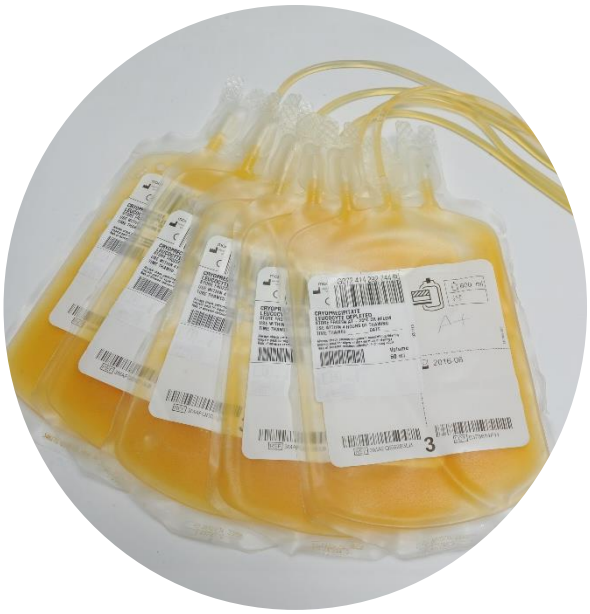
NHS
Blood and Transplant



2018 Audit of the use of Fresh Frozen Plasma, Cryoprecipitate, and Transfusions for Bleeding in Neonates and older Children

National Comparative Audit of Blood Transfusion

December 2021

Acknowledgements

We wish to thank all staff and hospitals who participated in the 2018 audit of the use of Fresh Frozen Plasma, cryoprecipitate and other blood components in neonates and older children. We recognise that those giving up their valuable time have been many and that this will inevitably have been on top of a heavy workload. We are equally grateful to colleagues for their valuable and constructive comments, including all members of the project group.

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Contents

Summary of Main Findings and Recommendations

This audit reviews the practice of the use of prophylactic fresh frozen plasma (FFP) and cryoprecipitate in neonates and older children, and of transfusions to treat bleeding and trauma. It is acknowledged that there is much excellent transfusion practice in this patient group, however this audit has identified many areas where practice may be improved at sites in the NHS. These cover organisational issues as well as transfusion care for individual infants and older children. A suggested local action plan to address the main findings is provided at the end of the report *(see Local action plan template, p67)*.

Organisational data

- Most, but not all sites transfusing the relevant age groups had local transfusion policies/guidelines. 87.3% of sites with a neonatal unit had a policy/local guideline for the transfusion of FFP and cryoprecipitate to neonates. Similarly, 83.3% of relevant sites had a policy/local guideline for the transfusion of FFP and cryoprecipitate to children *(see KPI 1, p11; Organisational Key points, p13)*.
    - *BSH guidelines (2016) state that hospitals should have clear guidelines on transfusion thresholds for different paediatric groups.*
- 26.3% of sites had policies of routinely checking coagulation screens on all preterm neonates, which could increase the risk of unnecessary FFP transfusion *(see KPI 2, p11; Organisational Key points, p13)*.
    - *BSH guidelines (2016) state that a policy of routine coagulation screening is inappropriate as results are difficult to interpret in neonates and routine testing may lead to increased transfusion of FFP without benefit.*
- 28.1% of sites had no major haemorrhage protocol (MHP) for children *(see Organisational Key points, p13)*.
    - *BSH guidelines (2016) state that hospitals which may encounter children with massive blood loss should have a dedicated children's major blood loss guideline, which would include advice on the correct age-adjusted volumes of blood components in an emergency.*
- For those sites that had an MHP, tranexamic acid use was not included in MHPs for children at 17.5% of sites *(see Organisational Key points, p13)*.
    - *BSH guidelines (2016) recommend that tranexamic acid should be used where massive blood loss is anticipated in children presenting with major traumatic injuries, according to the timing and dosage recommended by RCPCH (2012).*
- 40.4% of sites did not have a concessionary release policy for use of acceptable alternatives to 'paediatric' blood components in emergencies for major bleeding *(see Organisational Key points, p13)*.
    - *In order to avoid delays in blood provision, BSH guidelines (2016) recommend using pre-agreed hierarchies of alternative components in case specific blood components are not available in an emergency.*

Clinical audit

- 76.5% of neonates were transfused prophylactic FFP for 'abnormal coagulation', in the absence of surgery/invasive procedure *(see Neonatal Key points, p17; Reasons for initial FFP transfusion, p24).* 23.2% of the neonates stated to have 'abnormal coagulation' who had a coagulation test reported within the 24 hours prior to transfusion had an internationalised ratio (INR)/prothrombin time ratio (PTR) of < 1.5, not significantly abnormal (*Table 10, p31; Coagulation test Key points, p32*).
    - *BSH guidelines (BSH, 2016) recommend that there is no evidence to support the routine use of fresh frozen plasma (FFP) to try to correct abnormalities of the coagulation screen alone in non-bleeding neonates*.
- Prevention of intraventricular haemorrhage (IVH) was given as an additional reason for transfusion for around a third of all prophylactic FFP (32.9%; 73/222) and cryoprecipitate (39.1%; 27/69) transfusions given for 'abnormal coagulation the absence of invasive procedure or surgery' (*see Neonatal Key points, p17; Reasons for initial FFP transfusion, p24; Reasons for initial cryoprecipitate transfusion, p39*).
    - *BSH guidelines (2016) recommend that FFP should not be used for simple volume replacement or routinely for prevention of IVH.*
    - *The use of cryoprecipitate for this indication was unexpected. BSH guidelines (BSH, 2016) recommend that prophylactic cryoprecipitate should not be routinely administered to non-bleeding children with decreased fibrinogen including prior to surgery. It may be considered for fibrinogen < 1 g/l for surgery at risk of significant bleeding or to critical sites*.
- The volume (mL/kg) of neonatal prophylactic FFP and cryoprecipitate transfusions was > 20 mL/kg for 13.0% of FFP transfusions and > 10mL/kg for 41.5% of cryoprecipitate transfusions where data were available. For all children this was 17.6% for FFP and 31.7% for cryoprecipitate (*see Key clinical group Neonates, p15; Volume of FFP transfused, p29; Volume of cryoprecipitate transfused, p43*).
    - *BSH guidelines (2016) describe suggested transfusion volumes and indicate that care should be taken to avoid volume overload.*
- Volumes of prophylactic FFP and cryoprecipitate were < 10mL/kg for 15.4% FFP and < 5mL/kg for 15.9% cryoprecipitate transfusions where data were available (*see Volume of FFP transfused, p29; Volume of cryoprecipitate transfused, p43*).
    - *These volumes may be sub-therapeutic and are below those suggested by BSH (2016; for FFP 15-20mL/kg, with the higher volumes particularly in bleeding patients; for cryoprecipitate 5-10mL/kg).*
- 59.4% of children transfused with prophylactic FFP and 48.8% with cryoprecipitate who had cardiac surgery as the underlying condition were stated to have 'normal coagulation', and the majority were ≥ 1 month old; of these children transfused with FFP, 61.0% were stated to have been given FFP for pump priming/cardiac bypass, and all were > 2 months old (*see Key clinical group Cardiac surgery, p17; FFP Main underlying condition, p23; Cryoprecipitate Main underlying condition, p38; Reasons for initial cryoprecipitate transfusion, p39*).

    - *NATA cardiac surgery guidelines (Faraoini et al, 2019) suggest the addition of FFP to the cardiopulmonary bypass (CPB) prime in neonates (< 30 days) undergoing cardiac surgery with cardiopulmonary bypass. However, no recommendation could be made for infants and children.*
- Tranexamic acid was used for only 18.2% of cardiac surgery children transfused prophylactic FFP for 'abnormal coagulation' and surgery or invasive procedure, and for 64.3% of those transfused cryoprecipitate in the same setting (*see Key clinical group Cardiac surgery, p17; Section A Tranexamic acid in surgery, p33; Section B Tranexamic acid in surgery, p47*).
    - *BSH guidelines (2016) recommend that tranexamic acid should be considered in all children undergoing surgery where there is risk of significant bleeding. NATA cardiac surgery guidelines (Faraoini et al, 2019) recommend prophylactic administration of lysine analogs (either tranexamic acid or epsilon-aminocaproic acid) for all neonates and children undergoing surgery with CPB in order to reduce perioperative bleeding and transfusion.*
- Tranexamic acid was used for 83.3% (10/12) of the cases of trauma within 3 hours of trauma injury, but the numbers were small (*see Section C, Use of Tranexamic acid, p61*).
    - *According to BSH guidelines (2016), tranexamic acid should be used where massive blood loss is anticipated in children presenting with major traumatic injuries.*
- For children with major haemorrhage, the MHP was only activated in 55.6% of cases (*see Severity of the bleeding requiring transfusion, p54; Major haemorrhage protocol activated, p62*).
    - *Failure to activate the MHP in situations of major haemorrhage can lead to delayed transfusion and death (Naryan et al, SHOT 2021)*

Although many areas of practice do not have a strong evidence base, recommendations are provided for many of these areas by BSH and NATA guidelines, and in some cases there is high quality evidence from randomised controlled trial data.

It is recognised that the patient numbers in this National Comparative Audit are relatively small, but this reflects that neonatal and paediatric transfusions account for a small part of the overall transfusion activity in most hospitals.

Background

This audit reviews the practice of the use of fresh frozen plasma (FFP) and cryoprecipitate in paediatrics and neonatal medicine, both for prophylaxis and bleeding, by reference to standards in The British Society for Haematology (BSH) paediatric transfusion guidelines (BSH, 2016), and other guidelines (Faraoni et al, 2019). The audit extends the findings of a prior FFP National Comparative audit in 2009 which demonstrated that FFP was frequently transfused to children in absence of bleeding or need for procedures on the basis of coagulopathy alone (Stanworth et al, 2011). This was particularly the case for infants (42%) and mirrors similar findings from an Italian neonatal audit (Motta et al, 2014). Prophylactic use of FFP, including prior to surgery, is of unproven benefit at any age, and uncertainty for the neonatal population is compounded by the difficulty in defining a significant coagulopathy for this age group (Andrew et al 1987, 1988; Monagle et al, 2006). Minor abnormalities of the PTR or INR are poorly predictive of surgical bleeding (Segal and Dzik, 2005; BSH, 2008) and the effect of FFP in normalising the PT/INR is poor. Moreover, studies in preterm infants (Dani et al, 2009; Tran et al, 2012) have shown inconsistent benefits from coagulopathy screening and early plasma use for prevention of intraventricular haemorrhage, a serious bleeding complication of preterm babies.

This audit also explores use of fresh frozen plasma (FFP) and cryoprecipitate in paediatrics as part of the management of disseminated intravascular coagulation (DIC) by paediatricians and neonatologists. Data on transfusion support of children with DIC are limited and there are few specific guidelines for paediatrics. Recommendations are largely extrapolated from adult services, including the International Society on Thrombosis and Haemostasis harmonisation guidelines on DIC for adults (Wada et al, 2013). The BSH paediatric transfusion guidelines (BSH, 2016) recommended that FFP may be beneficial for children with DIC who have significant coagulopathy associated with clinically significant bleeding or prior to invasive procedures, and that cryoprecipitate may be given if the fibrinogen is less than 1.0 g/L despite FFP, or in conjunction with FFP for very low or rapidly falling fibrinogen.

Guidance on the management of major haemorrhage in children (BSH, 2016) has again been adapted from adult practice, including transfusion of FFP and red blood cells in ratios following the PROPPR study (Holcomb et al, 2015; BSH, 2015), and guidance on use of tranexamic acid. Increasing interest in the use of cryoprecipitate early in major haemorrhage in adults is also evident in paediatrics, but optimal practice is evolving and not well defined. Major haemorrhage protocols are recommended for children but consistency of implementation and appropriateness of use by hospitals are unknown. Moreover, it is not known how bleeding episodes not classified as major haemorrhage, but for which transfusions are given, are managed in children.

Aims of the audit

By reference to standards in guidelines, we wished to:

- Ascertain how FFP and cryoprecipitate are used for prophylactic transfusion.
- Improve understanding of the use of alternatives to plasma transfusion for infants and children.
- Improve understanding of the management of bleeding episodes in children, including implementation of Major Haemorrhage protocols.
- Compare practice with national recommendations.
- Identify clinical areas where further quality improvement initiatives should be targeted.

Audit standards

The audit standards were based on existing recommendations and key practice points from the BSH neonatal and paediatric transfusion guidelines (BSH, 2016). They were considered Key Performance Indicators (KPIs) in the initial report to hospitals (2018).

They are encapsulated in 4 Key Performance Indicators:

KPI 1: Trusts have a policy/local guideline for the transfusion of FFP and cryoprecipitate to neonates and children.

KPI 2: Trusts do not have a policy of routinely checking coagulation screens on all pre-term neonates.

KPI 3: Coagulation tests are performed before giving prophylactic FFP or cryoprecipitate.

KPI 4: Reason for the use of FFP or cryoprecipitate is documented in the patient's notes.

Methodology

All NHS hospitals in England were invited to participate in the audit, and hospitals in other UK countries were invited via their respective Blood Services.

Age groups included

Sites were asked to audit the medical and care records of 20 children receiving FFP and 20 children receiving cryoprecipitate in the prophylactic setting, and a sample of children (target 10) who had a transfusion as part of the management of active bleeding or trauma. For the purposes of the audit, 'children' were defined as all recipients who had not yet attained their 18th birthday. This included 'neonates' (defined for the purposes of the audit as those < 1 month), 'infants' (all those < 1 year), and 'older children' (from 1 to < 18 years).

Data collection method

Audit data collection was anonymised and could be either retrospective or prospective. Transfusion Laboratories supplied auditors with a list of children who had been transfused, and either records were obtained for audit (for retrospective data collection) or the auditors could visit the relevant clinical area (for prospective audit). The nature of the health professional filling in the audit form was not specified, but it was requested that where possible the main reason for giving FFP or cryoprecipitate should be given in conjunction with the clinical team, as should the description of the type of coagulopathy for children with 'abnormal coagulation'. In many cases, it is likely that the auditors would have been the site's Transfusion Practitioner although the clinicians were encouraged to take part.

A 'transfusion event' was defined as a prophylactic FFP transfusion, a prophylactic cryoprecipitate transfusion, or initiation of transfusion of blood components of any type given for bleeding. Children could be included in the audit more than once provided that sites did not audit the use of the same type of transfusion event more than once in the same child, e.g. a child could have both an FFP and cryoprecipitate transfusion event included.

For prophylactic FFP and cryoprecipitate transfusions, auditors were asked to capture the first transfusion during the admission or hospital visit in cases where more than one transfusion was given. The rationale for this was that we wanted to assess appropriateness of use based on the clinical picture as initially presented, recognising that ongoing transfusion indications may change as the clinical picture evolves.

For transfusions to treat bleeding, sites were encouraged to contribute data on any child who received a transfusion of any blood component as part of a plan to manage active bleeding. For these transfusions, details were requested on the first component transfused, and all subsequent components within the next 24 hours.

Auditors were also requested for information on local transfusion guidelines and policies in an organisational tool.

Data collection period

Data collection started on May 1st 2018 and ran at each site for 12 weeks following commencement. The date on which cases submitted occurred was not restricted to the data collection period and a minority of them occurred before May 1st 2018.

Analysis plan

Data collection required only the year of birth for patients over one year old on the date of transfusion. To obtain an age in days, we imputed patient's date of birth by randomly sampling from a multinomial distribution with probability of being born on a given day in their year of birth as reported by the Office for National Statistics (for further details see Appendix D; Additional methods). To convert gestational age from weeks and days into a decimal figure, we took the reported number of weeks and added the reported number of days divided by seven. So, a reported gestational age of 38 weeks and 2 days became 38 + (2/7) = 38.3 weeks.

Both PT and INR were included in the data collection for those receiving FFP and/or cryoprecipitate prophylactically, acknowledging that some hospitals may only report PT results as an INR. For comparative analyses in this audit, in the cases where only PT was reported, the PT ratio (PTR) was calculated using the midpoint of the local range (adult) where available or, if unavailable, the median midpoint across centres that provided a local range. The PTR results were considered similar enough to INR results for the purposes of the audit (the INR contains a minor adjustment, important for warfarin monitoring). A similar approach was taken for analysis of activated partial thromboplastin times (APTTs), or APT ratios (APTRs) and if indicated the APTR was calculated using local midpoints of ranges (adult) where available and, if unavailable, the median midpoint from all provided midpoints. Neonatal coagulation ranges for neonates as early as 30 weeks gestation show only minor prolongation compared to adults for the PT (Andrew et al, 1987, 1988), whereas there is significant prolongation for the APTT. Therefore, it was considered acceptable to present the PTR results unadjusted for the neonatal ranges for the purposes of the audit report. It is acknowledged that with more extreme prematurity, the PT will be more prolonged and this should be taken into account when reviewing the coagulation results for neonates in the report (Reverdiau-Moalic et al, 1996; Neary et al, 2015). The APTR results would require further adjustment in order to fully interpret their clinical significance.

In order to accurately reflect the auditors' responses to the questions in the audit tools, results have been presented using the same wording as was used in the questions as far as possible. All statistical analyses were carried out using the statistical package SAS Enterprise Guide (C) version 7.13 for Windows (2016 by SAS Institute Inc., Cary, NC, USA).

As with all audits, the quality of data is dependent upon the experience of the auditor and even more so on the quality of the patient record. Data are sometimes missing or sometimes incorrectly recorded. Every effort has been made by the audit team to clean and quality check the data submitted by the auditors. However, for some analyses, a small number of what seem to be outliers have been retained in the results, as reported by auditing sites.

Organisational data

57 out of the 64 sites included in the audit contributed organisational data.

Of the 57 sites, 50 sites treated adults and children, 5 were paediatric sites, 1 orthopaedic site and 1 was a women's hospital (including a neonatal unit).

Policies/local guidelines for transfusion of FFP and cryoprecipitate

KPI 1: Trusts have a policy/local guideline for the transfusion of FFP and cryoprecipitate to neonates and children

96.5% (55/57) of sites had a neonatal unit, and of those 87.3% (48/55) had a policy/local guideline for transfusion to neonates (7/55 did not).

94.7% (54/57) of sites transfuse children who are not in a neonatal unit and of those 83.3% (45/54) had a policy/local guideline for transfusion to children (9/54 did not).

Routine checking of coagulation screens on preterm neonates

KPI 2: Trusts do not have a policy of routinely checking coagulation screens on all pre-term neonates

70.2% (40/57) of sites met the audit standard of not having a policy of performing routine coagulation screens on all pre-term neonates. Unknown for 2 sites.

Additional key results from the organisational audit

52.7% (29/55) of sites provide age-related coagulation ranges for neonates and children to assist in the interpretation of test results.

31.6% (18/57) of hospitals used thromboelastography (TEG) or rotational thromboelastometry (RoTEM) to assess paediatric coagulation.

- 88.9% (16/18) used it in theatres
- 33.3% (6/18) used it in paediatric intensive care units (PICU)
- 27.8% (5/18) used it in A&E

Only 70.2% (40/57) of sites had a separate major haemorrhage protocol (MHP) in place for children. Unknown for 1 site.

Of the 40 sites that had a paediatric MHP, the number of times it had been activated in the previous 12 months was known for 90.0% (36/40) of hospitals. The majority of these hospitals had < 3 activations (2 had none, 20 had 1–2, 7 had 3–5, 3 had 6–9, and 4 had > 10).

Table 1: Features of the Major Haemorrhage Protocols and allied local paediatric policies (n = 57)			
Feature	**Yes (n & %)**	**No (n & %)**	**Unknown (n & %)**
For those with a paediatric MHP, tranexamic acid use is defined (n=40)	33 (82.5%)	7 (17.5%)	-
Paedipacks for emergency use in neonates	43 (75.4%)	13 (22.8%)	1 (1.8%)
Locally agreed concessionary release policy/ guidance document for acceptable alternatives to paediatric blood components in an emergency	32 (56.1%)	23 (40.4%)	2 (3.5%)
Policy or guidance on use of prothrombin concentrate for warfarin reversal in children	15 (26.3%)	41 (71.9%)	1 (1.8%)
Policy or guidance on use of fibrinogen concentrate in children[(1),(2)]	6 (10.5%)	17 (29.8%)	2 (3.5%)
Policy or guidance on the specific use of paediatric scores to help diagnose Disseminated Intravascular Coagulation	0 (0%)	54 (94.7%)	3 (5.3%)
7 of the 64 sites included in the audit did not complete organisational data and are excluded from this table. [(1)] 1 used instead of cryoprecipitate pools for older children; 1 - used for congenital hypofibrinogenaemia alone; 4 – Other [(2)] 32 (56.1%) sites do not use fibrinogen concentrate in children			

Key points relating to Organisational data:

- 87.3% (48/55) of sites with a neonatal unit had a policy/local guideline for the transfusion of FFP and cryoprecipitate to neonates. Similarly, 83.3% (45/54) of relevant sites had a policy/local guideline for the transfusion of FFP and cryoprecipitate to children.

Local polices guide clinicians and laboratory staff, improving standardisation of practice and the quality of care. Not all sites had a policy, and implementation would be a key step to improve practice.

- 26.3% (15/57) of sites had policies of routinely checking coagulation screens on all preterm neonates.

Neonatal coagulation testing should be initiated by a clinical picture suggesting a bleeding problem; there is no evidence to support routine testing and it may increase the risk of unnecessary transfusion, particularly if neonatal coagulation results are misinterpreted using adult normal ranges.

- Over a quarter of sites (28.1%;16/57) had no MHP for children (distinct from adults).

All hospitals who may treat children with major blood loss should have a dedicated MHP. Major haemorrhage in children will be a rare occurrence for many hospitals, and a paediatric MHP will help guide transfusion management and laboratory communication, reducing the risk of potentially life-threatening delays or errors in volumes for administration in an emergency clinical situation. Template paediatric MHPs are available (eg BSH, 2016), and may be used as the basis for developing a local MHP.

- For those sites that had a MHP, tranexamic acid use was not included in MHPs for children at 17.5% (7/40) of sites.

Tranexamic acid has been shown to reduce blood loss in both adults and children, and is recommended for massive blood loss, e.g. following paediatric trauma (RCPCH, 2012). Guidance on its use should be included in paediatric MHPs.

- 40.4% (23/57) of sites did not have a concessionary release policy for use of acceptable alternatives to 'paediatric' blood components in emergencies for major bleeding.

Concessionary release policies for use in emergency reduce the risk of confusion or delays in laboratory provision of appropriate blood components, particularly for neonates.

- 22.8% (13/57) of sites did not use paedipacks for emergency transfusion of neonates.

This is recommended good practice (BSH, 2016) to ensure neonates receive neonatal specification red cells, with additional safety features. Some hospitals may prefer to use large volume neonatal specification red cells rather than paedipacks, depending on their local usage and stock management.

Clinical audit

80 sites participated in the clinical audit (Appendix C). 16 sites reported that there were no transfusions to audit during the audit period. We report 675 transfusion events in 594 children from 64 sites. 62 sites were in England, 1 was in Northern Ireland and 1 was in Scotland. 18 children had their data fully excluded from the audit report (Appendix D Table A).

Table 2: Number of Transfusion Events Audited

Transfusion Events	National (n & %) n = 675	
Section A: FFP given prophylactically	417	61.8%
Section B: Cryoprecipitate given prophylactically	141	20.9%
Section C: ANY component given to treat bleeding or trauma	117	17.3%

NB: Some children were in more than one transfusion event category

Clinical audit KPIs

KPI 3: Coagulation tests are performed before giving prophylactic FFP and/or cryoprecipitate

For the purposes of the audit analysis, we defined a clinically relevant coagulation test as one conducted or reported within 24 hours preceding the prophylactic transfusion.

FFP: 63.1% (263/417) had a least one coagulation test known to be performed/reported within the 24 hours preceding the prophylactic FFP transfusion. 7.0 % (29/417) had at least one coagulation test more than 24 hours before the prophylactic FFP transfusion. 8.6%% (36/417) had at least one coagulation test but the transfusion time and/or test time was missing (Appendix D Table F).

Cryoprecipitate: 61.7% (87/141) had a least one coagulation test known to be performed within the 24 hours preceding the prophylactic cryoprecipitate transfusion. 4.3% (6/141) had at least one coagulation test more than 24 hours before the prophylactic cryoprecipitate transfusion. 15.6% (22/141) had at least one coagulation test but the transfusion time and/or test time was missing (Appendix D Table J).

KPI 4: Reason for the use of FFP and cryoprecipitate is documented in the patient's notes

Reason was documented in notes for 77.5% (323/417) of prophylactic FFP transfusion events, not documented in notes for 19% (78/417), and missing for 4% (16/417).

Reason was documented in notes for 66.0% (93/141) of prophylactic cryoprecipitate transfusion events, not documented in notes for 31% (43/141), and missing for 4% (5/141).

Use of prophylactic FFP and cryoprecipitate in key clinical groups

For both FFP and cryoprecipitate, the most common settings for transfusions were neonatal units (FFP 52.0%, 217/417; cryoprecipitate 36.2%, 51/141), theatre (FFP 19.4%, 81/417; cryoprecipitate 29.1%, 41/141), and PICU (FFP 13.4%, 56/417; cryoprecipitate 27.0%, 38/141).

For patients given prophylactic FFP and cryoprecipitate in theatre, cardiac surgery was the most common underlying condition for 60.5% (49/81) for FFP and 68.3% (28/41) for cryoprecipitate.

Further results are provided here for the following clinical groups: Neonatal units/neonates, PICU, Theatre/Cardiac surgery (see also Sections A and B).

1. Neonatal units/neonatal transfusions

Neonatal units were a major location for prophylactic transfusions of FFP (52.0%, 217/417) and cryoprecipitate (36.2%, 51/141). Neonates were a significant group of all cases for both FFP (56.1%, 234/417) and cryoprecipitate (44.0%; 62/141).

FFP

95.4% (207/217) of babies transfused on neonatal units were neonates (i.e. < 1 month of age; Appendix D Table B). The median age of neonates at the time of transfusion was 1 day (IQR 1-3 days). For the 97.8% (229/234) where gestational age was known, the median gestational age was 29.6 weeks (IQR 25.7-38.0).

The main underlying conditions for children transfused on the neonatal units were ‘ventilated preterm baby’ 45.6% (99/217), sepsis 20.7% (45/217), ‘perinatal event’ 9.7% (21/217).

‘Ventilated preterm babies’ constituted 24.9% (104/417) of all prophylactic FFP transfusions in the audit. These patients were transfused at a median of 1 day of life (IQR 1 - 2, n=103), were very pre-term with median gestational age 26.3 weeks (IQR 24.9 - 28.7, n=102), and of very low birth weight with a median weight of 0.80 kg (IQR 0.64 - 1.15, n=100).

For all infants born preterm at < 34 weeks gestation 77.0% (124/161) had the reason of ‘abnormal coagulation in the absence of invasive procedure or surgery’ as the main stated indication for transfusion. Prevention of IVH was given as a reason for FFP transfusion for 40.4% (65/161). (*See Section A for further details on gestational ages*).

Prevention of IVH was given as an additional reason for transfusion for 23.5% (98/417) of *all* cases of FFP transfusion. These children had a median age of 1 day (IQR 1-6) and gestational age 27.1 weeks (IQR 25.3-32.4); 80.6% (79/98) were neonates. Prevention of IVH was an additional reason for transfusion for 32.9% (73/222) of the FFP transfusions given for ‘abnormal coagulation the absence of invasive procedure or surgery’, of which 93.2% (68/73) were neonates.

The volume of FFP transfused was > 20 mL/kg for 13.0% (27/207) of the neonates where data was available (see Section A, Table 8).

Cryoprecipitate

The median age of neonates at the time of prophylactic cryoprecipitate transfusion was 3.5 days (IQR 1-7 days). The gestational age of all infants (< 1year) was known for 77.6% (76/98), with a median of 36.0 weeks (IQR 27.1-38.9). The volume transfused was > 10mL/kg for 41.5% (22/53) of the neonates where data were available.

Prevention of IVH was stated as an additional reason for transfusion of prophylactic cryoprecipitate for 25.5% (36/141) of *all* cases. These children had a median age of 4 days (IQR 1-65, n=35) and median gestational age of 30.1 weeks (IQR 26.4-38.3, n=26). 75% (27/36) of this group were transfused for 'abnormal coagulation in the absence of invasive procedure or surgery', and 81.5% (22/27) of these were neonates.

Prevention of IVH was an additional reason for transfusion for 39.1% (27/69) of the cryoprecipitate transfusions given for 'abnormal coagulation the absence of invasive procedure or surgery'.

1. <u>Key points relating to neonatal units/neonatal transfusions:</u>

- 52.0% (217/417) of FFP and 36.2% (51/141) of cryoprecipitate prophylactic transfusions were on neonatal units.

Neonatal units are key sites for education and optimisation of transfusion practice.

- 76.5% (179/234) of neonates had 'abnormal coagulation in the absence of invasive procedure or surgery' as the main reason for FFP transfusion (*these were 42.9% (179/417) of all FFP cases audited*).

Despite the BSH guideline (2016) recommendation that there is no evidence to support the routine use of FFP to try to correct abnormalities of the coagulation screen alone in non-bleeding neonates, the audit has identified common reporting of this indication; it is a key area where practice improvement should be targeted.

- Prevention of IVH was given as an additional reason for transfusion for around a third of all audited prophylactic FFP (32.9%; 73/222) and cryoprecipitate (39.1%; 27/69) transfusions given for 'abnormal coagulation the absence of invasive procedure or surgery'.
    - For the 161 preterm infants (born < 34 weeks gestational age), prevention of IVH was given as a reason for FFP transfusion for 40.4% (65/161).

BSH guidelines recommend against routine transfusion of FFP for prevention of IVH, in line with randomised controlled trial evidence for no benefit (NNNI Trial group, 1996). The significant usage of cryoprecipitate in the audit for this indication was unexpected and warrants further study.

- The volume (ml/kg) of FFP and cryoprecipitate transfusions was > 20 mL/kg in 13.0% (27/207) of FFP transfusions and > 10mL/kg in 41.5% (22/53) of cryoprecipitate transfusions where data were available.

These volumes exceed those currently recommended (BSH, 2016), and care should be taken to reduce the risk of transfusion associated circulatory overload (TACO).

2. Cardiac surgery

FFP

Cardiac surgery was the main underlying condition for 16.5% (69/417) children transfused with prophylactic FFP. 71.0% (49/69) were transfused in theatres, and 15.9% (11/69) in PICU. The median age at the time of transfusion was 1.2 years (IQR 4.5 months to 4.4 years, n=69) and the median weight was 8.65 kg (IQR 5.22 to 15.00 kg, n = 68).

59.4% (41/69) had 'normal coagulation', and cardiac surgery was the most common main underlying condition for patients transfused with 'normal coagulation (48.2%, 41/85). Only 1/41 was a neonate (< 1 month), 17/41 were ≥ 1 month and < 1 year, and 23/41 were ≥ 1 year old. Of these 41 with 'normal coagulation', 61.0% (25/41) were stated to have FFP for pump priming or cardiopulmonary bypass surgery, all were over 2 months of age.

26.2% (22/84) of children transfused FFP for abnormal coagulation prior to/during surgery or invasive procedures were undergoing cardiac surgery.

Cryoprecipitate

Cardiac surgery was the most common main underlying condition for children transfused with prophylactic cryoprecipitate (30.5%, 43/141). 65.1% (28/43) were transfused in theatre and 27.9% (12/43) in PICU. The median age at the time of transfusion was 7.6 months (IQR 3.1 months-5.9 years, n = 43). The median weight was 5.85 kg (IQR 3.66-13.00, n = 41).

48.8% (21/43) had 'normal coagulation', and cardiac surgery was also the most common main underlying condition for children transfused with 'normal coagulation' (70.0%, 21/30). Only 4/21 were neonates (< 1 month), 8/21 were ≥ 1 month and < 1 year, and 9/21 were ≥ 1 year old. 23.3% (7/30) of children transfused with 'normal coagulation' were stated to have cardiac bypass as a reason for transfusing.

38.9% (14/36) of children transfused cryoprecipitate for abnormal coagulation prior to/during surgery or invasive procedures were undergoing cardiac surgery.

Tranexamic acid in cardiac surgery

For children receiving FFP in the audit who were stated to be undergoing cardiac surgery, only 36.4% (24/66) received tranexamic acid. Only 18.2% (4/22) of children undergoing cardiac surgery with 'abnormal coagulation prior to or during invasive procedure or surgery' received tranexamic acid. For those undergoing cardiac surgery with 'normal coagulation' 45.5% (20/44) received tranexamic acid, and for the 25 with 'normal coagulation' and information that they were undergoing cardiac bypass surgery, it was 72.0% (18/25).

2. <u>Key points relating to cardiac surgery:</u>

- 16.5% (69/417) of prophylactic FFP and 30.5% (43/141) cryoprecipitate transfusions were given for children with cardiac surgery as their main underlying condition
- 59.4% (41/69) of children transfused with prophylactic FFP and 48.8% (21/43) with cryoprecipitate who had cardiac surgery as the underlying condition were stated to have 'normal coagulation', and the majority were ≥ 1 month old.
    - 61.0% (25/41) of these children with normal coagulation had FFP for pump priming/bypass, and none of these were neonates (all > 2 months old)

This significant use of prophylactic FFP and cryoprecipitate for children with cardiac surgery and normal coagulation, including a proportion stated to have received it for pump priming or cardiac bypass, is not based on strong evidence. Although the NATA guideline (Faraoni 2019) suggests adding FFP to the bypass prime to neonates < 30 days old, almost all those receiving FFP or cryoprecipitate for 'normal coagulation' were above this age. Further investigation is warranted as to the reasons for this practice and whether potentially avoidable transfusions can be minimised.

- Tranexamic acid was used for only 18.2% (4/22) of cardiac surgery children transfused FFP for 'abnormal coagulation' and surgery or invasive procedure.

Tranexamic acid is recommended for all children undergoing surgery with CPB prime (Faraoni et al, 2019), to reduce the risk of perioperative bleeding and transfusion. BSH (2016) similarly recommended its use for children undergoing cardiac surgery at high risk of significant bleeding. Local practice should be reviewed to encourage appropriate use of tranexamic acid in these patients.

3. PICU/sepsis

PICU was the third most common location for transfusion of FFP (13.4%, 56/417) and cryoprecipitate (27.0%, 38/141). For FFP transfusions on PICU, 48.2% were older children and 23.2% were neonates. 21.4% (12/56) of FFP transfusions on PICU were for children with sepsis, and 19.6% (11/56) with cardiac surgery.

Sepsis

FFP

16.3% (68/417) children transfused with FFP had sepsis as their main underlying condition. Most children that received FFP for sepsis were transfused within the neonatal period (median age 4 days, IQR 1 to 57 days, n=68), and infants transfused for sepsis had a median gestational age of 30.4 weeks (IQR 26.3 to 39.0 weeks, n=54) and median weight of 2.12 kg (IQR 0.90 to 3.96 kg, n=66).

73.5% (50/68) had 'abnormal coagulation' in the absence of surgical procedures. For the 306/417 children where the reason for transfusion included 'abnormal coagulation, the coagulopathy was described as sepsis for 6.9% (21/306) cases (Table 12).

Cryoprecipitate

- 12.8% (18/141) children transfused with cryoprecipitate had sepsis as their main underlying condition. For the 105/141 children transfused cryoprecipitate where the main reason for transfusion included 'abnormal coagulation' (with or without invasive procedure/surgery), the coagulopathy was described as sepsis in only 1.9% (2/105) cases ('DIC' was given for 14.3% ,15/105); (Table 23).

3. <u>Key points relating to PICU/sepsis:</u>

- 16.3% (68/417) of prophylactic FFP and 12.8% (18/141) of cryoprecipitate was transfused for children with sepsis as their main underlying condition.
- 73.5% (50/68) of children with sepsis transfused with prophylactic FFP were stated to have 'abnormal coagulation' in the absence of invasive procedure/surgery.

The BSH guidelines (2016) do not support the use of FFP or cryoprecipitate to correct coagulation results in the absence of surgery/invasive procedure in non-bleeding neonates or older children. It is important to ensure that patients are vitamin K replete (especially if there is an isolated increased PT); this may mean giving it routinely to sick children.

SECTION A: FFP given as prophylaxis

417 prophylactic transfusions of FFP were reported.

Baseline Characteristics of Children receiving Prophylactic FFP

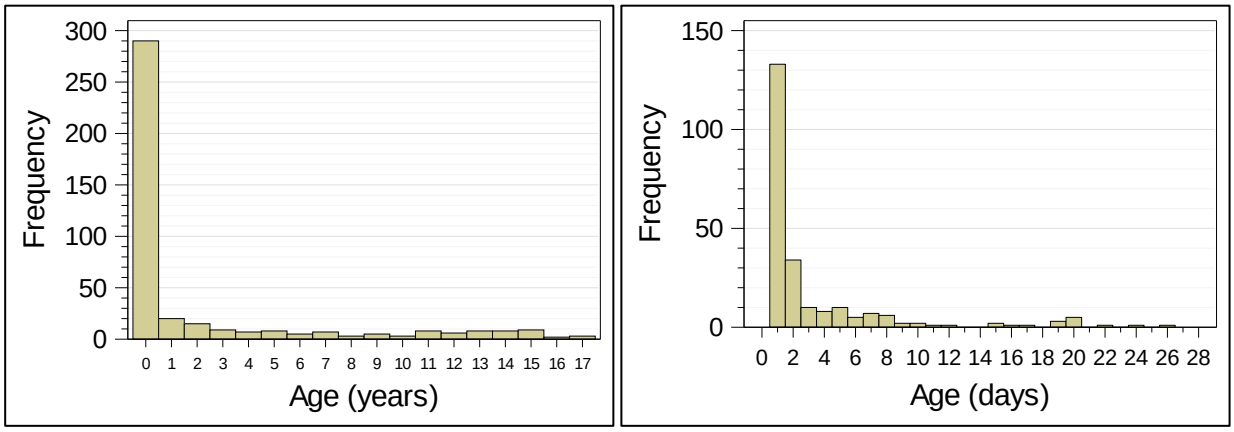
Age

Overall, the median age at the time of FFP transfusion was 8 days (IQR 1 day–2.1 years; range 1 day–17.7 years).

- The majority of children were less than 1 year of age (69.5%, 290/417).
- 56.1% (234/417) were neonates (< 1 month of age), and for these the median age was 1 day (IQR 1-3) (Appendix D Table B).
    - neonates were almost always transfused on neonatal units (88.5%).
- In theatres, 65.4% (53/81) were older children (≥ 1 year of age) and only 8.6% (7/81) were neonates.

Figure 1. Age distribution of children receiving prophylactic FFP.

a. All children **b. Neonates (< 1 month old)**



Gestational age

The gestational age of infants who received a transfusion was provided for 91.0% (264/290), with a median gestational age of 29.9 weeks (IQR 25.9–38.2, range 22.9–42.3) (Figure 2).

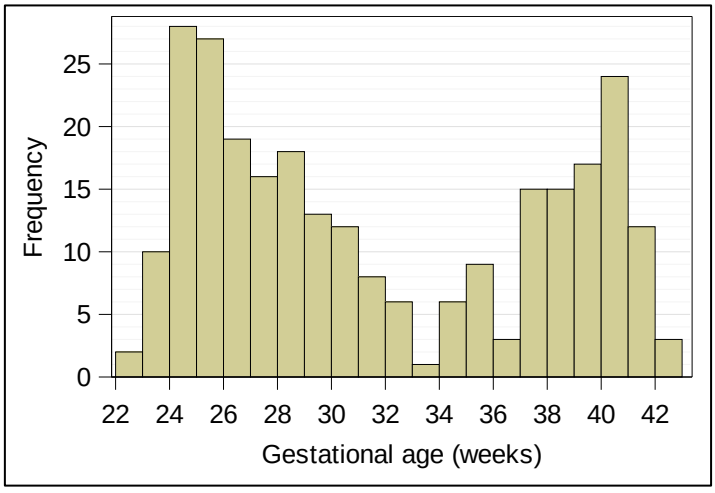
- For neonates, for the 97.8% (229/234) where gestational age was known, the median gestational age was 29.6 weeks (IQR 25.7–38.0, range 22.9–42.3) (Appendix D Figure A).

Preterm infants born at < 34 weeks gestation

The distribution of infant gestational ages separates into two groups, those born at < 34 weeks, and those born at ≥ 34 weeks. These groups have gestational age peaks at 24 weeks and 40 weeks ('term') respectively (Figure 2; see also Appendix D Figure A for similar pattern for neonatal gestational ages). For those born preterm at < 34 weeks:

- 94.4% (152/161) were transfused on neonatal units.
- the most common underlying diagnoses were 'ventilated preterm baby' (59.6%, 96/161) and sepsis (20.5%, 33/161).
- the majority (77.0%,124/161) had the main reason for transfusion as 'abnormal coagulation in absence of invasive procedure/surgery'; (normal coagulation 8.1%, 13/161).
- prevention of IVH was given as a reason for transfusion for 40.4% (65/161).

Figure 2: Gestational ages of children aged < 1 year receiving prophylactic FFP (n=264)



Weight

Weight at the time of transfusion was known for 94.0% (392/417) of cases. The median weight was 3.2 kg (IQR 1.0–11.6, range 0.1–94.0). (Appendix D Table C). The median weight of neonates (known for 224/234 neonates) was 1.2 kg (IQR 0.8–2.8).

Key points relating to age and weight:

- Overall median age at FFP transfusion was 8 days, and median weight was 3.2 kg.
- 56.1% (234/417) were neonates, with median age at transfusion of 1 day, median gestational age 29.6 weeks, and median weight at transfusion of 1.2kg.
- For the 161 preterm infants (born < 34 weeks gestational age), prevention of IVH was given as a reason for transfusion for 40.4% (65/161).

Neonates, in particular preterm neonates, are key recipients of prophylactic FFP and a particularly vulnerable, complex group of patients. It can be difficult to interpret neonatal coagulation results, particularly for very preterm babies, and local attention should be given to education and guidance on best transfusion practice for this group.

Location of prophylactic FFP transfusions and main underlying condition

Location

The majority of transfusions reported in this audit took place in neonatal units (52.0%, 217/417), theatres (19.4%, 81/417) or paediatric intensive care units (PICU; 13.4%, 56/417) (Table 3). Only 2.6% of transfusions (11/417) were on haematology/oncology/BMT wards (Table 3).

Neonates (< 1 month of age) were almost always transfused on neonatal units (88.5%, 207/234). The most common locations for transfusion of children ≥ 1 month were Theatres (40.7%, 74/182) or PICU (23.7%, 43/182) (Appendix D Table B).

Table 3: Location of prophylactic FFP transfusions

Location	National (n & %) n = 417	
Neonatal unit	217	52.0%
Theatre	81	19.4%
Paediatric Intensive Care Unit	56	13.4%
Paediatric ward	23	5.5%
Haematology/Oncology/Bone Marrow Transplant ward or day ward	17	4.1%
Paediatric High Dependency Unit	9	2.2%
Recovery	2	0.5%
Other *(listed below)*	11	2.6%
Missing	1	0.2%

Other (n=11)*:* Paediatric Liver Unit (4), A&E (2), Adult cardiothoracic CCU (1), Labour ward (1), and 3 with no further detail.

Main underlying condition

The main underlying conditions for which prophylactic FFP was given were 'ventilated pre-term baby' (24.9%), cardiac surgery (16.5%) and sepsis (16.3%) (Table 4; see Appendix D Table D for full details). These three main categories are described in the *Key clinical groups* section (p15).

Table 4: Main Underlying Medical or Surgical Condition

Main underlying condition	National (n & %) n = 417*	
Medical	**284**	**68.1%**
Ventilated preterm baby	104	24.9%
Sepsis	68	16.3%
Perinatal event	24	5.8%
Respiratory illness	17	4.1%
Leukaemia / Cancer / Bone marrow transplant	13	3.1%
Inherited disorders	13	3.1%
Other medical	43	10.3%
Missing	2	0.5%
Surgical	**133**	**31.9%**
Cardiac	69	16.5%
General surgery	17	4.1%
Necrotising enterocolitis	11	2.6%
Orthopaedic	10	2.4%
Other surgical	14	3.4%
Missing	12	2.9%

*Additional details in Appendix D Table D

Ventilated preterm babies

'Ventilated preterm babies' had a median age at the time of transfusion of 1 day (IQR 1–2, n=103). The median gestational age was 26.3 weeks (IQR 24.9–28.7, n = 102), with a median weight at the time of transfusion of 0.80 kg (IQR 0.64–1.15 kg, n=100). 81.7% (85/104) were transfused for 'abnormal coagulation' in the absence of surgical procedures.

Sepsis

Children with 'sepsis' had a median age at the time of transfusion of 4 days (IQR 1–57, n=68), and a median weight of 2.12 kg (IQR 0.90 to 3.96 kg, n=66). The median gestational age for those that were infants (<1 year of age) was 30.4 weeks (IQR 26.3–39.0, n=54). 73.5% with sepsis (50/68) were transfused for 'abnormal coagulation' in the absence of surgical procedures.

Cardiac Surgery
The median age at the time of transfusion for those with cardiac surgery as main underlying condition was 1.2 years (IQR 4.5 months to 4.0 years, n=69). The median weight was 8.65 kg (IQR 5.22 to 15.00 kg, n = 68).

- 59.4% (41/69) had 'normal coagulation'. 1 was a neonate (< 1 month), 17 were ≥ 1 month and < 1 year, and 23 were ≥ 1 year.
- Of the 41 with 'normal coagulation', 61.0% (25/41) were stated to have FFP for pump priming or cardiopulmonary bypass surgery, and all were over 2 months of age.

Key points relating to location and main underlying condition:

- 84.9% (354/417) prophylactic transfusions were in neonatal units, theatres or PICU
- The most common conditions associated with prophylactic transfusions in these locations were:
  - Neonatal unit (217) – 'ventilated preterm baby' 45.6% (99/217), sepsis 20.7% (45/217), 'perinatal event' 9.7% (21/217)
  - Theatre (81) – cardiac surgery 60.5% (49/81)
  - PICU (56) – sepsis 21.4% (12/56), cardiac surgery 19.6% (11/56).

These locations reflect the underlying conditions of the children transfused prophylactic FFP. Those with cardiac surgery may be transfused in theatre or post-operatively. See 'Key clinical group' Cardiac surgery' (p17) for further details and comment on prophylactic FFP transfusions for cardiac surgery.

Reasons for initial FFP transfusion

The reasons for giving the FFP transfusions are summarised in Table 5 overleaf. Auditors were asked to indicate the *main* reason for giving FFP (Table 5, highlighted rows), and whether prevention of IVH, fluid replacement, or bruising was an *additional* reason (Table 5, rows in italics; see also Table 6).

For FFP transfusions given for 'Normal coagulation with other reason', the other reasons stated by the auditors have also been incorporated into Table 5 (see also Appendix D Table E).

Table 5: Reasons for giving FFP

Reason	National (n & %) n = 417	
Abnormal coagulation before invasive procedure or surgery	**42**	**10.1%**
To prevent IVH	*11*	*2.6%*
As fluid replacement	*1*	*0.2%*
Bruising	*1*	*0.2%*
None of the above	*26*	*6.2%*
Missing	*3*	*0.7%*
Abnormal coagulation during invasive procedure or surgery	**42**	**10.1%**
To prevent IVH	*7*	*1.7%*
As fluid replacement	*2*	*0.5%*
Reversal of warfarin	*1*	*0.2%*
None of the above	*29*	*7.0%*
Missing	*3*	*0.7%*
Abnormal coagulation in the absence of invasive procedure or surgery	**222**	**53.2%**
To prevent IVH	*73*	*17.5%*
As fluid replacement	*12*	*2.9%*
Bruising	*13*	*3.1%*
None of the above	*115*	*27.6%*
Missing	*9*	*2.2%*
Normal coagulation with other reason	**85**	**20.4%**
To prevent IVH	*3*	*0.7%*
As fluid replacement	*14*	*3.4%*
Bruising	*5*	*1.2%*
*Cardiac bypass**	*25*	*6.0%*
Bleeding related	*5*	*1.2%*
Factor replacement	*3*	*0.7%*
Other surgery	*6*	*1.4%*
Other	*4*	*1.0%*
Missing	*20*	*4.8%*
Plasma exchange	**13**	**3.1%**
To prevent IVH	*1*	*0.2%*
As fluid replacement	*2*	*0.5%*
None of the above	*10*	*2.4%*
Missing	**13**	**3.1%**

*One child was also stated to have fluid replacement (not included in the table figures).

'Abnormal coagulation' group

73.4% (306/417) of children were described as having 'abnormal coagulation' by the auditors as part of the main reason for transfusion.

20.1% (84/417) were described as having abnormal coagulation *prior to or during surgery or invasive procedures*. Almost half of these were comprised by cardiac (26.2%, 22/84) and abdominal surgery (22.6%, 19/84) (Table 7).

53.0% (222/417) of children were described as having abnormal coagulation in the *absence* of invasive procedure or surgery.

- The majority of children in this group were neonates < 1 month old (81.0%; 179/222), transfused on the neonatal unit (78.38%, 174/222), with gestational age < 34 weeks (63%; 123/195). 38.3% (85/222) were 'ventilated preterm' neonates
- Other main underlying conditions were sepsis in 22.0% (49/222) and perinatal events in 9.0% (20/222).
- Additional reasons for transfusion were selected by the auditors for a proportion of these children: to prevent IVH for 32.9% (73/222); fluid replacement for 5.4% (12/222); bruising for 5.9% (13/222).

Normal coagulation group:

20.4% (85/417) of children were defined as having 'normal coagulation with other reason' by the auditors.

- Children tended to be older than in the 'abnormal coagulation' group with a median age of 1.2 years (IQR 76 d – 5.8 years). Only 23.5% (20/85) were neonates.
- The most common underlying conditions were cardiac surgery in 48.2% (41/85) or general surgery in 25.9% (22/85). 29.5% (25/85) were documented to be undergoing cardiopulmonary bypass.
- Transfusions were mostly given in theatres (57.6%; 49/85) and neonatal units (20.0%, 17/85).
- The most common reasons given for transfusion were cardiac bypass (29.4%, 25/85) and fluid replacement (16.5%, 14/85) (Table 5, see also Appendix D Table E). Only 11.8% (10/85) gave bruising or bleeding (presumed to be minor as this was prophylactic transfusion). For 23.5% (20/85), the auditor did not give a reason with normal coagulation.

Plasma exchange

Only 3.1% (13/417) children received prophylactic FFP for plasma exchange.

Key points relating to reasons for FFP transfusion:

- 53.0% (222/417) of children were transfused for abnormal coagulation in the *absence* of invasive procedure or surgery
  - the majority (81.0%, 179/222) were neonates
  - 32.9% (73/222) had prevention of IVH as a reason for transfusion
- 20.4% (85/417) of children were transfused for 'normal coagulation with other reason'
  - 57.6% (49/85) were transfused in theatre
  - 48.2% (41/85) had cardiac surgery as the underlying condition (29.5%, 25/85, known cardiac bypass)

A high proportion were transfused either for abnormal coagulation in the absence of procedure/surgery (particularly neonates) or 'normal coagulation' (particularly in theatre). This is not in line with BSH guidelines (2016) and many are likely to be inappropriate, increasing unnecessary risk. See also 'Key clinical groups' Neonates (p15) and Cardiac surgery (p17) for further discussion.

Additional reasons for FFP transfusion

Table 6: Additional reasons for FFP transfusion

Reason	National (n & %) n = 417	
None of the below	243	58.3%
To prevent intraventricular haemorrhage	98	23.5%
As fluid replacement	33	7.9%
Bruising	20	4.8%
Reversal of warfarin*	1	0.2%
Missing	22	5.3%

*Child was undergoing surgery

Prevention of IVH was stated as an additional reason in 23.5% of all cases (98/417). 73 of children in this group were transfused for 'abnormal coagulation in the absence of invasive procedure or surgery' while only 3 were for 'normal coagulation'.

- Children transfused for prevention of IVH had a median age of 1 day (IQR 1-6) and gestational age of 27.1 weeks (IQR 25.3-32.4). 80.6% (79/98) were < 1 month, 5.1% (5/98) were ≥1 month and < 1 year, and 13.3% (13/98) were ≥ 1 year.
- For the 73 children transfused with 'abnormal coagulation in the absence of invasive procedure or surgery', 93.2% (68/73) were neonates (< 1 month), 2.7% (2/73) were ≥ 1 month and < 1 year, 2.7% (2/73) were ≥ 1 year old, and 1 was missing age information.
- The most common underlying conditions were 'ventilated pre-term baby' in 46.9% (46/98) and sepsis in 20.4% (20/98).

Fluid replacement was an additional reason for 7.9% of children (33/417). 15 of these were transfused for normal coagulation (13.3%, 2/15 were cardiac surgery), and 12 for abnormal coagulation in the absence of procedure or surgery. The children had a median age of 20 days (IQR 4 days-3.9 years).

Key points relating to additional reasons for FFP transfusion:

- Prevention of IVH was given as a reason for transfusion of prophylactic FFP for 23.5% (98/417) of all children included in the audit
    - for preterm infants born at < 34 weeks gestation, prevention of IVH was given as a reason for transfusion for 40.4% (65/161).
- 7.9% (33/417) received FFP as fluid replacement

BSH guidelines (2016) recommend that FFP should not be used for simple volume replacement or routinely for prevention of IVH. See also 'Key clinical groups' Neonates (p15) regarding use for prevention of IVH.

Types of procedures

Table 7: Types of procedures patients transfused for 'abnormal coagulation' before/during invasive procedure or surgery were undergoing

Reason	National (n & %) n = 84	
Cardiac surgery	22	26.2%
Abdominal surgery	19	22.6%
Biopsy* *(details below)*	7	8.3%
Central line insertion	5	6.0%
Other surgery**	4	4.8%
Insertion/removal of UAC and/or UVC	2	2.4%
Other	13	15.5%
Lumbar puncture	*5*	*6.0%*
Drain insertion	*1*	*1.2%*
Pre ERCP planned	*1*	*1.2%*
No further detail given	*6*	*7.1%*
Missing	12	14.3%

*Biopsy sites (n=7): 2 bone marrow, 2 liver, 1 abdominal mass, 1 mediastinal mass, and 1 renal.
**3 neurosurgery, 1 orthopaedic surgery

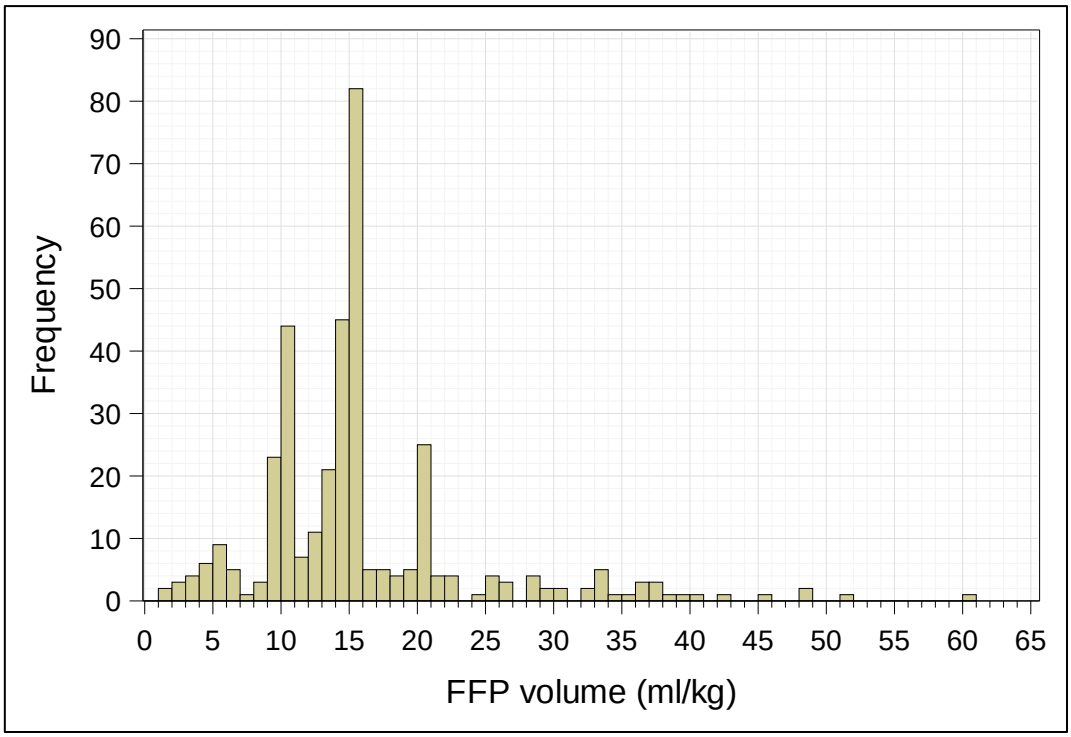
Volume of FFP transfused

The total volume of FFP transfused for each episode (defined as all FFP written up for transfusion at one time) was stated for 93% of (386/417) cases. The median volume was 50 mL (IQR 16-200, range 4-2000mL).

Volume of FFP by weight of patient

Due to 22 missing weights, 28 missing FFP volumes, and 3 missing both, the volume transfused (mL/kg) could only be calculated for 87% (364/417) of cases. The median volume transfused (mL/kg) was 15 mL/kg (IQR 10-17) (Figure 3).

Figure 3: Volume of FFP transfused (mL/kg)



Extreme FFP volumes (mL/kg) are not included in the figure (n=6 cases).

Table 8: Volume of FFP by weight and age of recipient

FFP volume transfused / weight of patient (mL/kg)	Age of prophylactic FFP recipient							
	Less than 1 month (n & %) n = 234		1 month to less than 1 year (n & %) n = 56		1 year or more than 1 year (n & %) n = 126		All ages (n & %) n = 417*	
Lower than 10	12	5.1%	7	12.5%	37	29.4%	**56**	**13.4%**
Between 10 and 20	168	71.8%	23	41.1%	52	41.3%	**244**	**58.5%**
Higher than 20	27	11.5%	18	32.1%	19	15.1%	**64**	**15.3%**
Missing	27	11.5%	8	14.3%	18	14.3%	**53**	**12.7%**
All	**234**	**100.0%**	**56**	**100.0%**	**126**	**100.0%**	**417**	**100.0%**

*One patient had missing age.

Key points relating to volume of FFP transfused:

- The FFP volume transfused for all cases where data available was:
  - < 10mL/kg for 15.4% (56/364)
  - 10-20mL/kg for 67.0% (244/364)
  - > 20 mL/kg for 17.6% (64/364)

Practice for volumes transfused continues to be variable. Low volumes may be sub-therapeutic, and high volumes may increase the risk of transfusion associated circulatory overload particularly in vulnerable recipients. BSH guidelines (2016) suggest 15-20mL/kg, with volumes at the higher range particularly in bleeding patients.

Type of FFP component transfused

Table 9: Type of FFP by age of recipient

Type of FFP	Age of prophylactic FFP recipient							
	Less than 1 month (n & %) (n = 234)		1 month to less than 1 year (n & %) (n = 56)		1 year or more than 1 year (n & %) (n = 126)		All ages (n & %) (n = 417*)	
Methylene-Blue	138	59.0%	14	25.0%	13	10.3%	166	39.8%
Solvent-detergent	56	23.9%	28	50.0%	102	81.0%	186	44.6%
Standard	18	7.7%	1	1.8%	2	1.6%	21	5.0%
Missing	22	9.4%	13	23.2%	9	7.1%	44	10.6%
All types	**234**	**100.0%**	**56**	**100.0%**	**126**	**100.0%**	**417**	**100.0%**

* One patient had missing age.

Note: guidance on use of plasma components has changed since the audit was performed (https://b-s-h.org.uk/media/18619/addendum-for-gl-on-transfusion-for-fetuses-neonates-and-older-children-aug-21-2020.pdf)

Coagulation tests

Coagulation tests relating to the initial FFP transfusion

Out of the 417 prophylactic FFP transfusion events audited, the date of the pretransfusion coagulation test result was available for 357 (85.6%) and the time for 351 (84.2%) transfusions.

Pre-transfusion coagulation test results

63.1% (263/417) had at least one coagulation test (i.e. PT/INR, APTT/APTR or fibrinogen) performed within the 24 hours preceding the prophylactic FFP transfusion (see Appendix D Table F). 7.0% (29/417) had at least one coagulation test more than 24 hours before the prophylactic FFP transfusion. 8.6% (36/417) had at least one coagulation test but the time of the transfusion or the test was missing.

INR or PTR values for those with 'abnormal coagulation' included in the main reason for transfusion

Of the 306 children with 'abnormal coagulation' included in the main reason for transfusion, only 228 (74.5%) had a INR/PTR result reported to be within 24 hours before transfusion.

Table 10: Results of INR or PTR pre-transfusion in all recipients with 'abnormal coagulation' included in the main reason for transfusion

INR or PTR (1) values from tests	Age of recipients							
	Less than 1 month (n & %) n = 204		1 month to less than 1 year (n & %) n = 32		1 year or more than 1 year (n & %) n = 69		All ages (n & %) n = 306*	
0.5 - <1.0	0	0.0%	1	3.1%	1	1.4%	2	0.7%
1.0 - <1.5	38	18.6%	3	9.4%	25	36.2%	66	21.6%
1.5-<2.0	60	29.4%	8	25.0%	11	15.9%	79	25.8%
2.0-<2.5	30	14.7%	2	6.3%	5	7.2%	37	12.1%
2.5-<3.0	16	7.8%	1	3.1%	2	2.9%	19	6.2%
3.0-<3.5	3	1.5%	0	0.0%	1	1.4%	4	1.3%
3.5-<4.0	8	3.9%	1	3.1%	0	0.0%	9	2.9%
4.0-<10.0	4	2.0%	0	0.0%	2	2.9%	6	2.0%
>=10.0 or greater than measurable (2)	5	2.5%	0	0.0%	1	1.4%	6	2.0%
Outside of 24 hours before or missing	40	19.6%	16	50.0%	21	30.4%	78	25.5%

(1) 37 are calculated PTRs, 33 are calculated using a local reference range (adult) and 4 calculated using a consensus average reference range. No INR/PTR values were < 0.5.
(2) One of the greater than measurable values was reported as '> 5'.
*One patient had missing age.

Note: although adult PT values were used to calculate the PTRs no further adjustment has been made to take account of neonatal coagulation ranges as this would have only a minor impact.

TEG/RoTEM performed within 24 hours prior to transfusion

Only 11 children had a TEG or RoTEM performed within 24 hours prior to the transfusion.

Coagulation test performed within 24 hours of the transfusion

Only 53.2% (222/417) children had a coagulation test known to have been performed within 24 hours after the transfusion commenced (see Appendix D Table H). For the purposes of the analysis, the stated start time of the FFP transfusion was used as the confirmation time point.

Key points relating to coagulation tests:

Where 'abnormal coagulation' was included in the reason for transfusion

- 25.5% (78/306) did not have an INR/PT test reported to us as within 24 hours prior to transfusion
- for those cases that did have a test within the 24 hours prior to transfusion, 29.8% (68/228) of results did not show significant coagulation abnormality, with INR/PTR of < 1.5
  - for neonates this was 23.2% (38/164), for older children (≥ 1 year) 54.2% (26/48).

These results indicate deviation from BSH guidance in a significant number of cases. The guidelines recommend that prophylactic FFP should not be administered to non-bleeding children with minor prolongation of the PT/APTT including prior to surgery, although it may be considered for surgery for critical sites. Minor abnormalities of the PT/INR are poorly predictive of surgical bleeding, and the effect of FFP in normalising the PT/INR is poor (studies on FFP have shown transfusing at PTR/INRs up to 1.8 to be of debatable benefit). Transfusing FFP in these cases is inappropriate and exposes children to unnecessary risk.

Although TEG/ROTEM is increasingly used in adult transfusion practice and there is interest in paediatrics, it is not well standardised for young children, in particular for neonates.

Additional treatments given

Table 11: Additional treatments given

	National (n & %) n = 417	
Vitamin K received in the 7 days prior to transfusion	220	52.8%
Additional transfusions of FFP given within the following 24 hours	98	23.5%
Cryoprecipitate given with the initial FFP/ following 24 hours	68	16.3%
Tranexamic Acid given with the initial FFP and/or in the following 24 hours	45	10.8%
Fibrinogen concentrate given with the initial FFP and/or in the following 24 hours	6	1.4%
Warfarin received in the 7 days prior to transfusion	5	1.2%
Other products given with the initial FFP and/or in the following 24 hours*	54	12.9%

*Human Albumin Solution (HAS) = 5 (9.3%); Prothrombin complex concentrate (PCC) = 4 (7.4%); Vitamin K = 4 (7.4%); Aprotinin = 3 (5.6%); Novo 7 (recombinant factor VIIa) = 1 (1.9%); and Missing = 37 (69%).

Tranexamic acid in surgery

Only 13.1% (11/84) of children transfused for 'abnormal coagulation prior to or during invasive procedure or surgery' received tranexamic acid. Of these only 18.2% (4/22) of children undergoing cardiac surgery and 5.3% (1/19) undergoing abdominal surgery (Table 7) received tranexamic acid.

For all children in the FFP audit stated to be undergoing cardiac surgery (from additional responses to QA11, not shown), only 36.4% (24/66) received tranexamic acid. For those undergoing cardiac surgery and stated to have 'normal coagulation' 45.5% (20/44) received tranexamic acid. For the 25 of with 'normal coagulation' undergoing cardiac bypass (Table 5), it was 72.0% (18/25).

Key points relating to tranexamic acid in surgery:

- Only 13.1% (11/84) of children transfused for 'abnormal coagulation prior to or during invasive procedure or surgery' received tranexamic acid.
- Only 36.4% (24/66) of children undergoing cardiac surgery received tranexamic acid.

Tranexamic acid should be considered for all children undergoing surgery at risk of significant bleeding, including cardiac surgery (BSH, 2016; Faraoni et al, 2019). This is a key area of patient blood management for children as for adults.

Adverse reaction to FFP

Only one child had a possible reaction after the FFP transfusion documented in the case notes (fever during infusion, no other signs of reaction). It was noted that this was likely to be due to underlying illness rather than reaction. Data were missing for 6 children. Although this might seem to suggest the adverse risk profile for plasma is low, there is likely to be considerable under-reporting.

Diagnosis of coagulopathy and DIC

For children with 'abnormal coagulation' the best description of the coagulopathy in the view of the clinical team

Auditors had indicated that there were 73.4% (306/417) cases where the main reason for transfusion included 'abnormal coagulation'. The definition of 'minor' abnormality was left to the auditors. Table 12 overleaf gives details.

Table 12		
Clinical Team description of the coagulopathy for those children where the main reason for transfusion included 'abnormal coagulation'	**National n & % (n = 306)**	
Minor abnormality of PT/APTT of uncertain cause	130	42.5%
DIC	27	8.8%
Due to liver disease	19	6.2%
Vitamin K deficiency	7	2.3%
Secondary to anticoagulation	3	1.0%
Other	106	34.6%
Prematurity	*25*	*8.2%*
Sepsis	*21*	*6.9%*
Congenital factor deficiency	*8*	*2.6%*
Neonatal coagulation	*6*	*2.0%*
Cardiac bypass	*4*	*1.3%*
Other (listed below)	*22*	*7.2%*
No further detail	*20*	*6.5%*
Missing	14	4.6%
Other (n=22): with thrombocytopenia (4), previous major bleed (3), cardiac surgery (2), ECMO (1), hypoxic ischaemic encephalopathy (1), minor bleed (1), plasma exchange (1), miscellaneous (5), and not relevant (4).		

Of the 27 cases described as DIC in Table 12, 24 were in the absence of invasive procedure or surgery, only 3 were prior to invasive procedure or surgery.

Key points relating to description of the coagulopathy:

- 42.5% (130/306) had a 'minor abnormality of PT/APTT of uncertain cause'.

A significant proportion of audited cases transfused for reasons including 'abnormal coagulation' stated that the coagulopathy was a minor abnormality of uncertain cause. This is not considered an appropriate indication for transfusion of prophylactic FFP as it is unlikely to be of benefit (BSH, 2016).

- 10.1% (31/306) were described as 'prematurity' or 'neonatal coagulation'.

Neonatal coagulation ranges are different from those of older children and adults, particularly for the APTT, so interpretation of results should take into account the PT and fibrinogen in addition. Coagulation results should be interpreted in the context of neonatal ranges (locally defined where available), and transfusions only given where the PT or APTT is significantly above the normal gestational and postnatal age-related reference range (BSH, 2016), together with clinically significant bleeding or prior to surgery or invasive procedures with a risk of significant bleeding.

- 88.9% (24/27) of those with DIC were transfused for 'abnormal coagulation in the absence of invasive procedure or surgery'.

BSH (2016) recommended, on the basis of international guidance for adults (Wada et al, 2013), that in the setting of DIC, FFP and cryoprecipitate should not be administered on the basis of laboratory tests alone, but restricted to those with signs of bleeding or where invasive procedures are planned (with the possible exception of children with acute promyelocytic leukaemia). The audit demonstrated a high proportion of those said to have DIC who were transfused prophylactic FFP against guidelines, on the basis of abnormal coagulation and no procedure/surgery.

Disseminated Intravascular Coagulopathy (DIC)

DIC was noted for 28 cases.

Table 13: Criteria for diagnosis of DIC for the 28 cases

Criteria for diagnosis	National n & % (n = 28)	
Prolonged PT(1)	3	10.7%
Prolonged APTT	4	14.3%
Low Fibrinogen	4	14.3%
Low platelets	8	28.6%
Raised D Dimers	2	7.1%
Other(2)	3	10.7%
Missing	4	14.3%

(1) For one case a second choice was defined as 'Raised D Dimers'.
(2) For two cases further details are 'Raised CRP', and 'Oozing, unable to take clotting'.

Note: one of the DIC cases had not stated 'abnormal coagulation' as a reason for transfusion

DIC score

In 54% of cases (15/28) a scoring system was not used, not known for 11 cases, missing for 2 cases.

Platelet transfusions

25% (7/28) of children with DIC received platelet transfusions.

Key points relating to DIC:

- There was no evidence of the use of scoring systems for diagnosis of DIC
- Criteria for diagnosis of DIC varied, and in only 3/28 cases were raised D Dimers included.

DIC scores have not been validated in children, and they are not universally used even in adult practice. It is not surprising that we found little evidence of their use in the clinical audit (only 1 case, in Section B), and that no hospital responding to the Observational data question had policy or guidance on the specific use of paediatric scores to help diagnose DIC. The choice of criteria for diagnosis of DIC in children is an area for future development.

SECTION B: Cryoprecipitate given as prophylaxis

141 prophylactic transfusions of cryoprecipitate were reported.

Baseline Characteristics of Children receiving Prophylactic cryoprecipitate

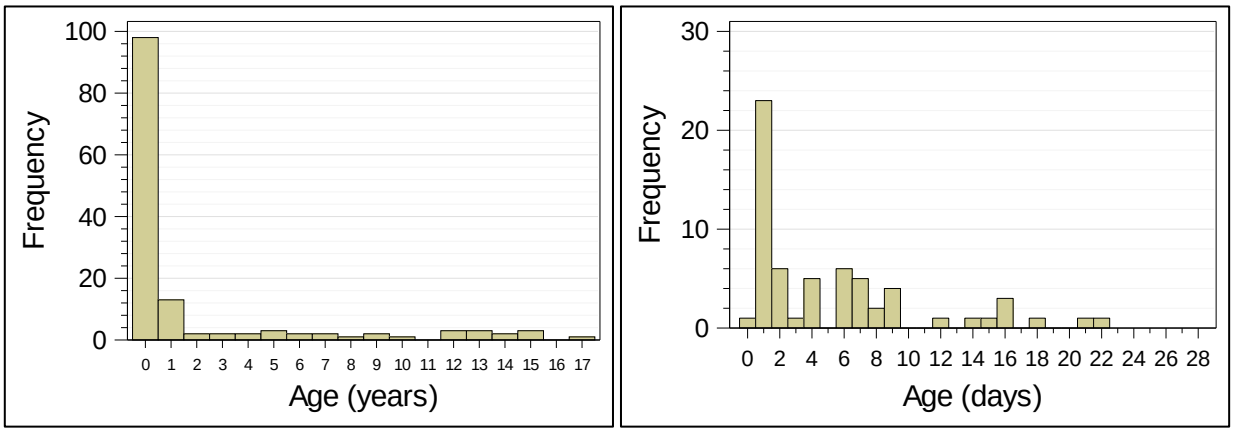
Age

Overall, the median age of those receiving prophylactic cryoprecipitate was 71 days (IQR 4 days–1.4 years; range 0 days - 17.8 years; data missing for 1 child)

- 70.0% (98/140) were infants (< 1 year)
- 44.0% (62/141) were neonates (median age 3.5 days, IQR 1-7).

Figure 4: Age distribution of children receiving prophylactic cryoprecipitate

a. All children **b. Neonates (< 1 month old)**



Gestational age

The gestational age of infants (< 1 year old) who received a cryoprecipitate transfusion was known for 76/98 (77.6%). The median gestational age was 36.0 weeks (IQR 27.1-38.9, range 23.1- 41.9) (Appendix D Figure B).

Weight

Weight at the time of transfusion was known for 133/141 (94%) cases. The median weight was 3.5 kg (IQR 2.2-8.7, range 0.3-94.0).

Key points relating to age and weight:

- Overall, the median age at cryoprecipitate transfusion was 71 days (slightly older than for those receiving FFP), and median weight was 3.5kg.
- 44.0% (62/141) of children who received cryoprecipitate were neonates

Neonates and infants < 1 year received more than two thirds of prophylactic cryoprecipitate transfusions to children.

Location of prophylactic cryoprecipitate transfusions and main underlying condition

Location

As for FFP, the majority of the transfusions reported in this audit took place in the neonatal unit (36.2%, 51/141), theatre (29.1%, 41/141), or PICU (27.0%, 38/141) (Table 14).

Table 14: Location of prophylactic cryoprecipitate transfusions

Location	National (n & %) n = 141	
Neonatal unit	51	36.2%
Theatre	41	29.1%
Paediatric Intensive Care Unit	38	27.0%
Paediatric ward	2	1.4%
Haematology/Oncology/Bone Marrow Transplant ward or day ward	2	1.4%
Paediatric High Dependency Unit	2	1.4%
Other *(listed below)*	4	2.8%
Missing	1	0.7%

Other (n=4): Adult intensive care unit (cardiac), Cardiac theatre, Liver ITU, and Paediatric liver unit.

Main underlying condition

The main underlying conditions for which cryoprecipitate was given were cardiac surgery (30.5%; 43/141), sepsis (12.8%; 18/141) and 'ventilated pre-term baby' (10.6%; 15/141) (Table 15).

Table 15: Main Underlying Medical or Surgical Condition

	National (n & %) n = 141	
Medical	**66**	**46.8%**
Sepsis	18	12.8%
Ventilated preterm baby	15	10.6%
Respiratory illness	9	6.4%
Perinatal event	7	5.0%
Inherited disorders	1	0.7%
Other medical	13	9.2%
Missing	3	2.1%
Surgical	**75**	**53.2%**
Cardiac	43	30.5%
Necrotising enterocolitis	3	2.1%
Orthopaedic (scoliosis)	3	2.1%
General surgery	2	1.4%
Other surgical	16	11.3%
Missing	8	5.7%

Additional details are in Appendix D Table I

Key points relating to location and main underlying condition:

- 92.2% (130/141) prophylactic cryoprecipitate transfusions were in neonatal units, theatres or PICU
- 53.2% (75/141) children receiving prophylactic cryoprecipitate had a surgical underlying condition, and for 30.5% (43/141) this was cardiac surgery.

The most common locations were the same as for those transfused prophylactic FFP, but a higher proportion had an underlying surgical condition, in particular cardiac surgery. As for FFP, the most common location was the neonatal unit.

Reasons for initial cryoprecipitate transfusion

The reasons for giving the cryoprecipitate transfusions are summarised in Table 16 overleaf. Auditors were asked to indicate the *main* reason for giving cryoprecipitate (Table 16, highlighted rows), and whether prevention of IVH, or bruising was an *additional* reason (Table 16, rows in italics; see also Table 17).

For cryoprecipitate transfusions given for 'Normal coagulation with other reason', the other reasons stated by the auditors have also been incorporated into Table 16.

Table 16: Reasons for giving cryoprecipitate

Reason	National (n & %) n = 141	
Abnormal coagulation before invasive procedure or surgery	8	5.7%
To prevent IVH	*1*	*0.7%*
Bruising	*0*	*0.0%*
Neither	*4*	*2.8%*
Missing	*3*	*2.1%*
Abnormal coagulation during invasive procedure or surgery	28	19.9%
To prevent IVH	*7*	*5.0%*
Bruising	*0*	*0.0%*
Neither	*19*	*13.5%*
Missing	*2*	*1.4%*
Abnormal coagulation in the absence of invasive procedure or surgery	69	48.9%
To prevent IVH	*27*	*19.1%*
Bruising	*5*	*3.5%*
Neither	*33*	*23.4%*
Missing	*4*	*2.8%*
Normal coagulation with other reason	30	21.3%
To prevent IVH	*1*	*0.7%*
Bruising	*0*	*0.0%*
Cardiac bypass	*7*	*5.0%*
Post-operative low fibrinogen	*3*	*2.1%*
Other(1)	*4*	*2.8%*
Missing	*15*	*10.6%*
Missing	6	4.3%

(1) "Cardiac surgery", "plasma exchange", "Post lines insertion for ECMO", and "Prevent haemorrhage peri operatively".

'Abnormal coagulation' group

74.4% (105/141) of children were described as having 'abnormal coagulation' by the auditors as part of the main reason for cryoprecipitate transfusion.

25.5% (36/141) were described as having abnormal coagulation *prior to or during surgery or invasive procedures*. Half of these were cardiac (38.9%, 14/36) or other surgery (11.1%, 4/36) (Table 18).

48.9% (69/141) of children who received prophylactic cryoprecipitate were described as having abnormal coagulation in the absence of invasive procedure or surgery.

- The majority of children in this group were neonates (65.2%; 45/69), and 20% (14/69) were 'ventilated preterm' neonates.
- The most common locations for cryoprecipitate transfusion were neonatal units (63.7%, 44/69) and PICU (30.4%, 21/69); the most common underlying condition was sepsis (23.2%, 16/69).
- Additional reasons for transfusion were selected by auditors for a proportion of these children: to prevent IVH in 39.1% (27/69) and bruising in 7.2% (5/69).

Normal coagulation group:

21% (30/141) of children who received prophylactic cryoprecipitate were defined as having 'normal coagulation with other reason' by the auditors.

- The median age of children who received cryoprecipitate and who had normal coagulation was 1.2 years (IQR 93 days-6 years. Only 16.7% (5/30) were neonates.
- The most common underlying condition was cardiac surgery (70.0%; 21/30). Only 4/21 were neonates (< 1 month), 8/21 were ≥ 1 month and < 1 year, and 9/21 were ≥ 1 year old.
- The most common reasons given for cryoprecipitate transfusion included cardiac bypass surgery 23.3% (7/30), post-operative low fibrinogen 10.0% (3/30), to prevent IVH 3.3% (1/30). (Table 16). For 50% (15/30) the auditor did not give a reason with normal coagulation.

Key points relating to reasons for cryoprecipitate transfusion:

- 48.9% (69/141) of children were transfused cryoprecipitate for 'abnormal coagulation in the *absence* of invasive procedure or surgery
  - the majority were neonates (65.2%; 45/69)
  - 48.9% (22/45) of these neonates had prevention of IVH as an additional reason for transfusion
- 21.3% (30/141) of children were transfused cryoprecipitate for 'normal coagulation with other reason'
  - cardiac surgery was the most common underlying condition (70.0%; 21/30)
  - for children with a cardiac surgery underlying condition, 48.8% (21/43) had 'normal coagulation'.

The main indications for transfusion of cryoprecipitate in children are DIC with bleeding, bleeding following cardiac surgery, and major haemorrhage (BSH, 2016). BSH recommends that cryoprecipitate may be considered for fibrinogen < 1g/L for surgery at risk of significant bleeding or to critical sites. The majority of cryoprecipitate transfusions audited would appear to be outwith guideline recommendations. There should be local review with clinicians as to the indications for transfusion of prophylactic cryoprecipitate to children. See 'Key clinical group' Cardiac surgery' (p17) for further details and comment on prophylactic cryoprecipitate transfusions for cardiac surgery.

Additional reasons for Cryoprecipitate transfusion

Prevention of intraventricular haemorrhage was stated as an additional reason for transfusion of prophylactic cryoprecipitate for 26% (36/141) of all cases. The median age of the children was 4 days (IQR 1-65, range 1 day - 13.9 years; n=35).

27/36 (75.0%) in this group were transfused for 'abnormal coagulation in the absence of invasive procedure or surgery'.

- For these 27 cases, 26 were infants (<1 year), 22 neonates, 4 aged ≥ 1 month but < 1 year, and 1 had missing age. Median age was 1.5 days (IQR 1-7 days; range 1-124 days).
- The median gestational age was 29.1 weeks (n=22; IQR 25.4-38.3; range 23.3-40.3 weeks).
- The most common main underlying conditions were sepsis (29.6%; 8/27) and ventilated preterm baby (22.2%; 6/27).

Table 17: Additional reason for cryoprecipitate transfusion

Reason	National (n & %) n = 141	
Neither to prevent intraventricular haemorrhage nor bruising	88	62.4%
To prevent intraventricular haemorrhage	36	25.5%
Bruising	5	3.5%
Missing	12	8.5%

Key points relating to additional reasons for cryoprecipitate transfusion:

- 25.5% (36/141) of all children had prevention of IVH given as a reason for transfusion of prophylactic cryoprecipitate
    - 81.5% (22/27) of cases transfused for IVH in addition to 'abnormal coagulation in the absence of invasive procedure or surgery' were neonates

This was a surprising finding and warrants further investigation, particularly for the neonates with 'abnormal coagulation' alone transfused to prevent IVH. A large randomised trial has demonstrated no benefit of FFP to prevent IVH in neonates (NNNI Trial group, 1996).

Type of procedure for those with abnormal coagulation

Table 18: Types of procedures patients transfused for 'abnormal coagulation' before/during invasive procedure or surgery were undergoing

Reason	National (n & %) n = 36	
Cardiac surgery	14	38.9%
Other surgery	4	11.1%
Biopsy(1)	2	5.6%
Removal of tunnelled central line	1	2.8%
Abdominal surgery	1	2.8%
Other(2)	3	8.3%
Missing	11	30.6%

(1) Biopsy sites: Renal and Skin/Muscle. Patient with Skin/Muscle biopsy also had Hickman line insertion, counted in 'Biopsy' category.
(2) 1 Drain insertion; 1 bleed; 1 no further detail given

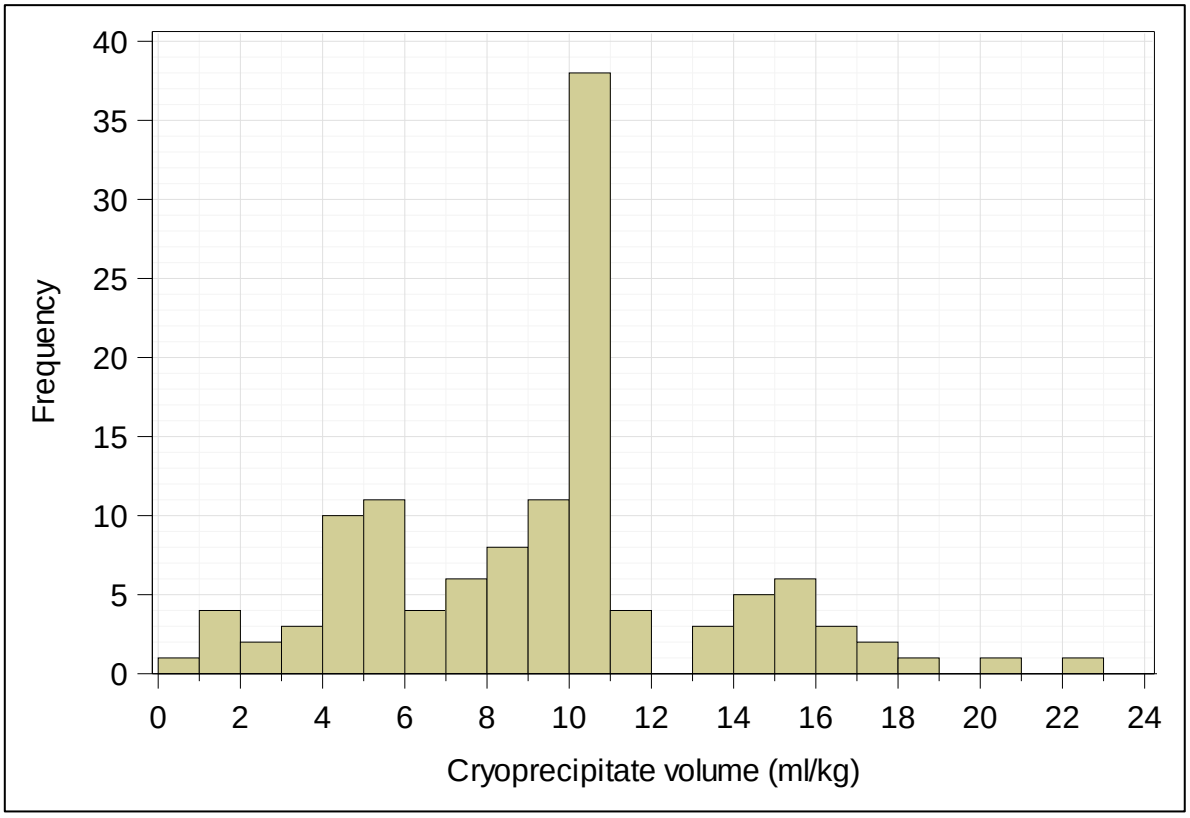
Volume of cryoprecipitate transfused

The total volume of cryoprecipitate transfused for each episode (defined as all cryoprecipitate written up for transfusion at one time) was stated for 94% (133/141) of cases. The median volume of cryoprecipitate was 40 mL (IQR 17-63, range 2.6-583mL).

Volume of cryoprecipitate volume by weight of patient

Due to 7 missing weights, 7 missing cryoprecipitate volumes, and 1 missing both, dose could only be calculated for 126/141 (89%) of cases. This median volume (mL/kg) was 10.0 mL/kg (IQR 6.0-10.5) (Figure 5).

Figure 5: Volume of cryoprecipitate transfused (mL/kg)



Extreme cryoprecipitate volumes (mL/kg) are not included in the figure (n=2 cases).

Table 19: Volume of cryoprecipitate by weight and age of recipient

Cryoprecipitate volume transfused / weight of patient (mL/kg)	Age of prophylactic cryoprecipitate recipient							
	Less than 1 month (n & %) n = 62		1 month to less than 1 year (n & %) n = 36		1 year or more than 1 year (n & %) n = 42		All ages (n & %) n = 141*	
Lower than 5	4	6.5%	3	8.3%	13	31.0%	20	14.2%
Between 5 and 10	27	43.5%	20	55.6%	18	42.9%	66	46.8%
Higher than 10	22	35.5%	13	36.1%	5	11.9%	40	28.4%
Missing	9	14.5%	0	0.0%	6	14.3%	15	10.6%
All	**62**	**100.0%**	**36**	**100.0%**	**42**	**100.0%**	**141**	**100.0%**

*One patient had missing age.

Type of cryoprecipitate transfused

Table 20: Type of cryoprecipitate transfused								
Type of cryoprecipitate	**Age of prophylactic cryoprecipitate recipient**							
	Less than 1 month (n & %)		**1 month to less than 1 year (n & %)**		**1 year or more than 1 year (n & %)**		**All ages (n & %)**	
	n = 62		**n = 36**		**n = 42**		**n = 141***	
Methylene-Blue	54	87.1%	26	72.2%	39	92.9%	120	85.1%
Pooled	*7*	*11.3%*	*1*	*2.8%*	*14*	*33.3%*	*22*	*15.6%*
Single	*45*	*72.6%*	*24*	*66.7%*	*23*	*54.8%*	*92*	*65.2%*
Missing	*2*	*3.2%*	*1*	*2.8%*	*2*	*4.8%*	*6*	*4.3%*
Standard	0	-	1	2.8%	2	4.8%	3	2.1%
Pooled	*0*	*-*	*0*	*-*	*1*	*2.4%*	*1*	*0.7%*
Single	*0*	*-*	*1*	*2.8%*	*1*	*2.4%*	*2*	*1.4%*
Missing	8	12.9%	9	25.0%	1	2.4%	18	12.8%
All types	**62**	**100.0%**	**36**	**100.0%**	**42**	**100.0%**	**141**	**100.0%**

* One patient had missing age.

Note: guidance on use of plasma components has changed since the audit was performed (https://b-s-h.org.uk/media/18619/addendum-for-gl-on-transfusion-for-fetuses-neonates-and-older-children-aug-21-2020.pdf)

Key points relating to volume of cryoprecipitate transfused:

- The volume transfused for all cases where data available was:
  - < 5ml/kg for 15.9% (20/126)
  - 5-10mL/kg for 52.4% (66/126)
  - > 10 ml/kg for 31.7% (40/126)

Practice continues to be variable. BSH guidelines (2016) suggest 5-10ml/kg for children. Low volumes may be subtherapeutic.

Coagulation tests

Pre-transfusion coagulation test results

At least one test result was known for 124/141 (87.9%) cases. There was a mixture of test results available, with some cases having only one test result while others had the full complement (see Appendix D Table J).

61.7% (87/141) had a least one coagulation test known to be performed within the 24 hours preceding the prophylactic cryoprecipitate transfusion. 4.3% (6/141) had at least one coagulation test more than 24 hours before the prophylactic cryoprecipitate transfusion. 15.6% (22/141) had at least one coagulation test result but the transfusion time and/or test time was missing.

Fibrinogen values for those that were defined as having abnormal coagulation

Of the 105/141 of children described as having 'abnormal coagulation' included in the main reason for transfusion by the auditors, we were only given information that 70 had a fibrinogen result within 24 hours before transfusion.

Table 21: Results of fibrinogen pre-transfusion in recipients with abnormal coagulation

Fibrinogen values from tests (g/L)	Age of prophylactic cryoprecipitate recipients with 'abnormal coagulation'							
	Less than 1 month (n & %) n = 54		1 month to less than 1 year (n & %) n = 27		1 year or more than 1 year (n & %) n = 23		All ages (n & %) n = 105*	
0.0 - <0.5	4	7.4%	**5**	18.5%	0	0.0%	9	8.6%
0.5 - <1.0	29	53.7%	10	37.0%	7	30.4%	46	43.8%
1.0 - <1.5	5	9.3%	2	7.4%	2	8.7%	9	8.6%
1.5 - <2.0	1	1.9%	0	0.0%	3	13.0%	4	3.8%
2.0 - 6.0	1	1.9%	1	3.7%	0	0.0%	2	1.9%
Outside of 24 hours before or missing	14	25.9%	9	33.3%	11	47.8%	35	33.3%
*One patient had missing age.								

TEG/RoTEM performed within 24 hours prior to transfusion

Only 5 children had a TEG or RoTEM performed within 24 hours prior to the transfusion.

Coagulation test performed within the 24 hours of the transfusion

121/141 children had a coagulation test performed. 61.7% (87/141) had any test performed within 24 hours after the transfusion commenced (see Appendix D Table K); 57.4% (81/141) had a fibrinogen test. For the purposes of the analysis, the start time of the cryoprecipitate transfusion was used as the confirmation time point.

Key points relating to coagulation tests:

Where 'abnormal coagulation' was included in the reason for cryoprecipitate transfusion i

- 33.3% (35/105) did not have a fibrinogen test known to be performed/reported within 24 hours prior to transfusion
- Of those that did have a test known within 24 hours prior to transfusion, 78.6% (55/70) had a fibrinogen level < 1.0g/L.
    - *for 21.4% (15/70) of those with a test within 24 hours, the fibrinogen was ≥ 1g/L*

A significant proportion of cryoprecipitate transfusions were given at fibrinogen levels higher than those recommended for prophylaxis in non-bleeding children (BSH, 2016). BSH recommended that cryoprecipitate prophylaxis may be considered for children with fibrinogen < 1g/L for surgery at risk of significant bleeding or to critical sites.

Additional treatments given

Table 22: Additional treatments given

	National (n & %) n = 141	
FFP given with the initial Cryoprecipitate/ following 24 hours	65	46.1%
Additional transfusions of Cryoprecipitate	36	25.5%
Tranexamic Acid given with the initial Cryoprecipitate/ following 24 hours	29	20.6%
Fibrinogen concentrate given with the initial Cryoprecipitate/ following 24 hours	7	5.0%
Other products given with the initial Cryoprecipitate/ following 24 hours*	12	8.5%

*HAS = 3 (25%); PCC = 2 (17%); Aprotinin = 1 (8.3%); Novo 7 = 1 (8.3%); and Missing = 5 (42%)

Tranexamic acid in surgery

Tranexamic acid was only given to 33.3% (12/36) children transfused for 'abnormal coagulation prior to or during invasive procedure or surgery'. Of these 12 children, 9 were undergoing cardiac surgery. For the cardiac surgery patients transfused for abnormal coagulation/surgery 64.3% (9/14) received tranexamic acid.

Only 52.4% (11/21) of audited children with normal coagulation and cardiac surgery as the main underlying condition received tranexamic acid. 85.7% (6/7) of those stated to be undergoing bypass surgery (Table 16) received tranexamic acid.

Key points relating to tranexamic acid in surgery:

- Only 33.3% (12/36) children transfused for 'abnormal coagulation prior to or during invasive procedure or surgery' received tranexamic acid.
    - for those with cardiac surgery it was 64.3% (9/14)

Tranexamic acid should be considered for all children undergoing surgery at risk of significant bleeding, including cardiac surgery (BSH, 2016; Faraoni et al, 2019).

Adverse reaction to cryoprecipitate noted in the case notes?

No child had an adverse reaction to cryoprecipitate. Data missing for 6 children.

Diagnosis of coagulopathy and DIC

For children with 'abnormal coagulation', the best description of the coagulopathy in view of the clinical team.

Auditors had indicated that there were 105/141 (74.5%) cases where the main reason for transfusion included 'abnormal coagulation'.

Table 23: What best describes the coagulopathy?	National n & % (n = 105)	
Minor abnormality of PT/APTT of uncertain cause	41	39.0%
DIC	15	14.3%
Due to liver disease	10	9.5%
Secondary to anticoagulation	4	3.8%
Other	26	24.8%
Cardiac bypass	*4*	*3.8%*
Prematurity	*3*	*2.9%*
Sepsis	*2*	*1.9%*
Other (listed below)	*16*	*15.2%*
No further details	*1*	*1.0%*
Missing	9	8.6%
Other (n=16): ECMO (2), cardiac surgery (2), post bleed (1), post-operative (1), previous major bleed (1), with thrombocytopenia (1), miscellaneous (4), and not relevant (4).		

Of the 15 cases described as DIC in Table 23, 12 were in the absence of invasive procedure or surgery, only 3 were prior to or during invasive procedure/surgery.

Key points relating to description of the coagulopathy:

- 39.0% (41/105) of those transfused cryoprecipitate for 'abnormal coagulation' had 'minor abnormality of PT/APTT of uncertain cause'
- 14.3% (15/105) of those transfused cryoprecipitate for 'abnormal coagulation' were stated as having DIC, and of these, 80.0% (12/15) were in the absence or invasive procedure or surgery.

As for FFP (see Section A, Key points relating to description of the coagulopathy, p35), BSH guidelines (2016) recommended that cryoprecipitate should not be administered on the basis of laboratory tests alone. The audit has highlighted this area for improvement of practice.

Disseminated Intravascular Coagulopathy (DIC)

15 children had DIC documented. 7/15 had criteria for diagnosis for DIC missing. 2/15 had a raised D-dimer.

Table 24: Criteria for diagnosis of DIC for the 15 cases

Criteria for diagnosis	**N**
Prolonged PT. Prolonged APTT. Low Fibrinogen. Low platelets. Raised D Dimers	**1**
Prolonged PT. Prolonged APTT. Low Fibrinogen. Raised D Dimers.	**1**
Prolonged PT, Prolonged APTT, Low Fibrinogen	**1**
Prolonged APTT, Low Fibrinogen, Low platelets	**1**
Prolonged PT, Low platelets	**1**
Low fibrinogen	1
Prolonged PT	1
Other	1
Missing	7

In one of the cases of DIC a scoring system was known to have been used. In 33.3% of cases (5/15) a scoring system was not used.

FFP transfusions prior to cryoprecipitate

2 children with DIC received a preceding FFP transfusion.

Platelet transfusions

46.7% (7/15) of children with DIC received platelet transfusions.

Key points:

- Criteria for diagnosing DIC were variable and there was little evidence of the use of DIC scoring systems

See *'Section A, Key points relating to DIC'* (p36) for comment.

SECTION C: Any component given to treat bleeding or trauma

This section refers to children who received FFP and or cryoprecipitate in the setting of bleeding or trauma.

117 cases were reported where any blood component was given to treat bleeding or trauma.

Key points:

- The two most common locations for transfusions for bleeding were NICU (34.2%, 40/117) and theatre (29.9%, 35/117).
- 'Major haemorrhage' was experienced by 30.8% (36/117) of patients. The Major Haemorrhage Protocol was activated in only 55.6% (20/36) of these cases.
- Tranexamic acid was only used in 51.5% (34/66) cases prior to or during surgery.
- Nearly all children with trauma (10/12) were given Tranexamic Acid within 3 hours of the trauma injury, but the numbers are small.
- Pre-transfusion Hb and platelet count data were only available for 42.7% (50/117) and 40.2% (47/117) cases respectively within 24 hours prior to bleeding/transfusion. *Knowing these values is essential in guiding transfusion decisions.*
- Specific ratios of blood components (e.g. 1:1 FFP:RBC) were requested for only 14.5% (17/117) of children (data missing for 10 children, 8.5%).
- Weight was, according to the audit data, not known for 8.5% (10/117) cases. *Knowing the weight is essential when calculating the correct volume of blood and blood components to administer.*
- 17.6% (16/91) patients weighing less than 50kg had all or some of their administered components prescribed in units as opposed to millilitres. *Prescribing components in mL/kg is recommended practice where the patient weighs less than 50kg.*

Baseline Characteristics of children transfused to treat bleeding or trauma

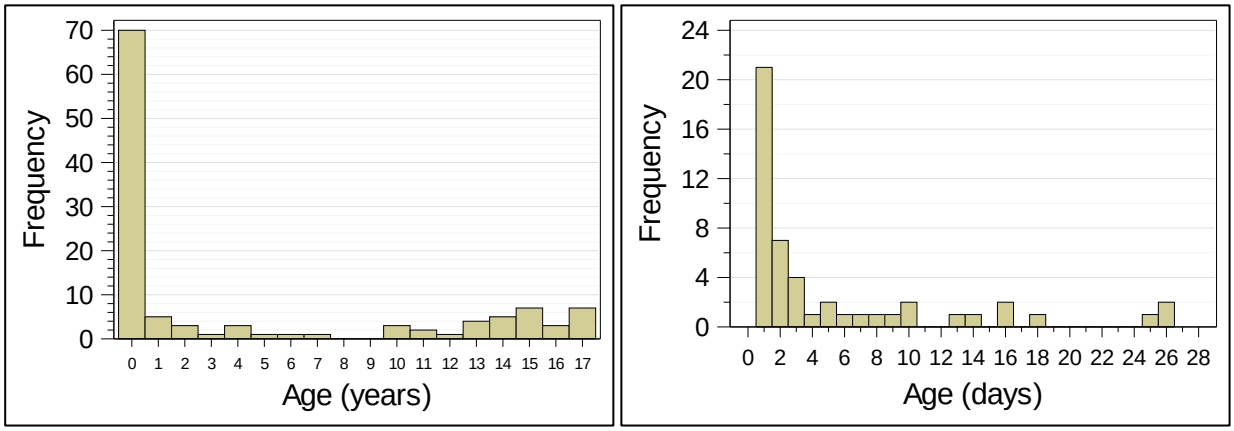
Age

Patients in this group were generally older than those in the prophylactic transfusion audited groups, with median age of 121 days (IQR 3 days - 10.9 years).

- 59.8% (70/117) of children were infants (< 1 year of age), with a median age of 5.5 days (IQR 1 - 51 days, range 1 day - 11.5 months).
- 41.9% (49/117) of children were neonates (< 1 month of age), with a median age of 2 days (IQR 1 - 7 days, range 1 - 26 days).

Figure 6. Age distribution of children receiving transfusion to treat bleeding or trauma

a. All children **b. Neonates (< 1 month old)**



Gestational age

The gestational age was known for 65 of the 70 children transfused for bleeding/trauma who were less than one year old. The median gestational age was 31.3 weeks (IQR 27.0 - 38.4, range 23.3 to 40.6). (Appendix D Figure C).

Weight

Weight was known for 91.5% (107/117) of cases. The median weight was 3.8 kg (IQR 1.6 - 26.5, range 0.5 to 94.0).

Location of transfusion to treat bleeding/trauma and main underlying condition

Location

The majority of these transfusions took place neonatal units (34.2%, 40/117), theatre (29.9%, 35/117), PICU (15.4%, 18/117), or A&E (12.0%, 14/117) (Table 25).

Table 25: Location of transfusion to treat bleeding or trauma

Location	National (n & %) n = 117	
Neonatal unit	40	34.2%
Theatre	35	29.9%
Paediatric Intensive Care Unit	18	15.4%
Haematology/Oncology/Bone Marrow Transplant ward or day ward	5	4.3%
Paediatric ward	3	2.6%
Other *(listed below)*	16	13.7%

Other (n=16): A&E (14), During transfer to another Trust site", and "Adult cardiac ICU".

Main underlying condition

The main underlying conditions for which blood components were given were cardiac surgery (23.9%, 28/117), ventilated pre-term baby (17.1%, 20/117), trauma (10.3% 12/117), and orthopaedic surgery (6.0%, 7/117)) (Table 26 and Appendix D Table L).

Table 26: Main Underlying Medical or Surgical Condition

Main underlying condition	National (n & %) n = 117	
Medical	**53**	**45.3%**
Ventilated preterm baby	20	17.1%
Sepsis	6	5.1%
Respiratory illness(1)	5	4.3%
Perinatal event (including FMH*)	5	4.3%
Inherited bleeding disorders	3	2.6%
Other medical(1)	9	7.7%
Missing	5	4.3%
Surgical	**64**	**54.7%**
Cardiac	28	23.9%
Orthopaedic	7	6.0%
General surgery	5	4.3%
Necrotising enterocolitis	3	2.6%
Other surgical (1)	18	15.4%
Trauma	*12*	*10.3%*
Missing	3	2.6%

(1) For more details see Appendix D Table L

* Feto-maternal haemorrhage

Neonates

Neonates were 41.9% (49/117) of all cases transfused for bleeding or trauma, with a median age of 2 days.

- The most common sites of bleeding given were ‘respiratory system’ (18.4%, 9/49), ‘intracranial’ (14.3%, 7/49) and cardiothoracic (10.2%, 5/49).

- The severity of bleeding requiring transfusion was ‘haemodynamic instability’ for 32.7% (16/49) and ‘major haemorrhage documented clinical or operation notes’ for 12.2% (6/49). 38.8% (19/49) were ‘in retrospect not significantly bleeding but clinically unstable’. For 16.3% (8/49), data were missing for severity of bleed. Overall, according to the definition given in section *‘Severity of the bleeding requiring transfusion’* (p54), 44.9% (22/49) had ‘significant bleeding (see Table 28 for comparison with all cases).

Trauma patients

The median age for the 12 trauma patients was 15 years (IQR 8.3 - 16.0).
In 58.3% (7/12) cases the paediatric emergency medicine (PEM) consultant was the trauma team leader (data missing for 2 cases).

In 41.7% (5/12) of cases there had been pre-hospital transfusion of blood components (data missing for 1 case). The type of component transfused was known for 3 cases: 1 FFP; 1 freeze-dried plasma; 1 red cells. The major haemorrhage protocol was activated for 75.0% (9/12) cases.

Key points relating to age, location and main underlying condition:

- The two most common locations for transfusion given for reasons of bleeding were neonatal units (34.2%, 40/117) and theatre (29.9%, 35/117).
- The most common underlying condition was cardiac surgery (23.9%, 28/117).
- 41.9% (49/117) of children transfused for bleeding were neonates, with a median age of 2 days
    - 'ventilated preterm baby' and 'perinatal event' were the underlying conditions for a total of 21.4% (25/117) of cases
- Only 12/117 children (10.3%) were transfused for treatment of trauma
    - 5/12 had received pre-hospital transfusion of blood components.
    - In 58.3% (7/12) cases the paediatric emergency medicine (PEM) consultant was the trauma team leader

A significant proportion of children treated for bleeding were neonates, and the neonatal unit was the most common location. Optimisation of the transfusion management of bleeding and suspected bleeding in neonates, including development of appropriate MHP guidance should be a focus for hospitals.

Cardiac surgery is a known key area for management of bleeding in children, but trauma is a relatively less common reason for transfusion in children.

Although 10% were transfused for trauma, bleeding occurred most commonly in locations other than A&E, and there is a need for paediatric teams to understand the principles of transfusion resuscitation in major blood loss and implementation of an MHP.

It is of interest that 58.3% of trauma cases were led by a PEM physician as trauma team leader, reflecting the increasing number of PEM specialists working at centres seeing seriously ill or injured children.

Severity of the bleeding requiring transfusion

The severity of the bleeding was categorised on the basis of the auditors' responses to the options given in the audit tool (Table 27). The auditors were given an option where in retrospect the bleeding was judged not to have been significant, to take account of diagnostic difficulty in some situations.

Table 27: Severity of bleeding requiring transfusion

Severity	National (n & %) n = 117	
Haemodynamic instability	32	27.4%
'Major haemorrhage' documented in clinical or operation notes	29	24.8%
In retrospect, not significantly bleeding but clinically unstable	28	23.9%
Blood loss of at least 40mL/kg within 3 hours	4	3.4%
Blood loss of at least 80mL/kg within 24 hours	3	2.6%
Missing	21	17.9%

Major haemorrhage

Overall, 30.8% (36/117) were categorised as having 'major haemorrhage' on the basis of the responses given to the options in the audit tool: 'major haemorrhage documented in clinical or operation notes' or 'blood loss ≥ 40mL/kg within 3 hours', or 'blood loss ≥ 80mL/kg within 24 hours' (Table 27).

- The children with major haemorrhage were most commonly transfused in theatre (41.7%, 15/36), A&E (33.3%, 12/36) and PICU (11.1%, 4/36).
- The underlying conditions included trauma (27.8%, 10/36), cardiac surgery (19.4%, 7/36) and orthopaedic surgery (13.9%, 5/36).
- The major haemorrhage protocol was activated in 55.6% (20/36) of these cases (11 cases in A&E, 4 in theatre, 2 in PICU, 2 in Haematology/oncology/bone marrow transplant ward or day ward, 1 in neonatal unit).

Haemodynamic instability

27.4% (32/117) were described as being 'haemodynamically unstable' (Table 27). A major haemorrhage protocol was used for 6.3% (2/32) cases.

- Children were most commonly transfused in neonatal units (43.8%, 14/32), theatre (28.1%, 9/32), and PICU (15.6%, 5/32).
- Underlying conditions included cardiac surgery (31.3%, 10/32), ventilated preterm baby (25.0%, 8/32) and sepsis (9.4%, 3/32).

Significant bleed

'Significant bleeding' (classified as either 'major haemorrhage' or 'haemodynamic instability') occurred in a total of 58.1%, (68/117) cases (Table 27).

Key points relating to severity of the bleeding requiring transfusion (where information was available):

- 58.1% (68/117) were transfused for 'significant bleeding' (including those with haemodynamic instability).
- 75.0% (27/36) of 'major haemorrhage' cases occurred in theatre or A&E, and trauma or cardiac surgery were the most common underlying conditions
- 23.9% (28/117) were in retrospect 'not significantly bleeding but clinically unstable'
    - for neonates this was a higher proportion, at 38.8% (19/49).

Major bleeding does occur in children and paediatric teams need to understand how and where to access local guidelines on transfusion resuscitation. A quarter of cases transfused for bleeding were in retrospect not significantly bleeding, 38.8% for neonates, illustrating the diagnostic difficulty in some situations. Caution with transfusion volumes and repeated clinical reassessment is vital for children transfused for major haemorrhage in order to avoid either over or under transfusion.

Main site(s) of the bleeding

Table 28: Main sites of bleeding

Site	National (n & %) n = 117	
Intracranial	13	11.1%
Respiratory system	12	10.3%
Gastrointestinal system	9	7.7%
Musculoskeletal	7	6.0%
Skin/subcutaneous	3	2.6%
Site of catheter/line insertion	3	2.6%
Nose/mouth	3	2.6%
Fetomaternal haemorrhage requiring transfusion at or after birth	3	2.6%
No significant bleeding confirmed	13	11.1%
Other	50	42.7%
Cardiothoracic	*14*	*12.0%*
Trauma or multiple sites of bleeding	*4*	*3.4%*
Other(1)	*4*	*3.4%*
No further details given	*28*	*23.9%*
Missing	1	0.9%

(1) Other: 2 Haematuria; 1 Gynaecological; 1 bleeding from umbilical cord

Blood components transfused in the first 4 hours after the start of the first blood component transfusion (including first component transfused)

A proportion of children had additional transfusions from 5 up to 24 hours after the start of the first blood component transfusion (data not shown).

Note: although there is apparently a significant percentage of missing data for the blood transfusions, due to the way the data were collected this may simply reflect that the components were not transfused.

Red cells

82.1% (96/117) of children received red cells (data missing for 15, 12.8%; the remainder cases stated not having received red cells)

- total red cell volume transfused was known for 80.0% (77/96): median 150mL (IQR 36 - 700)
- weight-related volume transfused (mL/kg) was known for 71.9% (69/96): median **15.3mL/kg** (IQR 12.4 - 26.6).

FFP

63.2% (74/117) received FFP (data missing for 25, 21.4%; the remainder cases stated not having received FFP).

- total FFP volume transfused was known for 78.4% (58/74): median 145 mL (IQR 33-500)
- weight-related volume transfused (mL/kg) was known for 70.3% (52/74): median **15mL/kg** (IQR 10-19.6).
- 23.1% (12/52) received < 10mL/kg, 17% (9/52) received > 20mL/kg.

Cryoprecipitate

33.3% (39/117) received cryoprecipitate (data missing for 46, 39.3%; the remainder cases stated not having received cryoprecipitate).

- total cryoprecipitate volume transfused was known for 82.1% (32/39): median 72.5mL (IQR 47.5 - 280)
- weight-related volume transfused (mL/kg) was known for 71.8% (28/39): median transfusion volume **10mL/kg** (IQR 6 - 15.1)
- 17.9% (5/28) received < 5mL/kg, 50% (14/28) received > 10mL/kg.

Platelets

33.3% (39/117) received platelets (data missing for 44, 37.6%; the remainder cases stated not having received platelets).

- total platelet volume transfused was known for 84.6% (33/39): median 250mL (IQR 50 -260)
- weight-related volume transfused (mL/kg) was known for 71.8% (28/39): median **12.5mL/kg** (IQR 5.3 to 16.6).

Key points relating to blood components transfused in the first 4 hours:

- The volume of red cells transfused (median 15.3mL/kg, IQR 12.4-26.6) was within the range that would be expected for transfusion of children with varying severity of bleeding.
- FFP was received by a high proportion of children within the first 4 hours after the start of the first blood component transfusion: 63.2% (74/117).
    - of those with known data, the volume transfused was < 10ml/kg for 23.1% (12/52)
- Cryoprecipitate and platelets were each transfused to a third of children.
    - of those with known data, the volume of cryoprecipitate was < 5mL/kg for 17.9% (14/28)

Typical paediatric MHPs would recommend an initial red cell transfusion of 20ml/kg in the situation of suspected major haemorrhage, but practice varies and some centres and protocols advocate repeated transfusion of 5mL/kg aliquots (e.g. Advanced Paediatric Life Support guidelines).

A significant proportion of FFP and cryoprecipitate transfusions within this 4 hour time period were likely to have been sub-therapeutic. For FFP, it is recommended that volumes of 20mL/kg should be used in major haemorrhage and other bleeding children (BSH, 2016); lower volumes risk being subtherapeutic. There is a similar risk for the children transfused low volumes of cryoprecipitate (below 5mL/kg).

Laboratory test results

The haemoglobin and platelet results are shown in Tables 29 and 30, respectively, for children who received either a red cell or a platelet transfusion in the first 4 hours. The 'pre-transfusion' and 'post-transfusion' test data were not precisely timed in relation to individual component transfusions, limiting the inferences that can be made.

Laboratory tests taken *prior to or within 1 hour* after the onset of bleeding (or suspected bleeding)

For the purposes of the audit analysis, taking into account the likely urgency of the situation in many cases, all results taken between 24 hours before and up to 1 hour after the start of the bleed or suspected bleed (or start of transfusion when the bleed time was missing) were classified as 'pre-transfusion' results. (Appendix D Table M).

Auditors were asked for the closest results prior to or within 1 hour after the onset of bleeding/suspected bleeding. If the time of the bleed onset was not known, they were asked to use results relating to the start of transfusion of the first component.

The date and time of bleed or suspected bleed was known for 55.5% (65/117) of cases. Of the remaining 52 cases, the date and time of first transfusion were known for 49/52 (94.2%). Overall, 114/117 (97.4%) had information on either timing of onset of bleed or start of transfusion of the first component, which were used for analysis of laboratory tests.

Haemoglobin

42.7% (50/117) cases had a haemoglobin result known to have been performed within 24 hours 'pre-transfusion' (i.e. including tests up to 1 hour after the start of bleed/suspected bleed/start of transfusion time) (Appendix D Table M).

Platelet count

40.2% (47/117) cases had a platelet result known to have been performed within 24 hours 'pre-transfusion' (i.e. including tests up to 1 hour after the start of bleed/suspected bleed/start of transfusion time) (Appendix D Table M).

Laboratory results at or up to 24 hours *after* start of transfusion of the first component

For the purposes of the audit analysis, results between 2 hours and within 24 hours of the start of transfusion of the first component were described as the 'post transfusion' results. (Appendix D Table N).

The start date and time of transfusion of first blood component was known for 113/117 cases, which were used for analysis of laboratory tests.

Haemoglobin

59.0% (69/117) cases had a haemoglobin result known to have been within 2 hours and 24 hours after the start of the transfusion (Appendix D Table N).
58 of these 69 cases received a red cell transfusion. 69.0% (40/58) of cases had 'significant bleeding' (Table 29).

Platelet count

59.0% (69/117) cases had a platelet result known to have been within 2 hours and 24 hours after the start of the transfusion (Appendix D Table N).
27 of these 69 cases received a platelet transfusion. 74.1% (20/27) of cases had 'significant bleeding' (Table 30).

Summary data on haemoglobin results for children who received a red cell transfusion in the first 4 hours

82.1% (96/117) children had evidence of receiving a red cell transfusion as part of their transfusion treatment for bleeding or trauma. Only 41.7% (40/96) of these had a haemoglobin result known to have been taken within 24 hours 'pre-transfusion' (Table 29).

For those children who had significant bleeding and received a red cell transfusion where a 'pre-transfusion' Hb result was known within 24 hours (44.8%, 26/58), the median Hb was 108 g/L (IQR 87 - 116) (Table 29). Where a 'post-transfusion' result was known within 24 hours (69.0%, 40/58), the median Hb was 113 g/L (IQR 95-130) (Table 29).

Table 29: Haemoglobin values (g/L) provided for those that had a red cell transfusion, by severity of bleed

Severity of bleed for those that had a red cell transfusion in the first 4 hours (n=96)	Pre-transfusion test performed between 24 hours before and 1 hour after bleed or transfusion				Post-transfusion test performed between 2 and 24 hours after start time of transfusion			
	n	Median	IQR	Range	n	Median	IQR	Range
Significant bleeding* (n=58)	**26**	**108**	**87-116**	**62-162**	**40**	**113**	**95-130**	**67-163**
Haemodynamic instability (n=23)	***10***	***102***	***78-127***	***62-162***	***18***	***116***	***95-133***	***67-162***
Major haemorrhage (n=35)	***16***	***108***	***94-115***	***63-149***	***22***	***113***	***95-127***	***84-163***
Major haemorrhage documented in clinical or operation notes (n=28)	*13*	*108*	*100-115*	*63-149*	*16*	*116*	*109-130*	*93-163*
Blood loss of at least 40 mL/Kg within 3 hours (n=4)	*2*	*86*	*79-93*	*79-93*	*4*	*91*	*85-97*	*84-98*
Blood loss of at least 80 mL/Kg within 24 hours (n=3)	*1*	*115*	*115-115*	*115-115*	*2*	*98*	*85-111*	*85-111*
No significant bleed (n=23)**	**9**	**95**	**86-119**	**72-154**	**8**	**128**	**109-158**	**103-172**
Missing severity (n=15)	**5**	**111**	**81-141**	**56-190**	**10**	**111**	**93-136**	**73-183**
All (n=96)	**40**	**108**	**84-120**	**56-190**	**58**	**113**	**98-133**	**67-183**

*'Significant bleeding' is the combination of 'Major haemorrhage' and 'Haemodynamic instability' cases
**In retrospect not significantly bleeding but clinically unstable
Note: the pre- and post-transfusion results in the table may not be from the same child

Summary data on platelet results for children that received a platelet cell transfusion in the first 4 hours

39/117 children had evidence of receiving a platelet transfusion as part of their transfusion treatment for bleeding or trauma. Only 38.5% (15/39) of these had a result known to have been taken within 24 hours 'pre-transfusion' (Table 30).

For those children who had significant bleeding and received a platelet transfusion where a 'pre-transfusion' platelet result was available within 24 hours (40.0%, 12/30) the median platelet count was 180 x 10^9/L (IQR 118 - 240) (Table 30). Where a 'post-transfusion' platelet result was available within 24 hours (66.7%, 20/30) the median platelet count was 143 x 10^9/L (IQR 114-191) (Table 30). In only 1 of the measurements within these defined timepoints was the platelet count below 50 x 10^9/L.

Table 30: Platelet counts (x 10^9/L) provided for those that had a platelet transfusion, by severity of bleed

Severity of bleed for those that had a platelet transfusion in the first 4 hours (n=39)	Pre-transfusion test performed between 24 hours before and 1 hour after bleed or transfusion				Post-transfusion test performed between 2 and 24 hours after start time of transfusion			
	n	Median	IQR	Range	n	Median	IQR	Range
Significant bleeding* (n=30)	**12**	**180**	**118-240**	**18-288**	**20**	**143**	**114-191**	**68-404**
Haemodynamic instability (n=9)	***3***	***83***	***18-188***	***18-188***	***8***	***159***	***132-240***	***115-404***
Major haemorrhage (n=21)	***9***	***202***	***160-278***	***55-288***	***12***	***136***	***78-182***	***68-381***
Major haemorrhage documented in clinical or operation notes (n=18)	*7*	*202*	*160-284*	*152-288*	*9*	*137*	*112-193*	*76-381*
Blood loss of at least 40mL/Kg within 3 hours (n=2)	*2*	*114*	*55-172*	*55-172*	*2*	*120*	*68-171*	*68-171*
Blood loss of at least 80 mL/Kg within 24 hours (n=1)	*0*	*-*	*-*	*-*	*1*	*71*	*71-71*	*71-71*
No significant bleed (n=4)**	**2**	**43**	**28-57**	**28-57**	**3**	**86**	**56-103**	**56-103**
Missing severity (n=5)	**1**	**54**	**54-54**	**54-54**	**4**	**76**	**66-124**	**60-166**
All (n=39)	**15**	**160**	**55-202**	**18-288**	**27**	**134**	**79-171**	**56-404**

*'Significant bleeding' is the combination of 'Major haemorrhage' and 'Haemodynamic instability' cases
**In retrospect not significantly bleeding but clinically unstable
Note: the pre- and post-transfusion results in the table may not be from the same child

Key points relating to laboratory test results:

- Only 41.7% (40/96) of children transfused with red cells had a Hb result known within 24 hours 'pre-transfusion' and only 60.4% (58/96) known within 24 hours 'post-transfusion' (accepting the limitations of the analysis definitions)
    - the median 'pre-transfusion' Hb where available was 108g/L, post-transfusion was 113g/L
- Only 62.9% (22/35) of those with 'major haemorrhage' had a Hb result known within 24 hours post-transfusion.
- For the children with 'significant bleeding' and a platelet count known within 24 hours 'pre-transfusion' (40.0%, 12/30), the median count was 180 x 10^9/L (IQR 118 - 240); within 24 hours 'post-transfusion' (for 66.7%, 20/30) it was 143 x 10^9/L (IQR 114-191).

The percentage of children with pre- and post-transfusion blood test results was surprisingly low. It is vital to monitor the impact of transfusions both clinically and with repeated laboratory testing in the bleeding situation, particularly major haemorrhage.

For major haemorrhage, it is suggested that the Hb should be maintained above 80g/L and platelets above 75 x 10^9/L. The audit results, where available, showed these Hb and platelet levels were achieved in the majority of cases.

TEG or RoTEM used to assess coagulation in the 24 hours after the onset of bleeding (or suspected bleeding)

TEG or RoTEM was only used to assess coagulation in only 12.8% of cases (15/117). Data were missing for 6 cases.

Non-transfusion interventions

Use of Tranexamic Acid

Surgery

Tranexamic Acid was used prior to or during surgery in 51.5% (34/66) of cases where the response to the question indicated there had been surgery.

Trauma

Tranexamic acid was used within 3 hours of trauma injury (non-surgical) for 15 cases

- the underlying conditions given were 'trauma' (10) and cardiac surgery (1)

Other products used to treat the bleeding (n=26); multiple products for one patient

Tranexamic acid 5; Vitamin K 4; PCC 3; Protamine 3; Fibrinogen concentrate 2; Novoseven 2; Aprotinin 1; Dexamethasone 1; and Missing 12.

Interventions undertaken to manage bleeding within 24 hours

- 76.9% (90/117) received supportive management only (including transfusion)
- 19.6% (11/56) of children who did not have a surgical bleeding required surgery
- 3.1% (2/64) of children who had surgical bleeding required a re-operation
- 1.7% (2/117) required interventional radiology
- 10.3% (12/117) information was missing

Key points relating to Use of tranexamic acid:

- Tranexamic acid was used for 10/12 of the cases of trauma

According to guidelines (BSH, 2016), tranexamic acid should be used where massive blood loss is anticipated in children presenting with major traumatic injuries.

Laboratory communication and blood prescribing

Major Haemorrhage Protocol (MHP) activated

The MHP was activated for 18.8% (22/117) of cases (data missing for 15 children, 12.8%). 55.6% (20/36) were children defined as a having ‘major haemorrhage’ and 2 had ‘haemodynamic instability’ (see Table 27 and associated text for details).

Of the 80 cases when the MHP was not activated, the laboratory was contacted to notify them of the bleeding in 42.5% (34/80) of cases (data missing on 26 children, 32.5%).

Urgent blood requests and group and screen samples

Blood was requested urgently from the laboratory in 80 cases.

- A valid group and screen sample was stated to have been available in the laboratory in 78.8% (63/80) of cases.
- For those where a sample was not available, a valid group and save sample was subsequently received in a median of 59.5 minutes (IQR 37.5-73.5) for the 8/17 cases in which the timing was known.

Red cell provision

36.5% (35/96) of children receiving red cells within the first four hours after the start of the first blood component transfusion (including first component transfused) received emergency Group O, D neg red cells (data missing for 1 child)

- of these 25.7% (9/35) were paedipacks (data missing for 9 children, 25.7%)
- 7/9 receiving paedipacks were neonates (2 were ≥ 1 year old).

Specific red cell/plasma/platelet ratios

Specific ratios were requested for 14.5% (17/117) of children (data missing for 10 children, 8.5%). 14/17 were children with ‘major haemorrhage’, and 11/17 had had the major haemorrhage protocol activated.
Ratios were:

- 8 cases FFP : red cell ratio 1:1
- 5 cases FFP : red cell ratio 1:2
- 2 cases FFP : platelet : red cell ratio 1:1:1
- 2 cases ratio data missing

Patients weighing less than 50 kg and components prescribed in millilitres:

- 15.4% (14/91) of children who weighed less than 50 kg had their components prescribed in units only, rather than millilitres
- 2.2% (2/91) of children had their components prescribed in both units and millilitres
- 79.1% (72/91) had their components prescribed in millilitres alone.

Data were missing for 3 children (3.3%).

Recorded delays to provision of blood transfusion support within 24 hours after bleeding onset

There were two recorded delays to transfusion (data missing for 11/117, 9.4%). Reasons were:

- ‘Blood initially issued was outdated.’

- ‘Delay in FFP issue due to 2 MHP patients requiring massive transfusion support at the same time. Unable to thaw > 12 frozen components at any one time. 20+ required at same time.’

Key points relating to laboratory communication and blood prescribing:

- The major haemorrhage protocol (MHP) was only activated in 55.6% (20/36) of cases defined as having ‘major haemorrhage’.

There is variability in transfusion practices for major bleeding, and the evidence base in neonates and older children is limited.

Clinicians should have a low threshold to activate the MHP in cases of suspected major bleeding in order to optimise communication between clinical and laboratory staff and facilitate the rapid provision of blood components.

Education should be provided to ensure clinicians and laboratory staff understand how and where to access information in local paediatric MHP’s.

Adverse reaction to blood transfusion

No adverse reactions were noted. Data were missing for 4 cases.

Bleeding patients with abnormal coagulation, clinical team's description of the coagulopathy

Table 31: What best describes the coagulopathy?	National n & % (n = 117)	
Minor abnormality of PT/APTT/Fibrinogen of uncertain	22	18.8%
Major haemorrhage	17	14.5%
DIC	9	7.7%
Secondary to anticoagulation	5	4.3%
Liver disease	4	3.4%
Vitamin K deficiency	1	0.9%
Other	14	12.0%
Cardiac bypass	*2*	*1.7%*
Prematurity	*3*	*2.6%*
Sepsis	*2*	*1.7%*
Other[1]	*3*	*5.1%*
No further detail given	*4*	*3.4%*
Missing	45	38.5%
Other (n=6): "Post-operative cardiac surgery"; "Patient being treated for unknown cause of anaemia and thrombocytopenia"; "Renal Problems. Cardiac arrest. Bleed."		

Note: 'missing' includes cases with no coagulopathy, so not responding to question

Disseminated Intravascular Coagulopathy (DIC)

DIC was noted for 9 cases. A DIC score was not used for any of the 9 cases

Table 32: Criteria for diagnosis of DIC for the 9 cases

Criteria for diagnosis	N
Prolonged PT, Prolonged APTT, Low Fibrinogen, Low platelets, Abnormal TEG/RoTEM	1
Prolonged PT, Prolonged APTT, Low Fibrinogen, Low platelets	1
Low Fibrinogen. Low platelets.	1
Prolonged PT	1
Prolonged APTT	1
Prolonged PT, Prolonged APTT, Low platelets, Raised D Dimers	1
Raised D Dimers	1
Blood film	1
Other	1

Other (n=1): "Active bleeding in surgery. Surgery aborted due to bleeding

Key points relating to description of the coagulopathy and DIC:

- For the 72/117 cases where a coagulopathy was described, 23.6% (17/72) were said to have coagulopathy due to major haemorrhage.

See 'Section A, Key points relating to DIC', (p36), for comment on DIC scoring.

Discussion

This audit has highlighted multiple areas of FFP and cryoprecipitate use where practice is not aligned with recommendations in national guidelines, including BSH (2016). These areas should be the focus of further local quality improvement initiatives and education.

In addition, a number of learning points are summarised below, which might be of value in the design of repeat audits of the practices of plasma and cryoprecipitate transfusion in children and neonates, or as topics for research.

- More clarity on why plasma transfusions are given for prevention of IVH in neonates, given that vascular and endothelial aetiologies for bleeding are far more likely to be relevant.
- Improved definitions and auditing of the types and severity of bleeding events.
- The continued practices of prophylactic use of FFP and cryoprecipitate, in the absence of bleeding, which raise questions about whether other clinical factors were relevant in the decision to transfuse, but which were not picked up by the audit proforma. Although it is difficult to make direct comparisons with the previous national comparative audit of FFP (National Comparative Audit, 2009) due to methodological differences, the theme of a significant proportion of transfusions for neonates and infants being for abnormal coagulation alone is unchanged. In the 2009 audit, 66% (93/140) of infants < 1 year old transfused for non-bleeding indications were transfused for ‘abnormal coagulation’ in the absence of invasive procedure or surgery, broadly similar to the current audit results. However, we do not know the overall numbers of transfusions of FFP transfused to infants for this indication currently in the UK compared to 2009.
- The uncertainties over local neonatal coagulation ranges and interpretation of neonatal coagulation results, in particular for very preterm babies and especially for the APTT/APTR, increase the difficulty in diagnosing clinically significant coagulopathy for this age group. Use of the APTR alone is of limited value in most situations, and interpretation of neonatal coagulation results should also take into account the PT and fibrinogen as well as gestational and postnatal age.
- Use of FFP and cryoprecipitate for children undergoing cardiac surgery with normal coagulation, including use for pump priming, requires further investigation and research as to evidence of benefit.
- The criteria for diagnosing DIC and managing DIC are poorly defined and validated in children and neonates – a difficult area for future understanding and development.

SUMMARY OF MAIN FINDINGS – A LOCAL ACTION PLAN TEMPLATE

Findings	Current guidance	What can we do?
Organisational		
Most but not all sites transfusing the relevant age groups had policies for transfusing FFP and cryoprecipitate to neonates and children.	BSH guidelines (2016) state that hospitals should have clear guidelines on transfusion thresholds for different paediatric groups.	**Ensure that we have clear guidelines that are available to clinical teams on transfusion thresholds for different paediatric groups.**
26% of sites had policies of routinely checking coagulation screens on all preterm neonates, which could increase the risk of unnecessary FFP transfusion.	BSH guidelines (2016) state that a policy of routine coagulation screening in neonates is inappropriate as results are difficult to interpret in and routine testing may lead to increased transfusion of FFP without benefit.	**If we still routinely screen, then discuss with local clinical teams with a view to amending local protocols, and re-educate if required.**
28% of sites had no major haemorrhage protocol (MHP) for children.	BSH guidelines (2016) state that hospitals which may encounter children with massive blood loss should have a dedicated children's major blood loss guideline, which would include advice on the correct age-adjusted volumes of blood components in an emergency.	**Check that our MHP for children is still appropriate, or develop one if we don't have one.**
For those sites that had an MHP, tranexamic acid use was not included in MHPs for children at 18% of sites.	BSH guidelines (2016)* recommend that tranexamic acid should be used where massive blood loss is anticipated in children presenting with major traumatic injuries, according to the timing and dosage recommended by RCPCH (2012).	**Ensure that our existing MHP for children includes the use of tranexamic acid, or ensure we include it in the MHP we intend to create.**
40% sites did not have a concessionary release policy for use of acceptable alternatives to 'paediatric' blood components in emergencies for major bleeding.	In order to avoid delays in blood provision, BSH guidelines (2016) recommend using pre-agreed hierarchies of alternative components in case specific blood components are not available in an emergency.	**Check that our local policy contains recommended hierarchies of alternative components, or build these into a policy if we don't have one.**

Clinical		
76.5% of neonates were transfused prophylactic FFP for 'abnormal coagulation', in the absence of surgery/invasive procedure. 23.2% of neonates that had a coagulation test reported within the 24 hours prior to transfusion had an INR/PTR of < 1.5, not significantly abnormal	BSH guidelines (2016) recommend that there is no evidence to support the routine use of fresh frozen plasma (FFP) to try to correct abnormalities of the coagulation screen alone in non-bleeding neonates.	**If we use FFP to correct abnormalities of the coagulation screen in non-bleeding neonates, discuss BSH guidelines with local clinical teams with a view to amending local protocols, and re-educate if required.**
Prevention of intraventricular haemorrhage (IVH) was an additional reason for transfusion in neonates for around a third of all FFP and cryoprecipitate transfusions given for abnormal coagulation in the absence of invasive procedure or surgery.	BSH guidelines (2016) recommend that FFP should not be used for simple volume replacement or routinely for prevention of IVH. The use of cryoprecipitate for this indication was unexpected. BSH guidelines recommended that prophylactic cryoprecipitate should not be routinely administered to non-bleeding children with decreased fibrinogen including prior to surgery. It may be considered for fibrinogen < 1 g/l for surgery at risk of significant bleeding or to critical sites.	**If we are using FFP for volume replacement or to prevent IVH, discuss BSH guidelines with local clinical teams with a view to amending local protocols, and re-educate if required.** **If we prophylactically administer cryoprecipitate to non-bleeding children with decreased fibrinogen, including prior to surgery, discuss BSH guidelines with local clinical teams with a view to amending local protocols, and re-educate if required.**
The volume (mL/kg) of neonatal prophylactic FFP and cryoprecipitate transfusions was > 20 mL/kg in 13.0% of FFP transfusions and > 10mL/kg in 41.5% of cryoprecipitate transfusions where data were available.	BSH guidelines (2016) describe suggested transfusion volumes and indicate that care should be taken to avoid volume overload. Suggested volumes are 15-20mL/kg for FFP (with volumes at the higher range particularly in bleeding patients), and 5-10mL/kg for cryoprecipitate.	**If the audit showed that we lack compliance with transfusion volumes, discuss BSH guidelines with local clinical teams and ensure that any local protocols are in keeping with BSH recommendations. Re-educate if required.**

Volumes of prophylactic FFP and cryoprecipitate were < 10mL/kg for 15.4% FFP and < 5mL/kg for 15.9% cryoprecipitate transfusions where data were available.	These volumes may be sub-therapeutic and are below those suggested by BSH (2016).	**If the audit showed that we lack compliance with transfusion volumes, discuss BSH guidelines with local clinical teams and ensure that any local protocols are in keeping with BSH recommendations. Re-educate if required.**
59.4% of children undergoing cardiac surgery transfused with prophylactic FFP and 48.8% with cryoprecipitate were stated to have 'normal coagulation', and the majority were ≥ 1 month old; of these children transfused with FFP, 61% were stated to have FFP for pump priming/cardiac bypass, and all were > 2 months old.	NATA cardiac surgery guidelines (Faraoini et al, 2019) suggest the addition of FFP to the CPB prime in neonates (< 30 days) undergoing cardiac surgery with cardiopulmonary bypass. However, no recommendation could be made for infants and children.	**We should review our audit data and discuss findings with cardiac teams.**
Tranexamic acid was used for 18.2% of cardiac surgery children transfused prophylactic FFP for 'abnormal coagulation' and surgery or invasive procedure, and for 64.3% of those transfused cryoprecipitate	BSH guidelines (2016) recommend that tranexamic acid should be considered in all children undergoing surgery where there is risk of significant bleeding. NATA cardiac surgery guidelines (Faraoini et al, 2019) recommend prophylactic administration of lysine analogs (either tranexamic acid or epsilon-aminocaproic acid) for all neonates and children undergoing surgery with CPB in order to reduce perioperative bleeding and transfusion.	**We should review our use of tranexamic acid in cardiac surgery and neonatal surgery, taking into consideration BSH recommendations.**
Tranexamic acid was used for 83.3% (10/12) of the cases of trauma within 3 hours of trauma injury, but the numbers were small.	According to BSH guidelines (2016), tranexamic acid should be used where massive blood loss is anticipated in children presenting with major traumatic injuries.	**We should review our use of tranexamic acid in trauma and major haemorrhage, taking into consideration BSH and RCPCH (2012) recommendations. Re-educate if required.**

For children with major haemorrhage, the MHP was only activated in 61% of cases.	Failure to activate the MHP in situations of major haemorrhage can lead to delayed transfusion and death (Naryan et al, SHOT 2021)	**We should review our MHP activations. For those patients where large volumes of product were given without MHP activation we should discuss those cases with clinicians.**

References

Andrew, M., Paes, B., Milner, R., Johnston, M., Mitchell, L., Tollefsen, D.M. & Powers, P. (1987) Development of the human coagulation system in the full-term infant. *Blood*, **70**,165-172.

Andrew, M., Paes, B., Milner, R., Johnston, M., Mitchell, L., Tollefsen, D.M., Castle, V. & Powers, P. (1988) Development of the human coagulation system in the healthy premature infant. *Blood*, **72**, 1651-1657.

British Society for Haematology Guideline: Chee, Y.L., Crawford, J.C., Watson, H.G., Greaves, M. (2008) Guidelines on the assessment of bleeding risk prior to surgery or invasive procedures. *British Journal of Haematology*, **140**, 496-504.

British Society for Haematology Guideline: Hunt, B.J., Allard, S., Keeling, D., Norfolk, D., Stanworth, S.J., Pendry, K., British Committee for Standards in Haematology. (2015) A practical guideline for the haematological management of major haemorrhage. *British Journal of Haematology,* **170**, 788-803.

British Society for Haematology Guideline: New, H.V., Berryman, J., Bolton-Maggs, P.H.B., Cantwell, C., Chalmers, E.A., Davies, T., Gottstein, R., Kelleher, A., Kumar, S., Morley, S.L., Stanworth, S.J. on behalf of the British Committee for Standards in Haematology. (2016) Guidelines on transfusion for fetuses, neonates, and older children. *British Journal of Haematology* **175**, 784-828.

Dani, C., Poggi, C., Ceciarini, F., Bertini, G., Pratesi, S. & Rubaltelli, F.F. (2009) Coagulopathy screening and early plasma treatment for the prevention of intraventricular haemorrhage in preterm infants. *Transfusion*, **49**, 2637-2644.

Faraoni, D., Meier, J., New, H.V., Van der Linden, P.J., Hunt, B.J. (2019) Patient Blood Management for Neonates and Children Undergoing Cardiac Surgery: 2019 NATA Guidelines. *Journal of Cardiothoracic and Vascular Anesthesia,* **33**, 3249-3263.

Holcomb, J.B., Tilley, B.C., Baraniak, S., Fox, E.E., Wade, C.E., Podbielski, J.M., del Junco, D.J., Brasel, K.J., Bulger, E.M., Callcut, R.A., Cohen, M.J., Cotton, B.A., Fabian, T.C., Inaba, K., Kerby, J.D., Muskat, P., O'Keeffe, T., Rizoli, S., Robinson, B.R., Scalea, T.M., Schreiber, M.A., Stein, D.M., Weinberg, J.A., Callum, J.L., Hess, J.R., Matijevic, N., Miller, C.N., Pittet, J.F., Hoyt, D.B., Pearson, G.D., Leroux, B. & van Belle, G.; PROPPR Study Group. (2015) Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs a 1:1:2 ratio and mortality in children with severe trauma: the PROPPR randomized clinical trial. *The Journal of the American Medical Association*, **313**, 471-482.

Monagle, P., Barnes, C., Ignjatovic, V., Furmedge, J., Newall, F., Chan, A., De Rosa, L., Hamilton, S., Ragg, P., Robinson, S., Auldist, A., Crock, C., Roy, N. & Rowlands, S. (2006) Developmental haemostasis. Impact for clinical haemostasis laboratories. Journal of *Thrombosis and Haemostasis*, **95**, 362-372.

Motta, M., Del, Vecchio, A., Perrone, B., Ghirardello, S. & Radicioni, M. (2014) Fresh frozen plasma use in the NICU: a prospective, observational, multicentred study. *Archives of Disease in Childhood. Fatal and Neonatal Edition*, **99**, F303-308.

Narayan, S. (Ed), Poles, D., et al. on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2020 Annual SHOT Report (2021).

National Comparative Audit of Blood Transfusion (2009) National Comparative Audit of the use of fresh frozen plasma. https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/14933/nca-audit_of_ffp_elsewheres2009.pdf (*accessed Dec 3 2021*).

Neary, E., McCallion, N., Kevane, B., Cotter, M., Egan, K., Regan, I., Kirkham, C., Mooney, C., Coulter-Smith, S., & Ní Áinle, F. (2015) Coagulation indices in very preterm infants from cord blood and postnatal samples. *Journal of Thrombosis and Haemostasis*, **13**, 2021–2030.

Northern Neonatal Nursing Initiative [NNNI] Trial Group. (1996) A randomized trial comparing the effect of prophylactic intravenous fresh frozen plasma, gelatin or glucose on early mortality and morbidity in preterm babies. *European Journal of Pediatrics,* **155**, 580-588.

Reverdiau-Moalic, P., Delahousse, B., Body, G., Bardos, P., Leroy, J., Gruel, Y. (1996) Evolution of blood coagulation activators and inhibitors in the healthy human fetus. *Blood* **88**, 900-906.

Royal College of Paediatrics and Child Health (RCPCH) (2012) Evidence Statement: Major Trauma and the use of Tranexamic Acid in Children. Available at: https://www.tarn.ac.uk/content/downloads/3100/121112_TXA evidence statement_final v2.pdf (*accessed Dec 2 2021*)

Segal, J.B. & Dzik, W.H. (2005) Paucity of studies to support that abnormal coagulation test results predict bleeding in the setting of invasive procedures: an evidence-based review. *Transfusion,* **45**, 1413-1425.

Stanworth, S.J., Grant-Casey, J., Lowe, D., Laffan, M., New, H., Murphy, M.F. & Allard, S. (2011) The use of fresh-frozen plasma in England: high levels of inappropriate use in adults and children. *Transfusion*, **51**, 62-70.

Tran, T.T., Veldman, A. & Malhotra, A. (2012) Does risk-based coagulation screening predict intraventricular haemorrhage in extreme premature infants? *Blood Coagulation and Fibrinolysis*, **23**, 532-536.

Wada, H., Thachil, J., Di Nisio, M., Mathew, P., Kurosawa, S., Gando, S., Kim, HK., Nielsen, J.D., Dempfle, C-E., Levi, M. & Toh, C.H. (2013) Guidance for diagnosis and treatment of disseminated intravascular coagulation from harmonization of the recommendations from three guidelines. *Journal of Thrombosis and Haemostasis*, **11**, 761–767.

Appendix A – Organisational Audit Tool

Organizational Audit Tool

1. Does your hospital have a neonatal unit? ☐ Yes ☐ No

2. Does your hospital transfuse children who are not in a neonatal unit? ☐ Yes ☐ No

3. Does your hospital have a policy/local guideline for the transfusion of FFP and cryoprecipitate:

to neonates? ☐ Yes ☐ No **to children?** ☐ Yes ☐ No

4. Does your hospital/neonatal unit have a policy of routine checking of coagulation screens on all preterm neonates?

☐ Yes ☐ No

5. Does your hospital laboratory provide age-related reference coagulation ranges for neonates and infants, to interpret these results?

☐ Yes ☐ No

5a. If 'Yes', what is the source of the ranges?

5b. What is your hospital's adult D Dimer range? | |

6. Does your hospital have a paediatric major haemorrhage policy, separate from an adult policy?

☐ Yes ☐ No

6a. If 'Yes', how many times has it been activated in the last 12 months?

☐ 1-2 ☐ 3 -5 ☐ 6 -9 ☐ >10 *(Insert number)* | |

7. Does your paediatric major haemorrhage policy define use of Tranexamic Acid?

☐ Yes ☐ No

8. Does your hospital provide paedipacks for emergency transfusion of neonates *(e.g. following delivery)*

☐ Yes ☐ No

9. Does your hospital have a locally agreed concessionary release policy/ guidance document for acceptable alternatives to paediatric blood components for use in an emergency *(e.g. major bleeding)*? Note: You may call this "Exceptional release", or similar.

☐ Yes ☐ No

10. Does your hospital have a policy/guidance on use of prothrombin concentrate for warfarin reversal in children? ☐ Yes ☐ No

11. Does your hospital have a policy/guidance on use of fibrinogen concentrate in children?

☐ Yes ☐ No ☐ Not used for children in our hospital

11a. If 'Yes' is it for (*please tick all that apply*):

☐ use instead of cryoprecipitate pools for larger children

☐ use in infant/paediatric cardiac surgery

☐ use for congenital hypofibrogenaemia alone

☐ other (please state)

12. Does your hospital have a policy/guidance on the specific use of paediatric scores to help diagnose Disseminated Intravascular Coagulation?

☐ Yes ☐ No

12a. If 'yes' is the source of the score (tick those that apply:

☐ International Society for Thrombosis and Haemostasis

☐ Other (please state)

13. Does your hospital use TEG/ROTEM to assess paediatric coagulation? ☐ Yes ☐ No

13a If 'Yes' , what areas is it used in?

☐ Theatre

☐ A&E

☐ PICU

☐ Other (please state)

National Comparative of Blood Transfusion Audit

NHS Blood and Transplant

Audit of the use of Fresh Frozen Plasma, Cryoprecipitate and other Blood Components in Neonates and Children

SECTION A - FFP given prophylactically

About this patient

A1. Where was the patient when the FFP was administered?
(Use the first component administered as a reference point and tick one option)

- ☐ Neonatal Unit
- ☐ Paediatric Intensive Care Unit
- ☐ Paediatric High Dependency Unit
- ☐ Haematology/Oncology/Bone Marrow Transplant ward or day ward
- ☐ Paediatric day care ward
- ☐ General paediatric ward
- ☐ Paediatric surgical ward
- ☐ Theatre
- ☐ Recovery
- ☐ A & E
- ☐ Adult ward
- ☐ Labour ward
- ☐ Other, please state: ____

A2. If on the date of transfusion the patient was over 1 year old, what was the patient's year of birth?

☐☐☐☐

If the patient was less than 1 year old, leave this blank and go to QA3. If not, go to QA6

A3. If on the date of transfusion the patient was less than 1 year old, what was their age in months?

☐☐

If the patient was less than 1 month old, go to QA4. Otherwise go to QA5

A4. If on the date of transfusion the patient was less than 1 month old, what was their age in days?

☐☐

Now go to QA5

A5. If on the date of transfusion the patient was less than 1 year old, what was their gestational age at birth?

☐ Weeks ☐ Days

A6. What was the most recent weight of the patient in Kg at the time of this transfusion? *If you are unable to find a record of the weight, please write "No record found"*

☐

A7. What is the main underlying medical or surgical condition? *(Tick one option)*

Medical
- ☐ Perinatal event
- ☐ Ventilated preterm baby
- ☐ Inherited disorders
- ☐ Bone Marrow Transplant
- ☐ Leukaemia / Cancer
  - ☐ Acute Lymphoblastic Leukaemia?
  - ☐ Promyelocytic Leukaemia (M3 Acute Myeloid Leukaemia)?
- ☐ Sepsis

- ☐ Respiratory illness
  - ☐ Mechanically ventilated? ☐ Not ventilated/non-invasive ventilation?

- ☐ Liver disease
- ☐ Thrombotic thrombocytopenic purpura
- ☐ Neurological disorder
- ☐ Renal disease

Surgical
- ☐ Cardiac
- ☐ Extracorporeal Membrane Oxygenation (ECMO)
  (for either cardiac or respiratory condition)

- ☐ Orthopaedic
  - ☐ craniofacial
  - ☐ scoliosis

- ☐ Necrotising enterocolitis
- ☐ General surgery
- ☐ Plastic surgery
- ☐ ENT surgery
- ☐ Trauma

If there is another main underlying medical or surgical condition, then please write it in the space below. ***OR*** *If you are unable to find the underlying reason, please write "Don't know" :*

☐

A8. Is the reason for this initial FFP transfusion documented in the patient's records? ☐ Yes ☐ No

A9. Which of these best describes the main reason for giving this initial FFP transfusion? *(Tick one option)*

☐ Before invasive procedure or surgery, with abnormal coagulation
☐ During invasive procedure or surgery, with abnormal coagulation
☐ Abnormal coagulation in the absence of invasive procedure or surgery
☐ Plasma exchange
☐ Normal coagulation with other reason (*please state in box; for intraventricular haemorrhage or fluid replacement see QA10*)

A10. In addition to the answer to QA9, do any of the following reasons for FFP transfusion apply?

☐ To prevent intraventricular haemorrhage
☐ As fluid replacement
☐ Reversal of warfarin
☐ Bruising
☐ None of the above

A11. If FFP was transfused as prophylaxis before or during a procedure or surgery, please indicate which:

☐ Not applicable

☐ Central line insertion ☐ Central line removal

☐ Tunnelled ☐ Non-tunnelled

☐ UAC or ☐ UVC (for neonates)

☐ Cardiac surgery
☐ Abdominal surgery
☐ Neurosurgery
☐ Biopsy (state site ***e.g. Liver, bone marrow, renal, other***)

☐ Other, please give details

A12. What was the total volume of FFP transfused for this episode (in mL)? ☐ mL

(An episode is defined as all the FFP written up for transfusion at one time)

A13. Was this FFP:

☐ Methylene-Blue?
☐ Solvent-detergent?
☐ Standard?

A14. What was the date of this initial FFP transfusion? D D M M ☐☐☐☐

A15. What was the start time of this initial FFP transfusion? H H : m m ☐☐☐☐

Please use 24 hour clock - (e.g.20:15)

A16. What were the coagulation tests relating to this initial FFP transfusion?

Please record the coagulation test results done before but nearest to the start time of the transfusion.

Date (dd/mm)	Time (hh:mm)	INR	PT(s)	APTT (s)	Fibrinogen (g/L)
Please tell us if these results are Raised (R), Normal (N) or Lowered (L)		R N L	R N L	R N L	R N L

☐ No result available

A17. Was TEG/RoTEM performed within 24 hours prior to transfusion?

☐ Yes ☐ No ☐ Not available

A18. Was a coagulation test performed within the 24 hours after the transfusion ended?

(Tick only, actual result not required; please record the time of coagulation test results done but if actual end time not known, then please estimate the time the transfusion ended)

Date (dd/mm)	Time (hh:mm)	INR	PT	APTT	Fibrinogen

☐ No result available

A19. Were any additional transfusions of FFP given within the 24 hours following this initial FFP transfusion? ☐ Yes ☐ No

A20. Was any cryoprecipitate given with the initial FFP episode and/or in the following 24 hours? ☐ Yes ☐ No

A21. Was any fibrinogen concentrate given with the initial FFP episode and/or in the following 24 hours? ☐ Yes ☐ No

A22. Was any tranexamic acid given with the initial FFP episode and/or in the following 24 hours? ☐ Yes ☐ No

A23. Were any other products given with the initial FFP episode and/or in the following 24 hours?
(e.g. Factor VIIa, Prothrombin Complex Concentrate) ☐ Yes ☐ No

A23a If yes, please give details:

A24. Did the patient receive Warfarin at any time in the 7 days prior to transfusion? ☐ Yes ☐ No

A25. Did the patient receive vitamin K at any time in the 7 days prior to transfusion? ☐ Yes ☐ No

A26. Was an adverse reaction to FFP noted in the case notes? ☐ Yes ☐ No

If yes, please describe the reaction

For patients where the reason given for transfusing FFP included 'abnormal coagulation' (QA9) fill in QA27-A31, as appropriate:

A27. If the main reason for FFP transfusion includes abnormal coagulation what, in the view of the clinical team, best describes the coagulopathy?
(Tick one option)

☐ Minor abnormality of PT/APTT of uncertain cause
☐ DIC
☐ Due to liver disease
☐ Secondary to anticoagulation
☐ Vitamin K deficiency
☐ Other (*please give details*)

If you ticked DIC in QA27, go to QA28. If not, you have finished SECTION A

A28. What were the laboratory results relating to this initial FFP transfusion in addition to the coagulation results stated in QA16?

Date (dd/mm)	Time (hh:mm)	D Dimer	Platelet count (x10^9/L)
Please tell us if the D Dimer results are Raised (R) or Normal (N		R N	

A29. What were the criteria for diagnosis *(Tick all that apply)*

☐ Prolonged PT
☐ Prolonged APTT
☐ Low Fibrinogen
☐ Low platelets
☐ Raised D Dimers
☐ Abnormal TEG/RoTEM *(e.g. abnormal fibrinolysis)*
☐ Blood film *(for fragments/schistocytes)*
☐ Other (please state)

A30. Was a DIC score used? ☐ Yes ☐ No ☐ D/K

A31. Were any platelets given with the initial FFP episode and/or in the following 24 hours? ☐ Yes ☐ No

END OF SECTION A

SECTION B - Cryoprecipitate given prophylactically

About this patient

B1. Where was the patient when the Cryo was administered?
(Use the first component administered as a reference point and tick one option)

- ☐ Neonatal Unit
- ☐ Paediatric Intensive Care Unit
- ☐ Paediatric High Dependency Unit
- ☐ Haematology/Oncology/Bone Marrow Transplant ward or day ward
- ☐ Paediatric day care ward
- ☐ General paediatric ward
- ☐ Paediatric surgical ward
- ☐ Theatre
- ☐ Recovery
- ☐ A & E
- ☐ Adult ward
- ☐ Labour ward
- ☐ Other, please state: ☐

B2. If on the date of transfusion the patient was over 1 year old, what was the patient's year of birth?

☐☐☐☐

If the patient was less than 1 year old, go to QB3. If not, go to QB6

B3. If on the date of transfusion the patient was less than 1 year old, what was their age in months?

☐☐

If the patient was less than 1 month old, go to QB4. If not, go to QB5

B4. If on the date of transfusion the patient was less than 1 month old, what was their age in days?

☐☐

Now go to QB5

B5. If on the date of transfusion the patient was less than 1 year old, what was their gestational age at birth?

☐ Weeks ☐ Days

B6. What was the most recent weight of the patient in Kg at the time of this transfusion? *If you are unable to find a record of the weight, please write "No record found"*

B7. What is the main underlying medical or surgical condition? *(Tick one option)*

Medical
- ☐ Perinatal event
- ☐ Ventilated preterm baby
- ☐ Inherited disorders
- ☐ Bone Marrow Transplant
- ☐ Leukaemia / Cancer
  - ☐ Acute Lymphoblastic Leukaemia?
  - ☐ Promyelocytic Leukaemia (M3 Acute Myeloid Leukaemia)?
- ☐ Sepsis

- ☐ Respiratory illness
  - ☐ Mechanically ventilated?
  - ☐ Not ventilated/non-invasive ventilation?

- ☐ Liver disease
- ☐ Thrombotic thrombocytopenic purpura
- ☐ Neurological disorder
- ☐ Renal disease

Surgical
- ☐ Cardiac
- ☐ Extracorporeal Membrane Oxygenation (ECMO)
  (for either cardiac or respiratory condition)

- ☐ Orthopaedic
  - ☐ craniofacial
  - ☐ scoliosis

- ☐ Necrotising enterocolitis
- ☐ General surgery
- ☐ Plastic surgery
- ☐ ENT surgery
- ☐ Trauma

If there is another main underlying medical or surgical condition, then please write it in the space below. ***OR*** *If you are unable to find the underlying reason, please write "Don't know" :*

B8. Is the reason for this initial Cryo transfusion documented in the patient's records? ☐ Yes ☐ No

B9. Which of these best describes the main reason for giving this initial Cryo transfusion? *(Tick one option)*

☐ Before invasive procedure or surgery, with abnormal coagulation
☐ During invasive procedure or surgery, with abnormal coagulation
☐ Abnormal coagulation in the absence of invasive procedure or surgery
☐ Normal coagulation with other reason (*please state in box; for intraventricular haemorrhage or fluid replacement see QB10*)

B10. In addition to the answer to QB9, do any of the following reasons for Cryo transfusion apply?

☐ To prevent intraventricular haemorrhage
☐ Bruising
☐ Neither

B11. If Cryo was transfused as prophylaxis before or during a procedure or surgery, please indicate which:

☐ Not applicable

☐ Central line insertion ☐ Central line removal

☐ Tunnelled ☐ Non-tunnelled

☐ UAC or ☐ UVC (for neonates)

☐ Cardiac surgery
☐ Abdominal surgery
☐ Neurosurgery
☐ Biopsy (state site ***e.g. Liver, bone marrow, renal, other***)

☐ Other, please give details

B12. What was the total volume of Cryo transfused for this episode (in mL)? mL

(An episode is defined as all the Cryo written up for transfusion at one time)

B13. Was this Cryo:

☐ Methylene-Blue? ☐ Pooled ☐ Single

☐ Standard? ☐ Pooled ☐ Single

B14. What was the date of this initial Cryo transfusion? D D M M

B15. What was the start time of this initial Cryo transfusion? H H : m m

Please use 24 hour clock - (e.g.20:15)

B16. What were the coagulation tests relating to this initial Cryo transfusion?

Please record the coagulation test results done before but nearest to the start time of the transfusion.

Date (dd/mm)	Time (hh:mm)	INR	PT(s)	APTT (s)	Fibrinogen (g/L)
Please tell us if these results are Raised (R), Normal (N) or Lowered (L)		R N L	R N L	R N L	R N L

☐ No result available

B17. Was TEG/RoTEM performed within 24 hours prior to transfusion?

Ye☐ No☐ No☐vailable

B18. Was a coagulation test performed within the 24 hours after the transfusion ended?

(Tick only, actual result not required; please record the time of coagulation test results done but if actual end time not known, then please estimate the time the transfusion ended)

Date (dd/mm)	Time (hh:mm)	INR	PT	APTT	Fibrinogen

☐ No result available

B19. Were any additional transfusions of Cryo given within the 24 hours following this initial Cryo transfusion? ☐ Yes ☐ No

B20. Was any FFP given with the initial Cryo episode and/or in the following 24 hours? ☐ Yes ☐ No

B21. Was any fibrinogen concentrate given with the initial Cryo episode and/or in the following 24 hours? ☐ Yes ☐ No

B22. Was any tranexamic acid given with the initial Cryo episode and/or in the following 24 hours? ☐ Yes ☐ No

B23. Were any other products given with the initial Cryo episode and/or in the following 24 hours?
(e.g. Factor VIIa, Prothrombin Complex Concentrate) ☐ Yes ☐ No

B23a If yes, please give details:

B24. Was an adverse reaction to Cryo noted in the case notes? ☐ Yes ☐ No

If yes, please describe the reaction

For patients where the reason given for transfusing Cryo included 'abnormal coagulation' (QB9) fill in QB25-31

B25. If the main reason for Cryo transfusion includes abnormal coagulation what, in the view of the clinical team, best describes the coagulopathy
(Tick one option)

☐ Minor abnormality of fibrinogen level of uncertain cause
☐ DIC
☐ Due to liver disease
☐ Secondary to anticoagulation
☐ Vitamin K deficiency
☐ Other (*please give details*)

If you ticked DIC in QB25, go to QB26 If not, you have finished SECTION B

B26. What were the laboratory results relating to this initial Cryo transfusion in addition to the coagulation results stated in QB16?

Date (dd/mm)	Time (hh:mm)	D Dimer	Platelet count (x10^9/L)
Please tell us if these results are Raised (R) or Normal (N		R N	

B27. What were the criteria for diagnosis *(Tick all that apply)*

- ☐ Prolonged PT
- ☐ Prolonged APTT
- ☐ Low Fibrinogen
- ☐ Low platelets
- ☐ Raised D Dimers
- ☐ Abnormal TEG/RoTEM *(e.g. abnormal fibrinolysis)*
- ☐ Blood film *(for fragments/schistocytes)*
- ☐ Other (please state)

B28. Was a DIC score used? ☐ Yes ☐ No ☐ Don't Know

B29. Was FFP given prior to the initial Cryo episode, within the preceding 24 hours?

Yes ☐ No ☐

B30. If Yes, was the fibrinogen level stated in QB16 taken following the FFP transfusion?

☐ Yes ☐ No ☐ Don't Know

B31. Were any platelets given with the initial Cryo episode and/or in the following 24 hours? ☐ Yes ☐ No

END OF SECTION B

SECTION C – ANY component given to treat bleeding or trauma

About this patient

C1. Where was the patient when the blood components were administered?
(Use the first component administered as a reference point and Tick one option)

- ☐ Neonatal Unit
- ☐ Paediatric Intensive Care Unit
- ☐ Paediatric High Dependency Unit
- ☐ Haematology/Oncology/Bone Marrow Transplant ward or day ward
- ☐ Paediatric day care ward
- ☐ General paediatric ward
- ☐ Paediatric surgical ward
- ☐ Theatre
- ☐ Recovery
- ☐ A & E
- ☐ Adult ward
- ☐ Labour ward
- ☐ Other, please state: ☐

C2. If on the date of transfusion the patient was over 1 year old, what was the patient's year of birth?

☐☐☐☐

If the patient was less than 1 year old, go to QC3. If not, go to QC6

C3. If on the date of transfusion the patient was less than 1 year old, what was their age in months?

☐☐

If the patient was less than 1 month old, go to QC4. If not, go to QC5

C4. If on the date of transfusion the patient was less than 1 month old, what was their age in days?

☐☐

Now go to QB5

C5. If on the date of transfusion the patient was less than 1 year old, what was their gestational age at birth?

☐ Weeks ☐ Days

C6. What was the most recent weight of the patient in Kg at the time of this transfusion? *If you are unable to find a record of the weight, please write "No record found"*

C7. What is the main underlying medical or surgical condition? *(Tick one option)*

Medical

- ☐ Perinatal event (including fetomaternal haemorrhage)
- ☐ Ventilated preterm baby
- ☐ Inherited bleeding disorder
- ☐ Bone Marrow Transplant
- ☐ Leukaemia / Cancer
  - ☐ Acute Lymphoblastic Leukaemia?
  - ☐ Promyelocytic Leukaemia (M3 Acute Myeloid Leukaemia)?
- ☐ Sepsis

- ☐ Respiratory illness
  - ☐ Ventilated?
  - ☐ Not ventilated?

- ☐ Liver disease
- ☐ Thrombotic thrombocytopenic purpura
- ☐ Neurological disorder
- ☐ Renal disease

Surgical

- ☐ Cardiac
- ☐ Extracorporeal Membrane Oxygenation (ECMO)
  (for either cardiac or respiratory condition)

- ☐ Orthopaedic
  - ☐ craniofacial
  - ☐ scoliosis

- ☐ Necrotising enterocolitis
- ☐ General surgery
- ☐ Plastic surgery
- ☐ ENT surgery
- ☐ Obstetric (pregnant mother)
- ☐ Trauma IF you ticked Trauma, please also answer QC8a,b & c

If there is another main underlying medical or surgical condition, then please write it in the space below. ***OR*** *If you are unable to find the underlying reason, please write "Don't know" :*

C8a. Was the trauma team leader a paediatric emergency medicine consultant?

Yes ☐ No ☐

C8b. Had there been pre-hospital transfusion of blood components?

Yes ☐ No ☐

C8c. If yes please tick which components were transfused:

☐ Red cells
☐ FFP
☐ Freeze-dried plasma

C9. **What was/were the main site(s) of the bleeding?** *(Tick as many as apply)*

☐ No significant bleeding confirmed
☐ Skin/subcutaneous
☐ Site of catheter / line insertion
☐ Nose/mouth
☐ Intracranial
☐ Gastrointestinal system
☐ Gynae
☐ Haematuria
☐ Musculoskeletal
☐ Obstetric
☐ Respiratory system
☐ Fetomaternal haemorrhage requiring transfusion at or after birth
☐ Other, *(Give details below)*

C10. What was the severity of the bleeding requiring transfusion?

☐ Major haemorrhage documented in clinical or operation notes
☐ Haemodynamic instability
☐ Blood loss of at least 40ml/Kg within 3 hours
☐ Blood loss of at least 80ml/Kg within 24 hours
☐ In retrospect, not significantly bleeding but clinically unstable

C11. What was the date and time the bleed (or suspected bleed) was first identified by clinicians?

D D M M

H H : m m

☐ Surgical bleeding so unable to tell ☐ Don't know

C12. If unable to tell or Don't know, what was the start time and date of the first component to be transfused because of the bleeding or trauma event?

D D M M

H H : m m

C13. What were the closest laboratory results of tests taken *prior to or within 1 hour after the onset of bleeding (or suspected bleeding)?* ***(whichever is closest to onset). If time of bleed onset not known, use results relating to the start of transfusion of the first component (QC12) instead.***

Date (dd/mm)	Time (hh:mm)	Hb g/L	Platelet count (x10^9/L)

Date (dd/mm)	Time (hh:mm)	INR	PT(s)	APTT (s)	Thrombin time (s)	Fibrinogen (g/L)
Please tell us if these results are Raised (R), Normal (N) or Lowered (L)		R N L	R N L	R N L	R N L	R N L

☐ No result available

C14. Was TEG/RoTEM used to assess coagulation in the 24 hours after the onset of bleeding (or suspected bleeding)?

☐ Yes ☐ No ☐ Not available

C15. What were the laboratory results at or up to 24 hours after start of transfusion of the first component?

Date (dd/mm)	Time (hh:mm)	Hb g/L	Platelet count (x10^9/L)

Date (dd/mm)	Time (hh:mm)	INR	PT(s)	APTT (s)	Thrombin time (s)	Fibrinogen (g/L)
Please tell us if these results are Raised (R), Normal (N) or Lowered (L)		R N L	R N L	R N L	R N L	R N L

☐ No result available *Please record a reason overleaf:.*

Reason why no result was available

☐ Patient transferred to another hospital
☐ Patient died
☐ No blood tests performed up to 24 hours of onset of bleeding
☐ Other, please state:

C16. Was tranexamic acid used within 3 hours of trauma injury (non-surgical)

☐ Yes ☐ No ☐ Not applicable

C17. Was tranexamic acid used prior to/during surgery?

☐ Yes ☐ No ☐ Not applicable

C18. Were any other products used to treat the bleeding?
(e.g. Factor VIIa, Prothrombin complex concentrate)

☐ Yes ☐ No

C18a. If yes, please state product(s) used:

C19. What interventions were undertaken to manage the bleeding within 24 hours *(Tick all that apply)*

☐ Supportive management only (including transfusion)
☐ Interventional radiology
☐ Surgery (if initial cause of bleed was not surgical)
☐ Re-operation

C20. What was the date and time transfusion of first blood component was commenced?

D D M M h h : m m

C21. If red cells were transfused, were they emergency Group O, D neg red cells?

☐ Yes ☐ No

C21a. If Yes, were these 'paedipacks'?

☐ Yes ☐ No

C22. Was a Major Haemorrhage protocol activated with Blood Transfusion (BT) Laboratory?

☐ Yes ☐ No ☐ Not documented/ Don't Know

C22a. If No, was the BT Laboratory phoned to notify them of the bleeding?

☐ Yes ☐ No

C23. If blood was requested urgently from the BT Laboratory was a valid G&S Sample held in the laboratory?

☐ Yes ☐ No ☐ Not applicable

C23a. If not, when was a G&S sample received by the laboratory?

D D M M h h : m m

C24. Were red cell and plasma/platelet volumes requested in a specific ratio?

☐ Yes ☐ No

C24a. If yes, was this ratio:

☐ FFP : red cells 1:1
☐ FFP : red cells 1:2
☐ FFP : platelets : red cells 1:1:1
☐ Other (please state)

C25. Which blood components and what volume were transfused in the first 4 hours after start of first blood component transfusion (including first component transfused)?

Component	Tick if transfused	If transfused, give total volume during the time period (mL)	If FFP or Cryo transfused, please tick type of component			
			MB	SD	Standard	Pre-thawed Standard
Red cells						
FFP						
Cryoprecipitate						
Platelets						

C26. Which blood components were transfused in from 5 up to 24 hours after start of first blood component transfusion?

Component	Tick if transfused	If transfused, give total volume during the time period (mL)	If FFP or Cryo transfused, please tick type of component			
			MB	SD	Standard	Pre-thawed Standard
Red cells						
FFP						
Cryoprecipitate						
Platelets						

C27. If the patient weighed less than 50 kg, were components prescribed in:

☐ Millilitres

☐ Units

☐ Patient did not weigh <50Kg

C28. Was an adverse reaction to blood transfusion noted in the case notes?

☐ Yes ☐ No

C28a. If yes, please describe, including nature of implicated blood component

C29. Were there any recorded delays to provision of blood transfusion support within 24 hours after bleeding onset?

☐ Yes ☐ No

C29a. If Yes, please describe

For patients with abnormal coagulation prior or within 1 hour after the onset of bleeding (or at time of first transfusion if onset of bleeding not known) (QC13) fill in QC30-33

C30. For patients with abnormal coagulation (QC13), what in the view of the clinical team best describes the coagulopathy? (*Tick one response*)

☐ Minor abnormality of PT/APTT/Fibrinogen of uncertain cause
☐ DIC
☐ Liver disease
☐ Secondary to anticoagulation
☐ Vitamin K deficiency
☐ Major haemorrhage
☐ Other (*please state*)

C31. If you selected DIC at QC30, what were the laboratory results in addition to the coagulation results stated in QC13)

Date (dd/mm)	Time (hh:mm)	D Dimers	Platelet count (x10^9/L)
Please tell us if these results are Raised (R) or Normal (N		R N	

C32. What were the criteria for diagnosis *(Tick all that apply)*

☐ Prolonged PT
☐ Prolonged APTT
☐ Low Fibrinogen
☐ Low platelets
☐ Raised D Dimers
☐ Abnormal TEG/RoTEM *(e.g. abnormal fibrinolysis)*
☐ Blood film *(for fragments/schistocytes)*
☐ Other (please state)

C33. Was a DIC score used? ☐ Yes ☐ No ☐ D/K

END OF SECTION C

Appendix C – List of participating sites that contributed data

Aintree University Hospital NHS Foundation Trust
Alder Hey Children's NHS Foundation Trust
Barnet Hospital
Basildon and Thurrock University Hospitals NHS Foundation Trust
Belfast Health and Social Care Trust
Birmingham Children's Hospital
Birmingham City Hospital
Birmingham Heartlands Hospital
Birmingham Women's Hospital
Bolton NHS Foundation Trust
Brighton and Sussex University Hospitals NHS Trust
Buckinghamshire Healthcare NHS Trust
Chelsea & Westminster Hospital
Colchester Hospital University NHS Foundation Trust
Croydon Health Services NHS Trust
East Kent Hospitals University NHS Foundation Trust
East Lancashire Hospitals NHS Trust
Epsom and St. Helier University Hospitals NHS Trust
Freeman Hospital
Gloucestershire Royal Hospital
Great Ormond Street Hospital For Children NHS Foundation Trust
Guys and St Thomas' NHS Foundation Trust
Homerton University Hospital NHS Foundation
King's College Hospital
Lancashire Teaching Hospitals NHS Foundation Trust
London North West University Healthcare NHS Trust
Luton and Dunstable University Hospital NHS Foundation Trust
Medway NHS Foundation Trust
Mid Cheshire Hospitals NHS Foundation Trust
Norfolk and Norwich University Hospitals NHS Foundation Trust
Oxford University Hospitals NHS Foundation Trust
Queen Elizabeth Hospital Greenwich
Queen's Hospital Romford
Queen's Medical Centre
Royal Manchester Children's Hospital
Royal National Orthopaedic Hospital NHS Trust
Royal Stoke University Hospital
Royal United Hospitals Bath NHS Foundation Trust
Royal Victoria Infirmary Newcastle
Sheffield Children's NHS Foundation Trust
South Tees Hospitals NHS Foundation Trust
St. George's University Hospitals NHS Foundation Trust
St. Mary's Hospital Manchester
Stockport NHS Foundation Trust
The Dudley Group NHS Foundation Trust
The Leeds Teaching Hospitals NHS Trust

The Queen Elizabeth Hospital Kings Lynn NHS Foundation Trust
The Royal Hallamshire Hospital
The Royal Hospital for Children Glasgow
The Royal London Hospital
The Royal Wolverhampton NHS Trust
University College London Hospitals NHS Foundation Trust
University Hospital Lewisham
University Hospital of South Manchester NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
University Hospitals Bristol NHS Foundation Trust
University Hospitals Coventry and Warwickshire NHS Trust
University Hospitals of Leicester NHS Trust
University Hospitals Plymouth NHS Trust
Walsall Healthcare NHS Trust
West Hertfordshire Hospitals NHS Trust
West Middlesex University Hospital
Wirral University Teaching Hospital NHS Foundation Trust
Wye Valley NHS Trust

Appendix D – Additional methods, tables and figures

Additional methods.

Calculation of patient age in days

Data collection required only the year of birth for patients over one year old on the date of transfusion. To obtain an age in days, we imputed a patient's full date of birth by randomly sampling from a multinomial distribution with probability of being born on a given day in their year of birth as reported by the Office for National Statistics (ONS). To view the ONS Open Government Licence visit http://www.nationalarchives.gov.uk/doc/open-government-licence/; or write to the Information Policy Team, The National Archives, Kew, Richmond, Surrey, TW9 4DU; or email: psi@nationalarchives.gsi.gov.uk. (Access data here: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/livebirths/adhocs/009036numberoflivebirthsbydate1995to2016inenglandandwales). The ONS probabilities of birth on a given day covered the time period from 1995 to 2016. To impute the age in days for a patient with a reported year of birth greater than 2016, we used the mean of the probabilities of being born on a given day over 1995-2016.

Data collection required only age in months for patients less than a year old but one month old or older on the date of transfusion. To obtain an age in days, we randomly sampled from a uniform distribution over their possible birth dates. For most cases, this sampling period was 30 days, but there were some cases where the year of birth or data from other sections of the audit allowed us to restrict this further.

We ran this random sampling for 10 different seeds in the computer algorithm and took the mean age in days as the imputed age used throughout this report.

Additional tables.

Table A: Data excluded by audit team after review of data.

Site code	Patient details	Details of exclusion
88	Audit episode 2, no further data	Fully excluded from report
176	Audit episode 6, form completed as bleeding/trauma patient, three-day-old patient, bleed identified on 01/07/2018	Fully excluded from report
161	Audit episode 11, no further data	Fully excluded from report
95	Audit episode 3, form completed as prophylactic FFP and cryo patient, patient born in 2004, initial cryo transfusion on 11/05/2018	Excluded from prophylactic FFP analysis (Section A)

103	Audit episode 1, form completed as prophylactic FFP and bleeding/trauma patient, one-day-old patient, component first transfused on 04/05/2018	Excluded from prophylactic FFP analysis (Section A)
74	Audit episode 1, form completed as bleeding/trauma patient, two-day-old patient, component first transfused on 08/07/2018	Fully excluded from report
46	Audit episode 9, form completed as prophylactic FFP and bleeding/trauma patient, patient born in 2004, bleed identified on 06/06/2018	Excluded from prophylactic FFP analysis (Section A)
97	Audit episode 24, form completed as bleeding/trauma patient, two-month-old patient, bleed identified on 15/05/2018	Fully excluded from report
97	Audit episode 25, form completed as prophylactic FFP and bleeding/trauma patient, six-day-old patient, component first transfused on 21/05/2018	Excluded from prophylactic FFP analysis (Section A)
97	Audit episode 27, form completed as bleeding/trauma patient, one-day-old patient, bleed identified on 12/07/2018	Fully excluded from report
42	Audit episode 1, form completed as prophylactic FFP and bleeding/trauma patient, one-day-old patient, component first transfused on 03/05/2018	Excluded from prophylactic FFP analysis (Section A)
1	Audit episode 27, form completed as prophylactic cryo and bleeding/trauma patient, patient born in 2004, bleed identified on 24/06/2018	Excluded from prophylactic cryo analysis (Section B)
153	Audit episode 24, form completed as prophylactic FFP patient, six-day-old patient, pre-transfusion coagulation tests performed on 10/07/2018	Fully excluded from report
153	Audit episode 30, form completed as prophylactic FFP and bleeding/trauma patient, five-day-old patient, initial FFP transfusion on 04/01/2018 and bleed identified on 05/01/2018	Excluded from bleeding/trauma patient analysis (Section C)
148	Audit episode 1, form completed as prophylactic FFP patient, patient born in 2014, initial FFP transfusion on 30/04/2018	Fully excluded from report
150	Audit episode 6, no further data	Fully excluded from report
150	Audit episode 13, form completed as prophylactic FFP patient, patient born in 2001, initial FFP transfusion on 06/07/2018	Fully excluded from report
150	Audit episode 19, form completed as prophylactic FFP and bleeding/trauma patient, patient born in 2016, initial FFP transfusion on 16/05/2018 and bleed identified on 15/05/2018	Fully excluded from report

3	Audit episode 3, form completed as prophylactic FFP and cryo and bleeding/trauma patient, patient born in 2016, bleed identified on 21/05/2018	Excluded from prophylactic FFP and cryo analysis (Sections A and B)
3	Audit episode 7, no further data	Fully excluded from report
3	Audit episode 9, form completed as prophylactic FFP patient, patient born in 2010, initial FFP transfusion on 26/06/2018	Excluded from prophylactic FFP analysis (Section A), and data used in bleeding/trauma patient analysis (Section C)
10	Audit episode 1, form completed as prophylactic FFP patient, patient born in 2016, initial FFP transfusion on 02/05/2018	Data used in prophylactic FFP and cryo analysis (Sections A and B)
31	Audit episode 1, form completed as prophylactic FFP and bleeding/trauma patient, one-day-old patient, initial FFP transfusion on 15/05/2018	Excluded from bleeding/trauma patient analysis (Section C)
108	Audit episode 1, form completed as prophylactic FFP and bleeding/trauma patient, nine-day-old patient, bleed identified on 05/05/2018	Excluded from prophylactic FFP analysis (Section A)
108	Audit episode 4, form completed as prophylactic FFP and cryo and bleeding/trauma patient, one-day-old patient, initial FFP transfusion on 29/05/2018, initial cryo transfusion on 28/05/2018, and bleed identified on 29/05/2018	Excluded from bleeding/trauma patient analysis (Section C)
108	Audit episode 9, patient born in 2018	Fully excluded from report
167	Audit episode 7, no further data	Fully excluded from report
167	Audit episode 13, form completed as prophylactic cryo and bleeding/trauma patient, patient born in 2016, initial cryo transfusion on 31/05/2018 and bleed identified on 31/05/2018	Fully excluded from report
84	Audit episode 9, form completed as prophylactic FFP and cryo patient, patient born in 2016, initial FFP and cryo transfusion on 20/06/2018	Fully excluded from report
84	Audit episode 14, no further data	Fully excluded from report
11	Audit episode 21, form completed as prophylactic FFP patient, patient born in 2013, initial FFP transfusion on 13/06/2021	Fully excluded from report

36	Audit episode 1, form completed as prophylactic FFP and bleeding/trauma patient, one-day-old patient, initial FFP transfusion on 24/04/2018	Excluded from bleeding/trauma patient analysis (Section C)
146	Audit episode 1, form completed as prophylactic FFP and bleeding/trauma patient, one-day-old patient, bleed identified on 28/06/2018	Excluded from prophylactic FFP analysis (Section A)

1. Tables relating to Section A

Table B: Location of prophylactic FFP transfusions, by age of recipient

Location	Age of children receiving prophylactic FFP							
	Less than 1 month (n & %) n = 234		1 month to less than 1 year (n & %) n = 56		1 year or more than 1 year (n & %) n = 126		All ages (n & %) n = 417*	
	n	col %	n	col %	n	col %	n	col %
Neonatal unit	207	88.5%	9	16.1%	0	0.0%	217	52.0%
Theatre/recovery	9	3.8%	21	37.5%	53	42.1%	83	19.9%
Paediatric Intensive Care Unit	13	5.6%	16	28.6%	27	21.4%	56	13.4%
Paediatric ward	2	0.9%	2	3.6%	19	15.1%	23	5.5%
Haematology/Oncology/Bone Marrow Transplant ward or day ward	0	0.0%	3	5.4%	14	11.1%	17	4.1%
Paediatric High Dependency Unit	2	0.9%	2	3.6%	5	4.0%	9	2.2%
Other	1	0.4%	2	3.6%	8	6.3%	11	2.6%
Missing	0	0.0%	1	1.8%	0	0.0%	1	0.2%
Total	**234**	**100.0%**	**56**	**100.0%**	**126**	**100.0%**	**417**	**100.0%**

*One patient had missing age.

Table C: Weight by age

Weight statistic	Age of children receiving prophylactic FFP			
	Less than 1 month (n = 234)	1 month to less than 1 year (n = 56)	1 year or more than 1 year (n = 126)	All ages (n = 417*)
Number reported	224 (95.7%)	51 (91.1%)	116 (92.1%)	392 (94.0%)
Median (kg)	1.2	4.8	19.1	3.2
IQR (kg)	0.8-2.8	3.0-6.0	13.7-40.7	1.0-11.6

*One patient had missing age.

Table D: Main underlying condition for children receiving prophylactic FFP		
	National (n & %) n = 417	
Medical	**284**	**68.1%**
Ventilated preterm baby	104	24.9%
Sepsis	68	16.3%
Perinatal event	24	5.8%
Respiratory illness	17	4.1%
Mechanically ventilated	*13*	*3.1%*
Non ventilated / invasive	*3*	*0.7%*
No further details	*1*	*0.2%*
Leukaemia / Cancer / Bone marrow transplant	13	3.1%
Acute Lymphoblastic Leukaemia	*5*	*1.2%*
Unspecified leukaemia/cancer	*5*	*1.2%*
Bone marrow transplant	*3*	*0.7%*
Inherited disorders	13	3.1%
Other medical	43	10.3%
Liver disease	*15*	*3.6%*
Neurological disorder	*7*	*1.7%*
Hypertensive Ischaemic Encephalopathy	*5*	*1.2%*
Renal disease	*4*	*1.0%*
Thrombotic Thrombocytopenic Purpura	*1*	*0.2%*
Other (listed below)	*11*	*2.6%*
Missing	2	0.5%
Surgical	**133**	**31.9%**
Cardiac	69	16.5%
General surgery	17	4.1%
Necrotising enterocolitis	11	2.6%
Orthopaedic	10	2.4%
Scoliosis	*7*	*1.7%*
Craniofacial	*2*	*0.5%*
Missing	*1*	*0.2%*
Other surgical	14	3.4%
Extracorporeal membrane oxygenation (ECMO)	*5*	*1.2%*
Neurosurgery	*4*	*1.0%*
Trauma	*2*	*0.5%*
Other (listed below)	*3*	*0.7%*
Missing	12	2.9%

Other medical (n = 11): “Anaemia and deranged clotting green aspirates and distended abdomen”;” Cardiac arrest at home”; “Exchange transfusion due to high bilirubin jaundice and haemolysis. Mum has SCD and anti-S.”; “GI bleed with malena”; “Hydrops Fetalis; Chylothorax L (Non-immune)”; “Neonatal encephalopathy”; “Post overdose and suicide attempt”; “PPHN”; “Severe hypotension”; “Unexplained hypotension”; “Don’t know”.
Other surgical (n = 3): “Congenital heart disease”; “Post renal transplant. 1/7 return to theatre for exploration. Perirenal haemorrhage and renal function V”; “Don’t know”.

Table E: Other reason for all those with normal coagulation in the absence of invasive procedure or surgery (as stated in QA9)		
Reason	**National (n & %) n = 85**	
Cardiac bypass	25	29.4%
As fluid replacement	14	16.5%
Bruising	5	5.9%
Bleeding related	5	5.9%
Factor replacement	3	3.5%
To prevent intraventricular haemorrhage	3	3.5%
Other surgery*	6	7.1%
Other**	4	4.7%
Missing	20	23.5%

*Other surgery (n=6): "~ Femur. Expandible nailing operation. Patient has McGuire Albright syndrome", Kasai procedure protocol, Liver transplant protocol, Neurosurgery, "REDO Cardiac surgery. Heparinised bleeding risk as REDO", and "Transfusion given during surgery".
**Other (n=4): "After significant blood transfusion", "Burns patient spiking temperature", "Nephrotic syndrome relapse treatment", and preterm protocol.

Table F: Availability of coagulation tests													
When did the pre-transfusion coagulation test occur relative to FFP transfusion (in hours)?	**PT/INR value available**			**APTT/APTR value available**			**Fibrinogen value available**			**Availability of any coagulation test**			**Total**
	Yes – valid value	Yes – value outside range*	No	Yes – valid value	Yes – value outside range*	No	Yes – valid value	Yes – value outside range*	No	All results (fibrinogen, PT/INR and APTT/APTR)	One or two out of fibrinogen, PT/INR, and APTT/APTR	No results	
>0-1 hours before transfusion	14	0	0	10	0	4	11	0	3	9	5	0	14
>1-2 hours before transfusion	18	0	2	17	1	2	12	0	8	12	6	2	20
>2-4 hours before transfusion	51	2	1	48	6	0	45	1	8	45	9	0	54
>4-6 hours before transfusion	62	2	2	59	4	3	50	0	16	48	18	0	66
>6-12 hours before transfusion	67	2	1	64	3	3	53	1	16	54	16	0	70
>12-24 hours before transfusion	41	0	0	39	1	1	30	2	9	32	9	0	41
>24-48 hours before transfusion	15	0	0	15	0	0	11	0	4	11	4	0	15
More than 48 hours before transfusion	14	0	0	14	0	0	9	0	5	9	5	0	14
After transfusion	20	1	1	19	1	2	15	0	7	15	6	1	22
Exact same time as transfusion	5	0	0	5	0	0	2	0	3	2	3	0	5
Missing time: Transfusion	30	0	0	27	0	3	22	0	8	22	8	0	30
Missing time: Coagulation test	3	0	59	3	0	59	3	0	59	3	0	59	62
Missing time: Transfusion and test	3	0	1	1	0	3	2	0	2	1	2	1	4
Total	**343**	**7**	**67**	**321**	**16**	**80**	**265**	**4**	**148**	**263**	**91**	**63**	**417**

*value outside range – outlier or greater than measurable; † PTR was calculated using a local average where available and, if unavailable, a consensus average across centre

Note: Green shading in this table indicates the timepoints of the data that were included in the analysis

Table G: Results of APTR pre-transfusion in all recipients with 'abnormal coagulation' included in the main reason for transfusion (as defined by QA9)								
APTR (1) values from tests	**Age of recipients**							
	Less than 1 month (n & %) n = 204		**1 month to less than 1 year (n & %) n = 32**		**1 year or more than 1 year (n & %) n = 69**		**All ages (n & %) n = 306***	
0.5 - <1.0	1	0.5%	0	0.0%	13	18.8%	14	4.6%
1.0 - <1.5	11	5.4%	4	12.5%	17	24.6%	32	10.5%
1.5 - <2.0	45	22.1%	5	15.6%	7	10.1%	57	18.6%
2.0 - <2.5	33	16.2%	2	6.3%	1	1.4%	36	11.8%
2.5 - <3.0	23	11.3%	1	3.1%	2	2.9%	26	8.5%
3.0 - <3.5	13	6.4%	0	0.0%	0	0.0%	13	4.2%
3.5 - <4.0	10	4.9%	0	0.0%	1	1.4%	11	3.6%
4.0-<12.0	16	7.8%	2	6.3%	1	1.4%	19	6.2%
>=12.0 or greater than measurable (1)	10	4.9%	2	6.3%	3	4.3%	15	4.9%
Outside of 24 hours before or missing	42	20.6%	16	50.0%	24	34.8%	83	27.1%

(1) 181 are calculated APTRs, 154 calculated using a local reference range (adult) and 27 using a consensus average reference range. No values < 0.5.
(2) One of the greater than measurable values was '> 7.0'.
*One patient had missing age.

Note: full interpretation of the APTRs values and significance of these results for neonates and infants should take into account postnatal and gestational ages.

Table H: Coagulation test performed within 24 hours of the transfusion					
When did the post-transfusion coagulation test occur relative to FFP transfusion (in hours)?	**INR test performed**	**PT test performed**	**APTT test performed**	**Fibrinogen test performed**	**Any test performed**
0-6 hours after start of transfusion	58	62	76	64	82
6-12 hours after start of transfusion	53	56	60	45	62
12-24 hours after start of transfusion	56	63	71	62	78
More than 24 after start of transfusion	13	23	23	20	25
Before start of transfusion	11	20	21	16	21
Missing time: Transfusion	18	17	21	16	24
Missing time: Coagulation test	0	3	3	3	3
Missing time: Transfusion and test	3	3	3	3	3
All	**212**	**247**	**278**	**229**	**298**

For the purposes of the analysis, the stated start time of the FFP transfusion was used as the confirmation time point.

Note: Green shading in this table indicates the timepoints of the data that were included in the analysis

2. Tables relating to Section B

Table I: Main underlying condition for children receiving prophylactic cryoprecipitate		
	National (n & %) n = 141	
Medical	**66**	**46.8%**
Sepsis	18	12.8%
Ventilated preterm baby	15	10.6%
Respiratory illness	9	6.4%
Mechanically ventilated	*8*	*5.7%*
Non ventilated / invasive	*1*	*0.7%*
Perinatal event	7	5.0%
Inherited disorders	1	0.7%
Other medical	13	9.2%
Liver disease	*9*	*6.4%*
Preterm	*2*	*1.4%*
Renal disease	*1*	*0.7%*
Neonatal encephalopathy	*1*	*0.7%*
Missing	3	2.1%
Surgical	**75**	**53.2%**
Cardiac	43	30.5%
Necrotising enterocolitis	3	2.1%
Orthopaedic (scoliosis)	3	2.1%
General surgery	2	1.4%
Other surgical	16	11.3%
Extracorporeal membrane oxygenation (ECMO)	*10*	*7.1%*
Neurosurgery	*3*	*2.1%*
Organ transplant	*2*	*1.4%*
Abnormal bowel - open abdomen Extreme prematurity.	*1*	*0.7%*
Missing	8	5.7%

Table J: Availability of coagulation tests													
When did the pre-transfusion coagulation test occur relative to cryoprecipitate transfusion (in hours)?	**PT/INR value available**			**APTT/APTR value available**			**Fibrinogen value available**			**Availability of any coagulation test**			**Tests performed at this time**
	Yes – valid value	Yes – value outside range*	No	Yes – valid value	Yes – value outside range*	No	Yes – valid value	Yes – value outside range*	No	All results (fibrinogen, PT/INR and APTT/APTR)	One or two out of fibrinogen, PT/INR, and APTT/APTR	No results	
0-1 hours before transfusion	1	0	0	1	0	0	1	0	0	1	0	0	**1**
>1-2 hours before transfusion	7	0	0	5	2	0	7	0	0	7	0	0	**7**
>2-4 hours before transfusion	19	2	1	21	1	0	21	0	1	20	2	0	**22**
>4-6 hours before transfusion	15	0	0	14	0	1	15	0	0	14	1	0	**15**
>6-12 hours before transfusion	27	2	0	28	0	1	25	0	4	25	4	0	**29**
>12-24 hours before transfusion	10	2	1	10	2	1	12	0	1	11	2	0	**13**
>24-48 hours before transfusion	3	0	0	2	0	1	3	0	0	2	1	0	**3**
More than 48 hours before transfusion	3	0	0	3	0	0	3	0	0	3	0	0	**3**
After transfusion	9	0	0	8	0	1	7	0	2	7	2	0	**9**
Missing time: Transfusion	19	0	0	16	2	1	14	0	5	14	5	0	**19**
Missing time: Coagulation test	3	0	16	3	0	16	3	0	16	3	0	16	**19**
Missing time: Transfusion and test	0	0	1	0	0	1	0	0	1	0	0	1	**1**
Total	**116**	**6**	**19**	**111**	**7**	**23**	**111**	**0**	**30**	**107**	**17**	**17**	**141**

*value outside range – outlier or greater than measurable
Note: Green shading in this table indicates the timepoints of the data that were included in the analysis

Table K: Coagulation test performed within 24 hours of the transfusion					
When did the post-transfusion coagulation test occur relative to cryoprecipitate transfusion (in hours)?	**INR test performed**	**PT test performed**	**APTT test performed**	**Fibrinogen test performed**	**Any test performed**
0-6 hours after start of transfusion	24	39	43	41	43
>6-12 hours after start of transfusion	9	15	15	15	16
>12-24 hours after start of transfusion	12	25	28	25	28
More than 24 after start of transfusion	4	7	7	7	8
Before start of transfusion	4	6	7	6	7
Missing time: Transfusion	14	10	16	10	16
Missing time: Coagulation test	0	2	2	2	2
Missing time: Transfusion and test	0	0	0	1	1

For the purposes of the analysis, the stated start time of the cryoprecipitate transfusion was used as the confirmation time point.
Note: Green shading in this table indicates the timepoints of the data that were included in the analysis

3. Tables relating to Section C

Table L: Main underlying condition for children receiving transfusion to treat bleeding or trauma		
	National (n & %) n = 117	
Medical	**53**	**45.3%**
Ventilated preterm baby	20	17.1%
Sepsis	6	5.1%
Respiratory illness	5	4.3%
Mechanically ventilated	*2*	*1.7%*
Non ventilated / invasive	*2*	*1.7%*
No further details given	*1*	*0.9%*
Perinatal event (including FMH)	5	4.3%
Inherited bleeding disorders	3	2.6%
Other medical	9	7.7%
Liver disease	*1*	*0.9%*
Renal disease	*1*	*0.9%*
Leukaemia / Cancer	*1*	*0.9%*
Other (listed below)	*6*	*5.1%*
Missing	5	4.3%
Surgical	**64**	**54.7%**
Cardiac	28	23.9%
Orthopaedic	7	6.0%
Scoliosis	*3*	*2.6%*
Craniofacial	*1*	*0.9%*
No further details given	*3*	*2.6%*
General surgery	5	4.3%
Necrotising enterocolitis	3	2.6%
Other surgical	18	15.4%
Trauma	*12*	*10.3%*
Liver transplant	*3*	*2.6%*
Extracorporeal membrane oxygenation (ECMO)	*2*	*1.7%00*
ENT surgery	*1*	*0.9%*
Missing	3	2.6%
Other medical (n=6): “Acute CMV infection leading to DIC”; “Dilated cardiomyopathy with severe biventricular dysfunction with LVAD support”; “Don't know. Baby unexpectedly unwell.”; “Metabolic emergency. Ornithine Transcarbamylase deficiency.”; “Out of hospital cardiac arrest. Subdural haemorrhages. Cerebral Oedema.”; “PV Bleeding - presented at E.D.”		

Table M: Timing of haemoglobin and platelet count tests 'pre-transfusion'				
When did the pre-transfusion Hb and platelets test occur?	**Haemoglobin value available** **Total count using bleed* or transfusion time (sub-count using transfusion time when bleed time was missing)**		**Platelet value available** **Total count using bleed* or transfusion time (sub-count using transfusion time when bleed time was missing)**	
	Value reported	**No value**	**Value reported**	**No value**
More than 24 hours before	2 (0)	0 (0)	2 (0)	0 (0)
>12-24 hours before	3 (0)	0 (0)	3 (0)	0 (0)
>6-12 hours before	3 (0)	0 (0)	3 (0)	0 (0)
>4-6 hours before	4 (2)	0 (0)	4 (2)	0 (0)
>2-4 hours before	6 (3)	0 (0)	6 (3)	0 (0)
>1-2 hours before	10 (1)	0 (0)	10 (1)	0 (0)
>0-1 hours before	13 (1)	0 (0)	12 (1)	1 (0)
Exact same time	5 (1)	0 (0)	4 (1)	1 (0)
>0-1 hours after	6 (3)	0 (0)	5 (2)	1 (1)
>1-2 hours after	9 (4)	0 (0)	9 (4)	0 (0)
>2-3 hours after	1 (1)	0 (0)	1 (1)	0 (0)
>3-4 hours after	4 (1)	0 (0)	4 (1)	0 (0)
>4-5 hours after	3 (2)	0 (0)	3 (2)	0 (0)
>5-6 hours after	4 (3)	0 (0)	4 (3)	0 (0)
>6-12 hours after	10 (5)	0 (0)	10 (5)	0 (0)
>12-24 hours after	14 (10)	0 (0)	14 (10)	0 (0)
More than 24 hours after	8 (8)	0 (0)	8 (8)	0 (0)
Missing time(s)	2† (N/A)	10 (N/A)	2† (N/A)	10 (N/A)
All within 24 hours before up to 1 hour after	**50 (11)**	**0 (0)**	**47 (10)**	**3 (1)**
All	**107 (45)**	**10 (0)**	**104 (44)**	**13 (1)**
	117 (45)		**117 (45)**	

† Hb and platelets provided for one case of missing transfusion and bleed time, and one case of missing test time.

* Bleed time is the start of the bleed or suspected bleed.

Note: Green shading in this table indicates the timepoints of the data that were included in the analysis

Table N: Timing of haemoglobin and platelet count tests 'post-transfusion'				
When did the post-transfusion Hb and platelets test occur relative to transfusion?	**Haemoglobin value available**		**Platelets value available**	
	Value reported	**No value**	**Value reported**	**No value**
Before transfusion	3	0	3	0
>0-1 hours after start of transfusion	7	0	7	0
>1-2 hours after start of transfusion	5	0	5	0
>2-3 hours after start of transfusion	7	0	7	0
>3-4 hours after start of transfusion	6	0	6	0
>4-5 hours after start of transfusion	3	0	3	0
>5-6 hours after start of transfusion	6	0	6	0
>6-12 hours after start of transfusion	22	0	22	0
>12-24 hours after start of transfusion	25	0	25	0
>24 hours after start of transfusion	5	0	4	1
Missing time: Hb/platelet test	0	24	0	24
Missing time: transfusion	2	0	2	0
Missing time: test and transfusion	0	2	0	2
All after 2 hours up to 24 hours after	**69**	**0**	**69**	**0**
All	**91**	**26**	**90**	**27**
	117		**117**	

Note: Green shading in this table indicates the timepoints of the data that were included in the analysis

Additional figures.

Figure A: Gestational ages of neonates receiving FFP prophylactically (n=229).

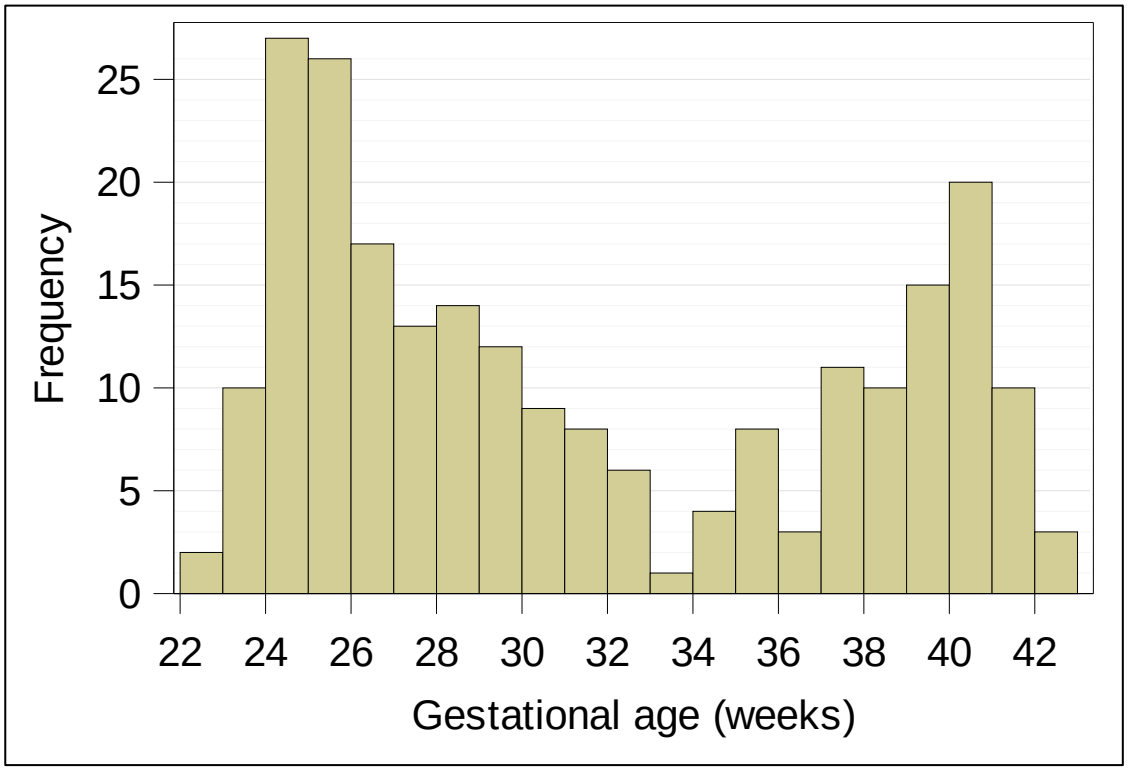


Figure B: Gestational ages of those receiving cryoprecipitate prophylactically, aged less than one year (n=76).

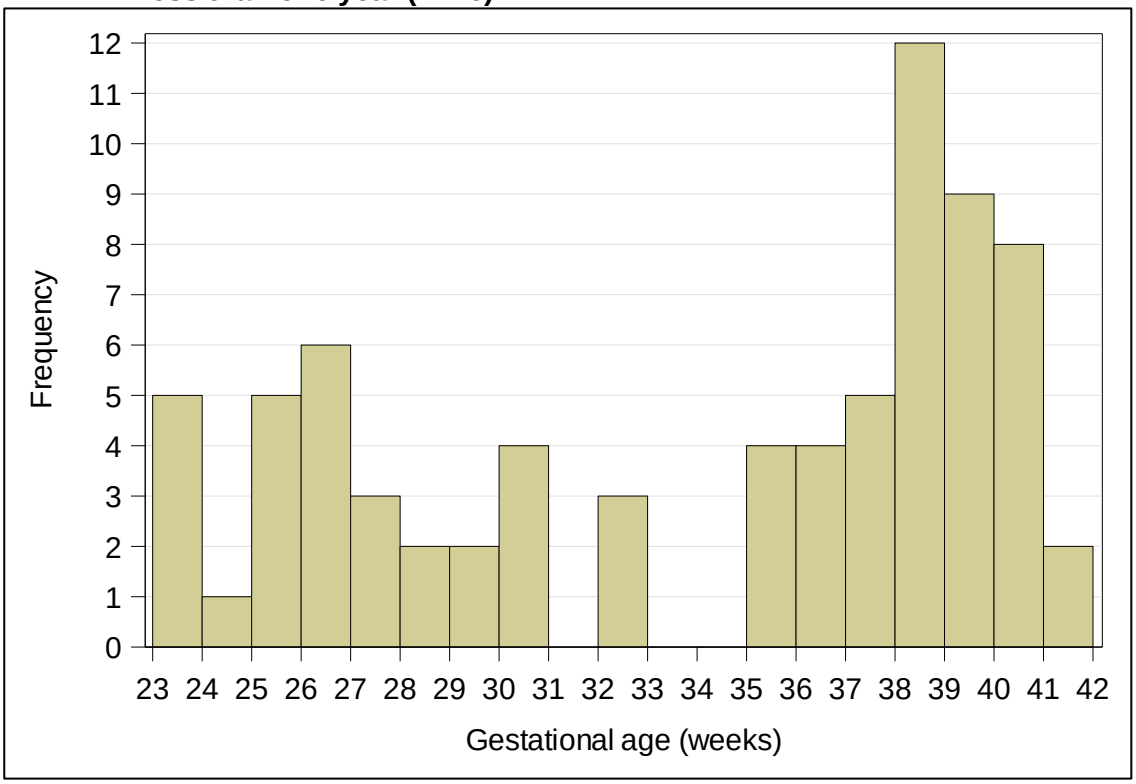


Figure C: Gestational ages of those receiving a transfusion of any component to treat bleeding or trauma, aged less than one year (n=65).