Reviewer's report

Title: An electronic clinical trial tool to recruit large patient samples and assess selection bias in general practice research

Version: 3 Date: 12 June 2010

Reviewer: Peter J Embi

Reviewer's report:

The authors have made many of the changes previously noted, and have provided a point-by-point response to the critiques that is very thorough and well organized. Most of the changes result in a significant improvement to this manuscript.

There are some key elements that remain to address however, several that the authors highlighted in their response for feedback, and I will focus on the main ones here that if addressed would improve the paper before publication.

One major one that I believe reflects a persistent methodological problem or at least a source of confusion is highlighted by the authors in their response starting under #6. This reviewer earlier commented that the authors should clarify the subjects of their study because the way the paper was/is written was confusing, by stating, “For instance, a few words should be added about the way in how the practices/physicians (the “subjects” of this study of a CTA intervention) were selected, how analysis of the data were conducted, etc.”

In response, the authors state that, “…Although we also mention the performance of doctors’ and practice staff, especially whether they have reached the target level of enrollment, these persons were not primarily in the center of our interest. In other words, the target of our study (i.e. the research subject) is neither the patients nor the physicians, but the performance of the EPR-based electronic tool in the midst of the “clinical study triangle” consisting of patients, practice personnel and study center (see page 8, lines 5ff). We hope the referee agrees with our point of view so that the comments in #8 and #9 (see below) can also be seen in a different light.”

I respectfully continue to disagree with the authors, and I think I understand why there remains some confusion and difference of view here. I will again attempt to point it out in some detail in the hopes of helping the authors understand what I meant and clarify the confusion and problematic methodologic descriptions that I believe persist. First, I understand the authors desire to appropriately state the aim of their study is to test their informatics intervention in the healthcare environment “triangle” they highlight. However, they seem to have conflated the “intervention” of this study with the “target” of the intervention as one and the same (i.e. the software tool) at various places in their response and in the revised text. In fact, this study is not unlike many other clinical informatics or even clinical trial intervention studies conducted in real-world settings wherein an intervention
With that said, I will make an expand on a few points and try to be more clear. My previous statements about “subjects” of the study were not references to the “research topic”, but instead to the “subjects” or targeted “participants” that are the focus of the intervention being studied. In this case, the “research subject” or focus of this study is certainly the software intervention (the tool + approach), much like the “research subject” or focus of a clinical drug trial is a particular pharmaceutical agent. However, the “research subjects” or participants of this study have to be identified not as the “tool” or a “triangle” that reflects the intervention plus environment, but in this case as the providers (or their practices) upon whom the software intervention is being tested. This is directly analogous to the case wherein the “research subjects” of a drug trial are the patients upon whom the drug is tested, even though the drug’s impact is the focus. Therefore, the “performance” of this tool alone is not the outcome of interest for this clinical study, per se, any more than the pharmacokinetics of a drug are the main interest of a therapeutic drug trial. The performance of the subjects affected by this tool is the outcome of interest. Indeed, this is directly analogous to many similar clinical informatics intervention studies, which are not unlike studies of drugs or other medical interventions in their study design. For examples, the authors need only look to studies like the prior studies of similar Clinical Trial Alert interventions that the authors now cite; those were applied in similar “triangles” wherein the primary intervention was the CTA software/approach, the “research subjects” were the providers upon whom the CTA was applied, and the outcomes of interest were the numbers or rates of patients recruited to the respective studies. In those cases, as with the current study, the topic was how the tool would affect recruitment, but to study and calculate impact, there had to be defined an intervention and a sample upon which to test its impact against some unit of analysis (e.g. recruitment rates). I go into this in such detail in order to hopefully clarify what I think is a critical point for this paper, and with hope that related sections will be clarified with regard to these study elements.

In addition, the authors could further address another persistent issue that seems to be adding confusion, namely the fact that study has multiple outcomes of interest: (1) recruitment rates, (2) survey efficiency, (3) selection bias. While I understand the desire to address the holistic view of the impacts of the intervention, it also means that the authors need to be careful not to conflate the multiple outcomes and underlying methodologies that derive from different underlying analyses. Here again, the details about the underlying osteoporosis study results can be confusing, since that’s not the main focus of this study. As the title suggests, this article is instead focused on issues of recruitment rates and analysis of bias. Fundamentally, the readership would benefit from some further clarification of this as an intervention study, where the “intervention” is the introduction of the clinical trial tool, and there are clear study participants and outcomes.

Given the discussion above, I hope the authors now agree that with regard to the
intervention of this study, responding to earlier comments addressed in response items #8 and #9 now requires different action.

Also, given the discussion above, I hope the authors’ response #14 regarding the last critique’s point about “intention to treat” analysis (which would not have excluded the poor performance of the two practices that failed to adhere to protocol) will be revisited. Once again, despite the authors explanation that, “Since we consider the clinical trial tool to be the “target” of our study, the expression “intention to treat” may be somewhat misleading,” the tool IS the intervention and cannot simultaneously be the study’s target population. As they state, the practices are the unit of analysis, and the practices’ performance after implementation of the tool is the outcome of interest. As such, those who performed poorly with the tool should be included in analysis, just as patients who fail to take a drug in a drug intervention trial are still included in the analysis in an intention-to-treat analysis. Alternatively, if the authors are not inclined to do this, they should explain that they opted not to conduct an intention to treat (or use) analysis by expanding on what they’ve already added.

Regarding the authors response topic #7 regarding the unit of analysis – I understand their dilemma. I would simply suggest then that this be discussed in the limitations section briefly.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests