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Transfusion Strategies in the Pre-Hospital Setting: Evaluating the Logistical Benefits of Pre-Hospital Whole Blood Transfusion, and a National Survey of Pre-Hospital Blood Transfusion

Harriet Tucker (harriet.tucker2@nhs.net)
Queen Mary University of London https://orcid.org/0000-0003-1629-6179
Laura Green
Queen Mary University of London
Karim Brohi
Blizard Institute of Cell and Molecular Science: Barts and The London School of Medicine and Dentistry Blizard Institute
Rebecca Cardigan
NHS Blood and Transplant
Ross Davenport
Blizard Institute of Cell and Molecular Science: Barts and The London School of Medicine and Dentistry Blizard Institute
Jane Davies
NHS Blood and Transplant
Dave Edmondson
NHS Blood and Transplant
William English
Barts Health NHS Trust
Joanne Griggs
Air Ambulance Kent Surrey Sussex
Al Hunter
NHSBT: NHS Blood and Transplant
Sophie Mitchinson
Air Ambulance Kent Surrey Sussex
Angela Maddison
Barts Health Pathology Service
Jonathon Scrimshaw
Barts Health NHS Trust
Simon Stanworth
NHS Blood and Transplant

Oliver Trampleasure
Barts Health NHS Trust
Andrew Whitehourse
London's Air Ambulance
Anne Weaver
London's Air Ambulance

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Abstract

Background

Pre-hospital blood component transfusion poses logistical challenges. Current patterns of pre-hospital blood use across the UK are not known. A potential benefit of providing a single combined component of whole blood is reduced need for multiple steps of administering separate components and more efficient use of time and resources by medical staff. .

Objectives

to undertake a detailed time-analysis of the steps of pre-hospital combined component transfusion against separate blood component transfusion, and to determine current UK pre-hospital transfusion practice and users' optimal pre-hospital transfusion strategy

Methods

A three-arm cross-over major haemorrhage simulation study compared: flow-time (time from decision-to-transfuse [DTT] to complete transfusion); touch-time (direct team 'hands on' contact time with transfusion process); and number of steps, people and equipment required for transfusion of 2 units of RCP [arm-A], 2 RBC + 2 TP [arm-B] or RBC + 2 Lyoplas [arm-C]). A national survey of current and optimal pre-hospital transfusion strategies was sent to 22 UK Air Ambulance Services (AAS) and 27 Major Trauma Centres (MTC) in December 2019.

Results

The simulation demonstrated that arm-A had a shorter flow-time (median 6min 31sec vs. 12min 20 sec, vs 16min 29 sec) and touch-time (median 2min 31 seconds vs. 5min 21sec vs. 15min 3sec) than arm-B and arm-C respectively, and required fewer steps, equipment and checks. 18 MTCs and 18 AAS responded to the national survey (response rates of 67 and 82%). 10 transfused RBC/plasma (5 TP/5 Lyoplas), 4 RBC only, 2 Lyoplas only, 1 RBC/Lyoplas/Fibrinogen, and 1 'red cell and plasma' (only available at one hospital site). 89% replied that a combined component transfusion would be desirable, as it would reduce patient mortality (83%) and tasks on scene (75%).

Conclusion

The time-analysis established the benefits for combined pre-hospital component transfusion in trauma patients. The national survey demonstrates the variation in current pre-hospital transfusion practice and reiterates that combined component transfusion pre-hospital may have logistical advantages over separate components.

Background

Balanced haemostatic resuscitation is the UK and European in-hospital standard of care for bleeding trauma patients[1],[2]. In-hospital studies suggest that RBC and plasma should be given together, in a 1:1 ratio[3] and evidence from military and civilian practice suggests that early administration of blood components may improve survival to hospital[4], decrease ongoing transfusion requirements, and decrease mortality[56]. Reported benefits suggest that pre-hospital red blood cell[7] and plasma administration may reduce mortality[8], platelet transfusions may be more effective when given very early[9] and earlier red cell transfusion may reduce mortality[10]. In addition, early administration of red blood cells (RBC), thawed fresh-frozen-plasma (TP) and platelets (PLT) in a near 1:1:1 ratio reduces in-hospital mortality and death from exsanguination at 24 hours[11].

UK air ambulances (AAS) are autonomous charities that operate as part of the of major trauma networks[12]. They transport patients to hospital and deliver specialist pre-hospital emergency medical care to incident scenes in order to provide on-scene and en route resuscitation. The pre-hospital clinicians are able to deliver blood components in the pre-hospital treatment and transfer of patients, but the details of exactly what these blood components are has not been reported.

Despite the benefits of early haemostatic resuscitation in bleeding trauma patients, and clear in-hospital guidelines, there is no clear national guidance for pre-hospital transfusion. No recently published UK survey reports current pre-hospital transfusion practice. Pre-hospital transfusion resuscitation may vary depending on economic and logistical factors, with some services transfusing RBC alone[13], and some RBC with a plasma component, either TP or lyophilised plasma ('Lyoplas')[14,15,16,17]. However, there is no national overview of this variation in practice, nor consensus regarding the optimal pre-hospital transfusion strategy

Transfusion of multiple blood components in the pre-hospital environment faces logistical and clinical challenges due to limited resources and personnel, weight and storage constraints, as the medical teams must carry and transport all equipment to the scene, and the potential delay in transferring patients to hospital due to the number of time-critical tasks needing to be performed at the scene of trauma.

The use of a combined component such as Whole Blood (WB)[18] or a Red Cell and Plasma component (RCP)[19] which is currently being used in London as part of a 2-year feasibility study may mitigate some of these challenges. No study has demonstrated the logistical and practical implications of combined versus separate blood components in the pre-hospital setting.

The aims of this study are to: to assess the logistical benefits of pre-hospital combined component transfusion against separate blood components, to determine current pre-hospital transfusion practice, and to understand the key users' optimal pre-hospital blood components

Methods

Simulation

Study Design, setting and participants

A three-armed cross over simulation study was carried out by three currently practicing helicopter emergency medical service (HEMS) crews in order to compare 3 different pre-hospital transfusion strategies. Each crew was comprised of a doctor and a paramedic. A single adult pre-hospital major haemorrhage ('Code Red')[20] scenario with a non-compressible abdominal and pelvic haemorrhage was used with the same mechanism of injury, clinical findings and physiological transfusion triggers across all three arms (Figure 1). All crews completed the same scenario three times with the different transfusion strategies.

Simulation study scenario

Interventions

The study contained three arms:

A: 2 units of RCP alone

B: 2 units of RBC and 2 units of TP;

C: 2 units of RBC and 2 units of lyophilised plasma (Lyoplas).

These three groups were selected as representing the three most frequently used transfusion strategies from the survey of current pre-hospital transfusion practice.

Measurements and Outcomes

The scenario timing start point was the crew's decision to transfuse (DTT). The end point was the complete transfusion of 2 units of RCP; 2 units of RBC and 2 units of TP; or 2 units of RBC and 2 units of lyophilised plasma. A physiological end point was not used.

The outcome measures were:

Flow-time (defined as the time from DTT to complete transfusion of units in each arm)

Touch-time (defined as the direct team 'hands on' contact time with the transfusion process, needed from DTT to complete transfusion of units in each arm)

Number of steps needed within the flow-time and for the transfusion of one blood component Number of team members needed within the flow-time

Number of pieces of equipment needed within the flow-time

Number of checks needed within the flow-time

Health care professional satisfaction with the different transfusion arms (Figure 2).

Simulation Study Outline

The scenario was developed and tested with different HEMS teams prior to use in the study. Prior to starting, all crew members (n = 6) were familiarised with all blood components and equipment needed to deliver blood product administration to eliminate unfamiliarity with equipment and components as a cause of difference in outcomes between arms. Peripheral intravenous access and location were standardised to provide the same flow rate in each simulation arm. All scenarios were filmed to allow full analysis and debriefing. Written consent was obtained from all participants prior to participation. Expired blood components, which would otherwise have been wasted, were used for the simulation, and training sets of lyophilised plasma were used. This simulation did not address any other aspects of clinical care nor other haemorrhage control interventions.

A debrief following the scenario examined team satisfaction with the different products, their cognitive burden during the transfusion, and allowed for informal feedback. This feedback was analysed to identify common themes.

Analysis

The results of the survey were collated and analysed. Shapiro Wilk tests were performed to assess normal distribution. Descriptive results and statistics are reported as numbers (%), or a series of means, standard deviations and median interquartile ranges (IQR) depending on whether data was normally or not-normally distributed. Items in the survey are reported in order of magnitude from highest to lowest. The results of the simulation study are reported as medians and IQRs. A Kruskal-Wallis test one-way ANOVA was used to analyse times measured between arms for statistical significance.

Survey

The main objectives of the survey were to establish current UK pre-hospital blood transfusion practice and establish clinicians' optimal pre-hospital transfusion strategy. Secondary aims were to establish users' desired key trial outcomes alongside demand and willingness to participate in a trial of pre-hospital whole blood transfusion.

Key stakeholders were identified as helicopter emergency medical services (HEMS) within air ambulance services (AAS), as these are the healthcare professionals currently able to transfuse blood components in the pre-hospital environment and major trauma centres (MTCs), the receiving hospitals for the majority of these patients. The UK has 22 HEMS and 27 MTCs[11]. Other pre-hospital healthcare professionals such as ambulance services, air ambulance and retrieval services, paramedics and British Association of Immediate Care (BASICS) doctors were not surveyed as at present they are unable to transfuse blood pre-hospital, or do not transfuse in the immediate post injury period.

The questionnaire was pre-piloted by five individuals of similar characteristics to the survey population, who provided written feedback to assist the authors to improve the survey. The survey was written using Google Forms and distributed via e-mail in December 2019 to MTC clinical directors via the national trauma director, and all AAS medical directors via the air ambulance association and PHOTON (the Pre-Hospital Operated Trainee Network). MTC clinical directors and AAS medical directors were asked to complete the survey themselves, or to delegate it to an appropriate experienced individual, representative of their organizational and individual experience and approach. Responses were collated in a spreadsheet (Google Sheets).

Respondents were asked to rank on a Likert Scale their preferred choices. (Appendix 1: survey questions). The survey was anonymous other than healthcare role (e.g. paramedic, ITU doctor, pre-hospital doctor). There were no financial inducements. There was a four-week closing date with reminders at weekly intervals. No ethical approval was needed as this was a service evaluation and no patient identifiable data was collected. According to the HRA decision tool, neither Health Research Authority (HRA) or Research Ethics Committee (REC) approval were required. Respondent consent was implied by written completion of the questionnaire.

Results

Simulation

The cross-over simulation demonstrated that transfusion of combined component (2 units of RCP) had a shorter flow-time and touch-time compared to other arms, and required fewer steps, pieces of equipment and checks to complete transfusion (Table 1). After one-way ANOVA, the differences in both flow time and touch time between group A and groups B and C were found to be statistically different, with a *p*-value of 0.017 and .00193, respectively (significance level of $p < 0.5$) (Table 1).

Table 1 Effect of different blood transfusion strategies on simulation outcomes

	Arm-A [2 RCP]	Arm-B [2 RBC + 2 TP]	Arm-C [2 RBC + 2 Lyoplas]	P
Flow Time Median (IQR)	6min 31sec (5min 07, 7min14)	12min 20sec (10min47, 13min53)	16min 29sec (13min11, 17min 02)	0.017
Touch Time Median (IQR)	2 min 31sec (2min07, 3min11)	5min 21sec (4min43, 6min07)	13min 03sec (11min48, 14min53)	0.0193
No. of steps	28	40	46	N/A
No. of pieces of equipment	4	10	12	N/A
No. of checks	8	16	16	N/A
No. of people	2	2	3	N/A

(RCP = Red cells and plasma combined; RBC = red blood cells; TP = thawed fresh frozen plasma; Lyoplas = Lyophilised plasma)

The number of steps directly linked to the transfusion of an individual blood component was counted (Figure 3). This process was repeated twice for in arm A (RCP), and four times in arms B and C (2 RBC + 2 TP and 2 RBC and 2 Lyoplas respectively).

Number of steps involved in the pre-hospital transfusion of one blood component

(RCP = red cell & plasma RBC = packed red blood cells TP = thawed fresh frozen plasma

Lyoplas = lyophilised plasma)

The crew satisfaction survey was performed immediately post completion of the third scenario, prior to discussion with other participating teams. All participants stated that a combined blood component delivered an improved transfusion strategy, led to increased scene efficiency, decreased use of resources, improved scene logistics, and was beneficial for both patients and crews (Table 2). This correlates with the responses from the national survey, described below.

Table 2 Participant responses to post simulation survey questions (n=6)

Question	Responses
What would your optimal pre-hospital transfusion practice be?	100%: blood component which mirrored in hospital practice, could be given quickly, easily and with minimal checks, equipment, and in the quickest time
Between these three scenarios, what transfusion strategy did you feel was optimal for the patient?	83% RCP 17% RBC + FFP.
Between these three scenarios, what transfusion strategy did you feel was optimal for the crew?	100% felt that if massive transfusion was indicated, less equipment, lines, access, blood warmers, and people were needed to give the RCP x2. 100% felt that Lyoplas was the most time consuming in terms of training, time and resources; also stated cold chain, storage and wastage implications of using ptFFP
Is there another transfusion strategy you would wish to see compared?	1 asked re use of pre-hospital cryoprecipitate.
Which transfusion strategy delivered a 2:2 ratio with the least use of resources/most efficient use of resources?	100% stated RCP (despite taking slightly longer to give each unit)
Which transfusion strategy needed fewer checks/equipment/steps to deliver a balanced 2:2 resuscitation?	100% stated RCP
Do you think there is a logistical and/or clinical benefit to using combined RCP vs component therapy?	100%: in those patients who had a major haemorrhage, RCP was quicker, easier, required fewer steps, less equipment, fewer checks, maximised blood warmer and intravenous access

Survey Results

Surveys were sent to 27 MTC and 22 AAS clinical leads. 67% (18) MTCs, and 82% (18) AAS responded, giving a 73% overall response rate. All questionnaires were returned fully completed. The MTC respondents were all doctors (from a range of specialties) whilst the AAS respondents comprised 13 doctors, 4 paramedics and 1 nurse (Figure 4).

Professional background of survey respondents

Current Transfusion Practice

Of the 18 AAS that responded, 28% (5) carried RBC & Lyoplas (3 within the RePHILL trial), 28% (5) RBC & TP, 22% (4) RBC only, 11% (two) Lyoplas only, 6% (one) RBC, Lyoplas, & fibrinogen, and 6%(one) RCP. MTCs will receive patients from more than one air ambulance service, hence patients arriving to MTCs could receive a range of different pre-hospital transfusion strategies. 94% of services linked with a nearby hospital to supply their blood components and one service had a co-located transfusion laboratory.

Future Transfusion Practice

89% of respondents replied that a combined component would be their optimal first choice of pre-hospital transfusion component; 75% preferred WB and 14% RCP (Figure 3). For those respondents that placed WB as their first choice, 96% placed either RCP or separate RBC, TP & PLT as their second optimal choice (figure 5)

Clinicians' optimal pre-hospital blood component

WB = whole blood; RCP = combined red cell and plasma; RBC/TP/Plt = separate components of red blood cells, thawed fresh frozen plasma, and platelets; RBC & TP = red blood cells and thawed FFP; RBC & Lyoplas = red blood cells and lyophilsed plasma; RBC, TP, PLT, Fibrinogen = separate red blood cells, thawed fresh frozen plasma, platelets and fibrinogen concentrate

The rationale behind choices included patient, clinician and logistical benefits (Table 3). 83% of respondents stated that the use of WB would reduce time to a balanced haemostatic resuscitation, and improve patient resuscitative, haemodynamic and coagulation parameters on hospital arrival. 75% stated WB use would reduce tasks and improve ease of blood component administration on scene.

Table 3 Users' perceived benefits of pre-hospital WB transfusion

Benefit	MTC (n) %	AA (n) %	Combined (n) %
Reduced time to administer a balanced haemostatic resuscitation	(14) 78	(16) 89	(30) 83
Improved resuscitative, haemodynamic and coagulation parameters at hospital arrival	(14) 78	(16) 89	(30) 83
Reduced tasks on scene	(13) 72	(14) 78	(27) 75
Increased ease of blood product administration	(15) 83	(12) 67	(27) 75
Reduced mortality	(10) 55	(15) 83	(25) 69
Reduced incidence of other adverse outcomes (e.g. Multi-organ failure, thrombo-embolic events)	(9) 50	(13) 72	(22) 61
Reduced scene time	(11) 62	(14) 78	(25) 69
Increased ease of blood component transport	(9) 50	(12) 67	(21) 58
Reduced in-hospital transfusion requirements	(7) 39	(10) 56	(17) 47
Reduced wastage of blood components	(6) 33	(10) 56	(16) 44
Reduced Incidence of transfusion reactions	(8) 44	(8) 44	(16) 44

Discussion

This is the first study to demonstrate the significant reduction in pre-hospital flow-time and touch-time gained by transfusing a combined blood component. This has important clinical significance and implications as the decreased times, especially touch time, will liberate crews to complete other time-critical interventions, reduce their cognitive burden with less interruption of critical processes[21], which reduces the potential for human error due to interruptions[22] and allows the team to perform blood transfusions more efficiently.

The use of a combined component had the shortest touch-time and flow time, and required fewer steps, people and equipment. The total volume of 2 RCP units (~940 mL) is only 100mL less than the total volumes of 2 RBC (500mL) and 2 TP (540mL). Therefore the above results may largely be due to the fewer number of steps required to administer RCP, such as fewer blood component safety checks. Most pre-hospital teams carry only one blood warmer, and venous or intraosseus access may be challenging and a rate limiting step in a haemodynamically unstable and shocked trauma patient; being able to transfuse two components simultaneously with a combined product may mitigate these limitations.

The use of lyophilised plasma led to longer flow and touch times, required more steps, and an additional person on scene to administer the product. Some of the advantages of Lyoplas over other plasma components (such as ease of storage, reduced wastage, and a longer shelf-life) have resulted in many services making the decision to use this product: however, the results show that TP performed better in almost all logistical outcomes used in the simulation, indicating that air ambulance services may need to review these factors when deciding on the most optimal transfusion strategy in pre-hospital environment[23].

The benefits of a combined component in reducing scene time may contribute to a reduced total duration of each patient episode. Thus use of a combined component could contribute to wider trauma system benefit, with increased availability of the limited resource of the HEMS team

The increasingly widespread practice of physician-paramedic delivered pre-hospital care facilitates the use of pre-hospital blood transfusions in traumatic injury, in appropriate patient groups. Experienced clinicians completed the survey, with their roles spanning many stages of the patient journey (from point of injury to ITU stay). The respondent sample thus represents a wide variety of user perspectives with a clear understanding of the complexities of pre-hospital blood transfusion. The responses share common themes, notably the perceived patient benefit from the use of whole blood, and the pre-hospital teams' emphasis on the importance of on scene variables such as scene time, tasks, and ease of blood component administration and storage. These perceived benefits to on scene logistics are reflected in the findings of the simulation study, where the use of a combined blood component was found to reduce the scene touch-time and flow-time, which may have the potential patient and clinician benefits as described by the survey.

The survey results are thus complementary to that of the simulation study, reflecting the actual and perceived benefits of pre-hospital combined component transfusion. It is also the most current published survey of pre-hospital transfusion practice in the UK, and highlights the range of pre-hospital transfusion strategies. This regional heterogeneity is consistent amongst both historical studies[24], and contemporary surveys of European practice[25] but also demonstrates the rapid development in blood product availability pre-hospital within the UK, the US, Scandinavia and Europe within the intervening four years, and the continuing lack of consensus regarding the benefits of pre-hospital blood product transfusion, which blood components should be transfused, and at what point in the patient pathway. The variation may, in part, be due to lack of clear, high-level pre-hospital evidence for any one transfusion strategy. A large prospective observational study[26] and a meta-analysis of observational studies[27] have been unable to provide a consensus; it is suggested that RBC use alone may reduce pre-hospital mortality[28], but there is conflicting evidence regarding the use of pre-hospital plasma and its effect on mortality[7, 29.] A subsequent systematic review[30] concluded that pre-hospital plasma infusion reduced 24-h mortality in haemorrhagic shock patients, but not 30-day mortality. There are currently two trials[31, 32] comparing pre-hospital transfusion against standard treatment (0.9% saline), whose results are awaited; however, it could be argued that the transfusion of crystalloid is no longer considered the standard of care for transfusion of bleeding trauma patients.

This variation in evidence and practice, alongside a perceived benefit to combined component transfusion in certain patient groups suggests that a pre-hospital multi-centre trial comparing different blood component transfusion strategies is needed. This is again highlighted by a recent systematic review[33] comparing the use of whole blood (WB) transfusion with component therapy in adult trauma patients with acute major haemorrhage, which concluded that there is insufficient evidence to support or reject the use of WB transfusion, and that larger trials are required to assess the efficacy and safety of WB transfusion in trauma.

Limitations

The survey was completed by only one representative from each AAS or MTC. It assumes that those responding would have the requisite expertise and opinion to make an informed response. However, looking at professional roles of the respondents, this represent a wide range of specialties and backgrounds, which gave breadth and depth to the responses. The survey may have been improved by sending it another round to the same respondents to assess for consistence, and to representatives from ambulance services, BASICS, and aeromedical transfer and retrieval teams. Only one service has had access to the red cell and plasma product, which may have biased the responses.

Within the simulation study each crew repeated the same scenario three times. This may have led to familiarity of process, increasing the speed of decision-making and thus affected the outcomes. However, this effect would have been the same across all three crews and all three simulations and thus any effect would be equally spread among all three arms. Time from scene arrival to first component infusion was not measured, which may have been a useful factor in relation to the survey's response of time to from injury to haemostatic resuscitation, and a clinical or physiological end point was not used which may not be truly representative of on scene decision making or end of transfusion time.

Conclusion

The results of both the simulation study and the survey add impetus to the need and demand for a combined component in the pre-hospital environment, with its relatively limited equipment and resources, in order to deliver a pre-hospital, early haemostatic resuscitation. There is variation in pre-hospital transfusion strategies within the United Kingdom and Europe. This may be due to a lack of consistent evidence in the pre-hospital setting, highlighting the need for future large multi-centre prospective trials. Furthermore, the pre-hospital availability of a combined component (such as Whole Blood or combined red cells and plasma) leads to a significant reduction in pre-hospital flow-time and touch-time, decreasing overall scene time, and facilitates a more effective use of resources, decreases the team cognitive burden, and may lead to a more rapid hospital transfer for traumatically injured bleeding patients.

Abbreviations

DTT: Decision to transfuse; RBC: red blood cells; RCP: combined red cells and plasma; FFP: fresh frozen plasma; tFFP: pre-thawed FFP; Lyoplas: Lyophilised Plasma; Plt: platelets; WB: whole blood; HR: Heart rate; SBP: systolic blood pressure; RR: respiratory rate; HEMS: Helicopter Emergency Medical Service; AAS: Air Ambulance Service; MTC: major trauma centre; BASICS: British Association of Immediate Care; ITU: intensive therapy unit; HRA: Health Research Authority; REC: Research Ethics Council

Declarations

Ethics approval and consent to participate

No ethical approval was needed as this was a service evaluation and no patient identifiable data was collected. According to the HRA decision tool neither Health Research Authority (HRA) or Research Ethics Committee (REC) approval were required. Respondent consent was implied by written completion of the questionnaire.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

HT designed the simulation study. HT and LG designed the survey. HT, LG, SS, RD, AH and AW reviewed the survey. HT analyzed and interpreted the data from both the study and the survey. HT and LG drafted manuscript. All authors read, reviewed and approved the final manuscript.

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Figures

Figure 1

40 year old male cyclist. Run over by turning Heavy Goods Vehicle. Injuries to pelvis and abdomen. Obvious marks to abdomen and pelvis, obvious pelvic deformity. No chest, neck or head injury. Low GCS due to hypoperfusion (E2V3M5). HR 130, SBP 70, RR 26, cool peripheries, pale, veins down. Poor initial response to 1:1, (HR 120, SBP 80) needs further 1:1.

Figure 1

All crews completed the same scenario three times with the different transfusion strategies.

Figure 2

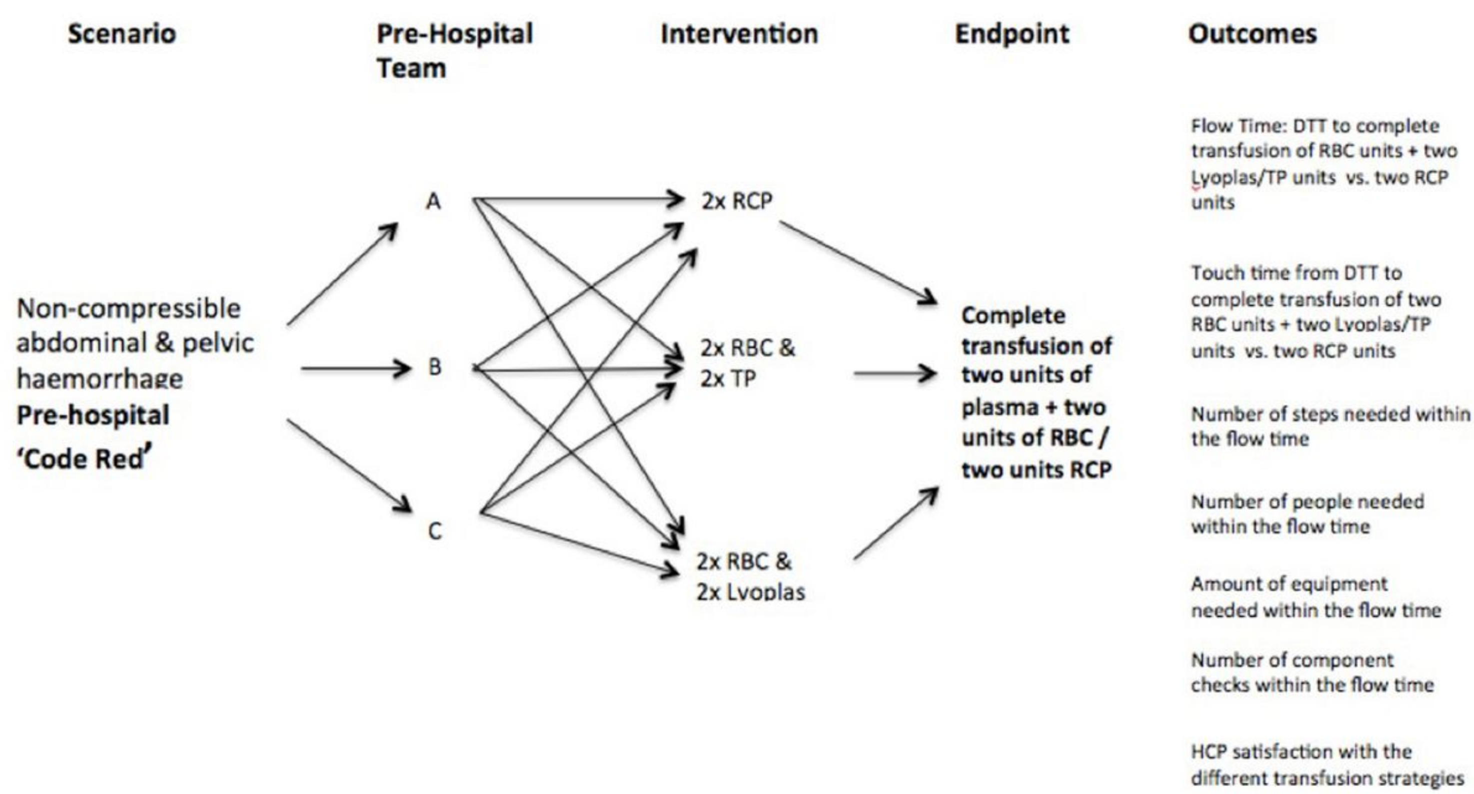

Figure 2

Health care professional satisfaction with the different transfusion arms

Figure 3

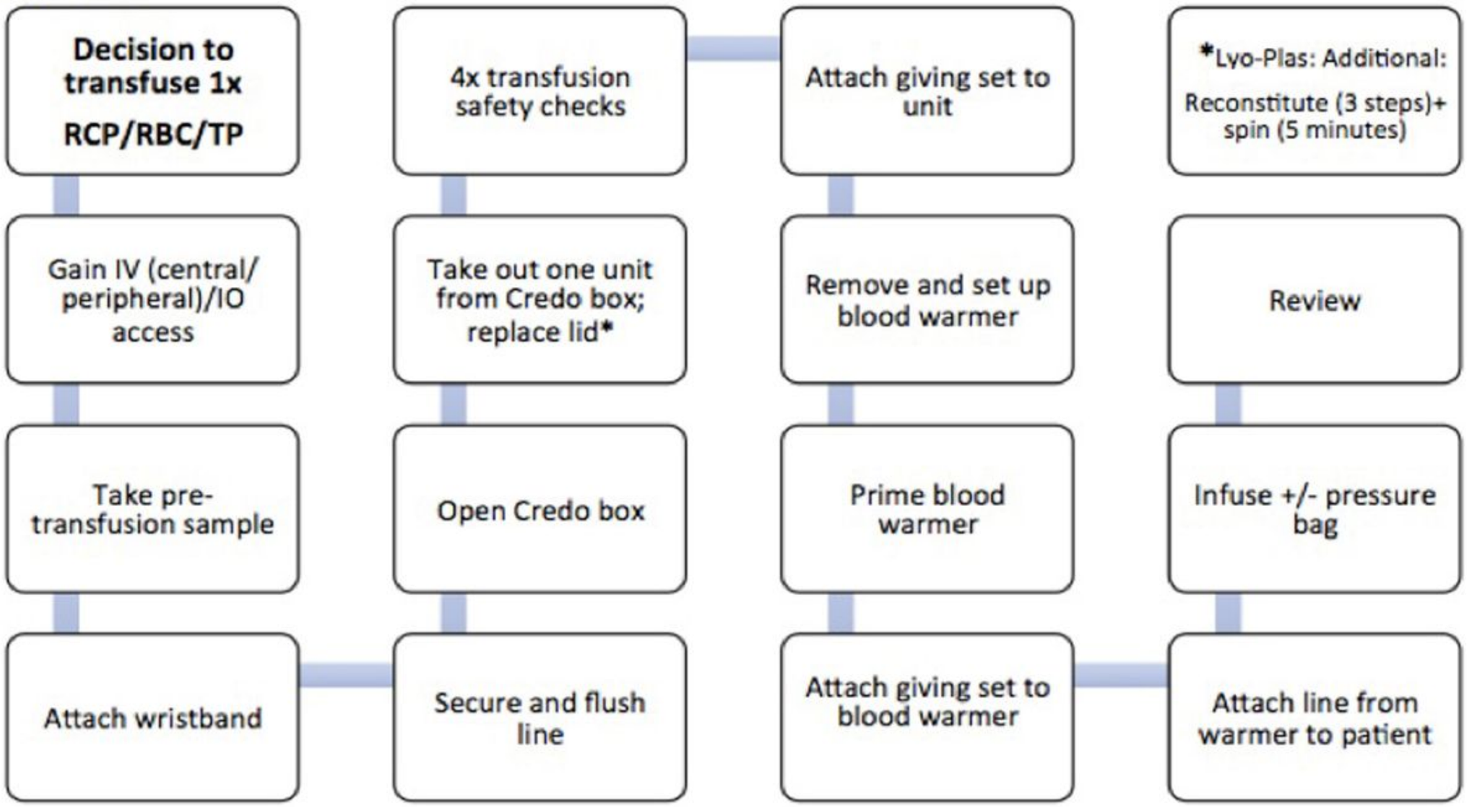

Figure 3

The number of steps directly linked to the transfusion of an individual blood component was counted . This process was repeated twice for in arm A (RCP), and four times in arms B and C (2 RBC + 2 TP and 2 RBC and 2 Lyoplas respectively). Number of steps involved in the pre-hospital transfusion of one blood component (RCP = red cell & plasma RBC = packed red blood cells TP = thawed fresh frozen plasma Lyoplas = lyophilised plasma)

Figure 4

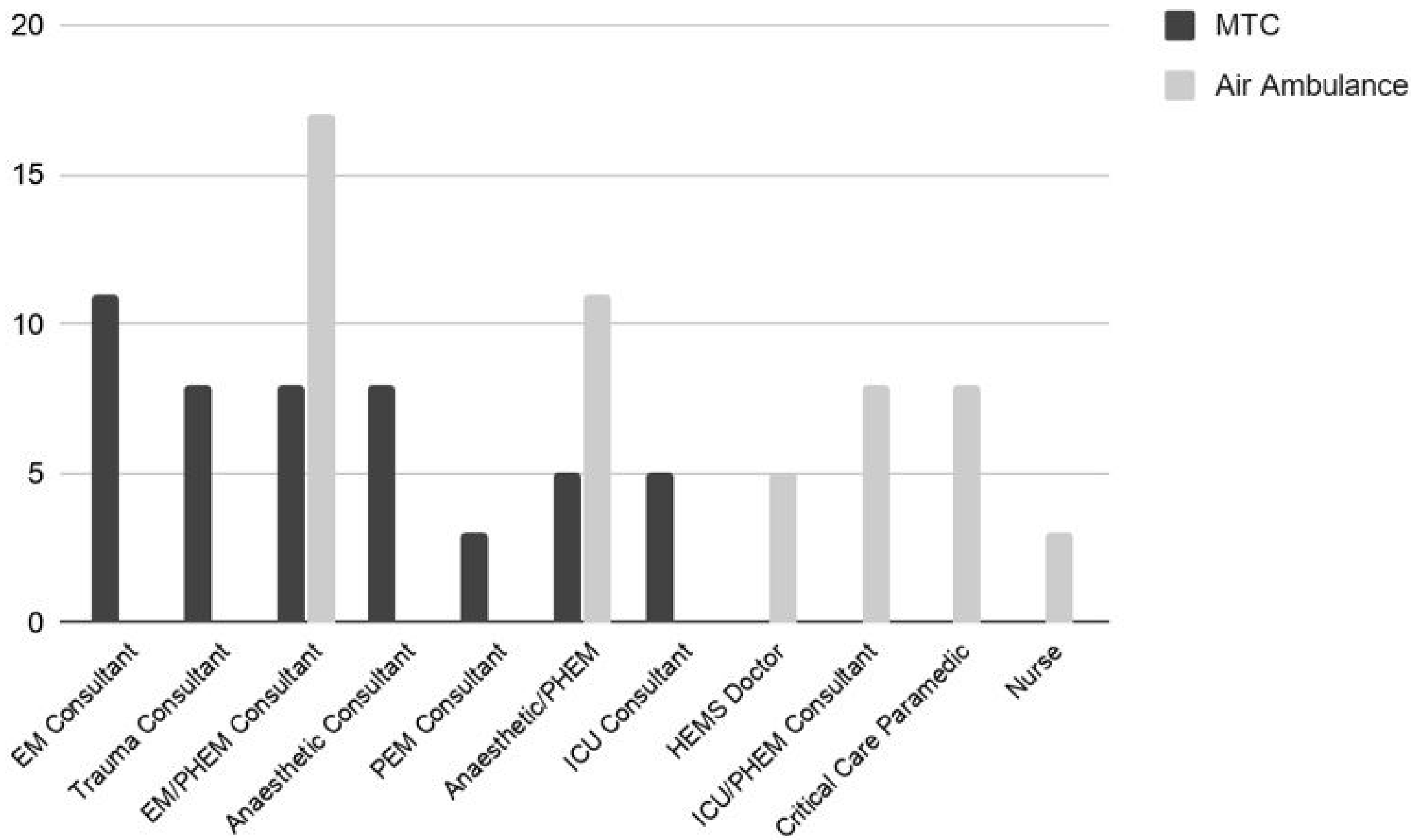

Figure 4

Professional background of survey respondents

Figure 5

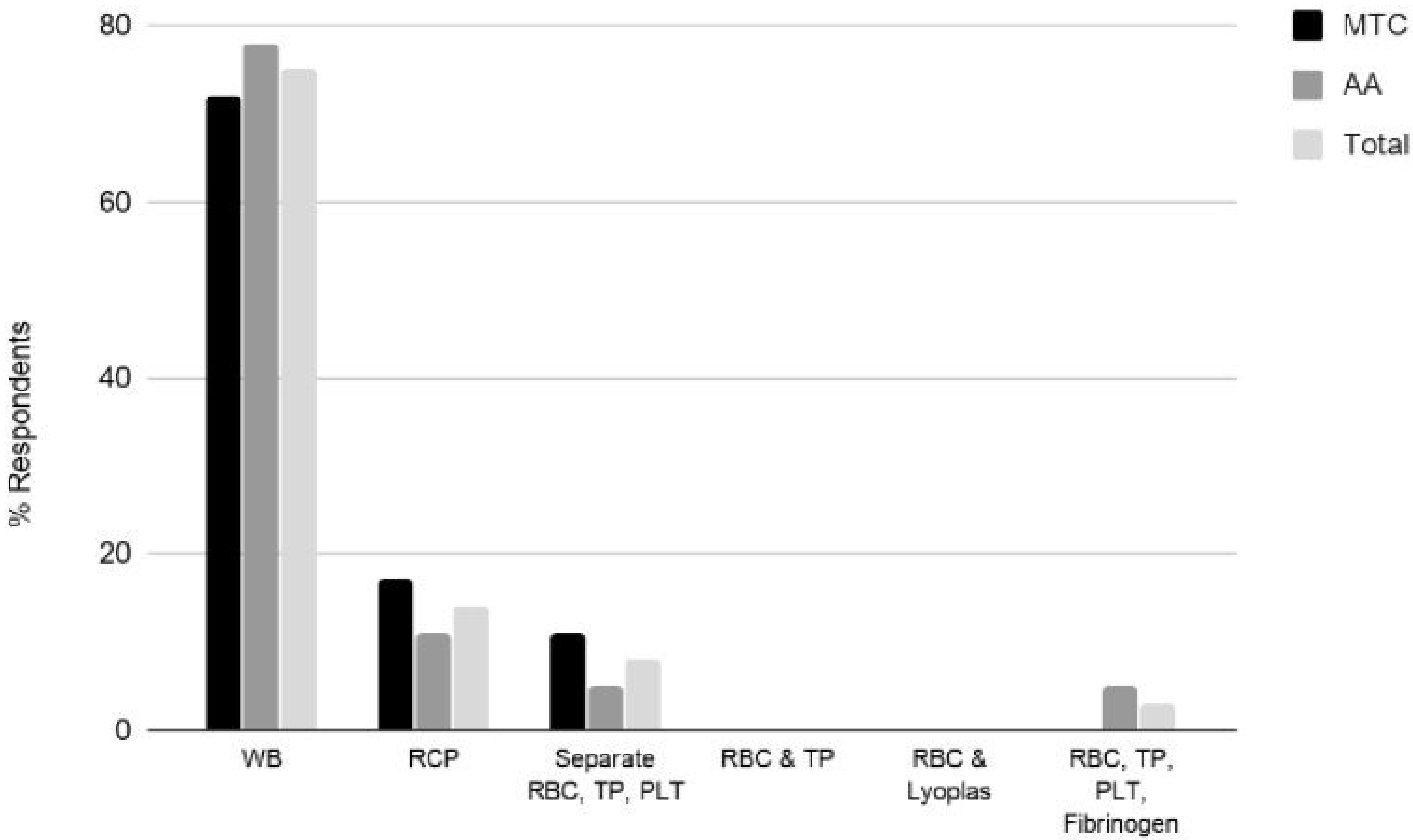

Figure 5

Clinicians' optimal pre-hospital blood component