Reviewer’s report

Title: A Systematic Review and Meta-Analysis of Interventions to Increase Stroke Thrombolysis

Version: 1 Date: 02 Feb 2019

Reviewer: Dominique Cadilhac

Reviewer's report:

The aim of this paper is to provide a summary of the literature using a systematic approach on the evidence for implementation interventions that might be effective to increase use of thrombolysis in patients with acute stroke. This is an important issues given there is wide variation in practice in different parts of the world and equitable access to this treatment even with the same country can be problematic.

I have read the paper and have a number of concerns and this might be addressed by the authors. The main issue I have is that the authors have undertaken meta-analyses of very diverse interventions. Therefore, the statistics for heterogeneity are very large (e.g. I² >75%) and this means that it is inappropriate to generate pooled effect size estimates. In other words, there are large inconsistencies and variation in the studies and they may not be similar enough clinically to be sensible to meta-analyse.

Aim: refers to efficacy but this is terminology for RCTs yet their review includes a range of study types. The authors need to change this to 'effectiveness' in particular because many of the studies are undertaken in real-world settings.

Also, in the aim it is stated that the intervention approaches and settings will be describe but this wasn't covered in detail. I think the authors need to expand Table 1. included studies and provide details of each included paper in a new row and provide information such as Study location, Design, Participants, Sample size, Intervention, Control, Outcome, Adverse events, Limitations.

It would also be better if Fig 1 followed the PRISMA format as per Moher D, Int J Surg 210 8(5): 336-341

In stroke pre/post design are problematic because 'stroke onset time' (necessary to determine if people are eligible for tPA) is often recorded better in the post phase and missing data in the pre phase can create distortions.

I think this paper could be redesigned to provide more detail of what interventions have been used, etc. The authors need to be clear how their paper adds to the literature and complements any other reviews that may have been undertaken on this topic.
It should be noted as a limitation in the Discussion that often organisational interventions to improve access to thrombolysis may not be published in journal articles. For example, government policies to increase access and pre-post assessments of impact of such policies.

If their literature review was completed in 2015, then any new advances could be mentioned in the Discussion. e.g the advent of Mobile Stroke Units. See authors Grotta J et al and the PRESTO group papers.

**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.

I am able to assess the statistics

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

Acceptable

**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