Reviewer’s report

Title: Publication and non-publication of clinical trials in PTSD: an overview

Version: 0 Date: 31 Jan 2019

Reviewer: Evan Mayo-Wilson

Reviewer's report:

Overall, I thought this was an interesting study, but it's not obvious what it adds to what is already known about this issue. For example, what does it add to these studies (Ross is referenced in the discussion, the others are not referenced):

Prayle AP, Hurley MN, Smyth AR. Compliance with mandatory reporting of clinical trial results on ClinicalTrials.gov: cross sectional study. BMJ. 2012;344:d7373


or this review


The authors should say more about the limitations of their findings. For example, previous studies suggest that the publication rate for registered trials is higher than for other trials (https://jamanetwork.com/journals/jama/fullarticle/2653434), so evidence about a cohort of registered trials would not generalize to all trials. Registered trials might be unlike trials published as abstracts (e.g., https://www.ncbi.nlm.nih.gov/pubmed/30480762, which is referenced but not discussed much) or trials identified through IRBs (e.g., https://www.ncbi.nlm.nih.gov/pubmed/15161896). It is unclear how to interpret the factors associated with journal publication for registered studies, which are systematically different to unregistered studies. For example, FDAAA 2007 applies to trials of FDA regulated products (drugs, biologics, devices), and applicable trials are much more likely than non-applicable trials to be registered. Applicable trials are also more likely to be reported in biomedical journals (which are often members of ICMJE and have registration requirements) compared with non-applicable trials that are more likely to be reported in psychology and allied health journals (which are not ICMJE members and do not have registration requirements). I conducted a study
about the registration of published clinical trials in clinical psychology journals (https://psycnet.apa.org/record/2016-28697-001); starting with a cohort of published studies, we learned that most clinical trials in psychology journals weren't registered. Registered trials in clinical psychology are the exception to the rule, and most clinical psych journals don't have registration requirements to my knowledge.

The authors should clarify the research question. I could not tell from the abstract or from the methods whether the goal was to assess (1) the publication rate for registered trials or (2) the registration rate for published trials. The Results seemed inconsistent with the Objectives and Methods. One could start with a cohort of registered studies and estimate the publication rate, or one could start with cohort of publications and estimate the registration rate.

It is unclear what it means where the authors say "53 (12.1%) were not identified in ICTRP with the search terms used". Search terms should be reported, and search strategies should have been validated and consistent for all databases/portals. I couldn't follow the flow chart (Figure 1). Although it is clear that the registers were searched in 2015, it's unclear when or how the authors searched for publications. Reproducible search strategies and exact dates should be reported for all searches. Results, including the number of citations retrieved from each database, should also be reported. If the authors are interested in time to publication and other outcomes with substantial lag, then the authors should have restricted their sample to trials with completion dates long before the search for journal articles. The authors report time to event analyses, but did all trials have enough time to experience the event (i.e., publication)? Because the Methods are incomplete, it's unclear whether the methods were appropriate.

The Results describe study characteristics like planned enrollment and actual sample size. It is unclear how this information relates to the Objectives described above. For example, the comparison of planned enrollment versus actual enrollment is not mentioned in the Methods. It is unclear whether the source of this information is the trial registration, published report, or both the trial registration and the published report. When the authors say "there was no difference between number planned and number enrolled" do they mean there was no numerical difference (e.g., 200 versus 200) or there was no important difference (e.g., 200 versus 198)? Tests for significance are reported for some variables, but these analyses are not mentioned in the methods and it is unclear which analyses were pre-specified and which analyses were undertaken post hoc.

The authors mention a protocol and should report whether they followed a pre-specified protocol and statistical analysis plan. If so, where can it be found? The data extraction form, statistical code, and dataset should be made available during peer review and should be made public upon publication (if not before).

There are several technical issues the authors should address:
- In some places, the authors discuss ICTRP as if it were a database. ICTRP is a search portal, which searches ClinicalTrials.gov and EudraCT as well as the other registries mentioned (such as ISRCTN and ANZCTR). All trials registered on ClinicalTrials.gov and EudraCT should also appear when searching ICTRP. Discrepancies between search results suggest there were errors in the search strategies.

- Please define "sponsor" and "secondary sponsors". "Sponsor" is a field on ClinicalTrials.gov, and the term is defined by FDAAA 2007 and 42 CFR Part 11. It is not synonymous with "funder", and the authors don't appear to be using the term according its statutory definition.

- For the purpose of this manuscript, please clarify the difference between a "trial" and a "clinical trial". The terms are often used interchangeably, and it is unclear what distinction the authors are making. Perhaps the authors mean "study" rather than "trial" when the word is used alone?

- How did the authors distinguish hospitals from universities in Table 1? Many university hospitals register studies under their institutional accounts (e.g., Johns Hopkins University, Yale University) and I don't know how the authors could make this distinction based on the name of the sponsor.

- How did the authors determine whether results were "positive", "negative" or "mixed"? Is "negative" the same as "null"? How did the authors handle non-inferiority and equivalence trials? Are these the results in registries (ClinicalTrials.gov) or the results in journal publications? What did the authors do if the results conflicted (e.g., results in a publication were "positive" and the results on ClinicalTrials.gov were "negative")? There's plenty of evidence that these often disagree, for example: Jones CW, Keil LG, Holland WC, Caughey MC, Platts-Mills TF. Comparison of registered and published outcomes in randomized controlled trials: a systematic review. BMC Med. 2015;13:282

The background and discussion are outdated and should consider the impact of 42 CFR Part 11 and new NIH registration and reporting requirements, which came into effect after searches for this study were conducted. The authors might also wish to note that APA guidelines include registration and reporting requirements for clinical trials published in APA journals (https://www.apastyle.org/jars). The discussion should acknowledge that there have been major developments in this area that make trials from 2015 (and before) unrepresentative of current registration and results reporting practices. [I am a co-author of the APA's JARS guidelines. The authors might choose to cite JARS, or not, at their discretion.] . The following references might be useful:


NOT-OD-16-149. National Institutes of Health. NIH policy on dissemination of NIH-funded clinical trial information.


42 CFR 11. Clinical trials registration and results information submission; Final rule

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I receive funding from FDA and NIH for research about trial registration and results reporting. I have received funding from PCORI and the Laura and John Arnold Foundation (now Arnold Ventures) for studies about research transparency. I openly refer to some of my research in my review.

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