Reviewer’s report

Title: Integrating genomic technologies in clinical practice: A novel approach

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Reviewer: hank greely

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BMC Medical Genomics Review

Major Compulsory Revisions
None

Minor Essential Revisions
None

Discretionary Revisions

This paper puts forth an interesting idea about how we should handle clinical genomic data in the future. I disagree with the author on whether we should follow his recommendations and think it highly unlikely that we actually will for them, but they are interesting and, I think, a useful contribution to the discussion.

1. The prose is decent, but the paper feels quite repetitive and a bit bloated at points. It should be cut by about 20 percent.

2. The idea of patients having control of their data, on a memory stick, CD, or some other hard form, seems problematic to me. For one things, patients will lose those devices, quickly and regularly. The actual sequence data will have to be kept somewhere in order to recreate them; given that it is stored somewhere, why not give patients control over who gets access to that data repository rather than give them the sole physical copy for purposes of control?

3. If patients have control over their genomic data, some will no doubt seek out the kinds of further information the author finds problematic. The author argues that CLIA and its equivalents will prevent them from getting information of clinical significance, but a) they might look up things themselves in various databases, b) some genomics labs may become CLIA certified (the arguments the author makes against this are weak – CLIA certification is not that demanding and various sequencing laboratories already have or are seeking CLIA certification), and c) some people or institutions will provide medical interpretations of sequence data without being CLIA certified, perhaps violating CLIA but in ways unlikely to cause them much difficulty.

4. Fundamentally, the idea that a clinician can ignore “incidental findings” that she could have found seems to me both ethically and legally unsound.
Responsibilities for incidental findings in research contexts may be controversial; the duties of a patient's physician to notice, for example, that the CAT scan, taken to look at the liver, happens to show a big mass on the pancreas are not. If a person's genome sequence showed a mutation consistent with Lynch syndrome and the geneticist had only examined the sequence areas linked to, say, breast and ovarian cancer because that's where the patient had a family history and concerns, I believe that would be deeply problematic. The author should rethink that point. This idea of "limited" genomic examinations is absolutely central to the author's point, but I think is – ethically, legally, and practically – unwise and, in any event, unobtainable. It may just be that the author and I disagree, but perhaps he can reinforce his arguments on this point.

5. I think I understand the author's idea for the "I-MPOSE" search, but it requires a very good database of genome/disease correlations. The author's suggestion of how to get to that database seem like just so much hand waving: "international advisory committees need to reach consensus." This is going to be a tremendously difficult and complex undertaking; this paper does not give it the attention it requires.

6. It is good that the author discloses the patent application covering "I-MPOSE." I am not a patent expert, but it is not at all clear to me that such a patent would be issued or, if issued, enforced. It is also not clear to me why the author wants there to be a patent, as he claims the use would be free of charge.

7. The author talks about the possible issues that gene patents cause in clinical applications of sequencing, but should at least note the possible implications of the recent Prometheus case from the US Supreme Court – a case that was decided after this article was submitted. It is deeply unclear what those implications are, but they clearly will be important. (I speak there as a lawyer.)

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

**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 significant competing interests.

I don't know that anyone could confidently answer your form by saying they have NO competing interests, at least when the paper involved has broad potential consequences. I am employed by a university that has a medical school; my wife is a physician in practice with the Kaiser Permanente medical system. The future of genomic medicine could, in theory, affect the ability or willingness of our employees to pay us and the ideas in this paper could affect the future of genomic medicine. More directly, I write and talk on topics related to this paper. If
it increases the interest in that field, I may have more opportunities to write, talk, travel, and so on that will affect my interests - or it may be "the answer" and all those opportunities may dry up. Either way, I believe we are talking about chances well under 1 percent of an income effect (in an unknown direction) of 1 percent or less at some uncertain time in the future - possibly after retirement - but I cannot honestly say there is no chance my family's interests will be unaffected.

Conflicts of interest are ubiquitous; conflicts policies that do not recognize that fact and seek assurances of absolute purity instead of assurances that any conflicts are likely to be insignificant are foolish. I think.