Reviewer's report

Title: Deficiencies in the transfer and availability of clinical trials evidence: a survey of existing systems and standards

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Reviewer: Atle Fretheim

Reviewer's report:

The authors have prepared a comprehensive, very long report (around 10,000 words) on a complex subject. Their stated objective is to "provide an overview of the existing systems and standards supporting the various processes in which, directly or indirectly, evidence from clinical trials is used". This is an extremely ambitious goal – too ambitious in my view. The authors will need to make several important changes – I think – to turn this into a manuscript that is publishable in the traditional peer-reviewed scientific literature.

I have not numbered or categorised my comments into "major or minor compulsory revisions", since my feedback at this stage is very general and indeed "major".

Firstly, the document is not organized in a way that makes it an easy read. Clearly this is a subjective point of view (mine), but after having started reading the document 5-6 times without being able to grasp its logic or direction (and therefore starting over after reading only a couple of pages, time and time again), I strongly feel that the authors should be obliged to make an effort at presenting a) their reasoning for preparing the report, and b) their findings, in a more accessible way. My trouble with the manuscript may partly be due to my limited insights in drug-regulatory processes (and/or stupidity), but I know enough about the field to belong to what I would think is the target audience.

The first problem is: What IS the problem? Why this report? The authors argue reasonably well for the need to improve the accessibility of key information “on past decisions and clinical trials” to facilitate the process market authorization, in particular to reduce the problem of late-stage failures in drug development (supposedly to avoid waste of time and money). I understand this and I was curious to learn more about the information used by regulatory agencies in their processes, and the authors’ analysis of how this could be improved.

However, the authors expand on the scope and include information systems for dealing with data-collection during the conduct of trials (not directly relevant to drug-regulatory agencies, I would think) and to the flow of information to clinicians and patients (not relevant to regulatory agencies). These are huge, complex areas by themselves and even in the current mega-length report (for a research paper, that is), these topics cannot be more than superficially explored. Also, the authors do not present an argument for why these topics are important
– are there major problems with the current handling of information during the conduct of trials? Are there major problems with how trial-findings are communicated to clinicians and patients? I am sure there are, but the authors have not presented arguments for this in the introductory parts of the manuscript, and therefore their decision to include practically all aspects of use of clinical trials information seems a bit strange.

An illustration of the problem with the current document: The main information channel for clinical findings to the public (especially clinicians) has traditionally been "research articles" in peer-reviewed medical journals. This "system" for supporting the use of clinical trials findings is barely mentioned in the current manuscript - likely to confuse many readers. A description of this "system" is a big task in itself, and the problems with basing dissemination of trial-findings on publication in journals are many - probably enough to fill several separate manuscripts.

Thus, my first proposal is to limit the current report to the specific issue related to information flow to regulatory agencies, for two main reasons: 1) The authors have explained quite well why this is an area where there is need for enquiry, and 2) This is a manageable scope for both the authors and the readers (and would likely make it easier to prepare a report with a more logical composition). I do believe that this could be a valuable contribution – it is unclear to many (of us) on exactly what basis drug regulatory decisions are being made, and a review and constructive critique of the information sources currently available to these agencies, is indeed welcome.

I am not sure the current approach qualifies as “science”. There is no clear, practical definition of what constitutes a scientific paper, but a purely descriptive report on the currently available information systems seems to me to be on the outer margins of what I would consider “science”. I would have expected this to be published as a "working paper" or “report” from the researchers’ institution or those funding them rather than as a scientific article. However, if the authors “focus” their manuscript as I have suggested, and strengthen their analytical component, I guess it would be easier to see this (a little bit more) as “science”. Whether this is "science" or not isn’t necessarily a big deal, and the editors can also propose to publish this as a “Debate”-article instead of “Research”-article, for example – if in the end considered publishable.

I have looked more or less randomly at some of the references, and I suggest that the authors double check to ensure that the statements in the text are in fact backed by the articles/documents that are being referred to (e.g. is reference 8 the most relevant regarding the “insufficient communication of important information to patients and professionals”? – perhaps, but it is definitively not a major theme of the referenced text).

If the authors decline my suggestion, I propose a thorough critical review on their part on how they can present both 1) why their work is important and 2) their thinking and findings in a more easily accessed way – with the aim of having the reader follow the step by step logic of the text as it is being read.
However, I strongly believe that this manuscript would be hugely improved if the authors take the unpleasant decision of cutting it down dramatically, and to focus only on what seems to be the main issue: What are the current systems that are being used to access clinical trial-findings for drug regulatory agencies, and how (i.e. analysis) can these be improved? Could be a great article – perhaps not a research article (or perhaps it could be), but at least an informative, useful debate/commentary paper.

**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.