Reviewer’s report

Title: Procalcitonin-guided diagnosis and antibiotic stewardship revisited

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Reviewer: Jean-Louis Vincent

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The authors review some recent studies on PCT.

The text is well written but it is very biased; this is not too surprising as the authors have been strong advocates of this biomarker, and have largely contributed to the field.

Although PCT is certainly a valuable marker, it is far from perfect.

This text should be either counterbalanced by another view or considerably revisited to underline the limitations of any biomarker, including PCT.

1. How were the studies selected? The negative multicentric study from ANZICS (published in the American Journal of Respiratory and Critical Care Medicine in 2014) is simply omitted. Likewise, the study by Oliveira et al showing PCT may not be superior to CRP for guiding antibiotic therapy.

2. The studies evaluating the place of PCT were not blinded; admittedly, it would be extremely difficult to have a blinded protocol, but this should be listed as a limitation.

3. How can one be sure that the antibiotic treatment was not too long in the control group? In other words, that reducing the duration of antibiotic therapy without the use of PCT could result in similar outcomes.

4. How can one be sure that PCT is superior to other biomarkers in this setting of reducing the duration of antibiotic therapy? This is supported by the study of Oliveira et al (Crit Care Med) which is not cited.

5. The cost of PCT is not even mentioned. The yearly hospital budget for routine measurement is very high. If the antibiotic treatment can indeed be shortened in the absence of PCT measurements, or with the support of cheaper CRP measurements, the cost/benefit may not be very reasonable.

6. The authors should more clearly recognize that biomarkers can only complement the clinical assessment and not replace it.

Specific comments
1. Background: "unnecessary and prolonged exposure to antimicrobial agents adversely affect patient outcomes (e.g., risk for clostridium difficile infection),": there is also a risk of emerging resistant organisms in the patient himself.

2. Middle of page 7: "Sepsis, as defined by SIRS criteria…": SIRS are not (or no longer) part of the sepsis criteria.

3. Page 8: "In addition, PCT was found to predict severity of illness.": this is true for any sepsis marker.

4. Page 10: "Thus, further investigation is needed in the surgical setting.": is it until PCT is shown superior to CRP? why not recognizing that CRP is just as good as PCT in this setting?

5. The Figure 1 seems promotional

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