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Title: Development of a nationwide out-of-hospital transfusion protocol: a modified RAND Delphi study

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Reviewer 1: Sheryl McDiarmid

Institution: Nursing, The Ottawa Hospital
General comments (author response in bold)

This manuscript summarizes a process used by group of 17 subject experts to develop 39 statements that will be used to provide guidance on the development of out-of hospital transfusion programs. The methodology is well described and is robust. The structure of the tables is particularly useful with succinct statements and corresponding rationale.

The discussion (interpretation) strengths and limitations are comprehensive. The future use of this starting document is well described.

The following comments are mainly suggestions to provide clarity of the manuscript from a reader perspective.

Page 3 Line 40 – suggest rewording from “We present a range of consensus statements which we hope will support efficient and safe OHT in CCTOs in Canada and other countries around the world” to “These consensus statements will support efficient and safe OHT in national and international critical care transport programs.”

Thank you, we agree that this change reads much better and have updated the abstract accordingly.

Page 4 Line 11 & 12 - is the use of fibrinogen or PCC being investigated generally or in patients requiring OHT?

We have clarified the sentence

‘In addition, the potential benefits of out-of-hospital administration of whole blood or blood products such as fibrinogen or prothrombin complex concentrate (PCC) in select patients are being investigated.’

Page 6 – the domains listed is there an order to them? Seems disconnected – maybe the following order would flow better and then the recommendations would need to be adjusted accordingly

1. General oversight.....
2. Initiation of OHT
3. Types of blood components
4. Storage and transport
5. Indications for and use
6. Resuscitation target
7. Delivery and monitoring of OHT

Thank you for the suggestion. The initial order of domains was actually different and the current order was suggested by the participants. As such, we are unable to change it.

Page 8 Table 1 – n=17 so probably 77 transfusion medicine specialist should be 7 and 88 from Ontario should be 8.

Yes, apologies for this oversight. Corrected now.

Is the intent for these guidelines to cover both adult and pediatric OHT? Were there pediatric specialists on the committee?

The guidelines are adult focused, we have clarified this in the limitations section. *'Finally, we did not provide any specific guidance on the pediatric population and no pediatric specialists participated in this research. While many of the principles can be applied to pediatric patients, we recommend involving local pediatric specialists when creating OHT guidelines for this population.'*

Page 16 Statement 6.1 should be reworded to say Tranexamic Acid (TXA) should be given within 3 hrs with any OHT for hemorrhagic shock due to trauma.

The current formulation of the statement was agreed amongst the study participants, to reflect indication (trauma within 3hrs) and evidence support early administration within this timeframe. As such, we are unable to change it.

Reviewer 2: Dr. Tim Nutbeam

Institution: Plymouth Hospitals NHS Trust

General comments (author response in bold)

Many thanks for asking me to review this paper. It is well written, is an appropriate use of Delphi methodology and will be useful locally and internationally. This is an important area of prehospital care practice where there is a lack of current guidance / standards so this paper will be very welcome.

Minor points:

1. The use of abbreviations is not standard throughout the paper: e.g. sometimes red blood cells is written in full / sometime RBCs.

Thank you for your feedback. We have reviewed abbreviations and standardized throughout. All abbreviations are spelled out once more at the beginning of each table/box, to avoid confusion.

2. Very minor referencing considerations: use of "." before or after reference (on one occasion it is both).

We have tidied this up, thank you.

3. To understand the methodology in more detail, could you confirm / explain in the manuscript:

- If the study group contributed as SME's (or if these two groups were completely separate)

We have added this to page 6

'The study team did not participate in the written survey rounds, NB and JVVf moderated the panel discussion but did not express opinions on statements discussed.'

- Were SME's allowed to interact completely anonymously (was this an option to them)
- Were the names / roles of the SME's known to each other (I appreciate their answers were anonymised)

We added the following to pages 6 and 7, respectively

'Participants were blinded to other participants' identities and responses during the written survey rounds.'

'For technical reasons, participants' identities and responses were not blinded during the panel discussion.'

'If participants preferred to remain anonymous, they were given the option to not actively participate in the panel discussion but to review the recording/transcription and provide written feedback to the study team.'

- What steps were taken (e.g. literature review) to derive original statements for first round considerations

Please see details now included on page 6.

'The initial statements and domains were drafted by JVVF, BN, JL and SM each provided written comments and revisions, which resulted in a second draft. The third and final draft was agreed on during a meeting of the whole study team (BN, JVVF, JL, SM).'

- Which of the participants were directly recruited (through contact with the study team) and which / how many were second order (this helps to understand any recruitment bias)

Details now added on page 8.

Overall, the study team identified 21 subject experts and a further eight were nominated by potential participants.'

- Were the results "validated" in anyway (and what are the next steps with this)

There was no validation at this point but we plan to measure adherence to / implementation of the recommendations by Canadian CCTOs. See page 21

'While outside the scope of this project, we have created a national collaboration and OHT working group with all Canadian CCTOs to assure processes are aligned as much as possible across the Canadian provinces, emerging evidence and new technology is reviewed in a timely and efficient manner, and quality improvement measures are shared across organizations. This collaboration will also ideally include a pan-Canadian OHT registry with consistent data entry from all participating CCTOs for quality assurance and future research projects. This will registry will allow us to measure adherence to these recommendations by Canadian CCTOs over the coming years.'

4. Add limitation around recruitment bias / study group recruiting SME's with a similar mind set to themselves and the potential influence on results.

Thank you for raising this limitation. We have included it in the limitations section, page 22

'As with any self-selecting group of experts, there is a risk of recruiting only participants with similar opinions. Based on participants' comments during the survey rounds and panel discussion, the study team was reassured that a wide range of opinion was captured during the study process.'