Author’s response to reviews

Title: Development of a computerised decision aid for thrombolysis in acute stroke care

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Author’s response to reviews: see over
Dear Dr Waterson,

Subject: MS: 1957059418138879

Title: Development of a computerised decision aid for thrombolysis in acute stroke care

Authors: Darren Flynn, Daniel J Nesbitt, Gary A Ford, Peter McMeekin, Helen Rodgers, Christopher Price, Christian Kray and Richard G Thomson

We would like to thank the reviewers for their helpful comments on our manuscript. Please find enclosed:

• A letter that responds to each point brought up by the reviewers (references to line / page numbers refer to the revised copy of the manuscript with changes highlighted in red text)
• A copy of the revised manuscript with changes in response to reviewer comments in red text

The word count for the revised manuscript (excluding title page, abstract, competing interests, list of abbreviations, author contributions, acknowledgements, references, five figures, four tables, and three additional files) = 5,506 words.

Please do contact me if you require any further information

Yours sincerely,

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DETAILED RESPONSES TO REVIEWER COMMENTS

The reviewer comments have been reproduced below, along with our responses in red text, and where applicable changes to the original manuscript.

REVIEWER #1: Richard Lindley

Reviewer’s report:
This is an important piece of work. The authors report a staged development of a computerised decision support system for acute stroke thrombolysis. Much of the controversy regarding this intervention is about the risk – and those who have had bad experiences have probably led the ongoing campaign against this treatment (e.g. those in the discipline of Emergency Medicine in Australia). The recent letter by Roger Shinton in the Lancet is further evidence that this conflict has not been resolved. The decision support system has clear face validity and this work describes the acceptability and early utility of the support tool by clinicians and patients and relatives.
Authors’ Response: We thank the reviewer for his positive comments on the importance of our manuscript.

1) Is the question posed by the authors well defined?
Yes.
This work is important as the explanation of risks and benefits are not straightforward, ischaemic stroke is common and often fatal or disabling, and the balance of risks and benefits remain controversial, even amongst clinicians. A simple, validated clinician support tool would be an important advance in emergency medicine.

Authors’ Response: We thank the reviewer for his positive comments on the need for the tool described in our manuscript.

2) Are the methods appropriate and well described?
The mixed methodology is appropriate for the work described. I note that the lead author performed the qualitative interviews and was the only researcher to analyse the transcripts. This could lead to bias as it is usual to have two independent analyses of transcripts for qualitative work. This potential weakness should be discussed. The authors should carefully review the content of the “Methods” section and consider how much content could be moved to the Results section without losing the “story” of the development. I note that a lot of the Methods section is actually your results.

Authors’ Response: Please see our response to comment 6 below regarding a single analyst performing the analysis of interviews. We have also reviewed the content of the methods sections, and we have moved details of the exploratory work to the introduction (and made a small amendment to our objectives (p7, line 9 - “informed by our initial exploratory work”). Specific sub-sections have been inserted to more clearly demarcate each phase of the development work, and all references to the results of the development phases (decision analytic model, workshops) have also been moved to corresponding sub-sections in the results.

3) Are the data sound?
Please see above.
Minor essential revision: Given the clear expertise of the authors in software development you should state the qualifications of the computer programmer and provide some details in the results section (for example, a computer sciences graduate with x years programming experience wrote the software, spending approximately y hours programming time on the project). It is good to have sufficient detail in your paper to allow replication and we need to know what your resources were in any replication.

Authors’ Response: On page 10, lines 6-9 of the methods sub-section (Development of alpha prototype), we have added details of the computer scientist’s experience along with the estimated total number of hours work need to conduct the programing to develop the alpha prototype: One of the authors (DN), a computing science graduate with 6 years of programming experience (with support from a senior computing scientist, CK) developed the software (spending approximately 10 weeks [370 hours] to develop the alpha prototype of COMPASS.

4) Does the manuscript adhere to the relevant standards for reporting and data deposition?
Please see above.

Authors’ Response: Please see our response to comment 2 above.
5) **Are the discussion and conclusions well balanced and adequately supported by the data?**

There are areas where this can be improved, see section 6.

**Authors’ Response: Please see our responses to comment 6 below.**

6) **Are the limitations of the work clearly stated?**

Minor essential revision: The authors discuss the small numbers. They should also acknowledge that the analysis of the interviews was performed by a single analyst, who may have introduced some biases, given the nature of the project. The need for ongoing adjustment of the support tool was discussed. This is very relevant as new data (Emerson et al Lancet 2014) will change the underlying assumptions in the tool.

**Authors’ Response:** We acknowledge the potential bias that may be introduced by analysis performed by a single author, and have added the following text on page 24, lines 16-20 of the revised manuscript. “Analysis of the interviews was also performed by a single author (DF), although any potential bias was minimised by engaging the other authors in the role of peer reviewers/debriefers (i.e., emerging themes were discussed within group meetings) to ensure the conceptual interpretations were a credible interpretation of the participants’ experiences.”

7) **Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?**

Yes.

8) **Do the title and abstract accurately convey what has been found?**

The abstract would benefit from major revision:

**Minor essential revisions:**

Page 2, line 8: you should add “by clinicians to patients/relatives”

Line 9, “using mixed methods we developed a computerised decision tool in an iterative staged process. We then tested the tool in simulated situations with final testing in real life stroke thrombolysis decisions in hospitals”.

I would recommend moving the text: “COMPASS 13 expresses predicted outcomes (bleeding complications, death, and extent of disability) with 14 and without thrombolysis, presented numerically (percentages and natural frequencies) and 15 graphically (pictographs, bar graphs and flowcharts)” currently in the Methods section of the abstract to the Results section.

Remove the duplicated sentence: No adverse effects of use of COMPASS were reported.

In Conclusions, I suggest deleting the text: “A mixed-methods feasibility study provided evidence that COMPASS may support clinicians to assess the value of treating individual stroke patients with thrombolysis, and may enhance patients and their relatives’ understanding of clinical outcome probabilities on benefits/risks of thrombolysis.”, and merely state that “Our structured development process led to the development of a gamma prototype computerized decision support tool. Initial evaluation has demonstrated reasonable acceptability amongst patients, relatives and clinicians. The impact of COMPASS on clinical outcomes requires wider prospective evaluation in clinical settings.”

**Authors’ Response:** We have amended the abstract (pp2-3) in accordance with the reviewer’s comments in the revised manuscript.
9) Is the writing acceptable?
Minor essential revision: I think the Method section could be shortened, with more “results” placed in the results section. Overall, more succinct writing could reduce the length of the manuscript.

Authors’ Response: We have shortened the methods section in response to the reviewer’s comment – please see our response to comment 2 above.

REVIEWER #2: Patrick Waterson

In general, I found this to be a well written and interesting paper. My main gripe is that it should be scaled down to be called something like ‘a preliminary (exploratory etc) study’. Your sample size is quite small, particularly as it relates to patients and relatives. That said, I think its worth publishing, but needs a revision.

Authors’ Response: We clearly acknowledge that our study has a small sample size and refer to it as a feasibility study. In our view, this reflects the preliminary nature of our work and in the discussion we emphasise the need for wider prospective evaluation of the Gamma prototype with larger samples.

- Could you help the non-medical reader by explain what is meant by ‘thrombolysis’ (I felt myself reaching for Wikipedia – never a good sign)

Authors’ Response: Thrombolysis refers to the breakdown of blood clots using pharmacological agents; commonly called ‘clot-busting drugs’. This has been added to introduction (page 1, lines 2-3) for the purposes of clarity.

- In general the language and style of the paper is very medical (not surprising I suppose given the authorship), but I would have thought a more expository style might help the reader to see the real worth of what you have done – can you simplify the language – maybe give it to a non-medical person to read and then look at their comments?

Authors’ Response: We thank the reviewer for highlighting the need to address specialist language to improve clarity, and we have wherever possible fully defined technical terminology in terms appropriate to the journal audience. We have endeavoured to address this throughout the manuscript, in particular in the introduction section (p4, paragraph 1; page 5, paragraph 1) by providing definitions of the following medical terminology:

- Acute ischaemic stroke
- Thrombolysis
- Symptomatic intracranial haemorrhage
- Door to needle time

- Page 4 – can you elaborate on what the ‘physician-related factors’ were

Authors’ Response: We have added the following text to page 5 (lines 3-5) “such as uncertainty about effectiveness, apprehensions about increased risk of SICH, and unresolved issues on relative contraindications for treatment
- Page 7 – ethnographic work – this would drive my sociology friends nuts – can you give more details? Ethnography has a very well documented set of research methods – a little more detail might help your establish your credibility in using the term.

Authors’ Response: We have included additional methodological detail on the ethnographic phase of the development process on pages 6 (lines 15-23) and page 7 (lines 1-6).

- Page 9, line 14 – what does ‘efficacious’ mean?

Authors’ Response: In this case it refers to efficiency of conveying probabilistic information on benefits and risks of treatment with and without thrombolysis. We have changed the word ‘efficacious’ to ‘efficient’ on page 15, line 11.

- Page 11 – delete double bracket – line 24

Authors’ Response: Done

Another general comment – your paper makes a lot of references to work you have already published – it makes it a little too self-referential – could you find the space (I know this is tough to do given word/page lengths – to explain the relation to your other work in a little more detail?

Authors’ Response: As described above, we have expanded on the methodological details of the ethnographic work and included more detail on the development process for the DAM. Full details of the DAM are presented in a sister manuscript, which has been peer-reviewed by BMC Medical Informatics and Decision Making (and revisions have been submitted with a decision on acceptance pending):

• MS: 1338577601137785 Development of a decision analytic model to support decision making and risk communication about thrombolytic treatment Peter J McMeekin Darren Flynn Gary Ford Helen Rodgers Jo Gray and Richard Thompson