

The Clinical Utility of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Nasal Screening to Rule Out MRSA Pneumonia: A Diagnostic Meta-analysis With Antimicrobial Stewardship Implications

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Background. Recent literature has highlighted methicillin-resistant *Staphylococcus aureus* (MRSA) nasal screening as a possible antimicrobial stewardship program tool for avoiding unnecessary empiric MRSA therapy for pneumonia, yet current guidelines recommend MRSA therapy based on risk factors. The objective of this meta-analysis was to evaluate the diagnostic value of MRSA nasal screening in MRSA pneumonia.

Methods. PubMed and EMBASE were searched from inception to November 2016 for English studies evaluating MRSA nasal screening and development of MRSA pneumonia. Data analysis was performed using a bivariate random-effects model to estimate pooled sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

Results. Twenty-two studies, comprising 5163 patients, met our inclusion criteria. The pooled sensitivity and specificity of MRSA nares screen for all MRSA pneumonia types were 70.9% and 90.3%, respectively. With a 10% prevalence of potential MRSA pneumonia, the calculated PPV was 44.8%, and the NPV was 96.5%. The pooled sensitivity and specificity for MRSA community-acquired pneumonia (CAP) and healthcare-associated pneumonia (HCAP) were 85% and 92.1%, respectively. For CAP and HCAP both the PPV and NPV increased, to 56.8% and 98.1%, respectively. In comparison, for MRSA ventilated-associated pneumonia, the sensitivity, specificity, PPV, and NPV were 40.3%, 93.7%, 35.7%, and 94.8%, respectively.

Conclusion. Nares screening for MRSA had a high specificity and NPV for ruling out MRSA pneumonia, particularly in cases of CAP/HCAP. Based on the NPV, MRSA nares screening is a valuable tool for AMS to streamline empiric antibiotic therapy, especially among patients with pneumonia who are not colonized with MRSA.

Keywords. MRSA nasal screening; pneumonia; antimicrobial stewardship; meta-analysis.

Current guidelines for the treatment of pneumonia published by the American Thoracic Society and Infectious Diseases Society of America (IDSA) recommend empiric methicillin-resistant *Staphylococcus aureus* (MRSA) coverage in at-risk patients, yet MRSA pneumonia has a low prevalence [1, 2]. Although initiating appropriate empiric antibiotics in a timely manner is critical, prescribers are often challenged in which patients to initiate anti-MRSA coverage to and when to deescalate therapy. Current guidelines do not provide guidance on deescalation before the availability of respiratory culture results, which may take up to 96 hours to process, or in their absence. As a result, anti-MRSA therapy, such as vancomycin, is frequently continued, contributing to unfavorable consequences of antimicrobial

overuse, including increased risk of adverse events, antimicrobial resistance, drug-drug interactions, and increased expense [3].

S. aureus, including MRSA, is a common colonizer of the nares. The absence of MRSA nares colonization has reported to be a negative predictor of MRSA pulmonary infections, specifically pneumonia. Traditionally, nares surveillance for MRSA is used for infection control and prevention purposes. However, recent literature has highlighted MRSA nasal screening as a useful antimicrobial stewardship screening test for avoiding unnecessary empiric MRSA therapy, including vancomycin [4, 5]. The objective of the current meta-analysis was to evaluate the diagnostic value of MRSA nasal screening in ruling out potential MRSA pneumonia.

METHODS

Literature Review

We reviewed PubMed and EMBASE from 1971 and 1974, respectively, to 1 March 2017 for studies in English evaluating MRSA nasal screening and development of MRSA pneumonia.

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We used the following search string: (methicillin-resistant *Staphylococcus aureus* OR MRSA) AND (nasal OR nares) AND (pneumonia OR respiratory OR lower respiratory tract infections). Citation titles and abstracts were reviewed for relevance, and full-text reviews were then performed on all potentially relevant studies. Bibliographies of included articles were reviewed for additional studies of relevance. Conference proceedings from IDWeek, the Interscience Conference on Antimicrobial Agents and Chemotherapy, and the European Congress of Clinical Microbiology and Infectious Diseases from 2007 to 2016 were also reviewed, using the keywords “nares” and “nasal” to identify unpublished studies.

Inclusion and Exclusion Criteria

Studies were included if they contained information on both positive rates of MRSA nasal surveillance screening using either culture or polymerase chain reaction (PCR) and reported the rates of culture confirmed MRSA pneumonia for community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), healthcare-associated pneumonia (HCAP), or ventilator-associated pneumonia (VAP). Studies were excluded if they were non-English, used only MRSA surveillance culture studies from other body sites (eg, throat swab samples), or zero-event studies (eg, absence of MRSA pneumonia diagnosed).

Outcomes

Outcomes evaluated for the clinical utility of MRSA nasal screening for predicting MRSA pneumonia included the performance characteristics of sensitivity, specificity, diagnostic odds ratios, likelihood ratios, positive predictive values (PPVs), and negative predictive values (NPVs). Factors affecting test performance and heterogeneity among studies were also assessed.

Data Extraction and Quality Assessment

Two investigators (D. M. P. and T. T. T.) independently reviewed the literature. Differences in article selection were resolved by consensus. Each investigator evaluated the included studies for possible sources of bias using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) checklist [6]. Data were extracted from the studies on rates of positive MRSA nasal surveillance screens, rates of MRSA pneumonia, study designs, setting, patient population and sample size, pneumonia classification and assessment definitions if present, respiratory culture type, and timing of surveillance screens.

Data Analysis

Performance characteristics were evaluated using a bivariate model for diagnostic meta-analysis to calculate the pooled sensitivities, specificities, diagnostic odds ratio, likelihood ratios, PPVs, and NPVs. Random-effects modeling was used on the assumption of heterogeneity in measurements among studies. PPVs and NPVs were calculated using the pooled MRSA

pneumonia prevalence among the included studies overall and by pneumonia type for CAP/HCAP, HAP, and VAP. Pooled prevalence was calculated using a random-effects model and excluded studies of only *S. aureus* pneumonia cohorts. Publication bias was assessed with the Deeks test [7].

Possible sources of heterogeneity were evaluated using meta-regression. Heterogeneity was determined with a Cochran *Q* statistic, with results considered significant at $P < .10$. Analyses were performed using Stata software version 14 (StataCorp) with the *metandi* and *metaprop_one* packages for pooled bivariate modeling and pooled prevalences, respectively. The *midas* package was also used for evaluating publication bias and heterogeneity. Review Manager software (version 5.3; The Cochrane Collaboration) was used to produce summary plots. This systematic review and meta-analysis was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Supplementary Table S1) [8].

RESULTS

The literature search resulted in 500 studies meeting key word criteria (Figure 1). After removal of duplicates, we reviewed titles and abstracts for 371 studies. Studies not relevant to our search were removed, yielding 69 studies for full review. Full-text review identified 18 nonrelevant studies, 21 studies with incomplete data, and 8 that did not meet inclusion criteria. In total, data were extracted from 22 studies for analysis, comprising 5163 patients.

Characteristics of the included studies are shown in Table 1 [4, 5, 9–28]. Of the 22 studies, 18 (81.8%) were retrospective studies, 3 (13.6%) were prospective cohorts, and the study design for 1 (4.5%) was not reported; 7 of the 22 studies (31.8%) were conference proceedings. Although most studies were conducted at teaching hospitals, 1 (4.5%) was conducted in a federal hospital, and the hospital setting was not reported in 5 (22.7%). Among the 22 studies, only 11 (50%) reported pneumonia classification; 3 studies (27.3%) evaluated CAP, HCAP, and VAP, 5 (45.5%) evaluated only VAP, 2 (18.2%) evaluated CAP/HCAP, and 1 (9.1%) evaluated “nosocomial” pneumonia.

The criteria used to diagnose pneumonia varied among the studies, with only 2 of 22 studies (9.1%) not reporting the criteria used. A majority of studies included radiographic, respiratory cultures, and clinical criteria to confirm diagnosis of pneumonia (Table 1). The MRSA nares surveillance methods used also varied among studies. PCR was used to detect MRSA in the nares in 11 studies (50%), culture-based identification was used in 4 (18.2%), 1 study (4.5%) used both PCR and culture-based identification, and the remaining studies did not specify the detection method (27.3%). The timing of obtaining MRSA nares surveillance culture was defined in 21 of 22 studies (95.5%). More than half of the studies obtained an MRSA nares

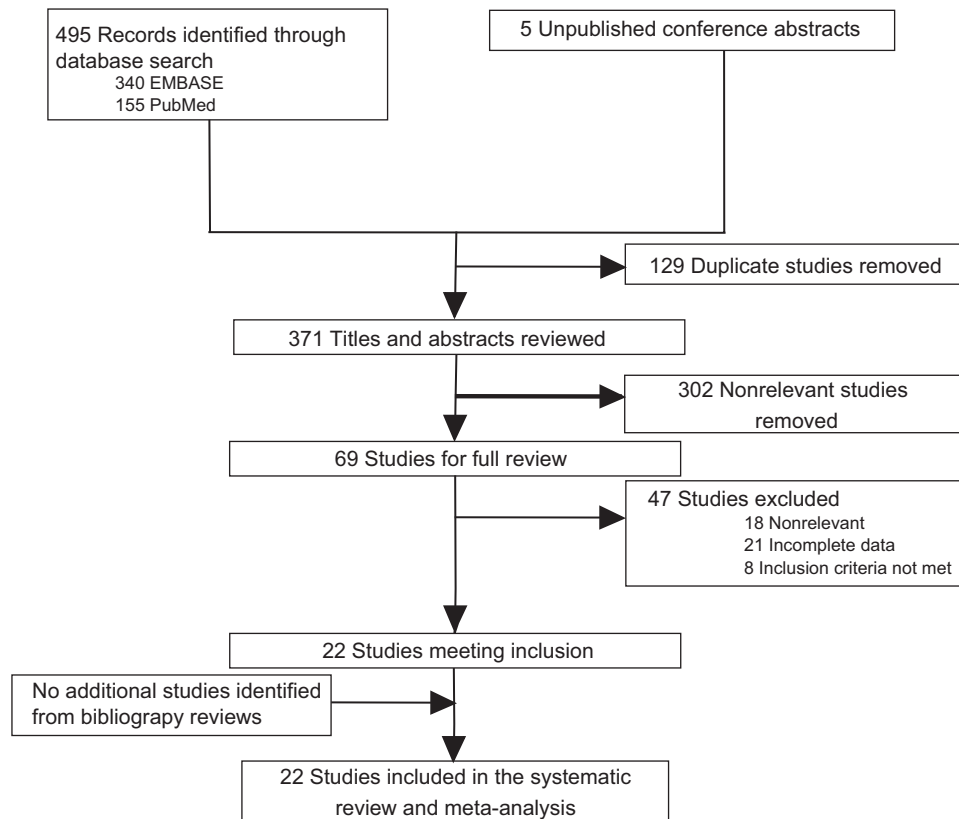


Figure 1. Flow diagram for literature review.

surveillance culture at admission to the hospital or the intensive care unit or within 24 hours of admission.

Pooled Prevalence and Diagnostic Performance

The pooled overall prevalence of MRSA pneumonia was 10% (95% confidence interval [CI], 8%–13%; $I^2 = 89.6\%$; $P < .001$) (Supplementary Figure S1). For VAP, the pooled prevalence was 8% (95% CI, 5%–11%; $I^2 = 49.9\%$; $P = .14$ and included only 3 of the 5 studies meeting criteria for analysis [9, 19, 22]. The prevalence was not conducted for CAP/HCAP, because only 2 studies met criteria and thus a pooled prevalence was not evaluated. Individual prevalence in those studies was 13.0% and 7.1% [4, 11].

Summarized results of the meta-analysis are shown in Table 2. For all types of pneumonia, the sensitivity, specificity, PPV, and NPV of MRSA nares screen to predict MRSA pneumonia were 70.9% (95% CI, 58.8%–80.6%), 90.3% (86.1%–93.3%), 44.8%, and 96.5%, respectively. For CAP/HCAP, the sensitivity, specificity, PPV, and NPV of the MRSA nares screen were higher at 85% (95% CI, 59.7%–95.6%), 92.1% (81.5%–96.9%), 56.8%, and 98.1%, respectively. However, for VAP the sensitivity and PPV were lowest, at 40.3% (95% CI, 17.4%–68.4%) and 35.7%, respectively; the specificity and NPV for VAP were 93.7% (77.1%–98.4%) and 94.8%, respectively. Supplementary Figure S2 shows the summary ROC curves by pneumonia type.

Heterogeneity

Meta-regression evaluations of the bivariate model for sources of heterogeneity suggested possible heterogeneity. In particular, heterogeneity was identified among prospective versus retrospective studies ($P = .01$), comparing PCR with other methods ($P = .01$), testing timing at admission with or without repeated tested, as compared with other timing ($P = .02$), and VAP studies compared with studies of other types of pneumonia ($P = .03$) (Table 3).

Publication Bias and Quality Assessments

Publication bias, evaluated using the Deeks funnel plot asymmetry test, did not show statistical significance ($P = .85$), reflecting symmetry to the data and a low probability of publication bias (Supplementary Figure S3). As reflected in the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2 figure (Supplementary Figure S4), the majority (>90%) of studies had a low risk of bias among all domains except the reference standard, with 59% of studies having a low risk of bias.

DISCUSSION

The use of MRSA nasal screens as a tool to guide deescalation of empiric anti-MRSA therapy was not included in the recent IDSA HAP/VAP guidelines, which recommend that empiric anti-MRSA therapy be given in a significant proportion of patients

Table 1. Characteristics of Included Studies

Authors and Year	Design	Sample Size, No.	Pneumonia Classification	Pneumonia Diagnostic Criteria	MRSA Surveillance Method	MRSA Surveillance Timing	Publication Type
Chan et al, 2012 [9]	Prospective cohort	388	VAP	Radiographic abnormality, quantitative BAL, and ≥ 1 sign of infection	Culture	At ICU admission, then weekly	Journal
Corne et al, 2005 [10]	NR	16	Unspecified	Radiographic abnormality, quantitative BAL or TBA, and clinical criteria	PCR	At ICU admission, then weekly	Journal
Dangerfield et al, 2014 [11]	Retrospective cohort	435	CAP, HAP, HCAP, VAP	Radiographic abnormality, blood and/or respiratory cultures (sputum, BAL, pleural), clinical criteria	PCR	1 mo before respiratory culture if outpatient or 1 wk before if inpatient	Journal
Giancola et al, 2016 [4]	Retrospective cohort	200	CAP, HCAP, HAP/VAP	Radiographic abnormality, sputum culture, clinical criteria	PCR	1 mo before respiratory culture if outpatient or 1 wk before if inpatient or < 3 d after respiratory culture	Journal
Gregg et al, 2011 [12]	Retrospective cohort	169	Unspecified	Quantitative or qualitative BAL, clinical criteria	Unspecified	NR	Conference proceeding
Hiatt et al, 2015 [13]	Retrospective cohort	297	Unspecified	Respiratory tract cultures (sputum, tracheal aspirate, BAL, or bronchial wash or brush)	Culture and PCR	Within 48 h before or after respiratory culture	Journal
Holmes et al, 2010 [14]	Retrospective cohort	145	Unspecified	Clinical sputum cultures	Unspecified	At surgical ICU admission	Journal
Jang et al, 2014 [15]	Prospective observational cohort	282	Unspecified	Radiographic abnormality, quantitative BAL, TBA or sputum, and ≥ 2 clinical criterion met	Culture	At ICU admission, 48 h after admission, and weekly until MRSA detected or patient discharged from ICU	Journal
Johnson et al, 2015 [16]	Retrospective cohort	72	CAP/HCAP	Respiratory tract cultures (sputum, tracheal aspirate, BAL, or bronchial wash or brush)	PCR	Within 48 h of admission	Journal
Kashuk et al, 2010 [17]	Retrospective cohort	176	VAP	Quantitative BAL, clinical criteria	Culture	Within 24 h of surgical ICU admission	Journal
Korobey et al, 2016 [18]	Retrospective cohort	93	Unspecified	Sputum culture	PCR	At ICU admission	Conference proceeding
Langsjoen et al, 2014 [19]	Retrospective cohort	56	VAP	NHSN surveillance VAP definition	PCR	At ICU admission	Journal
Marouni et al, 2010 [20]	Retrospective cohort	22	Unspecified	Radiographic abnormality, respiratory cultures, review of clinical data by expert panel	Unspecified	At ICU admission	Conference proceeding
McMahon et al, 2014 [21]	Retrospective cohort	1320	Unspecified	Tracheal aspirate or BAL	PCR	At admission	Conference proceeding
Mullins et al, 2013 [22]	Retrospective cohort	186	VAP	MV ≥ 48 h and BAL or tracheal aspirate	PCR	At ICU admission	Conference proceeding
Pollock et al, 2011 [23]	Retrospective cohort	76	Unspecified	Unspecified clinical diagnosis of pneumonia and microbiologic culture	Unspecified	At ICU admission then weekly	Conference proceeding
Rimawi et al, 2014 [24]	Retrospective cohort	275	CAP/HCAP	ATS/IDSA 2005 HAP/VAP/HCAP and 2007 CAP guideline definitions	PCR	At admission	Journal
Robicsek et al, 2008 [25]	Retrospective cohort	426	Unspecified	Positive respiratory culture with compatible chest X-ray and decision to treat	PCR	Within 1 d of respiratory culture	Journal
Rocha et al, 2013 [26]	Prospective cohort	21	VAP	Pneumonia developing ≥ 48 h after ICU admission with initiation of MV and ≥ 1 clinical criteria met	Unspecified	Within 48 h of ICU admission, if initial screen negative, cultures repeated every 2 d for duration of ICU stay	Journal
Sanuth et al, 2013 [27]	Retrospective cohort	23	CAP, HCAP, VAP	Unspecified	Unspecified	At ICU admission	Conference proceeding
Smith et al, 2017 [5]	Retrospective cohort	400	Nosocomial	Clinical diagnosis documented in electronic medical record with initiation of appropriate antibiotics and classified according to the 2005 ATS/IDSA guidelines	PCR	Before or within 48 h of ICU admission and a BAL, tracheal aspirate, or sputum culture within 7 d of MRSA screen	Journal
Tilahun et al, 2015 [28]	Retrospective cohort	165	Unspecified	Unspecified	Culture	Within 24 h of ICU admission	Journal

Abbreviations: ATS, American Thoracic Society; BAL, bronchoalveolar lavage; CAP, community-acquired pneumonia; HAP, hospital-acquired pneumonia; HCAP, healthcare-associated pneumonia; ICU, intensive care unit; IDSA, Infectious Diseases Society of America; MRSA, methicillin-resistant *Staphylococcus aureus*; MV, mechanical ventilation; NHSN, National Healthcare Safety Network; NR, not reported; PCR, polymerase chain reaction; TBA, tracheobronchial aspirate; VAP, ventilator-associated pneumonia.

Table 2. Performance Characteristics of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Surveillance Screening by MRSA Pneumonia Type

Type of Pneumonia	Studies, No.	Sensitivity (95% CI), %	Specificity (95% CI), %	Positive LR (95% CI)	Negative LR (95% CI)	DOR (95% CI)	PPV, %	NPV, %
All	22	70.9 (58.8–80.6)	90.3 (86.1–93.3)	7.28 (5.3–10.1)	0.32 (0.22–0.46)	24.6 (13.6–37.5)	44.8	96.5
CAP/HCAP	4	85.0 (59.7–95.6)	92.1 (81.5–96.9)	10.8 (5.1–23.0)	0.16 (0.06–0.48)	66.4 (28.5–154.6)	56.8	98.1
VAP	5	40.3 (17.4–68.4)	93.7 (77.1–98.4)	6.34 (1.94–20.8)	0.63 (0.42–0.98)	9.96 (2.63–37.6)	35.7	94.8

Abbreviations: CAP, community-acquired pneumonia; CI, confidence interval; DOR, diagnostic odds ratio; HCAP, healthcare-associated pneumonia; LR, likelihood ratio; MRSA, methicillin-resistant *Staphylococcus aureus*; NPV, negative predictive value; PPV, positive predictive value; VAP, ventilator-associated pneumonia.

who have pneumonia [1]. Thus, many patients are exposed to unnecessary antimicrobial therapy, leading to increased potential for adverse drug reactions, other drug effects, unnecessary drug costs, and increased costs of drug administration and monitoring [29]. However, several hospitals have already implemented stewardship practices that discontinue anti-MRSA antibiotics, especially vancomycin, based on negative MRSA nasal screen results [4, 5, 13, 30, 31].

Clinical outcomes, including mortality rates, have been noted to be similar among patients with therapy deescalations derived from MRSA nasal screens [11, 30]. A recent study using this deescalation approach demonstrated a decrease in MRSA therapy by approximately 2 days ($P < .001$) and reduced vancomycin serum level monitoring and dose adjustments by nearly 3-fold

($P = .02$), without a significant difference in clinical outcomes [31]. Another recent study observed a cost reduction of \$108 per patient for vancomycin medication costs and trough levels by using MRSA nasal screens for deescalation [5]. The relative cost of nasal *S. aureus* screening is minimal, providing an attractive way for antimicrobial stewardship programs (ASPs) to reduce unwarranted vancomycin therapy.

To our knowledge, ours is the first meta-analysis to evaluate the diagnostic value of MRSA nasal screens in ruling out MRSA pneumonia. Diagnostic odds ratio, the odds of positivity in disease relative to positivity in nondisease, reflected best overall performance among patients with CAP/HCAP [32]. These data can also be noted by the positive and negative likelihood ratios, ratios of positive and negative tests among

Table 3. Heterogeneity Assessment

Covariate	Studies, No.	Sensitivity, %	PValue	Specificity, %	PValue	Bivariate Model PValue
Study design						
Prospective	3	56	.31	80	<.01	.01
Retrospective	19	73		91		
Sample size						
<150 patients	9	72	.40	87	.02	.56
≥150 patients	13	70		91		
QUADAS-2 result						
Bias	14	71	.47	91	.01	.67
No bias	8	71		88		
Publication type						
Journal	15	71	.47	91	.01	.96
Conference proceeding	7	72		90		
Testing method						
PCR	12	78	.53	92	.01	.01
Other ^a	10	58		88		
Testing timings						
At admission (with or without repeat)	16	61	<.01	91	.05	.02
Other ^a	6	89		87		
Pneumonia diagnostic criteria						
Radiographic, culture, and clinical criteria	11	67	.18	92	.01	.56
Other ^a	11	75		88		
Pneumonia type						
VAP	5	40	.05	93	<.01	.03
Other ^a	17	77		89		

Abbreviations: PCR, polymerase chain reaction; QUADAS-2, Quality Assessment of Diagnostic Accuracy Studies; VAP, ventilator-associated pneumonia.

^aOther^a signifies a category different from the reference category, including data not reported.

diseased to the same result among nondiseased patients, with CAP/HCAP. However, we found that owing to the low PPV overall and in subsets by pneumonia type (CAP/HCAP, VAP), positive MRSA nares screens do not have predictive value in the diagnosis of MRSA pneumonia. However, the high NPV in our analysis supports the use of MRSA nasal screens as an ASP tool to rule out MRSA pneumonia. Conversely, we observed a low sensitivity (40.3%) in VAP suggesting a low utility in ruling out VAP MRSA pneumonia, probably related to artificial airways serving as an additional source of MRSA to the nasal passage.

The limitations in VAP were consistent during our analyses for sources of heterogeneity. Notably among bivariate analyses of heterogeneity, PCR testing performance was preferable. This is intuitive, because previous data have reflected improved performance of PCR compared with other methods, such as chromogenic culture; however, PCR is more expensive, at approximately \$26 per test versus only \$7 per test for chromogenic culture [33]. Beyond cost and performance, the time to result should also be considered, because PCR can provide actionable results for discontinuation of anti-MRSA therapy within 2 hours, which may take 2 days with culture-based testing. Finally, the timing of testing was associated with heterogeneity and is important to take into account when considering the clinical use of these surveillance tests.

Reported MRSA pneumonia rates are quite variable, ranging from <1% to 56% depending on the pneumonia criteria, although higher estimates may be attributable to sampling bias [11, 34]. We found an overall pooled MRSA pneumonia prevalence of 10%. This infrequent cause of pneumonia is accompanied by a clinical presentation, which includes a high severity score and may include acute onset of high fever, chills, severe hypoxemia, hypotension, cyanosis, bilateral rapid thick-walled cavitation, or hemoptysis [35, 36].

In addition to clinical evaluations, a possible approach for routine use of MRSA nasal screens by ASPs was noted by one of the aforementioned studies, which allowed for a per-protocol order of the MRSA nasal screen test by staff pharmacists in patients prescribed linezolid or vancomycin for possible or confirmed pneumonia as an extension of their hospital-approved vancomycin dosing protocol [31]. These results were flagged for their review and discussed with the prescribing provider if a potential deescalation opportunity occurred. This approach is consistent with data suggesting that nasal screening may occur after initiation of therapy, because MRSA persists in the respiratory tract during the first few days of therapy [4]. Alternatively, if incidental MRSA screen results are known within a week before diagnosis of pneumonia, these would be useful in discontinuing or not initiating anti-MRSA therapy [5, 11].

Notably, MRSA screens for therapy decisions should be avoided in patients with recent nasal decolonization before

screening and MRSA infection within 30 days before admission [5]. In patients with structural lung disease (eg, cystic fibrosis or bronchiectasis), MRSA nares screens may be discordant because colonization occurs more frequently in the lower respiratory tract and therefore should also be avoided. Moreover, in critically ill intensive care unit patients, more cautious deescalations may be considered with deescalations at 48 hours, because 98% of positive blood cultures for *Staphylococcus* occur within this time [37].

Our meta-analysis has limitations. Most of these data are from retrospective studies, which may be associated with increased bias, such as sampling bias of patients with available culture data, which probably occurred and would explain the relatively lower rates of MRSA among patients with VAP compared with other pneumonia types. Variation was present among studies in the pneumonia classification, and pneumonia diagnostic definitions were not always present. Verification bias may have occurred, in which nasal screen results influenced culture collection and/or clinical diagnosis. Moreover, the timing of the nasal swab collection in relation to the respiratory culture was not consistent or clearly defined among all studies.

There were variations MRSA pneumonia prevalence among studies, and therefore the performance of the screen may differ based on local epidemiology. However, we included conference proceedings in addition to published literature, which has been associated with more accurate pooled estimates because published trials are associated with larger produced estimates [38]. In addition, beyond pneumonia category, patient factors affecting individual risk for MRSA pneumonia, and thus affecting the pretest probability of disease, were not examined. Future studies should evaluate whether there is any impact of long-term care facilities, recent hospital admission, or other patient populations particularly at risk for MRSA pneumonia on the application of nares MRSA tests. Finally, there were a limited number of studies classifying specific pneumonia types, although screen performance was high among all types except VAP.

In conclusion, although a positive MRSA nares test result is not diagnostic of MRSA pneumonia, a negative result rapidly and effectively rules it out. MRSA nares screening, is a valuable tool for ASPs to deescalate empiric anti-MRSA therapy in patients with pneumonia who are not nasally colonized with MRSA, specifically those with CAP/HCAP. MRSA screening offers a rapid, inexpensive way for hospitals to avoid unnecessary and costly therapy that does not provide additional clinical benefit to the patient. With new IDSA CAP guidelines under development, consideration should be given to incorporating MRSA nares screening for ASP and diagnostic purposes. Additional studies are needed to fully evaluate the clinical outcomes associated with use of MRSA nares screens in patients with pneumonia.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Potential conflicts of interest. E. M. M. has received grant support from T2 biosystems, Atellas Pharma, and Sanofi-Aventis. T. T. T. has received honoraria for speaking and/or consulting from BioFire Diagnostics, GenMark Diagnostics, and Roche Diagnostics. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Kalil AC, Metersky ML, Klompas M, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clin Infect Dis* **2016**; 63:e61–e111.
2. Mandell LA, Wunderink RG, Anzueto A, et al; Infectious Diseases Society of America; American Thoracic Society. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis* **2007**; 44(suppl 2):S27–72.
3. Dellit TH, Owens RC, McGowan JE Jr, et al; Infectious Diseases Society of America; Society for Healthcare Epidemiology of America. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis* **2007**; 44:159–77.
4. Giancola SE, Nguyen AT, Le B, et al. Clinical utility of a nasal swab methicillin-resistant *Staphylococcus aureus* polymerase chain reaction test in intensive and intermediate care unit patients with pneumonia. *Diagn Microbiol Infect Dis* **2016**; 86:307–10.
5. Smith MN, Erdman MJ, Ferreira JA, Aldridge P, Jankowski CA. Clinical utility of methicillin-resistant *Staphylococcus aureus* nasal polymerase chain reaction assay in critically ill patients with nosocomial pneumonia. *J Crit Care* **2017**; 38:168–71.
6. Whiting PF, Rutjes AW, Westwood ME, et al; QUADAS-2 Group. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* **2011**; 155:529–36.
7. Deeks JJ, Macaskill P, Irwig L. The performance of tests of publication bias and other sample size effects in systematic reviews of diagnostic test accuracy was assessed. *J Clin Epidemiol* **2005**; 58:882–93.
8. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* **2009**; 6:e1000097.
9. Chan JD, Dellit TH, Choudhuri JA, et al. Active surveillance cultures of methicillin-resistant *Staphylococcus aureus* as a tool to predict methicillin-resistant *S. aureus* ventilator-associated pneumonia. *Crit Care Med* **2012**; 40:1437–42.
10. Corne P, Marchandin H, Jonquet O, Campos J, Bañuls AL. Molecular evidence that nasal carriage of *Staphylococcus aureus* plays a role in respiratory tract infections of critically ill patients. *J Clin Microbiol* **2005**; 43:3491–3.
11. Dangerfield B, Chung A, Webb B, Seville MT. Predictive value of methicillin-resistant *Staphylococcus aureus* (MRSA) nasal swab PCR assay for MRSA pneumonia. *Antimicrob Agents Chemother* **2014**; 58:859–64.
12. Gregg Z, Heffernan DA, Monaghan SF, et al. Nasal MRSA predicts ventilator-associated pneumonia and microbiology. *Surg Infect (Larchmt)* **2011**; 12(suppl 1):S2–82.
13. Hiatt J, Patel RK, Tate V, Smulian G, Kelly A. Using active methicillin-resistant *Staphylococcus aureus* surveillance nasal swabs to predict clinical respiratory culture results. *Am J Health Syst Pharm* **2015**; 72:S20–4.
14. Holmes JW, Williams MD. Methicillin-resistant *Staphylococcus aureus* screening and eradication in the surgical intensive care unit: is it worth it? *Am J Surgery* **2010**; 200:827–31.
15. Jang HC, Choi OJ, Kim GS, et al. Active surveillance of the trachea or throat for MRSA is more sensitive than nasal surveillance and a better predictor of MRSA infections among patients in intensive care. *PLoS One* **2014**; 9:e99192.
16. Johnson JA, Wright ME, Sheperd LA, Musher DM, Dang BN. Nasal methicillin-resistant *Staphylococcus aureus* polymerase chain reaction: a potential use in guiding antibiotic therapy for pneumonia. *Perm J* **2015**; 19:34–6.
17. Kashuk JL, Moore EE, Price CS, et al. Patterns of early and late ventilator-associated pneumonia due to methicillin-resistant *Staphylococcus aureus* in a trauma population. *J Trauma* **2010**; 69:519–22.
18. Korobey M, Sadaka F, Dumm A, et al. Predictive value of methicillin-resistant *Staphylococcus aureus* nasal swab PCR for MRSA pneumonia. *Crit Care Med* **2016**; 44:252.
19. Langsoen J, Brady C, Obenauf E, Kellie S. Nasal screening is useful in excluding methicillin-resistant *Staphylococcus aureus* in ventilator-associated pneumonia. *Am J Infect Control* **2014**; 42:1014–5.
20. Marouni A, Pacheco S, Bolon M, Wunderink RG. Diagnosis and treatment of pneumonia in the intensive care unit in the setting of methicillin-resistant *Staphylococcus aureus* surveillance. *Am J Respir Crit Care Med* **2010**; 181.
21. McMahon K, Stryjewski G. Value of MRSA nasal swab screening for predicting invasive MRSA respiratory infection. *Crit Care Med* **2014**; 42:A1475–A6.
22. Mullins B. Methicillin-resistant *Staphylococcus aureus* (MRSA) surveillance culture as a predictor for MRSA ventilator associated pneumonia. In: *IDWeek, 2013*. 2–6 October 2013, San Francisco CA.
23. Pollock J, Bethea A, Bown A. The clinical utility of nasal swabs as a predictor of methicillin resistant *Staphylococcus aureus* pneumonia. *Crit Care Med* **2011**; 39:163.
24. Rimawi RH, Ramsey KM, Shah KB, Cook PP. Correlation between methicillin-resistant *Staphylococcus aureus* nasal sampling and *S. aureus* pneumonia in the medical intensive care unit. *Infect Control Hosp Epidemiol* **2014**; 35:590–3.
25. Robicsek A, Suseno M, Beaumont JL, Thomson RB Jr, Peterson LR. Prediction of methicillin-resistant *Staphylococcus aureus* involvement in disease sites by concomitant nasal sampling. *J Clin Microbiol* **2008**; 46:588–92.
26. Rocha LA, Marques Ribas R, da Costa Darini AL, Gontijo Filho PP. Relationship between nasal colonization and ventilator-associated pneumonia and the role of the environment in transmission of *Staphylococcus aureus* in intensive care units. *Am J Infect Control* **2013**; 41:1236–40.
27. Sanuth B, Gerardo N, Khudeira Z. Methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia rate in patients with MRSA in the nares. *Crit Care Med* **2013**; 41:A201.
28. Tilahun B, Faust AC, McCorstin P, Ortegón A. Nasal colonization and lower respiratory tract infections with methicillin-resistant *Staphylococcus aureus*. *Am J Crit Care* **2015**; 24:8–12.
29. Cunha CB, Varughese CA, Mylonakis E. Antimicrobial stewardship programs (ASPs): the devil is in the details. *Virulence* **2013**; 4:147–9.
30. Boyce JM, Pop OF, Abreu-Lanfranco O, et al. A trial of discontinuation of empiric vancomycin therapy in patients with suspected methicillin-resistant *Staphylococcus aureus* health care-associated pneumonia. *Antimicrob Agents Chemother* **2013**; 57:1163–8.
31. Baby N, Faust AC, Smith T, Sheperd LA, Knoll L, Goodman EL. Nasal methicillin-resistant *Staphylococcus aureus* (MRSA) PCR testing reduces the duration of MRSA-targeted therapy in patients with suspected MRSA pneumonia. *Antimicrob Agents Chemother* **2017**; 61.
32. Glas AS, Lijmer JG, Prins MH, Bonsel GJ, Bossuyt PM. The diagnostic odds ratio: a single indicator of test performance. *J Clin Epidemiol* **2003**; 56:1129–35.
33. Paule SM, Mehta M, Hacek DM, Gonzales TM, Robicsek A, Peterson LR. Chromogenic media vs real-time PCR for nasal surveillance of methicillin-resistant *Staphylococcus aureus*: impact on detection of MRSA-positive persons. *Am J Clin Pathol* **2009**; 131:532–9.
34. Kollef MH, Shorr A, Tabak YP, Gupta V, Liu LZ, Johannes RS. Epidemiology and outcomes of health-care-associated pneumonia: results from a large US database of culture-positive pneumonia. *Chest* **2005**; 128:3854–62.
35. Rubinstein E, Kollef MH, Nathwani D. Pneumonia caused by methicillin-resistant *Staphylococcus aureus*. *Clin Infect Dis* **2008**; 46(suppl 5):S78–85.
36. Self WH, Wunderink RG, Williams DJ, et al. *Staphylococcus aureus* community-acquired pneumonia: prevalence, clinical characteristics, and outcomes. *Clin Infect Dis* **2016**; 63:300–9.
37. Pardo J, Klinker KP, Borgert SJ, Trikha G, Rand KH, Ramphal R. Time to positivity of blood cultures supports antibiotic de-escalation at 48 hours. *Ann Pharmacother* **2014**; 48:33–40.
38. Institute of Medicine. Finding what works in health care: standards for systematic reviews. Washington, DC: National Academies Press, **2011**.