Reviewer's report

Title: A national clinical decision support infrastructure to enable the widespread and consistent practice of genomic and personalized medicine

Version: 1 Date: 23 November 2008

Reviewer: Robert Greenes

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Major Compulsory Revisions
- No compulsory revisions are needed.

Minor Essential Revisions
1. Pre-requisites is usually a single non-hyphenated word.
2. Background, start of 2nd parag: “While genomic and personalized medicine are still…” should be “…is still…”.

Discretionary Revisions
1. I found that the arguments in this paper were weakened by a number of vague calls to action without a clear target for who would carry out the actions, and how they could be stimulated and sustained.
2. Also there is a clear slant toward a solution that is consistent with the identified proprietary interests of the authors. The argument would be more powerful if there were an author team that included individuals from institutions without such proprietary interests. There are at least 3 clinical knowledge sharing projects under way in the US that the authors do not mention.
3. The words genomics, genetic, molecular, and personalized are used in various combinations. What is the consistent point that is being made? Clearly, using genomic and proteomic techniques, we are better able to understand individual variation in both the manifestation of disease and the response to treatment. That should be the central point about this.
4. Discussion, 4th critical factor, projects the goal that “knowledge resources can be efficiently integrated into various clinical information systems in a plug-and-play manner”. “Plug and play” is a concept that is easy to talk about in a glib way, but in practice is very difficult. Most implementations of alerts, reminders, and other rule-based CDS, for example, combine both medical knowledge and business logic in terms of what event triggers the rule, when and in what application context it is executed, and how the results are conveyed to the user. These aspects are not separated and that appears to impede sharing. Such issues and others make this a far more complex problem than is implied by the “plug and play” goal, unless what is meant by “integrated into” information systems is defined in sufficiently limited terms.
5. Recommendations, number 2, suggests that there is novelty to the notion that genomic and personalized medicine CDS is similar to that for other CDS. The only difference is that there are very few rules that pertain to genomic factors to date. I think the authors would be better served by making the point that the need for sharing of CDS knowledge will only be exacerbated by the potential explosion of genomics-based rules, rather than implying that there is need for fusion of two disparate kinds of efforts.

6. The third recommendation, that of “leveraging existing resources” to the extent possible, is a weak statement. Referencing Table 2 only emphasizes the problem since it lists a large number of non-aligned, competing efforts that are not only part of the potential solution but part of the problem. It would be a much greater contribution if the authors could take a position on how these resources could be leveraged, what kind of authoritative body could be formed, and how decisions about such matters could be made in order to move forward rather than proliferate approaches to standardization.

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests