Reviewer’s report

Title: Clinical trial data reuse – overcoming complexities in trial design and data sharing

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Reviewer: Christian Ohmann

Reviewer’s report:

The topic discussed in the manuscript is certainly of major relevance for data sharing. Based upon own experiences with combining and pooling data from multiple different trials, potential hurdles, such as missing annotation, incomplete datasets and trial complexity are discussed and potential solutions addressed. Unfortunately, the manuscript cannot be accepted in its present form because it needs to be put into perspective with recent developments and the updated literature. The main points are:

1. The references about best practices for data sharing are not up to date and mis important documents (e.g. Ohmann et al., BMJ Open, 2017; Cancer Research UK with examples for good practice, https://www.cancerresearchuk.org/sites/default/files/hands_on_data_sharing_advice-_clinical.pdf). The discussion is much further than suggested in the manuscript.

2. This is similar with the discussion on benefits and risks for granting free access to such data. Here, it was recently proposed to provide different modes of access (e.g. open, managed) to cope with the different requirements (e.g. Banzi et al., Trials, 2019, 15:169, Hopkins et al., J Clin Epidemiol 2016; 70:17; Sydes et al., Trials, 2015; 16:104).

3. The reviewer agrees that detailed information about the original studies is necessary when data are combined across trials. Here, activities trying to link clinical trials with other data objects characterising the trial (e.g. study protocol, DMP, SAP, CRF, interim analysis, reports) are of major importance and should be at least mentioned (e.g. Goldacre et al., Trials, 2016; 17:184).

4. The suggestion that secondary users should collaborate closely with primary clinical trialists has been challenged by others (Ohmann et al., BMJ Open, 2017). This should at least be mentioned.

5. It can be agreed to the proposal to impose standards for data sharing but again there are already proposals in the literature, which need to be reflected.

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