Reviewer’s report

Title: Combining value of information analysis and ethical argumentation in decisions on participation of vulnerable patients in clinical research

Version: 0 Date: 31 Oct 2017

Reviewer: Richard Ashcroft

Reviewer’s report:

Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format.

Please overwrite this text when adding your comments to the authors.

This paper seeks to do two things. The first is to present arguments about whether a clinical trial of novel anticoagulants to treat pre-menopausal women with atrial fibrillation is ethically acceptable and economically justified. The second is to use this example as a test case for showing how a method for evaluating research proposals in ethical review can work effectively. This latter work builds on the work of Henry Richardson, a well-respected moral philosopher who has published important work in research ethics as well as in moral theory.

The paper strikes me as quite problematic. First of all, it seems to me that one can't _both_ use the method to evaluate the case _and_ use the case to justify the method. What one should do is take a case where the result is well-accepted, and show how the method works to produce the result which is accepted, only more efficiently and lucidly. And then having established the method, one can apply it to a novel case. You can't test a novel method on a novel case. You need a place to stand.

Secondly, the authors characterise the patient group in question as a "vulnerable group". The language of "vulnerable groups" is highly problematic, and there is now a very extensive literature on why this is so. The idea that women _as such_ are a vulnerable group has been very widely criticised for very many years, at least since the late 1970s, and in the recent literature I draw the authors’ attention to an important book by Francoise Baylis and others which discusses the status of women, in particular pregnant women, as research subjects very carefully.

Thirdly, it is not clear to me that the ethical arguments and the economic arguments belong in the same paper. REsearch Ethics COnmittees and IRBs rarely if ever consider economic arguments on whether a trial should proceed or not. Trial funders do consider economic arguments, as do purchasers of medicines once trialled and shown to be safe and effective. But otherwise these questions are kept separate.
It seems to me that the authors are trying to justify a trial they want to do - which is fine - but dressing this up as a novel contribution in bioethics - which it isn't, not least because it is not up to date with the scholarship.

So while there are some interesting arguments here, and I think the method has some promise, the paper needs a serious rethink before it could be considered for publication.

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?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?
4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal