Reviewer's report

Title: Procalcitonin-guided antibiotic use versus a standard approach for acute respiratory tract infections in primary care: study protocol for a randomised controlled trial and baseline characteristics of participating general practitioners [ISRCTN73182671]

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Reviewer: Michael S Niederman

Reviewer's report:

General

Briel and colleagues have described a protocol for the evaluation of antibiotic usage in a primary care setting. They propose to use procalcitonin to guide the use of antibiotics versus a standard approach to care. The presentation does not include any data from the study itself, but only data about the investigators who will be conducting the study. There are many unanswered questions about the protocol as presented. I do not believe as presented there will be great insights gained from reading this manuscript. It may be possible that this manuscript could be of value if it were clarified in the following areas.

1. In the introduction and throughout the manuscript, the authors state that they recruited general practitioners who are representative of all eligible general practitioners. There are absolutely no data presented to justify this statement. In fact, it is clear that they tried to recruit a number of general practitioners who did not accept recruitment. There may indeed be something very different about individuals who are willing to do the research versus those who weren't. This raises a key credibility question about the study, namely is it feasible to use this type of approach in a primary care practice.

2. I am still very confused about the protocol as it is designed. The authors suggest that the use of the protocol could lead to less antibiotic usage, but I am not clear about their concern of a Hawthorne effect. The Hawthorne effect implies that if patients are managed according to the protocol, then the control group might over time have different management. For this protocol to be relevant and valuable, it needs to be organized in the following fashion. The investigators need to determine first that based on clinical criteria, they will treat with antibiotics. Then, the PCT measurement is done. If indeed this is the protocol, then the decision to treat the controls has already been made, and the use of PCT data should not change the enrollment in that only patients in whom they have decided to treat with antibiotics will be considered controls. This is a critically important methodologic point which I do not feel is adequately addressed.

3. A more clear explanation of the evidence-based guidelines for antibiotic usage should be provided.

4. The authors never discuss the fact that even if their intervention does lead to less antibiotic usage it is a very labor intensive and potentially expensive approach. It seems unrealistic to believe that
patients will agree to have a blood test, wait for the results of the blood test to decide if they will get an antibiotic prescription and then return frequently for a followup blood test to decide when to stop the antibiotic therapy. The practicality of this approach in primary care seems doubtful and this issue is not discussed by the authors.

5. The authors state that followup of patients will be done in a blinded fashion by telephone. It seems impossible that the followup could be blinded since the interviewers could determine which patients had multiple blood tests and, therefore, which patients were enrolled in the procalcitonin monitoring group.

6. The authors have not listed antibiotic usage as a primary end point. Without this being a primary endpoint, I believe there is no point in doing the study. To simply say that the two management approaches, used in a low risk population, do not have different outcomes is a very un-ambitious study. This study will only have value if it leads to less antibiotic usage and as such, antibiotic usage deserves to be a primary end point.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

**Which journal?:** Not appropriate for BMC Medicine: an article of only archival interest, but might be suited to BMC Family Practice

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Quality of written English:** Acceptable

**Statistical review:** No