Reviewer's report

Title: The Natural History of Anemia in Hospitalized Community-acquired Pneumonia

Version: 1 Date: 18 November 2009

Reviewer: Marya Zilberberg

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Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

1. I have a major problem with the way the authors define anemia: at least borderline anemia threshold Hb is \( \leq 13 \) g/dL. By most definitions 13 g/dL is a normal value for men, and for women it is 12 g/dL and above. This is an important misclassification and the authors either need to explain why they used such definition and how the resulting misclassification has affected their estimates or re-do the analyses with more appropriate thresholds. While the authors attempt to explain this more fully in the text on page 5, their explanation does not address my concerns. I personally would be much more comfortable with Hb < 13 g/dL for men and <12 g/dL for women, with normals being \( \geq \) to the corresponding value. However, if you show me that it did not affect your results that much, I am willing to live with my discomfort.

Along the same lines, when the authors state on page 1 that “nearly 4 in 5 were anemic…” and “3 in 4 survivors…”, are they referring to the 13 g/dL threshold? If so, this may be overstating the magnitude of the problem.

2. In the Statistical Analysis section of the Methods the authors talk about models for anemia development and the 90-day mortality. The 90-day mortality model includes the additions of anemia and transfusions. How were these factors analyzed? After all anemia and transfusions are likely not independent of each other. In other words did the analysis assume independence of these events, which is not a correct approach, and if not, how was their interdependence handled statistically? If you considered them independent and put them in the same regression models, you need to check for their correlation, and, if positive, re-run a separate model including each one.

3. On page 8 when talking about enrollment numbers: it is unclear why you are jumping between 1,838 who had a Hb on day 1 and 1,893 with a Hb ever during hospitalization. By inference, it looks like you are including anyone with a Hb drawn ever during hospitalization. If so, how is baseline Hb defined?

To avoid this confusion I recommend that you define your inclusion and baseline Hb criteria more explicitly in the Methods.

4. In figure 3, referred to on page 9, the group with the lowest baseline Hb seems
to peter out around day 10 – is this because they are all dead or discharged or is this an error in the graph?

5. Similar to my suggestion in 3 above, please, define what you accepted as discharge Hb in the Methods.

6. On page 9 second line from bottom: “As expected” should be removed, as this is editorializing.

7. On page 10: again, anemia and transfusions are likely collinear and are by no means independent. You need to address this issue in your modeling, as it is likely not valid to include both anemia and TF as independent covariates into the same model.

8. Again on page 10 I am concerned that you are overstating the prevalence of anemia given your threshold definitions for Hb.

9. Your Discussion section is good. I would like some additional discussion of why you think chronic respiratory disease may be protective from development of anemia, since several studies have found a fairly high prevalence of anemia in COPD patients, though these were not confined to hospitalized patients. Some have in fact proposed that anemia in COPD develops during hospitalization and that may artificially inflate its prevalence estimate in this population. At any rate, this point is of interest and bears some discussion.

10. Finally, now that I have read the entire paper, I would suggest that you go back to the abstract and amend your conclusions. In my opinion, you have found that not all levels of anemia are clinically important, at least the way you have defined this importance relative to the 90-day mortality rate. Therefore, for a clinician it may be more helpful to know what levels of anemia he/she should worry about. Also, once you have addressed my TF issue, this should be brought out in the abstract as well.

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

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

Until three years ago I was employed by Johnson & Johnson, the manufacturer of erythropoietin, and I hold a minimal amount of their stock.