Reviewer's report

**Title:** A risk score for identifying Methicillin-resistant Staphylococcus aureus in patients presenting to the hospital with pneumonia

**Version:** 1  **Date:** 4 October 2012

**Reviewer:** Christopher Frei

**Reviewer's report:**

Overall: This study provides a novel approach to identify those patients at low risk for MRSA when presenting with pneumonia from the community. This study is strengthened by its large, multicenter design; however, there are things that need to be addressed prior to accepting this manuscript for publication.

**Major Compulsory Revisions**

**Abstract**

1. In the results section of the abstract, the sentences beginning with, “By design, MRSA prevalence...predictive value of 90.1%” should be replaced with these sentences from page 10 of the text, “[This study]...shows how the prevalence of MRSA rose with increasing score after stratifying the scores...when the score was # 6.”

2. I do not agree with the first sentence in the conclusion of the abstract. I don’t believe the authors can make the claim that “MRSA represents a common cause of pneumonia presenting to the hospital,” because they only studied culture-positive patients and this population is more likely to have a higher rate of MRSA. A pathogen is only identified in about 10-20% of patients with routine laboratory testing. The common belief is that other pathogens, like S. pneumoniae, are common causes of pneumonia, even in these cases where no pathogen is identified.

3. The abstract conclusion states the risk score identifies patients at ‘low risk’ for MRSA. While I agree with this conclusion, this is inconsistent with what is stated in the overall conclusion on page 15. The overall conclusion on page 15 seems to make some unsubstantiated claims.

4. I think that the best conclusion for the abstract would be some sentences from page 11 of the discussion, “A risk scoring tool based on...in whom anti-MRSA therapy can likely be withheld.”

**Methods**

1. Patients were excluded if they did not have “laboratory confirmation of bacterial etiology.” This leads me to believe this is a study of patients with culture-positive pneumonia. Is that what the authors intended to say? If so, there are major implications from trying to use this study to describe microbial etiology in pneumonia. They should recognize that pathogens are not identified in most
pneumonia cases. Also, they should tone down all the comments about how MRSA is so common in CAP. Recent studies published in other journals suggest that MRSA is responsible for only about 2.4% of CAP cases.

2. Please explain how multiple and mixed culture results were handled in the analysis (i.e., if a respiratory culture grew both MRSA and Pseudomonas aeruginosa, then how was that patient classified?).

3. The authors need to specify which variables were included in the logistic regression model and provide a rational for how these variables were chosen (e.g., P<0.05 in bivariable analysis).

4. I suggest including HCAP vs. CAP as one of the variables in the LR model if they investigators have not already done so to determine if HCAP is an independent predictor of MRSA.

5. The authors need to clearly explain why some variables were given a value of two points versus one point (e.g., what was the relative risk cut-off used?).

6. Paragraph 5, Lines 4-5 - Was a hypothesis test used to compare the AUROC for the determination and validation cohorts to 0.5? If so, please provide the description in the methods and the results.

7. Paragraph 1, Lines 8-10 – Explain how culture and susceptibility data were obtained (e.g., medical records or ICD-9 codes).

Results

1. The organization of the results section is confusing. It may be beneficial to the reader to delineate the cohorts being described. In paragraph 2, would state in the ‘development cohort’ then ‘validation cohort’ in paragraph 3 as described in the methods and figure 2.

2. In the third paragraph, I recommend to list specifically the eight variables independently associated with MRSA in the multivariable model – including OR and 95% CI. The sentences describing the point risk score should come before detailing the AUROCs – assuming the AUROCs are based on the scoring model.

3. The authors should report whether HCAP alone was an independent predictor of MRSA.

4. It may be impactful to include what proportion of the low risk subgroup were CAP patients versus HCAP patients. A clear distinction in this result may further support the notion of potential misclassification and overutilization of anti-MRSA agents.

Discussion

1. Paragraph 3, Lines 5-6 – The authors suggest that the presence of HCAP risk factors “fails to accomplish the goal” of stratifying patients by MRSA risk; however, their data show that HCAP patients were significantly more likely to be infected with MRSA relative to CAP patients. The authors should not make such a strong claim in their discussion, as the results suggest otherwise.

2. Paragraph 5, Lines 5-7 - This sentence stating “We show that the variables associated with MRSA may be distinct from those linked to resistant gram
negative organisms" is misleading. While it may be valid that there are distinct variables associated MRSA from resistant gram-negatives, this study demonstrated distinct variables associated with MRSA from all other pathogens of pneumonia (including common pathogens of CAP). Data comparing risk to ‘resistant gram negatives’ were not detailed.

3. Extremes of age (particularly younger <30 yrs), cerebrovascular disease, and dementia are new findings related to MRSA in pneumonia in this study. The authors’ comments on proposed rationale of these risk factors would be appreciated.

Conclusions
1. Re-state the conclusions to reflect that the risk tool may be used to identify patients at low risk for MRSA only, as the risk tool had a poor positive predictive value.

Tables and Figures
1. The authors need to add a table showing the results of the logistic regression model, including relative risks and 95% CIs.
2. Table 1: The cell containing ‘Recent hospitalization’ is defined as > 2 days compared to > 2 days in the results (pg. 10) and not specifically detailed in the study definition of HCAP in the methods section (pg. 8). Please reconcile.
3. Table 1: The cell containing ‘prior intravenous antibiotic therapy’ should contain ‘within the last 30 days’.
4. Table 1: Because “wound care in the last 30 days” was specified as a criteria for HCAP (pg. 8), these data should also be included in the table.
5. In Table 2, how was “recent antibiotic exposure” defined (i.e., prior 90 days)? Also, was this only intravenous antibiotic exposure? If so, please specify in the table.
6. In Figure 1, this high rate of MRSA in the CAP population suggests a different type of pneumonia population than most cohorts that have been studied. I think this has to do with the inclusion of only culture-positive patients in this sample. This should be acknowledged and/or explained.
7. Regarding Figure 2, I believe the categories should be renamed as follows:
   a. Low (<10%) # Low (0 to 1 pt)
   b. Medium (10 to 25%) # Medium (2 to 5 pts)
   c. High (>25%) # High (6 to 11 pts)

Minor Essential Revisions

Abstract
1. The word “cerebrovascular” is misspelled in the abstract.
2. Abstract - Results: Would clarify ‘prior antibiotics’ to ‘prior IV antibiotics’
3. Abstract - Results line 3: Uncapitalize “two”
Introduction
1. Paragraph 3 – add a reference after “For example, nursing home residence may be associated more with MRSA that P. aeruginosa”.

Methods
1. Paragraph 1, Lines 3-5 - The ICD-9-CM codes for pneumonia and sepsis should be included with a reference of other studies that have used these codes to define these diagnoses.
2. Paragraph 1, Line 5 - Change the ICD-9 definition to International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM).
   1. Paragraph 1, Line 7 – Explain how HAP and VAP were defined.
   2. Paragraph 2, Lines 5-7 – Explain how comorbidities were defined (e.g., ICD-9 codes or medical records).
   3. Paragraph 2, Lines 9-12 - An explanation and reference should be added following the variables used to define HCAP.
   4. Paragraph 2, Lines 13-16 - A reference should also be added following the definition of immunosuppression.
5. Endpoints and Covariates – Within the HCAP definition, was a recent hospitalization in the last 90 days require a stay of greater than 2 days? This needs to be clearly stated.

Results
1. Paragraph 1 – Provide a comparison of MRSA incidence in this study’s HCAP population to other studies and provide a reference and possible explanation of any differences.
2. Page 10, paragraph 2 – We recommend providing values (%) when comparing characteristics between MRSA and no-MRSA groups.
3. Paragraph 2 - What is meant by “correlated strongly”? Perhaps provide statistics.
4. Paragraph 3 - What is meant by “more strongly linked”? Perhaps provide statistics.

Discussion
1. Paragraph 1 – Provide a comparison of MRSA incidence in this study’s HCAP population to other studies and provide a reference and possible explanation of any differences.
2. Page 14, Paragraph 2 – This sentence should read “…and positive cultures of the respiratory can represent colonization and not true infection.”

Tables and Figures
1. The authors should add a table showing pathogen distribution, including separate columns for overall, CAP, and HCAP.
2. Table 1, The cell containing ‘Admission from nursing home or long term care facility’ should also include “skilled nursing facility” consistent with the rest of the manuscript.

Discretionary Revisions

General
1. Write out “two-thirds” and “one-third” throughout the paper.
2. Capitalize “Gram-negative” and “Gram-positive” throughout the paper.

Title
1. Un-capitalize “methicillin”.

Abstract
1. Results section - edit spacing of “< 30” and “score#6”.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

My institution has received investigator-initiated research funds from NIH, AstraZeneca, Bristol-Myers Squibb, Elan, Pfizer, and Ortho-McNeil for research I have conducted at my institution. I have personally received consulting funds from Forest and Ortho-McNeil Janssen (< $5,000 total) in the past five years.