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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

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3 **What fluids are given during air ambulance treatment of trauma patients**
4 **in the UK, and what might this mean for the future? Results from the**
5 **RESCUER observational cohort study**
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ABSTRACT

Objectives

We investigated how often intravenous fluids have been delivered during physician-led prehospital treatment of hypotensive trauma patients in the UK, and which fluids were given. These data were used to estimate the potential national requirement for prehospital blood products (PHBP) if evidence from ongoing trials were to report clinical superiority.

Setting

The Regional Exploration of Standard Care dUring Evacuation Resuscitation (RESCUER) retrospective observational study was a collaboration between 11 UK air ambulance services. Each was invited to provide up to 5 years of data, and total number of taskings during the same period.

Participants

Hypotensive trauma patients (systolic blood pressure <90mmHg or absent radial pulse), attended by a doctor.

Primary and secondary outcome measures

The primary outcome was the number of hypotensive trauma patients given prehospital fluids. Secondary outcomes were types and volumes of fluids. These data were combined with published data to estimate potential national eligibility for PHBP.

Results

Of 29,037 taskings, 729 (2.5%) were for hypotensive trauma patients attended by a physician. Half were aged 21–50 years; 73.4% were male. 537/729 (73.7%) were given fluids. 510 were

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3 given a single type of fluid; 27 received >1 type. The most common fluid was 0.9% saline,
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5 given to 486/537 (90.5%) of patients who received fluids, at a median volume of 750 (IQR
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7 300–1500) ml. 3% of patients received PHBP. Estimated projections for patients eligible for
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9 PHBP at these 11 services and in the whole UK were 313 and 794 patients per year
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11 respectively.
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15 **Conclusions**

16
17 One in 40 air ambulance taskings in the UK were manned by physicians to retrieve
18
19 hypotensive trauma patients. The most common fluid delivered was 0.9% saline. If evidence
20
21 justifies universal provision of PHBP, approximately 800 patients per year would be eligible
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23 in the UK, based on our data combined with those already published.
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28 **Keywords**

29
30 Prehospital care; trauma; emergency ambulance systems; helicopter retrieval; prehospital
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32 care, clinical management
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Strengths and limitations of this study

- This study reports data from the largest air ambulance collaboration to date, and illustrates the heterogeneity between air ambulance services in the UK with regards to provision of prehospital fluids for hypotensive trauma patients.
- The data from this study may be used by NHS leaders and blood transfusion services for regional and national resource management, by estimating the number of patients who would be eligible for prehospital blood products if evidence from ongoing trials justified universal provision throughout the UK.
- The study is limited by selection bias, since the majority of collaborating sites did not provide prehospital blood products; comparison is made with other published studies in order to place the current study data in context.

INTRODUCTION

Hypovolaemic shock following trauma may lead to reduced perfusion of vital organs, with resultant oxygen debt, tissue hypoxia, and acidosis. Intravenous resuscitation fluids are commonly given in this clinical scenario by prehospital teams during emergency evacuation to hospital, as recommended by the UK Ambulance Services Clinical Practice Guidelines and the National Institute for Health and Care Excellence (NICE).[1, 2] The principle aim of such an intervention is to restore circulatory volume and cardiac output, and improve perfusion of vital organs through increased microcirculatory flow. The most suitable fluid for prehospital resuscitation is controversial; there is no widespread consensus in the UK on which should be given to patients in this context, with a recent large prospective observational study[3] and a meta-analysis of observational studies[4] not offering a definitive answer. Some prehospital services within the UK now provide blood products in the prehospital environment,[5, 6] whereas others do not. There is some uncertainty regarding how many patients in the UK would require prehospital blood products (PHBP) if NHS leaders were to instigate universal national provision, since no nationwide assessment of fluid delivery in trauma patients has been conducted.

The UK air ambulances are autonomous charitable organisations which operate alongside National Health Service (NHS) ground ambulance services as components of major trauma networks. In addition to transporting injured patients to Trauma Units or regional Major Trauma Centres (as appropriate), air ambulances may deliver specialist prehospital emergency medical (PHEM) doctors and critical care paramedics (CCP) to incident scenes in order to provide on-scene and en-route resuscitation. These prehospital practitioners are able to deliver fluids in the prehospital treatment and evacuation of patients, but exactly what fluids have been delivered has not previously been examined in detail. There are three

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2
3 randomized controlled trials (RCTs) currently examining PHBP versus standard care
4 following trauma, from the USA, UK, and France.[7-9] In the UK, the Resuscitation with
5 PreHospItal bLood Products (RePHILL) trial is investigating whether packed red blood cells
6 and freeze-dried plasma are superior to 0.9% saline (designated as “standard care”) during
7 prehospital evacuation of trauma patients.[8] In order to place this trial into context of
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“standard care”, a study of current prehospital fluid resuscitation practice for trauma patients in the UK is warranted.

The aims of the current study were to determine how often resuscitation fluids are delivered in the UK for the prehospital treatment of hypotensive trauma patients, what types of fluids are most commonly delivered, and how these data might affect national resource planning for the universal provision of PHBP if the results of ongoing RCTs[7-9] show clinical efficacy.

METHODS

Study design and setting

All air ambulance services in the UK were invited to collaborate in a research project to investigate the delivery of prehospital fluids for trauma patients, designated as the Regional Examination of Standard Care dUring Evacuation Resuscitation (RESCUER) study, which employed a retrospective observational design. As a service evaluation using routine data, Research Ethics Committee approval was not required for this study (as confirmed by the online NHS Health Research Authority decision-making tool (<http://www.hra-decisiontools.org.uk/research/>)). Each contributing centre ensured that they had appropriate institutional approval for the use of all data.

National air ambulance research collaboration

All 22 air ambulance organisations in the UK were invited to collaborate in January 2016. First contact was made using a standardized, carbon copied email to representatives at each service, and then followed up at regular intervals by email and telephone until every centre declared that they wished to collaborate or declined. Co-ordination, communication and administration of the collaboration was undertaken at a single research centre in the West Midlands. Each centre was sent a study protocol and blank data sheet for completion. The time window for centres to respond to the request to provide data was a period of 12 months (January 2016 – December 2016). Identical blank datasheets were sent to centres in order to reduce the risk of bias or heterogeneity between centres.

Patient selection criteria

Inclusion criteria for this study were identical to the RePHILL study, an ethically approved UK-based randomised controlled trial of fluid delivery within the prehospital environment.[8] Patients were eligible if they had sustained a traumatic injury, were attended by a PHEM team (which included a physician), and had a systolic blood pressure (SBP) <90mmHg or absent radial pulse during their treatment and evacuation to hospital. These eligibility criteria were chosen because they represent the most likely criteria for the delivery of prehospital fluids by PHEM practitioners across the UK. Patients were excluded if they died before being given any fluids. Inter-hospital transfers were also excluded.

Data collection and management

Patients were identified at each air ambulance centre from contemporaneous prehospital documentation held by the ambulance services. Collaborators were asked to provide up to 5 years of retrospective data, but shorter periods were accepted, since it was anticipated that

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3 data storage and retrieval would vary between services. All centres were also asked to
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5 provide the total number of prehospital taskings during the same period in order to provide a
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7 contextual denominator. Details regarding patient characteristics included age and gender,
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9 mechanism of injury, and physiological parameters (such as blood pressure and heart rate).
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11 Details regarding medical evacuation included timings and delivery of prehospital tranexamic
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13 acid. The resuscitation fluid types and volumes were recorded for the entire prehospital
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15 period. Anonymised data were sent via password-encrypted NHS email to the central
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17 coordinator of the collaboration, and all data were combined. All data were screened by two
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19 authors (DNN and JMH) to ensure that eligibility criteria were correctly applied, and
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21 consistent between centres. These data were kept on a password-encrypted NHS computer
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23 within a restricted-entry research facility. The primary outcomes of interest were the type and
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25 volume of intravenous fluids delivered to patients during their prehospital treatment and
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27 evacuation to hospital. No power calculation was undertaken, since there were no
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29 comparisons planned at the outset of the study.
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33 For the purposes of potential future resource planning, an estimation was made for the
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35 projected number of patients per year that would be eligible for PHBP provision, on the
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37 assumption that the eligibility criteria would be the same as those in the current study. This
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39 was performed by dividing the total number of eligible patients at each site by the number of
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41 months of data provided by that site, and then multiplying by 12. These figures were added
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43 together in order to derive an approximate number of patients per year for the whole cohort
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45 of 11 sites. In order to provide an estimation for the total projected annual resource
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47 requirement for the UK, these data were combined with the data from 4 published studies[5,
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49 10-12], and then projected for all 22 UK sites on the assumption that these combined sites
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51 were a representative sample of the whole. This assumption was considered to be acceptable,
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53 since the included sites consisted of an adequate mix of urban and rural sites across the UK.
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RESULTS

National air ambulance collaboration

Of a possible 22 air ambulance services, 11 provided data for the collaboration. Four of the sites were willing to collaborate but could not be included because they did not have prehospital physicians on board, and a further 7 were unable to collaborate. Some reasons for non-collaborations were non-availability of personnel or time for research activity, desire not to duplicate data from other studies, and inadequate facilities to enable retrospective review of medical records of fluid data. All 22 sites provided basic data regarding aircraft, geographical locations, whether they carried doctors, and whether they provided prehospital blood products (Table 1).

Data collection tools

Of the 11 centres, all currently use dedicated electronic databases for data collection from air ambulance missions. One centre had also used paper records for part of their data collection. Two centres used only EasyTask (EuroAvionics Ltd, UK), two used only HEMSBase (Medic One Systems Ltd, UK), and one centre transferred from the former to the latter during the study period. Three centres used Access (Microsoft Inc, USA), and one used Filemaker (Apple Inc, USA). The remainder did not specify the electronic database that was used.

Patient characteristics

There were 29,037 taskings during the relevant study period, and patient level data was provided for 729 (2.5%) patients who fulfilled all study inclusion criteria. Figure 1 illustrates the number of patients and the date ranges provided by all centres. Their demographic and injury details are shown in Table 2.

Table 1. Summary of service provision by UK air ambulance charities

Air ambulance	Aircraft	Air Base	Carries doctor?	Carries blood products?
Cornwall Air Ambulance Trust [‡]	HMED01	Newquay	No**	No
Derbyshire, Leicester and Rutland Air Ambulance*	HMED54	East Midlands Airport	Yes	No
Devon Air Ambulance	HMED70	Exeter	Yes	No
	HMED71	Eaglescott	No	No
Dorset & Somerset Air Ambulance*	HMED10	Henstridge	Yes	Yes
East Anglian Air Ambulance*	HMED85	Norwich	Yes	No
	HMED88	Cambridge	Yes	No
Essex and Herts Air Ambulance*	HMED07	Earls Colne	Yes	No
	HMED55	North Weald	Yes	No
Great North Air Ambulance	HMED58	Langwathby	Yes	Yes
	HMED63	Durham Tees Valley	Yes	Yes
Great Western Ambulance Service*	HMED65	Filton	Yes	Yes
Hampshire & Isle of Wight Air Ambulance	HMED56	Thrupton	Yes	Yes
Kent Surrey Sussex Air Ambulance	HMED21	Marden	Yes	Yes
	HMED60	Redhill	Yes	Yes
Lincolnshire and Nottinghamshire Air Ambulance*	HMED29	RAF Waddington	Yes [†]	No
London's Air Ambulance	HMED27	Royal London/Northolt	Yes	Yes
	HMED28	Royal London/Northolt	Yes	Yes
Magpas*	HMED66	RAF Wyton	Yes	No
Midlands Air Ambulance*	HMED03	Cosford	Yes	No
	HMED06	Strensham	No	No
	HMED09	Tatenhill	No	No
North West Air Ambulance [‡]	HMED08	Blackpool Airport	No**	No
	HMED72	Barton Airfield	No**	No
	HMED75	Barton Airfield	No**	No
Scottish Ambulance Service*	HMED02	Inverness	No	No
	HMED05	Glasgow	Yes	Yes
Scotland's Charity Air Ambulance [‡]	HMED76	Perth Airport	No	No
Thames Valley Air Ambulance	HMED24	RAF Benson	Yes	Yes
Wales Air Ambulance Charitable Trust	HMED57	Swansea	Yes	Yes
	HMED59	Welshpool	Yes	Yes
	HMED61	Caernarfon	No	No
Warwickshire and Northamptonshire Air Ambulance*	HMED53	Coventry Airport	Yes	No
Wiltshire Air Ambulance [‡]	HMED22	Devizes	No	Yes
Yorkshire Air Ambulance*	HMED98	Nostell	Yes	No
	HMED99	Topcliffe	No	No

*Collaborators; [‡]Ineligible for current study; **Did not carry doctors during the majority of study period; [†]Ad hoc basis only for some of study period

Table 2. Study patient characteristics

Characteristic	Denominator*	N (%)
Male gender	683	501 (73.4)
Age category	716	
0 - 10		34 (4.7)
11 - 20		69 (9.6)
21 - 30		141 (19.7)
31 - 40		90 (12.6)
41 - 50		106 (14.8)
51 - 60		111 (15.5)
61 - 70		69 (9.6)
71 - 80		54 (7.5)
>80		42 (5.9)
Mechanism of injury	695	
Road traffic accident		
In vehicle		207 (29.8)
Pedestrian		104 (15.0)
Motorcyclist		90 (12.9)
Cyclist		35 (5.0)
Unspecified		17 (2.4)
Fall		92 (13.2)
Assault		62 (8.9)
Self-harm		39 (5.6)
Leisure and sports		14 (2.0)
Industrial		8 (1.2)
Crush		8 (1.2)
Railway		7 (1.0)
Agricultural		4 (0.6)
Impalement		3 (0.4)
Limb amputation		2 (0.3)
GSW		2 (0.3)
Dog bites		1 (0.1)
Blunt or penetrating injury	707	
Blunt		654 (92.5)
Penetrating		53 (7.5)

*indicates number with available data. Summary data are expressed using this number as a denominator.

Timing of evacuation

The time interval between the emergency call and arrival of the medical team was available for 597 patients; the median was 25 (IQR 19 – 35) minutes. The combined on-scene and transfer time (interval between arrival of medical team and arrival of patient in hospital) was available for 566 patients, and the median was 53 (IQR 39 – 73) minutes.

Resuscitation during evacuation

The initial physiological parameters that were obtained during treatment for all patients during the prehospital period (combined on-scene and transfer) are summarised in Table 3. During prehospital treatment of the patients, 342 (46.9%) patients received TXA. 192 (26.3%) patients received no fluids. Of the 537 (73.7%) patients who received at least one type of fluid, 510 (95.0%) received a single type of fluid, and 27 (5.0%) received more than one type. The types of fluid delivered to patients during their prehospital treatment and transfer to hospital are summarised in Table 4. 521 (97.0%) received crystalloid fluids only, 11 (2%) received blood products only, and 5 (1%) received both crystalloids and blood products.

Table 3. Initial physiological parameters for patients during prehospital treatment and evacuation

Parameter	1 st recorded	2 nd recorded	3 rd recorded
Systolic Blood Pressure*	82 (60 – 95)	85 (68 – 104)	91 (70 – 112)
Heart Rate*	98 (77 – 120)	97 (76 – 120)	98 (80 – 119)

*All values are given as median and interquartile range in parentheses

Of all patients that received prehospital fluids, 0.9% saline was given to 486/537 (90.5%), with a median volume administered of 750 (IQR 300–1500) ml. Figure 2 illustrates the frequency distribution of volume of 0.9% saline delivered to study patients during their

prehospital treatment and transfer, and ranged from 40ml to 4000ml. Hartmann's solution was delivered to 33/537 (6.1%) patients with a median volume of 750 (IQR 500 – 1375) ml. 24/537 (4.5%) patients were given hypertonic saline, with a median volume of 350 (IQR 162 – 350) ml.

Table 4. Type of intravenous fluid delivered to patients during their prehospital treatment and transfer to hospital.

Fluids	N (%)
Total	729 (100)
Single type of fluid	
0.9% saline	464 (63.6)
Hartmann's	31 (4.3)
PRBCs	10 (1.4)
Hypertonic saline	4 (0.5)
10% dextrose	1 (0.1)
Multiple types of fluid	
0.9% saline and hypertonic saline	20 (2.7)
0.9% saline and PRBCs	4 (0.5)
0.9% saline and Hartmann's	1 (0.1)
Hartmann's and PRBCs	1 (0.1)
PRBCs and FFP	1 (0.1)
No fluids	192 (26.3)

PRBC: packed red blood cells; FFP: fresh frozen plasma

National resource management projection

When the projected number of patients fulfilling eligibility criteria were examined for each study site, there was a wide range of eligible patients, ranging from 4 – 83 patients per year (Figure 1). The combined total number of patients that fulfilled eligibility criteria for all 11 air ambulance services was 297 per year. In addition, published data one collaborating site

(Great Western Ambulance Service (68/year),[12]) were combined with the data from the current study, giving a total of 313 patients per year for the 11 collaborating services. This figure represents the estimated number of patients per year that would require provision of blood products for 11/22 UK air ambulance services if clinical evidence from RCTs were to justify their universal provision.

In order to estimate the number of potentially eligible patients in the whole UK, further data from 3 non-collaborating sites (Thames Valley Air Ambulance (30/year);[10] Kent Surrey & Sussex Air Ambulance (80/year);[5] and London's Air Ambulance (82/year)), [11] were added to the current study data, giving a combined total of 505 patients per year from 14 services. Based on the assumption that the sample was representative of the population, the estimated projection for all 22 sites in the UK was 794 patients per year.

Table 5. Published data regarding prehospital blood transfusion by UK air ambulances

	Thames Valley Air Ambulance	Kent Surrey Sussex Air Ambulance	London's Air Ambulance	Great Western Air Ambulance
Reference	Raith <i>et al</i> [10]	Lyon <i>et al</i> [5]	Rehn <i>et al</i> [11]	Hooper <i>et al</i> [12]
RESCUER Collaborator	No	No	No	Yes
Publication type	Full text	Full text	Abstract	Abstract
Date range	Jan 14 – Feb 16	Feb 13 – Dec 14	Jan 12 – Dec 15	Aug 15 – Jul 16
N	63	147	321	62
N/year*	30	80	82	68
Age, median (range)	40 (13 - 89)	42 (9 - 92)	31	Not reported
Male, %	74.6	78	79	Not reported
Blunt injury, %	84	90	61	Not reported
Median ISS	34	30	Not reported	Not reported
ISS > 15, %	95	90	Not reported	Not reported
Units of PRBCs	Median, 2	Mean, 2.4	Median, 2 (IQR 1-3)	Not recorded

ISS: injury severity score; PRBC: packed red blood cells

*The same technique is used to calculate patients per year as described in Figure 1

DISCUSSION

The current study has found that one in every 40 air ambulance taskings in the UK during the study period was for a hypotensive trauma patient that was attended by a physician, and that three quarters of these patients were given intravenous fluids. The most common type of fluid delivered in this context was 0.9% saline, which was administered to more than 90% of those patients who received any fluid. Our findings confirm that the most common prehospital fluid for hypotensive trauma patients in the UK is 0.9% saline, at an average of 750ml. If ongoing RCTs[7-9] provide enough evidence for universal national provision of PHBP throughout the UK, the data from the current study estimate that just over 300 patients per year would fulfil eligibility criteria for these 11 air ambulance services, and just under 800 patients per year for the whole UK. The current study utilised a relatively straightforward study design to establish a national air ambulance research collaboration in the UK, and was able to examine data from 729 patients evacuated by 11 air ambulance services that supported a range of urban and rural areas. To our knowledge the largest previous air ambulance collaboration involved 9 air ambulance services in the USA.[13]

The majority of air ambulance services who collaborated in this study were those which do not provide prehospital blood products. UK NICE Guidelines support the delivery of crystalloid fluid in the absence of blood products,[2] and recent European guidelines recommend isotonic crystalloid fluid be delivered to hypotensive trauma patients.[14]

However, it is acknowledged that there are 14 helicopters in 10 services which currently provide blood products during prehospital evacuation in the UK (Table 1). The retrospective and sampling nature of the study meant that either non-participation, or newly instigated provision of blood products may not have been captured within the data sets, and that the current study findings are subject to selection bias. Nevertheless, our study was able to

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3 illustrate the regional heterogeneity amongst services, and provide an estimated projection
4 that might be utilized by NHS leaders for service provision, if results from RCTs show
5 clinical superiority of PHBP. Four of the air ambulance services that carry blood on board
6 have published data on their use of prehospital blood products (Table 5).[5, 10-12] The
7 demographics of these patients are similar to that found in our study (Table 2), with
8 predominantly adult males under the age of 50 years, and blunt trauma. The data from
9 London's Air Ambulance shows the unique case mix of this urban, trauma only service with
10 a relatively higher proportion of penetrating trauma. Most patients in these case series were
11 transfused an average of 2 units (approximately 600ml of blood). The number of patients
12 transfused per year from these 4 cohort studies ranges from 30 – 82 patients per year, which
13 is in keeping with the range of eligible patients from the RESCUER study data (Figure 1).
14 The current study sample is likely to represent the patients who would be eligible for PHBP if
15 it were considered to be the optimal evidence-based management strategy, since the
16 eligibility criteria were identical to those that have been approved by a Research Ethics
17 Committee for an ongoing RCT of prehospital blood products versus crystalloid fluids for
18 trauma.[8]
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Two randomised controlled trials have investigated the efficacy of crystalloid delivery to
trauma patients within the prehospital environment when compared to delayed delivery (in
hospital).[15, 16] The first of these reported that prehospital crystalloid delivery was
associated with higher mortality and number of complications amongst patients with
penetrating torso injury when compared to delayed delivery.[16] The second reported no
significant difference in mortality between early or delayed crystalloid infusion, but protocol
compliance was poor.[15] Further observational studies also have conflicting results
regarding prehospital crystalloid delivery, reporting equivalent,[17, 18] superior,[19] or

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3 poorer[20] outcomes when compared to no fluid delivery. The current study reports a wide
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5 range of volumes of crystalloid delivered to trauma patients—including no fluid at all—
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7 which would be based on the clinical parameters during the prehospital period, and physician
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9 judgment. It is likely that a tailored approach is required for prehospital resuscitation,[21] and
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11 specific patient groups should be investigated separately in order to determine which may
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13 benefit from prehospital crystalloid resuscitation fluid. Our study demonstrates that large
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15 scale collaboration of prehospital services in the UK is feasible, and provides a framework
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17 for such bespoke investigations to be undertaken. A UK national research collaborative is
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19 warranted in order to design and implement studies regarding outcomes following prehospital
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21 fluid resuscitation.
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26 Organisations such as the World Health Organization and the Institute of Medicine of the
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28 National Academies have reported that there is a relative lack of evidence in prehospital
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30 practice when compared to other medical specialties.[22, 23] Several factors hinder
31
32 prehospital research, most obviously the need for a small prehospital team to prioritise
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34 clinical care over the research process. Other factors may include limited data storage and
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36 access, and logistic, manning, and financial constraints. Treating research as a normal rather
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38 than extraordinary part of prehospital practice may improve study participation.[24] Recent
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40 UK collaborations have utilised research networks[25-27] and student-led associations[28] to
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42 answer questions related to clinical practice, but to our knowledge there has been no previous
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44 large-scale UK air ambulance research collaboration.
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50 **Limitations and future research**

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52 The prehospital air ambulance services in the UK are heterogenous, and each is run
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54 independently. We used the overall number of tasking as a contextual denominator but
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3 recognise that this is only an approximate measure, since some services are tasked only to
4 trauma, others attend trauma and medical emergencies, and others attend lower acuity
5 “admission avoidance” cases as well as medical and trauma emergencies. This study found
6 that each air ambulance uses its own data collection tool, and had different quantities
7 accessible for retrospective analysis. There were wide variations in data provided by each site
8 in both date ranges available, and number of patients (as seen in Figure 1). These variations
9 between sites may be due to a combination of differences in search strategies used within the
10 electronic records and genuine differences in workload between centres. Such a limitation is
11 likely to be compounded by retrospective methodology, and future studies may reduce bias
12 by using prospective data collection. Furthermore, heterogeneity may be reduced if sites
13 agree to standardise data collection, storage, and access. Although this might appear
14 straightforward, the reality is more complex due to the independent and autonomous nature
15 of air ambulance charities. Future collaborations may be optimised by adopting a centralised
16 structure, with consensus established between centres *a priori* about how to realise a true
17 national research collaborative.
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35 Some patients included in this study received intravenous hypertonic saline as a type
36 of intravenous fluid within the pre-hospital environment. Most services have well defined
37 criteria for its use relating to raised intracranial pressure and brain herniation in head injured
38 patients, and it is not used for volume resuscitation of the hypovolaemic patient.
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44 As each air ambulance service strives for improvements and optimal clinical
45 outcomes, changes and developments in service provision are commonplace. This study
46 presents the current state of the services at the time of writing, but these are subject to change
47 as practice evolves. Our estimated projections of PHBP resource requirements are likely to be
48 limited by being derived from retrospective data and the assumption that service
49 requirements will not change. Any increase or decrease in service demand will lead to under
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3 or over-estimation respectively. Furthermore, these data only represent those patients that
4
5 may require fluids following trauma, and did not include patients that require fluids for other
6
7 indications such as obstetric or gastrointestinal haemorrhage. Ongoing prospective data
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9 collection on both a regional and national scale would be required in order to optimise
10
11 resource provision for the UK.
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14 The current study did not examine clinical outcomes following fluid resuscitation.
15
16 Physician-led prehospital care often involves multiple simultaneous interventions, and the
17
18 retrospective observational design would not provide sufficiently robust data to allow
19
20 attribution of effect to interventions. Future collaborative research should focus on funded,
21
22 ethically-approved protocols that aim to investigate interventions and their outcomes. Such
23
24 work might benefit from centralised coordination by a recognised air ambulance entity such
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26 as the Air Ambulance Association.
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31 **CONCLUSION**

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34 Amongst 11 participating UK air ambulance services that carry physicians, there were 29,037
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36 total taskings, of which 2.5% retrieved hypotensive trauma patients. Of these, three-quarters
37
38 were given intravenous fluids. The most common fluid type in this context was 0.9% saline,
39
40 with a median volume of 750ml. There is heterogeneity amongst UK services, with just under
41
42 half currently providing prehospital either blood products or crystalloid fluids, and the
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44 remainder providing crystalloid fluids only. If randomised controlled trials report clinical
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46 superiority of prehospital blood products for trauma patients, and universal provision is
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48 planned by NHS leaders, we estimate that just over 300 patients per year would require these
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50 within the 11 air ambulance services sampled, and just under 800 patients per year in the
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52 whole UK.
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Contributors

DNN, IMS, NC, and MJM conceived, designed and developed the study protocol. DNN and JMH facilitated the multicentre collaboration. DNN, JMH, NC, and all RESCUER collaborators performed data collection. DNN and JMH combined and cleaned data from all sites in the study. DNN, JMH, JR, IMS, HD, and GP analysed and interpreted the data. The manuscript was written by DNN, and was critically appraised by JHM, JR, IMS, NC, GP, HD, and MJM. Further appraisal and revisions were made by all RESCUER collaborators for the final version of the manuscript.

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Competing interests

All authors declare that they have no competing interests. DNN, JMH, IS, NC, GP, HD, and MJM are investigators in the RePHILL (Resuscitation with PreHospItaL bLood Products) study, a multi-centre randomised controlled trial of prehospital blood product administration versus standard care for traumatic haemorrhage.

Patient consent

Not applicable

Ethics approval

As a service evaluation using routine data, Research Ethics Committee approval was not required for this study (as confirmed by the online NHS Health Research Authority decision-making tool (<http://www.hra-decisiontools.org.uk/research/>)). Each contributing centre ensured that they had appropriate institutional approval for the use of all data.

Data sharing statement

No extra data are available.

References

1. Brown SN, Kumar D, Millins M, Mark J, Association of Ambulance Chief E, Joint Royal Colleges Ambulance Liaison C, et al. UK ambulance services clinical practice guidelines 20162016.
2. National Clinical Guideline C. National Institute for Health and Care Excellence: Clinical Guidelines. Major Trauma: Assessment and Initial Management. London: National Institute for Health and Care Excellence (UK)
Copyright (c) National Clinical Guideline Centre, 2016.; 2016.

- 1
2
3 3. Holcomb JB, Swartz MD, DeSantis SM, Greene TJ, Fox EE, Stein DM, et al.
4
5 Multicenter Observational Prehospital Resuscitation on Helicopter Study (PROHS). *J*
6
7 *Trauma Acute Care Surg* 2017.
- 8
9 4. Smith IM, James RH, Dretzke J, Midwinter MJ. Prehospital Blood Product
10
11 Resuscitation for Trauma: A Systematic Review. *Shock* 2016;46(1):3-16.
- 12
13 5. Lyon RM, de Sausmarez E, McWhirter E, Wareham G, Nelson M, Matthies A, et al.
14
15 Pre-hospital transfusion of packed red blood cells in 147 patients from a UK helicopter
16
17 emergency medical service. *Scand J Trauma Resusc Emerg Med* 2017;25(1):12.
- 18
19 6. Lockey DJ, Weaver AE, Davies GE. Practical translation of hemorrhage control
20
21 techniques to the civilian trauma scene. *Transfusion* 2013;53 Suppl 1:17s-22s.
- 22
23 7. Brown JB, Guyette FX, Neal MD, Claridge JA, Daley BJ, Harbrecht BG, et al.
24
25 Taking the Blood Bank to the Field: The Design and Rationale of the Prehospital Air Medical
26
27 Plasma (PAMPer) Trial. *Prehosp Emerg Care* 2015;19(3):343-50.
- 28
29 8. Slinn G. A study comparing pre-hospital administration of packed red blood cells and
30
31 freeze-dried plasma with administration of normal saline in patients with low blood pressure
32
33 after major injuries [Available from: <http://isrctn.com/ISRCTN62326938>.]
- 34
35 9. Jost D, Lanoe V. Pre-hospital Administration of Lyophilized Plasma for Post-
36
37 traumatic Coagulopathy Treatment (PREHO-PLYO) Bethesda: National Institutes of
38
39 Health2017 [Available from: <https://clinicaltrials.gov/ct2/show/NCT02736812>.]
- 40
41 10. Raitt JE, Norris-Cervetto E, Hawksley O. A report of two years of pre-hospital blood
42
43 transfusions by Thames Valley Air Ambulance. *Trauma*;0(0):1460408617706388.
- 44
45 11. Rehn M, Weaver A, Eshelby S, Lockey D. London's Air Ambulance: 3 year
46
47 experience with pre-hospital transfusion. *Resuscitation*;96:156.
- 48
49 12. Hooper N, Baskerville M, Pynn HJ, Hooper TJ. Pre-hospital Blood – Developing a
50
51 Service. *Trauma* 2017;19(3):234.
- 52
53
54
55
56
57
58
59
60

- 1
2
3 13. Holcomb JB, Swartz MD, DeSantis SM, Greene TJ, Fox EE, Stein DM, et al.
4
5 Multicenter observational prehospital resuscitation on helicopter study. *J Trauma Acute Care*
6
7 *Surg* 2017;83(1 Suppl 1):S83-S91.
8
- 9 14. Rossaint R, Bouillon B, Cerny V, Coats TJ, Duranteau J, Fernandez-Mondejar E, et
10
11 al. The European guideline on management of major bleeding and coagulopathy following
12
13 trauma: fourth edition. *Crit Care* 2016;20:100.
14
- 15 15. Turner J, Nicholl J, Webber L, Cox H, Dixon S, Yates D. A randomised controlled
16
17 trial of prehospital intravenous fluid replacement therapy in serious trauma. *Health Technol*
18
19 *Assess* 2000;4(31):1-57.
20
- 21 16. Bickell WH, Wall MJ, Jr., Pepe PE, Martin RR, Ginger VF, Allen MK, et al.
22
23 Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso
24
25 injuries. *N Engl J Med* 1994;331(17):1105-9.
26
- 27 17. Kaweski SM, Sise MJ, Virgilio RW. The effect of prehospital fluids on survival in
28
29 trauma patients. *J Trauma* 1990;30(10):1215-8; discussion 8-9.
30
- 31 18. Cayten CG, Murphy JG, Stahl WM. Basic life support versus advanced life support
32
33 for injured patients with an injury severity score of 10 or more. *J Trauma* 1993;35(3):460-6;
34
35 discussion 6-7.
36
- 37 19. Hampton DA, Fabricant LJ, Differding J, Diggs B, Underwood S, De La Cruz D, et
38
39 al. Prehospital intravenous fluid is associated with increased survival in trauma patients. *J*
40
41 *Trauma Acute Care Surg* 2013;75(1 Suppl 1):S9-15.
42
- 43 20. Haut ER, Kalish BT, Cotton BA, Efron DT, Haider AH, Stevens KA, et al.
44
45 Prehospital intravenous fluid administration is associated with higher mortality in trauma
46
47 patients: a National Trauma Data Bank analysis. *Ann Surg* 2011;253(2):371-7.
48
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 21. Geeraedts LM, Jr., Pothof LA, Caldwell E, de Lange-de Klerk ES, D'Amours SK.
4
5 Prehospital fluid resuscitation in hypotensive trauma patients: do we need a tailored
6
7 approach? *Injury* 2015;46(1):4-9.
8
- 9 22. Sasser S VM, Kellermann A, Lormand JD. Prehospital trauma care systems. Geneva:
10
11 World Health Organization, 2005.
12
- 13 23. Medicine Io. Emergency Medical Services: At the Crossroads. Washington, DC: The
14
15 National Academies Press; 2007. 310 p.
16
- 17 24. Pocock H, Deakin CD, Quinn T, Perkins GD, Horton J, Gates S. Human factors in
18
19 prehospital research: lessons from the PARAMEDIC trial. *Emerg Med J* 2016;33(8):562-8.
20
21
- 22 25. Tiboni S, Bhangu A, Hall NJ. Outcome of appendicectomy in children performed in
23
24 paediatric surgery units compared with general surgery units. *Br J Surg* 2014;101(6):707-14.
25
- 26 26. Population-based cohort study of outcomes following cholecystectomy for benign
27
28 gallbladder diseases. *Br J Surg* 2016;103(12):1704-15.
29
- 30 27. Bhangu A, Koliass AG, Pinkney T, Hall NJ, Fitzgerald JE. Surgical research
31
32 collaboratives in the UK. *Lancet* 2013;382(9898):1091-2.
33
34
- 35 28. Chapman SJ, Glasbey JC, Khatri C, Kelly M, Nepogodiev D, Bhangu A, et al.
36
37 Promoting research and audit at medical school: evaluating the educational impact of
38
39 participation in a student-led national collaborative study. *BMC Med Education* 2015;15:47.
40
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FIGURE LEGENDS

Figure 1. Date ranges and number of included patients according to anonymised collaborating site.

*Number of patients per year are derived by the number of patients divided by the number of months of data provided, multiplied by 12

Figure 2. Volumes of 0.9% saline delivered to study patients

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SITE	2011	2012	2013	2014	2015	2016	Patients per year*
A	n = 63						13
B	n = 49						11
C	n = 74						10
D		n = 14					4
E		n = 20					5
F		n = 223					83
G		n = 79					25
H		n = 39					12
I			n = 79				39
J					n = 76		79
K					n = 13		15

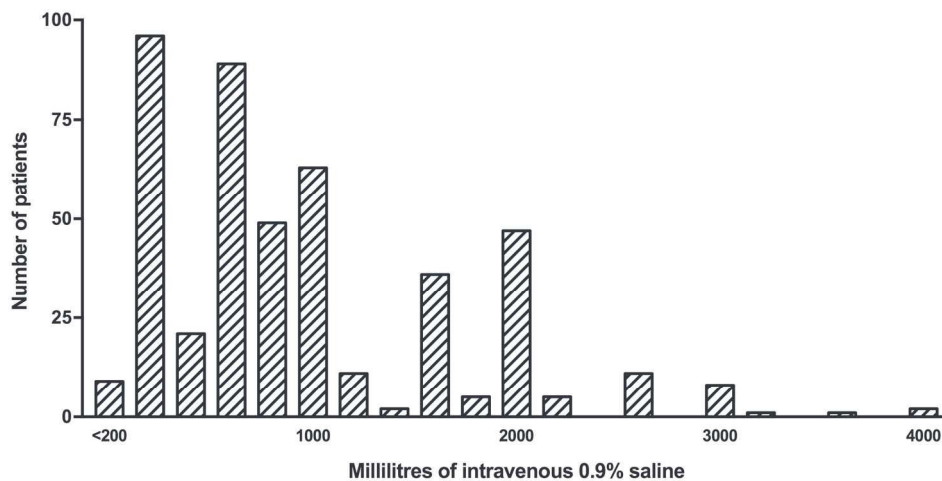


Figure 2. Volumes of 0.9% saline delivered to study patients

Figure 2. Volumes of 0.9% saline delivered to study patients

172x100mm (300 x 300 DPI)

Review only

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Title page
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Abstract
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6,7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7,8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7,8
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	8
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7,8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8,9
Bias	9	Describe any efforts to address potential sources of bias	7,8
Study size	10	Explain how the study size was arrived at	9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	9
		(b) Describe any methods used to examine subgroups and interactions	9
		(c) Explain how missing data were addressed	N/A
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	

Continued on next page

Results			Page
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10, & Table 1
		(b) Give reasons for non-participation at each stage	10
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10; Table 2
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	No follow up
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	13,14
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	All Results reported this way
		(b) Report category boundaries when continuous variables were categorized	Throughout
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18,19,20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	20
Generalisability	21	Discuss the generalisability (external validity) of the study results	19,20
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	21

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

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

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Primary Subject Heading:	Emergency medicine
Secondary Subject Heading:	Health services research, Health informatics, Public health
Keywords:	clinical management, prehospital care, helicopter retrieval, emergency ambulance systems, TRAUMA MANAGEMENT, Prehospital care

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Manuscripts

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3 **What fluids are given during air ambulance treatment of trauma patients**
4 **in the UK, and what might this mean for the future? Results from the**
5 **RESCUER observational cohort study**
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ABSTRACT

Objectives

We investigated how often intravenous fluids have been delivered during physician-led prehospital treatment of hypotensive trauma patients in the UK, and which fluids were given. These data were used to estimate the potential national requirement for prehospital blood products (PHBP) if evidence from ongoing trials were to report clinical superiority.

Setting

The Regional Exploration of Standard Care dUring Evacuation Resuscitation (RESCUER) retrospective observational study was a collaboration between 11 UK air ambulance services. Each was invited to provide up to 5 years of data, and total number of taskings during the same period.

Participants

Hypotensive trauma patients (systolic blood pressure <90mmHg or absent radial pulse), attended by a doctor.

Primary and secondary outcome measures

The primary outcome was the number of hypotensive trauma patients given prehospital fluids. Secondary outcomes were types and volumes of fluids. These data were combined with published data to estimate potential national eligibility for PHBP.

Results

Of 29,037 taskings, 729 (2.5%) were for hypotensive trauma patients attended by a physician. Half were aged 21–50 years; 73.4% were male. 537/729 (73.7%) were given fluids. 510 were

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3 given a single type of fluid; 27 received >1 type. The most common fluid was 0.9% saline,
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5 given to 486/537 (90.5%) of patients who received fluids, at a median volume of 750 (IQR
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7 300–1500) ml. 3% of patients received PHBP. Estimated projections for patients eligible for
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9 PHBP at these 11 services and in the whole UK were 313 and 794 patients per year
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11 respectively.
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16 **Conclusions**

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18 One in 40 air ambulance taskings manned by physicians retrieved hypotensive trauma
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20 patients. The most common fluid delivered was 0.9% saline. If evidence justifies universal
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22 provision of PHBP, approximately 800 patients/year would be eligible in the UK, based on
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24 our data combined with others published. Prospective investigations are required to confirm
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26 or adjust these estimations.
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31 **Keywords**

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33 Prehospital care; trauma; emergency ambulance systems; helicopter retrieval; prehospital
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35 care, clinical management
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Strengths and limitations of this study

- This study's main strength is that it reports data from the largest air ambulance collaboration to date, and might be used by NHS leaders and blood transfusion services to estimate regional and national resource requirements.
- The study is limited by selection bias, since the majority of collaborating sites did not provide prehospital blood products; comparison is made with other published studies in order to place the current study data in context.
- Since only hypotensive trauma patients were eligible for this study, no data are available regarding other patient groups that might require fluid resuscitation, such as those with gastrointestinal or obstetric haemorrhage.
- The study is further limited by unavailability of haematological data (such as haemoglobin level) within the prehospital environment, as well as limited data regarding specific injury details or severity scores.
- Patient outcomes were not examined within the limitations of this retrospective observational study, and future prospective investigations should aim to examine these in relation to specific interventions.

INTRODUCTION

Hypovolaemic shock following trauma may lead to reduced perfusion of vital organs, with resultant oxygen debt, tissue hypoxia, and acidosis. Intravenous resuscitation fluids are commonly given in this clinical scenario by prehospital teams during emergency evacuation to hospital, as recommended by the UK Ambulance Services Clinical Practice Guidelines and the National Institute for Health and Care Excellence (NICE).[1, 2] The principle aim of such an intervention is to restore circulatory volume and cardiac output, and improve perfusion of vital organs through increased microcirculatory flow. The most suitable fluid for prehospital resuscitation is controversial; there is no widespread consensus in the UK on which should be given to patients in this context, with a recent large prospective observational study[3] and a meta-analysis of observational studies[4] not offering a definitive answer. Some prehospital services within the UK now provide blood products in the prehospital environment,[5, 6] whereas others do not. There is some uncertainty regarding how many patients in the UK would require prehospital blood products (PHBP) if NHS leaders were to instigate universal national provision, since no nationwide assessment of fluid delivery in trauma patients has been conducted.

The UK air ambulances are autonomous charitable organisations which operate alongside National Health Service (NHS) ground ambulance services as components of major trauma networks. In addition to transporting injured patients to Trauma Units or regional Major Trauma Centres (as appropriate), air ambulances may deliver specialist prehospital emergency medical (PHEM) doctors and critical care paramedics (CCP) to incident scenes in order to provide on-scene and en-route resuscitation. These prehospital practitioners are able to deliver fluids in the prehospital treatment and evacuation of patients, but exactly what fluids have been delivered has not previously been examined in detail. There are three

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3 randomized controlled trials (RCTs) currently examining PHBP versus standard care
4 following trauma, from the USA, UK, and France.[7-9] In the UK, the Resuscitation with
5 PreHospItal bLood Products (RePHILL) trial is investigating whether packed red blood cells
6 and freeze-dried plasma are superior to 0.9% saline (designated as “standard care”) during
7 prehospital evacuation of trauma patients.[8] In order to place this trial into context of
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“standard care”, a study of current prehospital fluid resuscitation practice for trauma patients in the UK is warranted.

The aims of the current study were to determine how often resuscitation fluids are delivered in the UK for the prehospital treatment of hypotensive trauma patients, what types of fluids are most commonly delivered, and how these data might affect national resource planning for the universal provision of PHBP if the results of ongoing RCTs[7-9] show clinical efficacy.

METHODS

Study design and setting

All air ambulance services in the UK were invited to collaborate in a research project to investigate the delivery of prehospital fluids for trauma patients, designated as the Regional Examination of Standard Care dUring Evacuation Resuscitation (RESCUER) study, which employed a retrospective observational design. As a service evaluation using routine data, Research Ethics Committee approval was not required for this study (as confirmed by the online NHS Health Research Authority decision-making tool (<http://www.hra-decisiontools.org.uk/research/>)). Each contributing centre ensured that they had appropriate institutional approval for the use of all data. All air ambulance services undertake their own internal performance and quality reviews.

National air ambulance research collaboration

All 22 air ambulance organisations in the UK were invited to collaborate in January 2016. First contact was made using a standardized, carbon copied email to representatives at each service, and then followed up at regular intervals by email and telephone until every centre declared that they wished to collaborate or declined. Co-ordination, communication and administration of the collaboration was undertaken at a single research centre in the West Midlands. Each centre was sent a study protocol and blank data sheet for completion. The time window for centres to respond to the request to provide data was a period of 12 months (January 2016 – December 2016). Identical blank datasheets were sent to centres in order to reduce the risk of bias or heterogeneity between centres.

Patient selection criteria

Prior to the start of the study, it was considered likely that there would be heterogeneity amongst air ambulance services with regards to their site-specific protocols for fluid resuscitation eligibility. Inclusion criteria for this study were therefore chosen *a priori* to be identical to those of an ethically approved UK-based randomised controlled trial (the RePHILL study) that investigates fluid delivery within the prehospital environment.[8] Within these eligibility criteria, patients were included if they had sustained a traumatic injury, were attended by a PHEM team (which included a physician), and had a systolic blood pressure (SBP) <90mmHg or absent radial pulse during their treatment and evacuation to hospital. The assumption was made that prehospital personnel would utilise the contralateral radial pulse in the presence of an upper limb injury. 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

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3 study period. Patients were excluded if they died before being given any fluids. Inter-hospital
4 transfers were also excluded.
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8 9 **Data collection and management**

10 Patients were identified at each air ambulance centre from contemporaneous prehospital
11 documentation held by the ambulance services. Collaborators were asked to provide up to 5
12 years of retrospective data, but shorter periods were accepted, since it was anticipated that
13 data storage and retrieval would vary between services. All centres were also asked to
14 provide the total number of prehospital taskings during the same period in order to provide a
15 contextual denominator. Details regarding patient characteristics included age and gender,
16 mechanism of injury, and physiological parameters (such as blood pressure and heart rate).
17 Details regarding medical evacuation included timings and delivery of prehospital tranexamic
18 acid. The resuscitation fluid types and volumes were recorded for the entire prehospital
19 period. Only prehospital records were examined by air ambulance services, and in-hospital
20 records were not available for included patients.
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35 Anonymised data were sent via password-encrypted NHS email to the central
36 coordinator of the collaboration, and all data were combined. All data were screened by two
37 authors (DNN and JMH) to ensure that eligibility criteria were correctly applied, and
38 consistent between centres. These data were kept on a password-encrypted NHS computer
39 within a restricted-entry research facility. The primary outcomes of interest were the type and
40 volume of intravenous fluids delivered to patients during their prehospital treatment and
41 evacuation to hospital. No power calculation was undertaken, since there were no
42 comparisons planned at the outset of the study.
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52 For the purposes of potential future resource planning, an estimation was made for the
53 projected number of patients per year that would be eligible for PHBP provision, on the
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3 assumption that the eligibility criteria would be the same as those in the current study. This
4 was performed by dividing the total number of eligible patients at each site by the number of
5 months of data provided by that site, and then multiplying by 12. These figures were added
6 together in order to derive an approximate number of patients per year for the whole cohort
7 of 11 sites. In order to provide an estimation for the total projected annual resource
8 requirement for the UK, these data were combined with the data from 4 published studies[5,
9 10-12], and then projected for all 22 UK sites on the assumption that these combined sites
10 were a representative sample of the whole. This assumption was considered to be acceptable,
11 since the included sites consisted of an adequate mix of urban and rural sites across the UK.
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29 **RESULTS**

30 **National air ambulance collaboration**

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33 Of a possible 22 air ambulance services, 11 provided data for the collaboration. Four of the
34 sites were willing to collaborate but could not be included because they did not have
35 prehospital physicians on board, and a further 7 were unable to collaborate. Some reasons for
36 non-collaborations were non-availability of personnel or time for research activity, desire not
37 to duplicate data from other studies, and inadequate facilities to enable retrospective review
38 of medical records of fluid data. All 22 sites provided basic data regarding aircraft,
39 geographical locations, whether they carried doctors, and whether they provided prehospital
40 blood products (Table 1).
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Data collection tools

Of the 11 centres, all currently use dedicated electronic databases for data collection from air ambulance missions. One centre had also used paper records for part of their data collection.

Two centres used only EasyTask (EuroAvionics Ltd, UK), two used only HEMSBase (Medic One Systems Ltd, UK), and one centre transferred from the former to the latter during the study period. Three centres used Access (Microsoft Inc, USA), and one used Filemaker (Apple Inc, USA). The remainder did not specify the electronic database that was used.

Patient characteristics

There were 29,037 taskings during the relevant study period, and patient level data was provided for 729 (2.5%) patients who fulfilled all study inclusion criteria. Figure 1 illustrates the number of patients and the date ranges provided by all centres. Their demographic and injury details are shown in Table 2.

Timing of evacuation

The time interval between the emergency call and arrival of the medical team was available for 597 patients; the median was 25 (IQR 19 – 35) minutes. The combined on-scene and transfer time (interval between arrival of medical team and arrival of patient in hospital) was available for 566 patients, and the median was 53 (IQR 39 – 73) minutes.

Table 1. Summary of service provision by UK air ambulance charities

Air ambulance	Aircraft	Air Base	Carries doctor?	Carries blood products?
Cornwall Air Ambulance Trust [‡]	HMED01	Newquay	No**	No
Derbyshire, Leicester and Rutland Air Ambulance*	HMED54	East Midlands Airport	Yes	No
Devon Air Ambulance	HMED70	Exeter	Yes	No
	HMED71	Eaglescott	No	No
Dorset & Somerset Air Ambulance*	HMED10	Henstridge	Yes	Yes
East Anglian Air Ambulance*	HMED85	Norwich	Yes	No
	HMED88	Cambridge	Yes	No
Essex and Herts Air Ambulance*	HMED07	Earls Colne	Yes	No
	HMED55	North Weald	Yes	No
Great North Air Ambulance	HMED58	Langwathby	Yes	Yes
	HMED63	Durham Tees Valley	Yes	Yes
Great Western Ambulance Service*	HMED65	Filton	Yes	Yes
Hampshire & Isle of Wight Air Ambulance	HMED56	Thrupton	Yes	Yes
Kent Surrey Sussex Air Ambulance	HMED21	Marden	Yes	Yes
	HMED60	Redhill	Yes	Yes
Lincolnshire and Nottinghamshire Air Ambulance*	HMED29	RAF Waddington	Yes [†]	No
London's Air Ambulance	HMED27	Royal London/Northolt	Yes	Yes
	HMED28	Royal London/Northolt	Yes	Yes
Magpas*	HMED66	RAF Wyton	Yes	No
Midlands Air Ambulance*	HMED03	Cosford	Yes	No
	HMED06	Strensham	No	No
	HMED09	Tatenhill	No	No
North West Air Ambulance [‡]	HMED08	Blackpool Airport	No**	No
	HMED72	Barton Airfield	No**	No
	HMED75	Barton Airfield	No**	No
Scottish Ambulance Service*	HMED02	Inverness	No	No
	HMED05	Glasgow	Yes	Yes
Scotland's Charity Air Ambulance [‡]	HMED76	Perth Airport	No	No
Thames Valley Air Ambulance	HMED24	RAF Benson	Yes	Yes
Wales Air Ambulance Charitable Trust	HMED57	Swansea	Yes	Yes
	HMED59	Welshpool	Yes	Yes
	HMED61	Caernarfon	No	No
Warwickshire and Northamptonshire Air Ambulance*	HMED53	Coventry Airport	Yes	No
Wiltshire Air Ambulance [‡]	HMED22	Devizes	No	Yes
Yorkshire Air Ambulance*	HMED98	Nostell	Yes	No
	HMED99	Topcliffe	No	No

*Collaborators; [‡]Ineligible for current study; **Did not carry doctors during the majority of study period; [†]Ad hoc basis only for some of study period

Table 2. Study patient characteristics

Characteristic	Denominator*	N (%)
Male gender	683	501 (73.4)
Age category	716	
0 - 10		34 (4.7)
11 - 20		69 (9.6)
21 - 30		141 (19.7)
31 - 40		90 (12.6)
41 - 50		106 (14.8)
51 - 60		111 (15.5)
61 - 70		69 (9.6)
71 - 80		54 (7.5)
>80		42 (5.9)
Mechanism of injury	695	
Road traffic accident		
In vehicle		207 (29.8)
Pedestrian		104 (15.0)
Motorcyclist		90 (12.9)
Cyclist		35 (5.0)
Unspecified		17 (2.4)
Fall		92 (13.2)
Assault		62 (8.9)
Self-harm		39 (5.6)
Leisure and sports		14 (2.0)
Industrial		8 (1.2)
Crush		8 (1.2)
Railway		7 (1.0)
Agricultural		4 (0.6)
Impalement		3 (0.4)
Limb amputation		2 (0.3)
GSW		2 (0.3)
Dog bites		1 (0.1)
Blunt or penetrating injury	707	
Blunt		654 (92.5)
Penetrating		53 (7.5)

*indicates number with available data. Summary data are expressed using this number as a denominator.

Resuscitation during evacuation

The initial physiological parameters that were obtained during treatment for all patients during the prehospital period (combined on-scene and transfer) are summarised in Table 3. During prehospital treatment of the patients, 342 (46.9%) patients received TXA. 192 (26.3%) patients received no fluids. Of the 537 (73.7%) patients who received at least one type of fluid, 510 (95.0%) received a single type of fluid, and 27 (5.0%) received more than one type. The types of fluid delivered to patients during their prehospital treatment and transfer to hospital are summarised in Table 4. 521 (97.0%) received crystalloid fluids only, 11 (2%) received blood products only, and 5 (1%) received both crystalloids and blood products.

Table 3. Initial physiological parameters for patients during prehospital treatment and evacuation

Parameter	1 st recorded	2 nd recorded	3 rd recorded
Systolic Blood Pressure*	82 (60 – 95)	85 (68 – 104)	91 (70 – 112)
Heart Rate*	98 (77 – 120)	97 (76 – 120)	98 (80 – 119)

*All values are given as median and interquartile range in parentheses

Of all patients that received prehospital fluids, 0.9% saline was given to 486/537 (90.5%), with a median volume administered of 750 (IQR 300–1500) ml. Figure 2 illustrates the frequency distribution of volume of 0.9% saline delivered to study patients during their prehospital treatment and transfer, and ranged from 40ml to 4000ml. Hartmann's solution was delivered to 33/537 (6.1%) patients with a median volume of 750 (IQR 500 – 1375) ml. 24/537 (4.5%) patients were given hypertonic saline, with a median volume of 350 (IQR 162 – 350) ml.

Table 4. Type of intravenous fluid delivered to patients during their prehospital treatment and transfer to hospital.

Fluids	N (%)
Total	729 (100)
Single type of fluid	
0.9% saline	464 (63.6)
Hartmann's	31 (4.3)
PRBCs	10 (1.4)
Hypertonic saline	4 (0.5)
10% dextrose	1 (0.1)
Multiple types of fluid	
0.9% saline and hypertonic saline	20 (2.7)
0.9% saline and PRBCs	4 (0.5)
0.9% saline and Hartmann's	1 (0.1)
Hartmann's and PRBCs	1 (0.1)
PRBCs and FFP	1 (0.1)
No fluids	192 (26.3)

PRBC: packed red blood cells; FFP: fresh frozen plasma

National resource management projection

When the projected number of patients fulfilling eligibility criteria were examined for each study site, there was a wide range of eligible patients, ranging from 4 – 83 patients per year (Figure 1). The combined total number of patients that fulfilled eligibility criteria for all 11 air ambulance services was 297 per year. In addition, published data one collaborating site (Great Western Ambulance Service (68/year),[12]) were combined with the data from the current study, giving a total of 313 patients per year for the 11 collaborating services. This figure represents the estimated number of patients per year that would require provision of blood products for 11/22 UK air ambulance services if clinical evidence from RCTs were to justify their universal provision.

In order to estimate the number of potentially eligible patients in the whole UK, further data from 3 non-collaborating sites (Thames Valley Air Ambulance (30/year);[10] Kent Surrey & Sussex Air Ambulance (80/year);[5] and London's Air Ambulance (82/year)), [11] were added to the current study data, giving a combined total of 505 patients per year from 14 services. Based on the assumption that the sample was representative of the population, the estimated projection for all 22 sites in the UK was 794 patients per year.

Table 5. Published data regarding prehospital blood transfusion by UK air ambulances

	Thames Valley Air Ambulance	Kent Surrey Sussex Air Ambulance	London's Air Ambulance	Great Western Air Ambulance
Reference	Raïtt <i>et al</i> [10]	Lyon <i>et al</i> [5]	Rehn <i>et al</i> [11]	Hooper <i>et al</i> [12]
RESCUER Collaborator	No	No	No	Yes
Publication type	Full text	Full text	Abstract	Abstract
Date range	Jan 14 – Feb 16	Feb 13 – Dec 14	Jan 12 – Dec 15	Aug 15 – Jul 16
N	63	147	321	62
N/year*	30	80	82	68
Age, median (range)	40 (13 - 89)	42 (9 - 92)	31	Not reported
Male, %	74.6	78	79	Not reported
Blunt injury, %	84	90	61	Not reported
Median ISS	34	30	Not reported	Not reported
ISS > 15, %	95	90	Not reported	Not reported
Units of PRBCs	Median, 2	Mean, 2.4	Median, 2 (IQR 1-3)	Not recorded

ISS: injury severity score; PRBC: packed red blood cells

*The same technique is used to calculate patients per year as described in Figure 1

DISCUSSION

The current study has found that one in every 40 air ambulance taskings during the study period was for a hypotensive trauma patient that was attended by a physician, and that three quarters of these patients were given intravenous fluids. The most common type of fluid delivered in this context was 0.9% saline, which was administered to more than 90% of those patients who received any fluid. Our findings confirm that the most common prehospital fluid for hypotensive trauma patients in the UK is 0.9% saline, at an average of 750ml. If ongoing RCTs[7-9] provide enough evidence for universal national provision of PHBP throughout the UK, the data from the current study estimate that just over 300 patients per year would fulfil eligibility criteria for these 11 air ambulance services, and just under 800 patients per year for the whole UK. The current study utilised a relatively straightforward study design to establish a national air ambulance research collaboration in the UK, and was able to examine data from 729 patients evacuated by 11 air ambulance services that supported a range of urban and rural areas. To our knowledge the largest previous air ambulance collaboration involved 9 air ambulance services in the USA.[13]

The majority of air ambulance services who collaborated in this study were those which do not provide prehospital blood products. UK NICE Guidelines support the delivery of crystalloid fluid in the absence of blood products,[2] and recent European guidelines recommend isotonic crystalloid fluid be delivered to hypotensive trauma patients.[14]

However, it is acknowledged that there are 14 helicopters in 10 services which currently provide blood products during prehospital evacuation in the UK (Table 1). The retrospective and sampling nature of the study meant that either non-participation, or newly instigated provision of blood products may not have been captured within the data sets, and that the current study findings are subject to selection bias. Nevertheless, our study was able to

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3 illustrate the regional heterogeneity amongst services, and provide an estimated projection
4 that might be utilized by NHS leaders for service provision, if results from RCTs show
5 clinical superiority of PHBP. Four of the air ambulance services that carry blood on board
6 have published data on their use of prehospital blood products (Table 5).[5, 10-12] The
7 demographics of these patients are similar to that found in our study (Table 2), with
8 predominantly adult males under the age of 50 years, and blunt trauma. The data from
9 London's Air Ambulance shows the unique case mix of this urban, trauma only service with
10 a relatively higher proportion of penetrating trauma. Most patients in these case series were
11 transfused an average of 2 units (approximately 600ml of blood). The number of patients
12 transfused per year from these 4 cohort studies ranges from 30 – 82 patients per year, which
13 is in keeping with the range of eligible patients from the RESCUER study data (Figure 1).
14 The current study sample is likely to represent the patients who would be eligible for PHBP if
15 it were considered to be the optimal evidence-based management strategy, since the
16 eligibility criteria were identical to those that have been approved by a Research Ethics
17 Committee for an ongoing RCT of prehospital blood products versus crystalloid fluids for
18 trauma.[8]
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Two randomised controlled trials have investigated the efficacy of crystalloid delivery to
trauma patients within the prehospital environment when compared to delayed delivery (in
hospital).[15, 16] The first of these reported that prehospital crystalloid delivery was
associated with higher mortality and number of complications amongst patients with
penetrating torso injury when compared to delayed delivery.[16] The second reported no
significant difference in mortality between early or delayed crystalloid infusion, but protocol
compliance was poor.[15] Further observational studies also have conflicting results
regarding prehospital crystalloid delivery, reporting equivalent,[17, 18] superior,[19] or

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3 poorer[20] outcomes when compared to no fluid delivery. The current study reports a wide
4 range of volumes of crystalloid delivered to trauma patients—including no fluid at all—
5 which would be based on the clinical parameters during the prehospital period, and physician
6 judgment. It is likely that a tailored approach is required for prehospital resuscitation,[21] and
7 specific patient groups should be investigated separately in order to determine which may
8 benefit from prehospital crystalloid resuscitation fluid. Our study demonstrates that large
9 scale collaboration of prehospital services in the UK is feasible, and provides a framework
10 for such bespoke investigations to be undertaken. A UK national research collaborative is
11 warranted in order to design and implement studies regarding outcomes following prehospital
12 fluid resuscitation.
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26 Organisations such as the World Health Organization and the Institute of Medicine of the
27 National Academies have reported that there is a relative lack of evidence in prehospital
28 practice when compared to other medical specialties.[22, 23] Several factors hinder
29 prehospital research, most obviously the need for a small prehospital team to prioritise
30 clinical care over the research process. Other factors may include limited data storage and
31 access, and logistic, manning, and financial constraints. Treating research as a normal rather
32 than extraordinary part of prehospital practice may improve study participation.[24] Recent
33 UK collaborations have utilised research networks[25-27] and student-led associations[28] to
34 answer questions related to clinical practice, but to our knowledge there has been no previous
35 large-scale UK air ambulance research collaboration.
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50 **Limitations and future research**

51 The prehospital air ambulance services in the UK are heterogenous, and each is run
52 independently. We used the overall number of tasking as a contextual denominator but
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3 recognise that this is only an approximate measure, since some services are tasked only to
4 trauma, others attend trauma and medical emergencies, and others attend lower acuity
5 “admission avoidance” cases as well as medical and trauma emergencies. This study found
6 that each air ambulance uses its own data collection tool, and had different quantities
7 accessible for retrospective analysis. There were wide variations in data provided by each site
8 in both date ranges available, and number of patients (as seen in Figure 1). These variations
9 between sites may be due to a combination of differences in search strategies used within the
10 electronic records and genuine differences in workload between centres. Such a limitation is
11 likely to be compounded by retrospective methodology, and future studies may reduce bias
12 by using prospective data collection. Furthermore, heterogeneity may be reduced if sites
13 agree to standardise data collection, storage, and access. Although this might appear
14 straightforward, the reality is more complex due to the independent and autonomous nature
15 of air ambulance charities. Future collaborations may be optimised by adopting a centralised
16 structure, with consensus established between centres *a priori* about how to realise a true
17 national research collaborative.
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35 Some patients included in this study received intravenous hypertonic saline as a type
36 of intravenous fluid within the pre-hospital environment. Most services have well defined
37 criteria for its use relating to raised intracranial pressure and brain herniation in head injured
38 patients, and it is not used for volume resuscitation of the hypovolaemic patient.
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44 The amount of data available for each patient within the resource-limited prehospital
45 setting was relatively low when compared to studies within the in-hospital environment. The
46 current study is therefore limited by lack of desirable parameters such as haemoglobin, or
47 arterial blood gas parameters within the prehospital period. Furthermore, no in-hospital
48 parameters were available in the current study, since data were collected exclusively from
49 prehospital records. Detailed descriptions of injuries were not available within the framework
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3 of prehospital data collection, and injury severity scores (ISS) were not available for patients.
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5 Glasgow Coma Scales were not available, and it was unknown how many patients may have
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7 had an isolated brain injury. It is acknowledged that blood pressure and pulse are not the most
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9 ideal parameters for the decision to transfuse. There may be more sensitive and specific
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11 criteria, such as shock index or injury severity, as demonstrated in a recent large trauma
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13 registry study[29]. However, a pragmatic approach was used in order to determine patient
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15 eligibility, reflecting the practice currently used within UK prehospital services.

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18 Within the framework of a retrospective observational study, it was not possible to
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20 examine the decision-making process for each patient who was eligible for fluid
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22 resuscitation. Some eligible patients did not receive fluids, and it is likely that some patients
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24 that did not fit our inclusion criteria were given fluid resuscitation. Such uncertainty could be
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26 better addressed by prospective investigations that sought to examine real-time decision
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28 processes. Although each individual air ambulance service conducts their own internal
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30 performance and quality reviews, specific details from these were beyond the scope of the
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32 current study, and not included.

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35 As each air ambulance service strives for improvements and optimal clinical
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37 outcomes, changes and developments in service provision are commonplace. This study
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39 presents the current state of the services at the time of writing, but these are subject to change
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41 as practice evolves. Our estimated projections of PHBP resource requirements are likely to be
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43 limited by being derived from retrospective data and the assumption that service
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45 requirements will not change. Any increase or decrease in service demand will lead to under
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47 or over-estimation respectively. Furthermore, these data only represent those patients that
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49 may require fluids following trauma, and did not include patients that require fluids for other
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51 indications such as obstetric or gastrointestinal haemorrhage. It is also acknowledged that
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53 data from the current study may not necessary be applicable to selected patients, such as
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3 those more severely injured, with severe shock, with longer transport times, or in the military
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5 context of remote damage control resuscitation.
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7 The current study did not examine clinical outcomes following fluid resuscitation.
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9 Physician-led prehospital care often involves multiple simultaneous interventions, and the
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11 retrospective observational design would not provide sufficiently robust data to allow
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13 attribution of effect to interventions. Future collaborative research should focus on funded,
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15 ethically-approved protocols that aim to investigate interventions and their outcomes. Such
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17 work might benefit from centralised coordination by a recognised air ambulance entity such
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19 as the Air Ambulance Association.
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24 **CONCLUSION**

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27 Amongst 11 participating UK air ambulance services that carry physicians, there were 29,037
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29 total taskings, of which 2.5% retrieved hypotensive trauma patients. Of these, three-quarters
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31 were given intravenous fluids. The most common fluid type in this context was 0.9% saline,
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33 with a median volume of 750ml. There is heterogeneity amongst UK services, with just under
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35 half currently providing prehospital either blood products or crystalloid fluids, and the
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37 remainder providing crystalloid fluids only. If randomised controlled trials report clinical
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39 superiority of prehospital blood products for trauma patients, and universal provision is
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41 planned by NHS leaders, we estimate that just over 300 patients per year would require these
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43 within the 11 air ambulance services sampled, and just under 800 patients per year in the
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45 whole UK. These estimations require prospective investigations to confirm or adjust.
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22 **Contributors**

23
24 DNN, IMS, NC, and MJM conceived, designed and developed the study protocol. DNN and
25
26 JMH facilitated the multicentre collaboration. DNN, JMH, NC, and all RESCUER
27
28 collaborators performed data collection. DNN and JMH combined and cleaned data from all
29
30 sites in the study. DNN, JMH, JR, IMS, HD, and GP analysed and interpreted the data. The
31
32 manuscript was written by DNN, and was critically appraised by JHM, JR, IMS, NC, GP,
33
34 HD, and MJM. Further appraisal and revisions were made by all RESCUER collaborators for
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36 the final version of the manuscript.
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50 **Competing interests**

51
52 All authors declare that they have no competing interests. DNN, JMH, IS, NC, GP, HD, and
53
54 MJM are investigators in the RePHILL (Resuscitation with PreHospItaL bLood Products)
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3 study, a multi-centre randomised controlled trial of prehospital blood product administration
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5 versus standard care for traumatic haemorrhage.
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8 9 **Patient consent**

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11 Not applicable
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14 15 **Ethics approval**

16
17 As a service evaluation using routine data, Research Ethics Committee approval was not
18
19 required for this study (as confirmed by the online NHS Health Research Authority decision-
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21 making tool (<http://www.hra-decisiontools.org.uk/research/>)). Each contributing centre
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23 ensured that they had appropriate institutional approval for the use of all data.
24
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28 29 **Data sharing statement**

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31 No extra data are available.
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34 35 **References**

- 36
37 1. Joint Royal Colleges Ambulance Liaison Committee and Association of Ambulance
38
39 Chief Executives (2016) *UK Ambulance Services Clinical Practice Guidelines*
40
41 2016. Bridgwater: Class Professional Publishing.
- 42
43 2. National Clinical Guideline Centre (UK). Major Trauma: Assessment and Initial
44
45 Management. London: National Institute for Health and Care Excellence (UK); 2016 Feb.
46
47 (NICE Guideline, No. 39.) [Available from:
48
49 <https://www.ncbi.nlm.nih.gov/books/NBK344252>]
50
- 51
52 3. Holcomb JB, Swartz MD, DeSantis SM, et al. Multicenter observational prehospital
53
54 resuscitation on helicopter study. *J Trauma Acute Care Surg.* 2017;83(1 Suppl 1):S83-s91.
55
56
57
58
59

- 1
2
3 4. Smith IM, James RH, Dretzke J, et al. Prehospital Blood Product Resuscitation for
4
5 Trauma: A Systematic Review. *Shock* 2016;46(1):3-16.
6
- 7 5. Lyon RM, de Sausmarez E, McWhirter E, et al. Pre-hospital transfusion of packed red
8
9 blood cells in 147 patients from a UK helicopter emergency medical service. *Scand J Trauma*
10
11 *Resusc Emerg Med* 2017;25(1):12.
12
- 13 6. Lockey DJ, Weaver AE, Davies GE. Practical translation of hemorrhage control
14
15 techniques to the civilian trauma scene. *Transfusion* 2013;53 Suppl 1:17s-22s.
16
- 17 7. Brown JB, Guyette FX, Neal MD, et al. Taking the Blood Bank to the Field: The
18
19 Design and Rationale of the Prehospital Air Medical Plasma (PAMPer) Trial. *Prehosp Emerg*
20
21 *Care* 2015;19(3):343-50.
22
- 23 8. Smith IM, Crombie N, Bishop JR, et al. RePHILL: Protocol for a randomised
24
25 controlled trial of pre-hospital blood product resuscitation for trauma. *Transfus Med* (in
26
27 press)
28
- 29 9. Jost D, Lanoe V. Pre-hospital Administration of Lyophilized Plasma for Post-
30
31 traumatic Coagulopathy Treatment (PREHO-PLYO) Bethesda: National Institutes of Health
32
33 2017 [Available from: <https://clinicaltrials.gov/ct2/show/NCT02736812>].
34
35
- 36 10. Raitt JE, Norris-Cervetto E, Hawksley O. A report of two years of pre-hospital blood
37
38 transfusions by Thames Valley Air Ambulance. *Trauma* 2017 doi:
39
40 10.1177/1460408617706388
41
- 42 11. Rehn M, Weaver A, Eshelby S, et al. London's Air Ambulance: 3 year experience
43
44 with pre-hospital transfusion. *Resuscitation*;96:156.
45
46
- 47 12. Hooper N, Baskerville M, Pynn HJ, et al. Pre-hospital Blood – Developing a Service.
48
49 *Trauma* 2017;19(3):234 doi: 10.1177/1460408617712136
50
51
52
53
54
55
56
57
58
59

- 1
2
3 13. Holcomb JB, Swartz MD, DeSantis SM, et al. Multicenter observational prehospital
4 resuscitation on helicopter study. *J Trauma Acute Care Surg* 2017;83:S83-S91.
5
6
- 7 14. Rossaint R, Bouillon B, Cerny V, et al. The European guideline on management of
8 major bleeding and coagulopathy following trauma: fourth edition. *Crit Care* 2016;20:100.
9
10
- 11 15. Turner J, Nicholl J, Webber L, et al. A randomised controlled trial of prehospital
12 intravenous fluid replacement therapy in serious trauma. *Health Technol Assess*
13 2000;4(31):1-57.
14
15
- 16 16. Bickell WH, Wall MJ, Jr., Pepe PE, et al. Immediate versus delayed fluid
17 resuscitation for hypotensive patients with penetrating torso injuries. *N Engl J Med*
18 1994;331(17):1105-9.
19
20
- 21 17. Kaweski SM, Sise MJ, Virgilio RW. The effect of prehospital fluids on survival in
22 trauma patients. *J Trauma* 1990;30(10):1215-8; discussion 8-9.
23
24
- 25 18. Cayten CG, Murphy JG, Stahl WM. Basic life support versus advanced life support
26 for injured patients with an injury severity score of 10 or more. *J Trauma* 1993;35(3):460-6;
27 discussion 6-7.
28
29
- 30 19. Hampton DA, Fabricant LJ, Differding J, et al. Prehospital intravenous fluid is
31 associated with increased survival in trauma patients. *J Trauma Acute Care Surg* 2013;75(1
32 Suppl 1):S9-15.
33
34
- 35 20. Haut ER, Kalish BT, Cotton BA, et al. Prehospital intravenous fluid administration is
36 associated with higher mortality in trauma patients: a National Trauma Data Bank analysis.
37 *Ann Surg* 2011;253(2):371-7.
38
39
- 40 21. Geeraedts LM, Jr., Pothof LA, Caldwell E, et al. Prehospital fluid resuscitation in
41 hypotensive trauma patients: do we need a tailored approach? *Injury* 2015;46(1):4-9.
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 22. Sasser S VM, Kellermann A, Lormand JD. Prehospital trauma care systems. Geneva:
4 World Health Organization, 2005. [Available from:
5 http://www.who.int/violence_injury_prevention/publications/services/39162_oms_new.pdf]
6
7
8
9 23. Institute of Medicine. 2007. *Emergency Medical Services: At the Crossroads*.
10 Washington, DC: The National Academies Press. doi: 10.17226/11629.
11
12
13 24. Pocock H, Deakin CD, Quinn T, et al. Human factors in prehospital research: lessons
14 from the PARAMEDIC trial. *Emerg Med J* 2016;33(8):562-8.
15
16
17 25. Tiboni S, Bhangu A, Hall NJ. Outcome of appendicectomy in children performed in
18 paediatric surgery units compared with general surgery units. *Br J Surg* 2014;101(6):707-14.
19
20
21 26. CholeS Study Group, West Midlands Research Collaborative. Population-based
22 cohort study of outcomes following cholecystectomy for benign gallbladder diseases. *Br J*
23 *Surg* 2016;103(12):1704-15.
24
25
26
27 27. Bhangu A, Koliass AG, Pinkney T, et al. Surgical research collaboratives in the UK.
28 *Lancet* 2013;382(9898):1091-2.
29
30
31
32 28. Chapman SJ, Glasbey JC, Khatri C, et al. Promoting research and audit at medical
33 school: evaluating the educational impact of participation in a student-led national
34 collaborative study. *BMC Medical Education* 2015;15:47.
35
36
37
38 29. David JS, Voiglio EJ, Cesareo E, et al. Prehospital parameters can help to predict
39 coagulopathy and massive transfusion in trauma patients. *Vox Sang* 2017;112(6):557-66.
40
41
42
43
44
45
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FIGURE LEGENDS

Figure 1. Date ranges and number of included patients according to anonymised collaborating site.

*Number of patients per year are derived by the number of patients divided by the number of months of data provided, multiplied by 12

Figure 2. Volumes of 0.9% saline delivered to study patients

SITE	2011	2012	2013	2014	2015	2016	Patients per year*
A	n = 63						13
B	n = 49						11
C	n = 74						10
D		n = 14					4
E		n = 20					5
F		n = 223					83
G		n = 79					25
H		n = 39					12
I			n = 79				39
J					n = 76		79
K					n = 13		15

Figure 1. Date ranges and number of included patients according to anonymised collaborating site.
 *Number of patients per year are derived by the number of patients divided by the number of months of data provided, multiplied by 12

256x131mm (300 x 300 DPI)

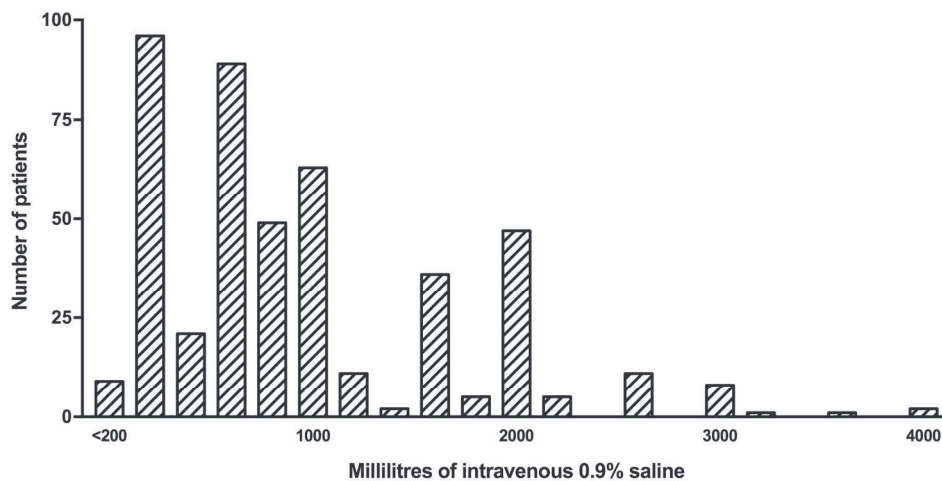


Figure 2. Volumes of 0.9% saline delivered to study patients

Figure 2. Volumes of 0.9% saline delivered to study patients

172x100mm (300 x 300 DPI)

Review only

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Title page
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Abstract
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6,7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7,8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7,8
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	8
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7,8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8,9
Bias	9	Describe any efforts to address potential sources of bias	7,8
Study size	10	Explain how the study size was arrived at	9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	9
		(b) Describe any methods used to examine subgroups and interactions	9
		(c) Explain how missing data were addressed	N/A
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	

Continued on next page

Results			Page
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10, & Table 1
		(b) Give reasons for non-participation at each stage	10
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10; Table 2
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	No follow up
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	13,14
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	All Results reported this way
		(b) Report category boundaries when continuous variables were categorized	Throughout
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18,19,20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	20
Generalisability	21	Discuss the generalisability (external validity) of the study results	19,20
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	21

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.