PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	What fluids are given during air ambulance treatment of trauma patients in the UK, and what might this mean for the future? Results from the RESCUER observational cohort study
AUTHORS	Naumann, David; Hancox, James; Raitt, James; Smith, Iain; Crombie, Nicholas; Doughty, Heidi; Perkins, Gavin; Midwinter, Mark

VERSION 1 – REVIEW

REVIEWER	Joseph Galante UC Davis United States
REVIEW RETURNED	10-Oct-2017

GENERAL COMMENTS	This is an interesting paper. While it has a very low impact on patient care, it serves as the foundation of developing future studies. The authors were correct in their limitations. Which patients has bleeding other than trauma and which patients were traumatic brain injuries. A broader question is why did the patients get fluid at all and where should have fluid been given but was not? What were the protocols of the air ambulances to administer fluid. How many incidents of performance or quality review identified opportunities for improvement. When all of these factors are taken into account the authors may want to reconsider their number of 300 patients. Methods: Including patients with no palpable radial pulse may be a confounder if the patient had an injury to the upper extremity which cause the radial artery to become occluded.

REVIEWER	JEAN STEPHANE DAVID CHU Lyon Sud, Anesthesia and Intensive Care, Hospices Civils de Lyon, France and University Claude Bernard Lyon 1, Lyon, France
REVIEW RETURNED	04-Nov-2017

GENERAL COMMENTS	I would like to thanks you for this study because doing research in the prehospital setting is hard. My main criticism in this study is the assumption that low blood pressure mean haemorrhage and then RBC transfusion. I think low blood pressure is not enough to decide if the patient need blood because the low pressure may be in relation with other source of shock such as neurogenic shock in case of spinal injury. Using the Shock Index is probably more relevant. But the best is to determine the haemoglobin (Hgb) with a POC device such as the Hemocue.

	The design of the study should have been to determine how much patients presented with a Hgb < 7 (or 9) at hospital admission and then to define witch clinical criteria (if not using a POC) may help to predict a low hgb at admission. The risk of using only SBP is to over-transfuse the patients. Using clinical criteria has been suggested to predict massive transfusion and TIC in a recent paper that aimed to determine which prehospital criteria were associated with coagulopathy or MT (See David JS et al. Vox Sang 2017). In this paper the intensity of prehospital resuscitation were associated with both coagulopathy and TIC. No study had shown a benefit from prehospital transfusion. However, for selected patients (more severely injured), with decrease haemoglobin and severe shock and/or for the patients with longer transport times (mountain, rural area), that may be useful as well as in the military context of the tactical damage control. In the methods section, it is not clear why critical care paramedics were excluded from the study !? If "absent radial pulse" is not very precise, measuring the SBP with a automatic monitor is feasible for almost all prehospital patient, and provide accurate measure. When reading the results, almost 25 % of the patients had no fluids at all but it is not reported how much of them had severe TBI. It is also not reported how much patients had vasopressor that may be very useful to increase the pressure, especially in case of severe TBI. Otherwise you should exclude patients with TBI. It is reported that 3 % of the patients received PHBP. I suppose that means "RBC" or other products ? For these patients, how was the haemoglobin at admission ? Within the recommended range of 7-9 g/L ? Lower ? higher ? In the results, ISS, GCS and outcome should be reported. In the reference section, it is not possible to find few references such as Hooper N, Trauma 2017 ...

VERSION 1 – AUTHOR RESPONSE

REVIEWER 1:

1. This is an interesting paper. While it has a very low impact on patient care, it serves as the foundation of developing future studies. The authors were correct in their limitations. Which patients has bleeding other than trauma and which patients were traumatic brain injuries. A broader question is why did the patients get fluid at all and where should have fluid been given but was not? What were the protocols of the air ambulances to administer fluid?

Authors' response: We have now clarified the patient eligibility criteria in the revised "patient selection criteria" section of the Methods (page 8). Before embarking on this study, it was clear that there would be variations in protocols across the air ambulances in terms of giving fluids. Since we wished to apply consistent eligibility criteria to all patients in the study, we decided to apply the eligibility criteria from a well-known prehospital randomised controlled trial (the RePHILL trial). This has the benefit of having Research Ethics Committee approved eligibility criteria. Unfortunately we were not able to examine in detail the decision-making process for each eligible patient, since those data were not available. We have added this to the Limitations section (4th paragraph of Limitations, page 21), since we agree with the reviewer that these details would be of interest.

2. How many incidents of performance or quality review identified opportunities for improvement? When all of these factors are taken into account the authors may want to reconsider their number of 300 patients.

Authors' response: All air ambulance services undertake their own performance and quality reviews. This statement has been added to the "Study design and setting" paragraph of the Results section (page 7). Unfortunately, we did not have access to the specific details of such reviews from all 11 air ambulance services, and therefore did not include such details within the manuscript. We have added this as a Limitations (within the 4th paragraph of Limitations, page 21). We have also made it clear in the Conclusion (page 22) (and abstract) that "300" is just an estimation, which requires prospective investigation in order to clarify.

3. Methods: Including patients with no palpable radial pulse may be a confounder if the patient had an injury to the upper extremity which cause the radial artery to become occluded.

Authors' response: In our methodology, we made the assumption that prehospital personnel would take this into consideration within their normal practice. Within the framework of a retrospective study, we considered this assumption to be acceptable. We have now added a short statement about this within the "Patient selection criteria" paragraph of the Methods section (page 8).

REVIEWER 2:

1. I would like to thanks you for this study because doing research in the prehospital setting is hard. My main criticism in this study is the assumption that low blood pressure mean haemorrhage and then RBC transfusion. I think low blood pressure is not enough to decide if the patient need blood because the low pressure may be in relation with other source of shock such as neurogenic shock in case of spinal injury. Using the Shock Index is probably more relevant.

Authors' response: We agree with the reviewer that there are some limitations with using the blood pressure to determine transfusion, and that shock index may be of greater value. However, in the resource- and time-limited prehospital setting, it is blood pressure and pulse that are most commonly used to determine requirement for fluid resuscitation of trauma patients in the UK, as reflected by NICE Guidelines (NG 39, published Feb 2016). We deliberately used the eligibility criteria from a prehospital RCT that investigates fluid resuscitation because it has already been approved by a Research Ethics Committee, and we considered that the eligibility criteria would be as acceptable as possible within the limitations discussed. We therefore did not use shock index. This is now added to the 3rd paragraph of the Limitations section (pages 20-21), since we agree that it is a limitation.

2. But the best is to determine the haemoglobin (Hgb) with a POC device such as the Hemocue. The design of the study should have been to determine how much patients presented with a Hgb < 7 (or 9) at hospital admission and then to define witch clinical criteria (if not using a POC) may help to predict a low hgb at admission. The risk of using only SBP is to over-transfuse the patients. Using clinical criteria has been suggested to predict massive transfusion and TIC in a recent paper that aimed to determine which prehospital criteria were associated with coagulopathy or MT (See David JS et al. Vox Sang 2017). In this paper the intensity of prehospital resuscitation were associated with both coagulopathy and TIC.

Authors' response: We agree that other criteria than SBP would be ideal. However, we have used a pragmatic approach, and included patients according to current UK prehospital practice. We have discussed this limitation in the 3rd paragraph of the Limitations section (pages 20-21), and have included the reference (David JS et al. Vox Sang 2017) as suggested by the reviewer (Reference 29).

3. No study had shown a benefit from prehospital transfusion. However, for selected patients (more severely injured), with decrease haemoglobin and severe shock and/or for the patients with longer transport times (mountain, rural area), that may be useful as well as in the military context of the tactical damage control.

Authors' response: We agree that these represent special scenarios, and have now referred to this within the 5th paragraph of the limitations section (pages 21-22).

4. In the methods section, it is not clear why critical care paramedics were excluded from the study!?

Authors' response: We have revised the "Patient selection criteria" paragraph of the Methods to explain this further (page 8). We decided to use the specific eligibility criteria from an ethically-approved RCT in order to address the fact that there would be different protocols across the UK air ambulance services. The decision to only include prehospital services with PHEM-trained physicians was made on the basis that this was the setting most likely to be amenable to prehospital transfusion of blood products during the study period

5. If "absent radial pulse" is not very precise, measuring the SBP with a automatic monitor is feasible for almost all prehospital patient, and provide accurate measure.

Authors' response: In our methodology we used either SBP or pulse as criteria. All included services have access to automatic BP monitors.

6. When reading the results, almost 25 % of the patients had no fluids at all but it is not reported how much of them had severe TBI. It is also not reported how much patients had vasopressor that may be very useful to increase the pressure, especially in case of severe TBI. Otherwise you should exclude patients with TBI.

Authors' response: Unfortunately, we did not have access to specific anatomical injury details, due to the nature of prehospital data collection during the study period. We have acknowledged this a limitation within the 3rd paragraph of the Limitations section (pages 20-21).

7. It is reported that 3 % of the patients received PHBP. I suppose that means "RBC" or other products ? For these patients, how was the haemoglobin at admission ? Within the recommended range of 7-9 g/L ? Lower ? higher ? In the results, ISS, GCS and outcome should be reported.

Authors' response: All of the data within this study were gather exclusively from prehospital records, and no in-hospital records were available. This has now been clarified in the "Data collection and management" section of the Methods (page 9). We acknowledge that this is a limitation in asking further research questions. Unfortunately, ISS and GCS were not available. In the UK, ISS is assigned centrally by the Trauma and Audit Research Network (TARN) using hospital identifiers, but no hospital identifiers were available to us because we did not follow patients up once they entered the hospital. We have added this limitation to the 3rd paragraph of the Limitations study (pages 20-21).

8. In the reference section, it is not possible to find few references such as Hooper N, Trauma 2017 ...

Authors' response: We have now checked all of the references, and added the DOI numbers for the articles that have been published online (such as Hooper 2017). We have also updated Reference 8.

VERSION 2 – REVIEW

REVIEWER	Joesph Galante UC Davis Medical Center Sacramento, CA, USA
REVIEW RETURNED	19-Nov-2017

GENERAL COMMENTS	The paper still has flaws but the authors have done their best to mitigate these flaws. I am not sure about the subject selection, it may not be the group the authors are trying to study. The inability to know why a fluid was given and if there were missed opportunities could impact the authors results and conclusions. The one saving grace for this manuscript is this. In an very difficult environment (pre-hospital EMS) the authors at least have identified that normal saline (a drug with many side effects) is being used predominantly to resuscitate patients in shock. This will be a heavily cited paper for future research on pre-hospital fluid resuscitation.

REVIEWER	Jean Stephane DAVID Département d'Anesthésie Réanimation, Centre Hospitalier Lyon Sud, Hospices Civils de Lyon, F-69495 Pierre Benite cedex, France ; Faculté de Médecine Lyon Est, Université Claude Bernard Lyon 1, Lyon, France None in relation with "fluids"
REVIEW RETURNED	20-Nov-2017

GENERAL COMMENTS	Dear Authors. Thanks for the revision. However, the bibliographic style is still not in accordance with that of the BMJ Open. I would suggest also to reduce the length of both discussion and conclusion. Conclusion should be different than an abstract (no number ...)