Reviewer’s report

Title: Ethical values supporting the disclosure of incidental and secondary findings in clinical genomic testing: a qualitative study

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Reviewer: Katherine Saylor

Reviewer's report:

Title:

Autonomy, non-maleficence and beneficence as guiding values for the reporting of incidental and secondary findings in genomic testing: a qualitative study

Summary:

Saelaert and co-authors report how professionals at Belgian medical genetics centers justify their personal opinions and center policies about reporting incidental or secondary genetics findings to patients. The authors conducted focus groups that included clinical geneticists, laboratory geneticists, genetic counselors, and other professionals, and analyzed transcripts thematically to identify instances where participants discussed bioethical principles. The authors found that participants appealed to patient autonomy to justify the right to know and the right not to know (including IF opt-out policies), beneficence to justify mandatory reporting of actionable incidental findings, and non-maleficence to justify not seeking or reporting secondary findings. The authors describe how participants adjudicate conflicts between these principles, in particular to justify mandatory IF reporting despite the violation of autonomy. In the discussion, the authors characterize genetics center professionals justification of mandatory reporting as epistemic, technological, soft paternalism.

Review:

The focus group data study combined with ethical analysis provides a valuable perspective on how ethical principles are used in practice. I hope that this study is published because I think that it is a useful combination of empirical and philosophical analysis. The study is well-situated in the literature, and the basic arguments for and against seeking and reporting ISFs are well described in the introduction. The study population and setting is relevant to understanding how real-world decisions about ISFs are made, at least by professionals in genetics clinics. Going beyond reporting and classifying what focus group participants said, the authors relate specific appeals to principles (beneficence, non-maleficence, autonomy) to broader a justification for determining which principle to follow (soft paternalism). However, the organization of the results and discussion is somewhat difficult to follow and needs reworking, and some possible policy options outside of justifying mandatory IF reporting are left unexplored.
Major comments:

1. Most participants view IFs and SFs as distinct, and the CMGs have different policies for IFs vs. SFs. But the distinction in genetic testing practice is not always obvious to me. Genetics labs have access to all ISFs once the exome is run, but they have to actively look for them. Unlike an x-ray or a karyotype (classic incidental finding scenarios), it is unlikely that clinicians will happen upon a variant in a gene they weren't specifically looking at. Unless you are considering chromosomal abnormalities or misattributed paternity, I cannot think of many common IFs that aren't actually SFs. Are there specific examples of IFs that participants discussed? In what situation would BRCA variants be IF and not SF? Sometimes, the authors write IFs when ISFs might be relevant, such as in much of the discussion. It may be that participants think they are talking about IFs but they are really talking about SFs—the authors should take a critical view.

2. Focus group participants sometimes slip into talking about reproductive utility when the focus group prompt was for adult conditions. Does this matter? Why did the authors want to restrict the conversations to adult conditions?

3. Methods:
   a. Focus groups: Provide a justification for using focus groups instead of individual interviews.
   b. Participant recruitment: Who specifically was approached at the Belgian College of Medical Genetics-- representatives or directors from each CMG? How were participants recruited to ensure the right people from each CMG were included (describe the "purposive sampling approach")? Did the researchers try to recruit participants with certain roles, as shown in table 2 (clinical geneticist, etc.)? Did a single contact at each CMG help identify relevant people to include in the focus group? Were some participants subordinate to other participants in the same group?

4. The results are organized according to principles of beneficence, non-maleficence and autonomy, however, the discussion focuses on different types of paternalism. Consider the possibility of re-analyzing the focus group transcripts according to the types of paternalism described in the discussion.

5. Most focus group participants make statements in support of whichever policy their particular Center has (with some noted exceptions). But it is likely that the participants were not the people who made the policies. This implies to me that instead of having deep commitments to principles that give rise to opinions/policies, the participants find ways to justify existing policies with principles. I would suggest more discussion of the distinction between principles guiding policy opinions vs. using principles to rationalize existing policies.
6. Participants describe limiting panels so that they do not have to face the possibility of IFs. Is this a shirking of professional duty? Outside of genetics, primary care practitioners would typically seek all IFs that can benefit the patients' care or lead to referrals to other specialists. How do clinicians delineate the boundary of their duties?

7. The discussion focuses almost entirely on mandatory reporting of IFs. However, the authors should also address to the right to know SFs and whether non-maleficence or justice overrides that autonomy-based right.

8. Related to 6, can the authors propose a hierarchy of values that CMG participants use? It seems like autonomy to not know is paramount if patients were fully competent, but since we assume they are not, then beneficence of reporting IFs trumps. Non-maleficence is thought to be relevant to SFs that haven't been observed, but not to IFs that have been observed. Autonomy related to the right to know SFs is overruled by justice concerns regarding resource costs.

9. I am struggling to understand the distinction between epistemic and soft paternalism in the characterization of mandatory IF reporting. Is it "epistemic" paternalism because patients don't yet know the results and telling them improves their knowledge of their genetic predispositions? Or is it "epistemic" paternalism because patients are incompetent and don't know the value of knowing IFs? Which refers to the fact that a patient doesn't know their BRCA status, and which refers to the possibility that some patients don't know whether BRCA status matters? I think that "epistemic" refers to not having the results yet, and "soft" refers to not knowing the value. (Lines 380-406). But later, Line 457, the authors describe "epistemic competence", which indicates understanding the value of information enough to be able to make an opt-out decision. I think that incompetence regarding the value of IFs is what makes it soft paternalism rather than hard paternalism (which would be disclosing to patients who are well informed but still do not want the information). Calling it epistemic incompetence confuses the two concepts. Starting in line 380, the authors say that the intervention of disclosing IFs is an epistemic intervention — patients are given information. I encourage the authors to do more to distinguish between the epistemic intervention and the soft paternalism.

Minor comments:

1. I appreciate the critique of participants' view that wanting to know is rational and not wanting to know is emotional. (Starting line 443). I also appreciate the caveat that reporting IFs might not actually result in better clinical outcomes (line 478-493). These critiques call out the biased views of participants that dictate how they apply and prioritize principles, perhaps giving undue justification to mandatory reporting of potentially useless or harmful IFs.

2. In general, avoid passive voice. Instead, use active voice e.g. "this study empirically investigates how medical genetics professionals consider these principles... and how they resolve value conflicts".
3. There are some minor grammatical and word choice errors, so the manuscript would benefit from copy editing. For example, pg. 15 line 377: "but it is conform the recommendations…", also pg. 19 line 484: "Criticists doubt…"

4. In the abstract, the authors should state what type of "professionals" were included in the focus groups (medical genetics professionals?).

5. In the abstract, state which principles were invoked to support which clinical or policy decisions. E.g. Participants invoked respect for autonomy to support patient opt-out options, beneficence to support mandatory reporting of some IFs, and non-maleficence to support minimal reporting of SFs.

6. The ACMG only recommends opportunistic screening for significant, highly penetrant, actionable variants, so it should not be construed as recommending widespread screening (line 72 vs. line 80-82).

7. All of the statements were made by focus group participants, not the CMGs. The results are often attributed to the Centers for Medical Genetics (CMGs) rather than to individual participants or even to the focus group. It would be more accurate to write that individual participants in the focus groups stated certain opinions. Or that that the focus group participants were in consensus on something. Policies can be attributed to CMGs, but opinions, justifications, and statements should be attributed to the individual participants.

8. I would like to see the role of the participants who are quoted. For example, I would like each quote to be labeled "P8, FG3, genetic counselor". Were there any notable differences across type of participant?

9. The fact that it is "technological" paternalism seems unimportant to the justification of mandatory reporting.

10. Line 474-476: The moral harm is decreased by patients' RETROSPECTIVE approval of the epistemic intervention. While this may be true, it is possible that patients change their preferences to deal with the fact that they have the knowledge and cannot un-know it.

11. Line 524: Even if resources do not increase for genetic testing, it is likely that the costs of testing will go down and the clinical value of genetic information will go up in the future.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes
Are the conclusions drawn adequately supported by the data shown?
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Yes

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