Reviewer's report

Title: Improved survival with initial methicillin-resistant Staphylococcus aureus therapy in high-risk community-onset pneumonia patients: application of a new risk score

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Reviewer: Marya Zilberberg

Reviewer's report:

1. Is the question posed by the authors well defined? -- YES
2. Are the methods appropriate and well described? -- Well described but there are some issues (see below)
3. Are the data sound? -- YES
4. Do the figures appear to be genuine, i.e. without evidence of manipulation? -- YES
5. Does the manuscript adhere to the relevant standards for reporting and data deposition? -- YES
6. Are the discussion and conclusions well balanced and adequately supported by the data? -- NO
7. Are limitations of the work clearly stated? -- Incompletely
8. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? -- YES, but not all
9. Do the title and abstract accurately convey what has been found? -- I am not sure I can agree completely with the investigators' conclusions
10. Is the writing acceptable? -- VERY GOOD

This is a retrospective cohort study among elderly VA patients asking a very important question of whether a MRSA risk score can limit use of anti-MRSA therapies to only those patients who are deemed to be at high risk for MRSA pneumonia without compromising clinical outcomes, namely 30-day mortality. This is a critical question to ask, and the authors do a good job setting up the rationale for what they did. Unfortunately, I do not feel that the question has been answered conclusively, but rather has provided some interesting fodder for further inquiry.

Major

The biggest issue for me is the tremendous probability of confounding by indication in these data. That is, based on what is reported, patients in the lower risk strata who received anti-MRSA treatment were much sicker than those who did not, which would go hand-in-hand with their higher mortality. The fact that the adjusted analyses still showed this increased mortality to me suggests at least a
strong possibility of residual confounding rather than treatment effect. Were they also more likely to be treated for Gram-negative pathogens as well? If so, how do you know that it was not either those pathogens if present or overtreatment or undertreatment for those pathogens that impacted mortality? Have the investigators considered using propensity matching, for example, which may be better at reducing such confounding than a simple regression? Another consideration should be given to including in the analyses pneumonia mortality model built specifically for administrative data such as these (Rothberg MB, Pekow PS, Priya A et al. PLoS One. 2014 Jan 31;9(1):e87382.)

I realize that you looked at the ICD-9 codes for specific organisms, but I am not aware of any data that support their accuracy. And in fact the low proportions of organisms indicate that this is not a very sensitive way to identify these potential pathogens.

Another concern is that this is a very high mortality population. In a recent study published by our group from Premier Perspective database (cited above) reported unadjusted mortality in the 7% range. In the current study unadjusted mortality is 20%. Granted, this is an older population of mostly white men, but this needs to be addressed at the very least as a limitation.

Another concern is the timing of the data. Why use such old data? Is there not reason to think that practices have changed so significantly as to make your results less applicable? We know that treatment of and mortality in severe sepsis, for example, have changed dramatically in the last 10-15 years. Furthermore, the ATS-IDSA HCAP treatment guidelines were published in 2005. And even the uniform ATS-IDSA CAP guideline did not come out until 2007. Could it mean that there was likely to be less uniformity to pneumonia treatment in the time period examined than in the current time, and this would impact mortality in a way that you might not have captured adequately? Again, at the very least this requires elaboration as a limitation.

Minor

On page 6, lines 131-134: Why were only these types of medications examined. What about other antimicrobials? What about PPIs and statins, both of which have been reported to impact mortality in pneumonia?

Page 6, lines 140-142: The authors describe differences from the Shorr score that were applied here. Can you justify these differences? Can you say how that may have impacted your findings? Is this a limitation that should be mentioned explicitly?

On page 7, lines 167-168: you said that all unbalanced characteristics from table 2 were included in your mortality model. Why is this? Is it not more appropriate to include only those characteristics that unbalanced in the unadjusted mortality analysis as well as those others that may have biologic plausibility or evidence from other studies to have an impact on the outcome? By including the unbalanced characteristics for MRSA therapy, are you not entangling MRSA
therapy with mortality a priori?

There are number of other studies that have examined guideline concordant therapy as it impacts outcomes that should be reviewed.

Limitations paragraph needs to include other potential limitations as mentioned above.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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

Declaration of competing interests:

I have received research and/or consulting funding from Cubist, Pfizer, Astellas, Theravance and Tetraphase.