy > 3 days, n (%)	Colonization vs. no colonization	Chi-squared test	No	• 19/46 (42%) vs. 24/57 (43%) • Denominator and percentages reported, numerator calculated • Study states no statistical significance (p=NR)	Uehara 2001[41]	• Screened on admission (at <24hrs of age), weekly on Monday, and 1 day before discharge. Additional cultures performed according to clinical requirements. • Finding reported as not significant • Timing of whether occurred before or after colonization unknown • Study provided percentages only; number of infants calculated.
Antibiotic therapy, after day 11 of life, n (%)	Colonization vs. no colonization	Chi-squared test	No	• 21/46 (46%) vs. 31/57 (54%) • Denominator and percentages reported, numerator calculated • Study states no statistical significance (p=NR)	Uehara 2001[41]	• Screened on admission (at <24 hrs of age), weekly on Monday, and 1 day before discharge. Additional cultures performed according to clinical requirements.

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	Results	Author Year	Comments
Antibiotic therapy, days, mean ± SD	MRSA infection vs no infection	Student's t test	No	**Univariate analysis:** • 9.57 days ±5.89 vs. 7.52 days ±4.33 • p=0.207	Huang 2005[35]	
Antimicrobial therapy (ampicillin) within 24 hours of birth, n/N (%)	MRSA infection vs. no infection	Fisher exact test	Yes	**Univariate analysis:** • 19/28 (67.9%) vs.394/895 (44.4%) • p=0.019	Sakaki 2009[34]	
Antimicrobial therapy (cefotaxime) within 24 hours of birth, n/N (%)	MRSA infection vs. no infection	Fisher exact test	No	**Univariate analysis:** • 4/28 (14.3%) vs.150/895 (17.0%) • p=1.0	Sakaki 2009[34]	
Antimicrobial therapy (gentamicin) within 24 hours of birth, n/N (%)	MRSA infection vs. no infection	Fisher exact test	No	**Univariate analysis:** • 0/28 (0%) vs.17/895 (1.9%) • p=1.0	Sakaki 2009[34]	
Antimicrobial therapy (cefazolin) within 24 hours of birth, n/N (%)	MRSA infection vs. no infection	Fisher exact test	No	**Univariate analysis:** • 0/28 (0%) vs.28/895 (3.2%) • p=1.0	Sakaki 2009[34]	
Antimicrobial therapy (amikacin) within 24 hours of birth, n/N (%)	MRSA infection vs. no infection	Fisher exact test	No	**Univariate analysis:** • 0/28 (0%) vs.7/895 (0.8%) • p=1.0	Sakaki 2009[34]	
Any catheterization, n (%)	Colonization vs. no colonization	Chi-squared or Fisher's exact test	No	• 10/11 (91%) vs. 193/240 (80%) • p = 0.695	Kuo 2013[36]	• Specimens obtained from nares and umbilicus on two dates: Oct 11, and Dec 12, 2011 • Included endotracheal tube, CVC, Foley catheter, chest tube, arterial catheter, and any other drainage tube at time of sampling.
Blood transfusion	Infection or colonization vs. no infection or colonization	Univariate logistic regression	No	• Colonization or infection was not associated with blood transfusion: OR = 6.9 (0.72–335); p = 0.12	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites
Central venous line	Infection or colonization vs. no infection or colonization	Univariate logistic regression	No	• Colonization or infection was not associated with a central venous line: OR = 1.4 (0.02–118); p = 1.0	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	Results	Author Year	Comments
Central line utilization, n (%)	Infection or colonization vs. no MRSA detected	NR	Yes	≥ 50%of length of stay: • Colonized: 17/128 (13%) • Infected: 17/63 (27%) • No MRSA detected: 183/2089 (9%) < 50% of length of stay: • Colonized: 23/128 (18%) • Infected: 12/63 (19%) • No MRSA detected: 86/2089 (4%) None: • Colonized: 88/128 (68%) • Infected: 34/63 (54%) • No MRSA detected: 1820/2089 (87%) • p < 0.001	Song 2010[28]	• Active screening for MRSA on admission and weekly thereafter • Study provided only one p value for all categories • Study compared colonized/infected to those with no MRSA detected • Presence of characteristic may have occurred before or after sampling that determined MRSA status • Intervention could have occurred before or after colonization/ infection
[a]Central line, OR (95% CI)	Infection or colonization vs. no infection or colonization	Poisson regression	Yes (univariate) No (multivariate)	Univariate analysis • Colonization or infection associated with prolonged central line use: OR = 1.07 (1.04–1.11), p=NR Multivariate analysis • Not significant, p=NR	Song 2010[22]	• Nasal swabs collected on admission and weekly thereafter • No data given for multivariate analysis
Central venous access device days, n (%)	Colonization vs. no colonization	Pearson's chi-squared test, chi-squared test for linear trend, or Fisher's exact test	Yes	Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • >14 days: 28/100 (28.0%) vs. 87/732 (11.9%) • 1-14 days: 23/100 (23.0%) vs. 171/732 (23.4%) • No device: 49/100 (49.0%) vs. 472/732 (64.5%) • p < 0.001	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days (median 4 days [range: 1-6]) after admission to NICU
Central venous access device, n (%)	Colonization vs. no colonization	Chi-squared test of Fisher's exact test	Yes	• 51/187 (27.3%) 192/535 (35.9%) • p = 0.01	Geraci 2014[6]	• Weekly nasal and rectal swabs obtained. For the 1st 6 months, universal admission screening was performed
Central venous catheter, n (%)	Colonization vs. no colonization	Chi square or Fisher's exact test	No	• 5/11 (45%) vs. 114/204 (48%) • p=1.000	Kuo 2013[36]	• Specimens obtained from nares and umbilicus on 2 dates: Oct 11, and Dec 12, 2011
Central venous catheter at onset (presence of), n/N (%)	MRSA infection vs no infection	Chi-squared or Fisher's exact test	No	**Univariate analysis:** • 16/21 (76.2%) vs. 10/21 (47.6%) • p=0.111	Huang 2005[35]	•
Peripheral venous line	Infection or colonization vs. no MRSA	Univariate logistic regression	No	• Colonization or infection was not associated with having a peripheral venous line: OR = 0.1 (0–-1.11); p = 0.07	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	Results	Author Year	Comments
Endotracheal intubation, n (%)	Infection vs. no infection	Chi- squared test	Yes	• 10/12 (83%) vs 31/68 (46%) • OR = 5.97 (1.22–29.31); p=NR	Khoury 2005[32]	• Single screening of patients on Oct 14, 2001. Newly admitted patients were screened until August 2002 and the periumbilical and perirectal sites were screened
Endotracheal intubation (with mechanical ventilation)	Colonization or infection vs. no MRSA	Univariate logistic regression	No	• Colonization or infection was not associated with mechanical ventilation with intubation: OR = 0.9 (0.69–1.21); p = 0.60	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites
Endotracheal intubation, days, n (%)	Colonization vs. no colonization	Pearson's chi-squared test, chi-squared test for linear trend, or Fisher's exact test	Yes	Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • > 3 days: 23/10 (23.0%) vs. 98/ 732 (13.4%) • 1-3 days: 16/100 (16.0%) vs. 51/732 (7.0%) • No: 61/100 (61.0%) vs. (582/732 (79.5%) • p < 0.001	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days (median 4 days [range: 1-6]) after admission to NICU.
Endotracheal intubation	Colonization vs. no colonization	Chi-squared test or Fisher's exact test	No	• 37/187 (19.9%) vs. 114/535 (21.3%) • p = 0.33	Geraci 2014[6]	• Weekly nasal and rectal swabs obtained. For the 1st 6 months, universal admission screening was performed.
Endotracheal intubation, n (%)	Colonization vs. no colonization	Chi-squared or Fisher's exact test	No	• 4/11 (36%) vs. 78/240 (33%) • p = 0.753	Kuo 2013[36]	• Specimens obtained from nares and umbilicus on two dates: Oct 11, and Dec 12, 2011
Intubation, n (%)	Colonization vs. no colonization	Chi-squared test	No	• 15/46 (33%) vs. 15/57 (26%) • Denominator and percentages reported, numerator calculated • Study states no statistical significance (p=NR)	Uehara 2001[41]	• Screened on admission (at <24 hrs of age), weekly on Monday, and 1 day before discharge. Additional cultures performed according to clinical requirements.
Extracorporeal membrane oxygenation procedure, n (%)	Colonization or infection vs. no MRSA detected	NR	Yes	• Colonized: 3/128 (2%) • Infected: 5/63 (8%) • No MRSA detected: 42/2089 (2%) • p = 0.007	Song 2010[28]	• Active screening for MRSA on admission and weekly thereafter • Study provided only one p value for all categories • Study compared colonized/infected to those with no MRSA detected • Presence of characteristic may have occurred before or after sampling that determined MRSA status • Intervention could have occurred before or after colonization/ infection

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	Results	Author Year	Comments
Gavage feeding, n (%)	Infection vs. no infection	Chi-squared test	Yes	• 12/12 (100%) vs. 38/68 (56%) • The odds of infection was associated with gavage feeding: 10.33 (1.28–83.37); p=NR	Khoury 2005[32]	• Single screening of patients on Oct 14, 2001; newly admitted patients were screened through January 2002. Periumbilical and perirectal sites were screened
Hyperalimentation, days, mean ± SD	MRSA infection vs no infection	Student's t test	No	**Univariate analysis:** • 10.0 days ±11.8 vs. 6.0 days ±5.51 • p=0.166	Huang 2005[35]	
Incubator (stay in), days, mean ± SD	MRSA infection vs no infection	Student's t test	No	**Univariate analysis:** • 13.4 days ±18.1 vs. 7.0 days ±8.5 • p=0.150	Huang 2005[35]	
Intraventricular hemorrhage, n/N (%)	MRSA infection vs no infection	Chi-squared or Fisher's exact test	No	**Univariate analysis:** • 5/21 (22%) vs. 2/21 (9%) p=NR but no significant difference between both groups	Huang 2005[35]	
Kangaroo care	Infection or colonization vs. no MRSA	Univariate logistic regression	No	• Colonization or infection was not associated with kangaroo care: OR = 0.8 (0.18–3.47); p = 1.0	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites
Gastric tube	Infection or colonization vs. no MRSA	Univariate logistic regression	No	• Colonization or infection was not associated with a gastric tube: OR = 5.6 (0.62–276); p = 0.18	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites
Nasogastric tube, days, n (%)	Colonization vs. no colonization	Pearson's chi-squared test, chi-squared test for linear trend, or Fisher's exact test	Yes	Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • >14 days: 43/100 (43.0%) vs. 107/732 (14.6%) • 1–14 days: 18/100 (18.0%) vs. 159/732 (21.7%) • No tube: 38/100 (38.0%) vs. 462/732 (63.1%) • p <0.001	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4 days [range: 1-6]).
Nasogastric tube, n (%)	Colonization vs. no colonization	Chi-squared test or Fisher's exact test	No	• 71/187 (38%) vs. 201/535 (37.6%) • p = 0.47	Geraci 2014[6]	• Weekly nasal and rectal swabs obtained. For the 1st 6 months, universal admission screening was performed.
Nasogastric tube, n (%)	Colonization vs. no colonization	Chi-squared or Fisher's exact test	No	• 10/11 (91%) vs. 165/240 (69%) • p = 0.181	Kuo 2013[36]	• Specimens obtained from nares and umbilicus on two dates: Oct 11, and Dec 12, 2011
Parenteral nutrition, OR (95% CI:)	Infection or colonization vs. no MRSA	Univariate logistic regression	No	• Colonization or infection was not associated with parenteral nutrition: OR = 0.4 (0.04–3.91); p = 0.63	Nübel 2013[45]	• Weekly screening of nasopharyngeal and perineal sites
Parenteral nutrition, n (%)	Colonization vs. no colonization	Pearson's chi-squared test, chi-squared test for linear trend, or Fisher's exact test	No	Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • 72/100 (72.0%) vs. 472/732 (64.5%) • p = 0.14	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4 days [range: 1-6]).
Parenteral nutrition, n (%)	Colonization vs. no colonization	Chi-squared test or Fisher's exact test	No	• 80/187 (42.8%) vs. 270/535 (50.5%) • p = 0.07	Geraci 2014[6]	• Weekly nasal and rectal swabs obtained. For the 1st 6 months, universal admission screening was performed.

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	Results	Author Year	Comments
First feeding by tube, n/N (%)	MRSA infection vs. no infection	Fisher exact test	Yes	**Univariate analysis:** • 11/28 (39.3%) vs. 689/895 (77.0%) p<0.001	Sakaki 2009[34]	
nCPAP, n (%)	Colonization vs. no colonization	Pearson's chi-squared test, chi-squared test for linear trend, or Fisher's exact test	Yes	Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • >3 days: 28/100 (28.0%) vs. 61/732 (8.3%) • 1-3 days: 14/100 (14.0%) vs. 71/732 (9.7%) • No nCPAP: 58/100 (58.0%) vs. 599/732 (81.8%) • p <0.001	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4 days [range: 1–6]).
nCPAP, n, (%)	Colonization vs. no colonization	Chi-squared test of linear trend or Fisher's exact test	No	• 39/187 (20.9%) vs. 102/535 (19.1%) • p = 0.30	Geraci 2014[6]	• Weekly nasal and rectal swabs obtained. For the 1st 6 months, universal admission screening was performed.
Mechanical ventilation, days, mean ± SD	MRSA infection vs no infection	Student's t test	No	**Univariate analysis:** • 6.19 days ±8.49 vs. 3.67 days ±5.76 p=0.266	Huang 2005[35]	
Respiratory support utilization, n (%)	Colonization or infection vs. no MRSA detected	NR	Yes	≥ 50% length of stay: • Colonized: 29/128 (23%) • Infected: 17/63 (27%) • No MRSA detected: 326/2089 (16%) • < 50% length of stay: • Colonized: 32/128 (25%) • Infected: 15/63 (24%) • No MRSA detected: 396/2089 (19%) None: • Colonized: 67/128 (52%) • Infected: 31/63 (49%) • No MRSA detected: 1367/2089 (65%) • p = 0.001	Song 2010[28]	• Active screening for MRSA on admission and weekly thereafter • Study provided only one p value for all categories • Study compared colonized/infected to those with no MRSA detected • Presence of characteristic may have occurred before or after sampling that determined MRSA status
[a]Respiratory support utilization, OR (95% CI)	Colonization or infection vs. no MRSA	Poisson regression	Yes (univariate) Yes (multivariate)	• Univariate analysis: MRSA colonized or infected patients had respiratory support: OR = 1.06 (1.03–1.09), p=NR • Multivariate analysis: Prolonged ventilator use was statistically significant risk factor after adjusting for confounding variables: OR = 3.30 (1.25–8.74), p=NR	Song 2010[22]	• Nasal swabs collected on admission and weekly thereafter.
[a]Respiratory support, ventilator, n (%)	Colonization or infection vs. no MRSA	Chi-squared test	Yes	• 21/26 (80.7%) vs. 179/593 (30%) • p < 0.0001	Reboli 1989[38]	• Weekly culture of nares, pharynx, or endotracheal tubes • Study note: ventilator use was related to low birthweight and so not an independent risk factor
Surgical procedure	Colonization vs. no colonization	Pearson's chi-squared test, chi-squared test for linear trend, or Fisher's exact test	No	Subset of 832 with negative first nasal swab: acquired MRSA vs. no MRSA: • 14/100 (14.0%) vs. 69/732(9.4%) • p = 0.13	Giuffre 2015[37]	• Active screening (weekly), first nasal swab obtained a mean of 3.91 days after admission to NICU (median 4 days [range: 1–6]).

Risk Factor	Outcome	Analytical Statistics	Statistically Significant Finding	Results	Author Year	Comments
Surgical procedure, n (%)	Colonization vs. no colonization	Chi-squared test	No	• Surgery: 8/187 (4.3%) vs. 38/535 (7.1%) • p =0.10	Geraci 2014[6]	• Weekly nasal and rectal swabs obtained. For the 1st 6 months, universal admission screening was performed.
Surgical procedure, n (%)	Colonization vs. no colonization	Chi-squared or Fisher's exact test	No	• 3/11 (27%) vs. 71/240 (30%) • p=1.000	Kuo 2013[36]	• Specimens obtained from nares and umbilicus on two dates: Oct 11, and Dec 12, 2011
Surgery, n/N (%)	MRSA infection vs no infection	Chi-squared or Fisher's exact test	No	**Univariate analysis:** • 5/21 (22%) vs. 2/21 (9%) • p=NR but no significant difference between both groups	Huang 2005[35]	

Abbreviations: CI = confidence interval, IQR = interquartile range, MRSA = methicillin-resistant *staphylococcus aureus*, MSSA = methicillin-susceptible *staphylococcus aureus*, OR = Odds ratio, SD = standard deviation

4. Risk of Bias

Table 65 Risk of Bias of Observational Studies

Author Year	All study groups derived from similar source/ reference populations	Attrition not significantly different across study groups	Measure of exposure is valid	Measure of outcome is valid	Investigator blinded to endpoint assessment or outcomes are objective	Potential confounders identified	Statistical adjustment for potential confounders done	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Azarian 2016[52]	✓	✓	✓	✓				✓	Moderate
Carey 2010[30]	✓		✓	✓	✓	✓		✓	Low
Cohen-Wolkowiez 2007[29]	✓	✓	✓	✓		✓		✓	Low
Delaney 2013[1]	✓		✓	✓	✓	✓		✓	Low
Ericson 2015[31]	✓		✓	✓	✓	✓		✓	Low
Garcia 2014[43]	✓	✓	✓	✓		✓	✓	✓	Low
Geraci 2014[6]	✓		✓	✓	✓	✓		✓	Low
Graham 2002[50]	✓		✓	✓	✓	✓	✓		Low
Giuffre 2013[37]	✓		✓	✓	✓	✓	✓	✓	Low
Huang 2005[35]	✓	✓	✓	✓		✓	✓		Low
Huang 2006[24]	✓		✓	✓	✓			✓	Moderate
Huang 2015[26]	✓		✓	✓	✓			✓	Moderate
Julian 2015[12]	✓		✓	✓	✓	✓	✓	✓	Low
Khoury 2005[32]	✓		✓	✓	✓				High
Kuo 2013[36]	✓		✓	✓	✓	✓		✓	Low

4. Risk of Bias

Author Year	All study groups derived from similar source/ reference populations	Attrition not significantly different across study groups	Measure of exposure is valid	Measure of outcome is valid	Investigator blinded to endpoint assessment or outcomes are objective	Potential confounders identified	Statistical adjustment for potential confounders done	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Lazenby 2012[40]	✓		✓	✓	✓	✓	✓	✓	Low
Macnow 2013[44]	✓		✓	✓	✓	✓	✓	✓	Low
Maraqa 2011[33]	✓		✓	✓	✓	✓	✓	✓	Low
Nübel 2013[45]	✓	✓	✓	✓	✓			✓	Low
Pierce 2017[48]	✓		✓	✓	✓	✓	✓		Low
Reboli 1989[38]	✓		✓	✓	✓			✓	Moderate
Sakakai 2009[34]	✓	✓	✓	✓		✓	✓	✓	Low
Schultz 2009[46]	✓	✓	✓	✓		✓	✓	✓	Low
Song 2010[28]	✓		✓	✓	✓	✓	✓		Low
Song 2010[22]	✓	✓	✓	✓	✓				Moderate
Uehara 2001[41]	✓		✓	✓	✓	✓			Moderate
Washam 2018[42]	✓	✓	✓	✓	✓	✓	✓	✓	Low

5. Evaluation of the Risk of Bias of an Individual Study

Instructions:

1) Answer each question *Yes* or *No*.
2) Divide the total number of answers by the total number of questions on the appropriate checklist (Note: for descriptive outbreak studies that did not report a funding source, the question was excluded from the calculation.)
3) The Risk of Bias was rated as follows:

Study Type	% of Items Reported	Risk of Bias
Observational, Diagnostic	≤ 50%	High
	> 50% and < 75%	Moderate
	≥ 75%	Low
Descriptive	≤ 50%	High
	> 50%	Moderate

5.A. Checklist for Observational Studies

1. Were all study groups derived from similar source/ reference populations?
2. Was attrition not significantly different across study groups?
3. Was the measure of exposure valid?
4. Was the measure of outcome valid?
5. Were investigators blinded to endpoint assessment or are the outcomes objective?
6. Were potential confounders identified?
7. Were statistical adjustments done for potential confounders?
8. Were funding source(s) disclosed and no obvious conflict of interest?

5.B. Checklist for Diagnostic Studies

1. Did the study avoid using a case-control design?
2. Did the study enroll all suitable patients or consecutive suitable patients within a time period?
3. Were readers of the diagnostic test of interest blinded to the results of the reference standard?
4. Were patients assessed by a reference standard regardless of the test's results?
5. Was the funding for this study derived from a source that does not have a financial interest in its results?

5.C. Checklist for Descriptive Studies

1. Did the study enroll all suitable patients or consecutive suitable patients within a time period?
2. Was the study prospectively planned?
3. Were independent or blinded assessors used to assess subjective outcomes?
4. Was the study's funding derived from a source that would not benefit financially from results in a particular direction?

5.D. Translating Risk of Bias into GRADE Tables

- When the risk of bias was rated as "High" for >75% of studies making up the evidence base for a given outcome, one point was deducted for Study Quality in the GRADE table.

6. HICPAC Recommendation Categorization Scheme (2019)

Table 66 Strength of Recommendations

Strength	Definition	Implied Obligation	Language
Recommendation	A Recommendation means that we are confident that the benefits of the recommended approach clearly exceed the harms (or, in the case of a negative recommendation, that the harms clearly exceed the benefits). In general, Recommendations should be supported by high- to moderate-quality evidence. In some circumstances, however, Recommendations may be made based on lesser evidence or even expert opinion when high-quality evidence is impossible to obtain, and the anticipated benefits strongly outweigh the harms or when then Recommendation is required by federal law.	A Recommendation implies that healthcare personnel/healthcare facilities "should" implement the recommended approach unless a clear and compelling rationale for an alternative approach is present.	The wording of the Recommendation should specify the setting and population to which the Recommendation applies (eg, adult patients in intensive care unit settings). • Action verbs, eg, use, perform, maintain, replace • Should, should not • Recommend/ is recommended, recommend against/ is not recommended • Is indicated/ is not indicated
Conditional Recommendation	A Conditional Recommendation means that we have determined that the benefits of the recommended approach are *likely* to exceed the harms (or, in the case of a negative recommendation, that the harms are likely to exceed the benefits). Conditional Recommendations may be supported by either low-, moderate- or high-quality evidence when: • there is high-quality evidence, but the benefit/harm balance is not clearly tipped in one direction • the evidence is weak enough to cast doubt on whether the recommendation will consistently lead to benefit • the likelihood of benefit for a specific patient population or clinical situation is extrapolated from relatively high-quality evidence demonstrating impact on other patient populations or in other clinical situations (eg, evidence obtained during outbreaks used to support probable benefit during endemic periods) • the impact of the specific intervention is difficult to disentangle from the impact of other simultaneously implemented interventions (eg, studies evaluating "bundled" practices) • there appears to be benefit based on available evidence, but the benefit/harm balance may change with further research • benefit is most likely if the intervention is used as a supplemental measure in addition to basic practices	A Conditional Recommendation implies that healthcare facilities/ personnel "could," or could "consider" implementing the recommended approach. The degree of appropriateness may vary depending on the benefit vs. harm balance for the specific setting.	The wording of the Conditional Recommendation should specify the setting and population to which the Conditional Recommendation applies when relevant, including: – select settings (eg, during outbreaks) – select environments (eg, ICUs) – select populations (eg, neonates, transplant patients). • Consider • Could • May/ may consider
No Recommendation	No Recommendation is made when there is both a lack of pertinent evidence and an unclear balance between benefits and harms.	n/a	"No recommendation can be made regarding"

Table 67 Justification for Choice of Recommendation Strength

Components	What to include	Comments
Supporting Evidence	List the number and type(s) of available evidence used.	eg, "… 10 observational studies"
Level of Confidence in the Evidence	Level of confidence is low/moderate/high (See Table 3).	eg, "The level of confidence in this evidence is low, as observational studies are at increased risk of bias"

6. HICPAC Recommendation Categorization Scheme (2019)

Components	What to include	Comments
Benefits	List the favorable changes in outcomes that would likely occur if the Recommendation were followed.	Be explicit, clear about pros/cons
Risks and Harms	List the adverse events or other unfavorable outcomes that may occur if the Recommendation were followed.	Be explicit, clear about pros/cons
Resource Use	Describe (if applicable) direct costs, opportunity costs, material or human resources requirements, facility needs, etc, that may be associated with following the Recommendation.	HICPAC does not perform its own cost analyses and is not obliged to address cost if analyses are not available and no useful statements can be made. State clearly if information on resource use is lacking.
Benefit-Harm Assessment	Classify as "preponderance of benefit over harm" (or vice versa) or a "balance of benefit and harm." Description of this balance can be from the individual patient perspective, the societal perspective, or both.	Recommendations are possible when clear benefit is not offset by important harms or costs (or vice versa); conversely, when the benefit is small or offset by important adverse factors, the balance between benefit and harm prevents a Recommendation.
Value Judgments	Summarize value judgments used by the group in creating the Recommendation; if none were involved, state "none."	Translating evidence into action often involves value judgments, which include guiding principles, ethical considerations, or other beliefs and priorities. Stating them clearly helps users understand their influence on interpreting objective evidence.
Intentional Vagueness	State reasons for any intentional vagueness in the Recommendation; if none was intended, state "none."	Recommendations should be clear and specific, but if the group chooses to be vague, acknowledging their reasoning clearly promotes transparency. Reasons for vagueness may include insufficient evidence; inability to achieve consensus among panel regarding evidence quality, anticipated benefits/harms, or interpretation of evidence; legal considerations; economic reasons; ethical/religious issues.
Exceptions	List situations or circumstances in which the Recommendation should not be applied.	

Table 68 Aggregate Level of Confidence in Effect Estimate*

Level of Confidence	Description
High	Highly confident that the true effect lies close to that of the estimated size and direction of the effect. For example, confidence in the evidence is rated as "High" when there are multiple studies with no major limitations, there are consistent findings, and the summary estimate has a narrow confidence interval.
Moderate	The true effect is likely to be close to the estimated size and direction of the effect, but there is a possibility that it is substantially different. For example, confidence in the evidence is rated as "Moderate" when there are only a few studies and some have limitations but not major flaws, there is some variation between study results, or the confidence interval of the summary estimate is wide.
Low	The true effect may be substantially different from the estimated size and direction of the effect. For example, confidence in the evidence is rated as "Low" when supporting studies have major flaws, there is important variation between study results, the confidence interval of the summary estimate is very wide, or there are no rigorous studies.

*Based on Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) and the Canadian Task Force on Preventive Health Care

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8. Acronyms and Abbreviations

Abbreviation	Expansion
*	Critical outcome by which decisions are made
BSI	Bloodstream Infection
CDC	Centers for Disease Control and Prevention
CLABSI	Central Line-Associated Bloodstream Infection
FDA	Food and Drug Administration
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HICPAC	Healthcare Infection Control Practices Advisory Committee
IV	Intravenous
MRSA	Methicillin-Resistant *Staphylococcus aureus*
MSSA	Methicillin-Sensitive *Staphylococcus aureus*
NICU	Neonatal Intensive Care Unit
PCR	Polymerase Chain Reaction
RCT	Randomized Controlled Trial
S. aureus	*Staphylococcus aureus*
TAP	Targeted Assessment for Prevention
VLBW	Very Low Birthweight