Headline Data: Deaths, Major Morbidity and ABO-Incompatible Transfusions 3

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Key SHOT messages

- Transfusion in the UK continues to be safe and SHOT data for the last 10 years show the risk of death from transfusion as 0.92 per 100,000 components issued. This includes all deaths reported with imputabilities ranging from possible, probable, or confirmed
- Non-infectious complications, especially procedural errors and errors related to transfusion decisions continue to be the most common causes of transfusion-related deaths in the UK. Delays in transfusion and pulmonary complications (mainly TACO) were the main causes of reported transfusion-related deaths in 2021 contributing to 77.1% (27/35 deaths reported to SHOT in 2021)
- Errors (including near miss) continue to account for majority of the reports. In 2021, 2569/3161 (81.3%) of all reports were due to errors
- Near miss events continue to account for a large proportion, 1155/3161 (36.5%) of the incidents reported to SHOT
- Inadequate staffing, lack of adequate training, poor supervision and poor safety culture have been identified as contributory to numerous incidents reported to SHOT. These need to be addressed urgently to reduce the risk to patient safety. Ensuring process-based safety for transfusions through a multipronged approach, adequate training, appropriate resources, having user-centred design and learning from experiences are essential
- Overriding alerts and flags on LIMS continue to contribute to errors reported. Incorporating human factors principles into designing alerts and avoiding unnecessary alerts will help improve usability and reduce errors
- Trends in pathological transfusion reactions, such as febrile, allergic, hypotensive, and haemolytic reactions are similar to previous years. All staff involved in transfusions must be competent and confident in recognising and appropriately managing transfusion reactions in recipients

The recommendation from last year remains pertinent and safety messages emerging from haemovigilance data must inform safety initiatives in all healthcare organisations not just for safer transfusions but for overall safer patient care.

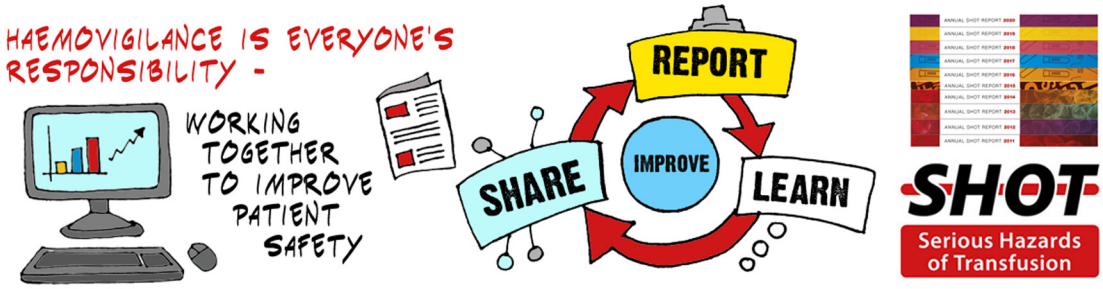
Recommendation

- NHS Trusts/Health Boards must use intelligence from all patient safety data including national haemovigilance data to inform changes in healthcare systems, policies, and practices to embed the lessons learnt and truly improve patient safety

Action: Hospital chief executives and medical directors, National Blood Transfusion Committee (or the equivalent for the devolved countries), hospital transfusion teams

Abbreviations used in this chapter

ABOi	ABO-incompatible
BSH	British Society for Haematology
CCP	COVID-19 convalescent plasma
CMV	Cytomegalovirus
FAHR	Febrile, allergic and hypotensive reactions
FFP	Fresh frozen plasma
IBCT	Incorrect blood component transfused
ISTARE	International Surveillance of Transfusion-Associated Reactions and Events
LIMS	Laboratory information management system
MB	Methylene blue
NHS	National Health Service
NM	Near miss
PAS	Platelet additive solution
RBRP	Right blood right patient
SaBTO	The Advisory Committee on the Safety of Blood, Tissues and Organs
SCRIPT	SHOT Collaborative Reviewing and reforming IT Processes in Transfusion
SMART	Specific, measurable, achievable, realistic, and timely
SRNM	Specific requirements not met
TACO	Transfusion-associated circulatory overload
UCT	Uncommon complications of transfusion
UK	United Kingdom
vCJD	Variant Creutzfeldt Jakob Disease
WBIT	Wrong blood in tube



Introduction

Haemovigilance is instrumental in improving transfusion safety, both for donors and patients. Without it, there would be no way to assess the safety of blood components. Haemovigilance is designed to protect patients and blood donors and enables the dissemination of knowledge amongst professionals to minimise the risk of adverse events. Haemovigilance is not a recordkeeping function but focuses on proactively identifying safety issues ('signals') and taking actions to minimise or mitigate risk to patients and donors. SHOT reporting is mainly a passive process while being professionally mandated, analysis of these data is limited by the report being submitted and the details included in the submitted report by reporters. This highlights the importance of a good reporting culture with reporters providing as much detail as possible. Analysis of the submitted reports from both a qualitative and quantitative standpoint forms the basis of signal detection, identification of key learning points and recommendations. Haemovigilance data from 2021 show that while transfusions are generally safe in the UK, there are definite areas for concern where actions are urgently needed to improve transfusion safety, and these are elaborated further in this chapter and throughout the Annual SHOT Report. The risk of death related to transfusion in the UK is 1 in 62,753 components issued and the risk of serious harm is 1 in 17,431 components issued.

Serious adverse reactions and events related to transfusion are reported to SHOT and errors continue to account for most of the reports 2569/3161 (81.3%) (Figure 3.1).

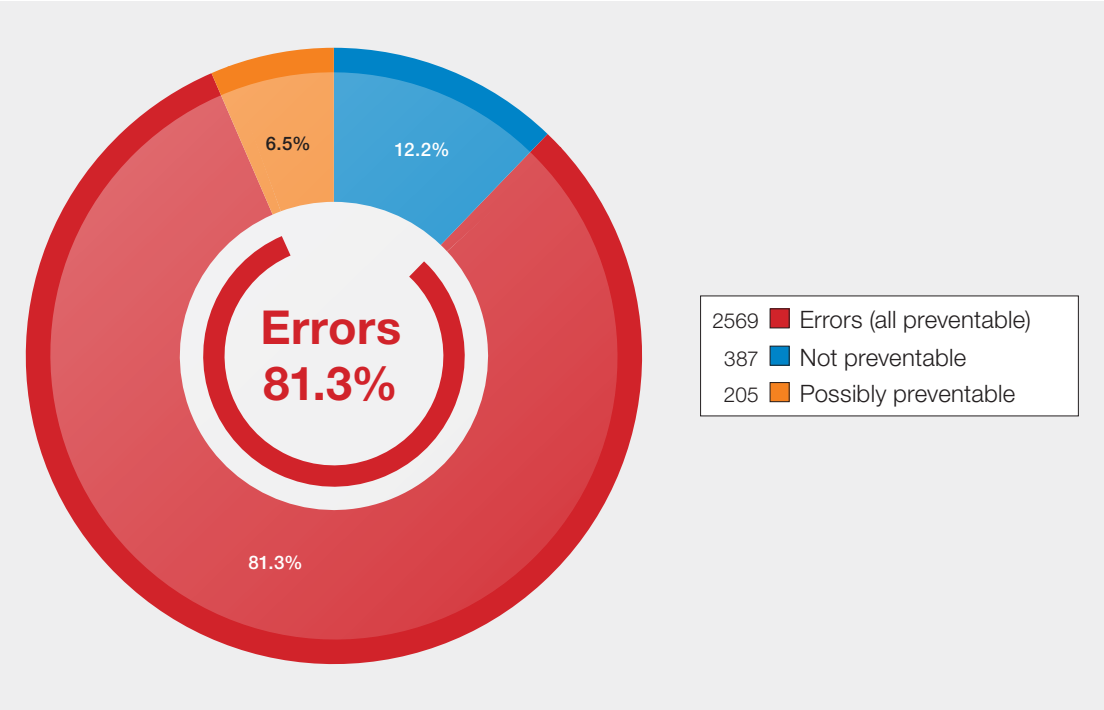


Figure 3.1: Errors account for most reports: 2569/3161

Figure 3.2 shows the trends in transfusion errors reported to SHOT as a percentage of total reports 2014-2021. There is a slight downward trend, but errors continue to contribute to more than 80% of submitted reports and with similar errors reported year on year, it is clear that learning from these incidents is not optimal and incident investigations may not be effective. All systemic causal and contributory factors must be addressed to ensure better transfusion safety.

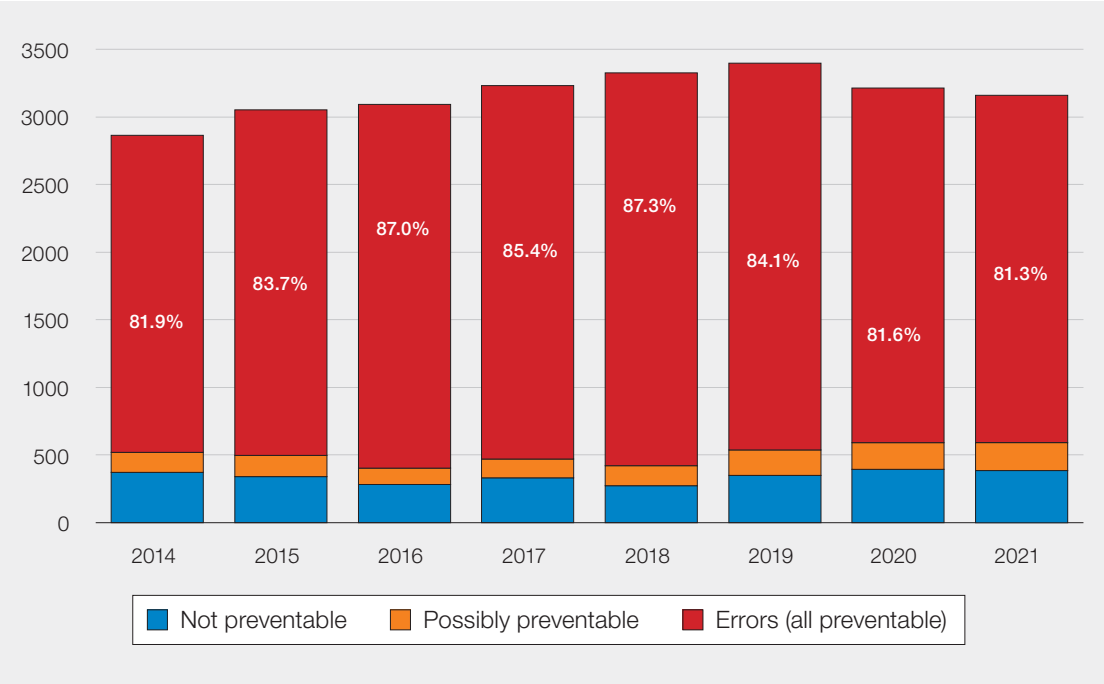


Figure 3.2: Errors as a percentage of total reports 2014-2021

Deaths related to transfusion n=35

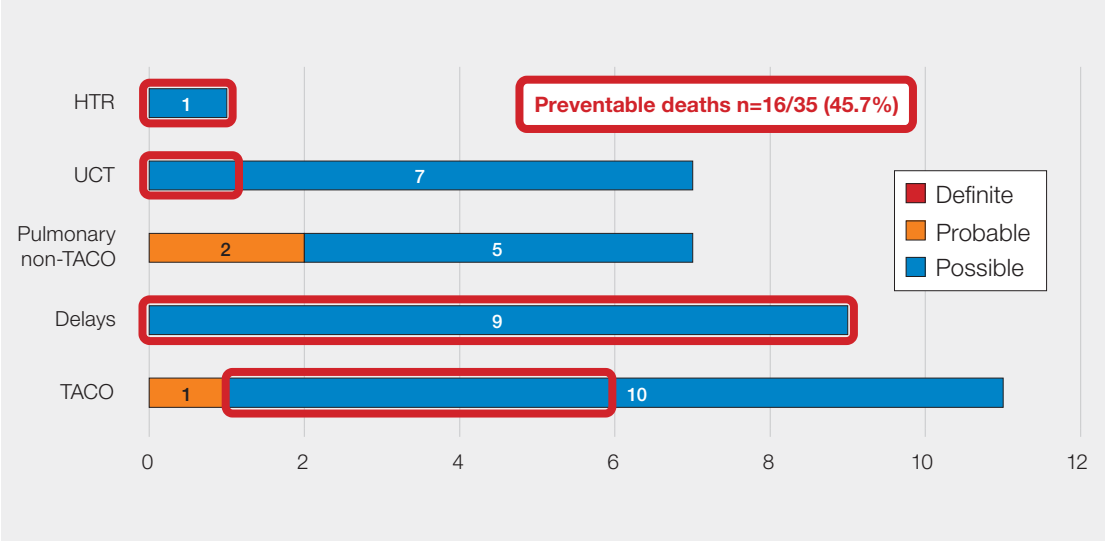
All deaths reported to SHOT are assessed for imputability i.e., the relationship of the blood transfusion to the reaction. The imputability criteria are detailed in the table below

Table 3.1: Definition of imputability levels

		Imputability
N/A	Not assessable	When there is insufficient data for imputability assessment
0	Excluded or unlikely	When there is conclusive evidence beyond reasonable doubt for attributing the adverse reaction to causes other than the blood or blood components or where the evidence is clearly in favour of alternative causes
1	Possible	When the evidence is indeterminate for attributing the adverse reaction either to the blood or blood component or where there may be alternative causes
2	Likely/probable	When the evidence is clearly in favour of attributing the adverse reactions to the blood or blood component
3	Certain	When there is conclusive evidence beyond reasonable doubt

Deaths reported in 2021 were noted mostly relating to TACO (n=11), pulmonary non-TACO (n=7) and delays (n=9). The key factors identified in the transfusion-related deaths are discussed in the relevant chapters of this Annual SHOT Report. Figure 3.3 shows the distribution of deaths related to transfusion reported in 2021.

Figure 3.3: Deaths related to transfusion (with imputability) reported in 2021 n=35



HTR=haemolytic transfusion reactions; UCT=uncommon complications of transfusion; TACO=transfusion-associated circulatory overload

TACO and delays continue to be the leading causes of transfusion-related deaths in the UK, accounting for 20/35 deaths reported (57.1%). A TACO checklist was not completed prior to transfusion in 5/11 cases potentially representing missed opportunities to identify and mitigate risks in vulnerable patients. Incident investigation was carried out in 10 of the TACO deaths reported. Transfusion delays continue to contribute significantly to patient deaths and communication issues were identified in 3/9 cases as one of the most important contributory factors. A higher number of deaths were reported due to non-TACO pulmonary causes and in the UCT category. All are described in detail in the respective chapters with COVID-19 infection and sequelae also noted to be contributing to the patient decline in several cases.

Haemolytic transfusion reaction was responsible for 1 of the deaths reported in 2021, this was a thalassaemia intermedia patient in her 70s with a history of previous transfusion reactions who inadvertently received antigen-positive blood. Acute haemolytic transfusion reaction was listed on the death certificate as a significant condition contributing to death. This case is a reminder that haemolytic transfusion reactions can be lethal and highlights the importance of obtaining previous transfusion history and antibody status. Avoiding alloimmunisation is key especially in multi-transfused patients.

Where deaths are potentially avoidable, it is vital that thorough incident investigations using human factors principles are performed and are generally of good quality with SMART (specific, measurable, achievable, realistic, and timely) improvement actions. The COVID-19 pandemic has been cited as a contributory factor in several of these cases relating to staff pressures and high levels of patient admissions.

Major morbidity n=126

Febrile, allergic or hypotensive transfusion reactions and pulmonary complications continue to account for most of the cases with major morbidity. These are detailed further in the respective subject chapters in this report.

Major morbidity is defined in the SHOT definitions document as:

- Intensive care or high dependency admission and/or ventilation, renal dialysis and/or renal impairment
- Transfusion induced coagulopathy in association with treatment for major haemorrhage (due to the dilution of haemostatic factors following unbalanced resuscitation or overuse of crystalloid/colloid
- Evidence of acute intravascular haemolysis e.g. haemoglobinaemia, gross haemoglobinuria
- Life-threatening acute reaction requiring immediate medical intervention
- Persistent viral infection
- Acute symptomatic confirmed infection
- Sensitisation to D or K in an individual of childbearing potential
- Reaction resulting in a low or high Hb level of a degree sufficient to cause risk to life unless there is immediate medical intervention

Potential for major morbidity is defined as:

- Potential risk of D or K sensitisation in an individual of childbearing potential

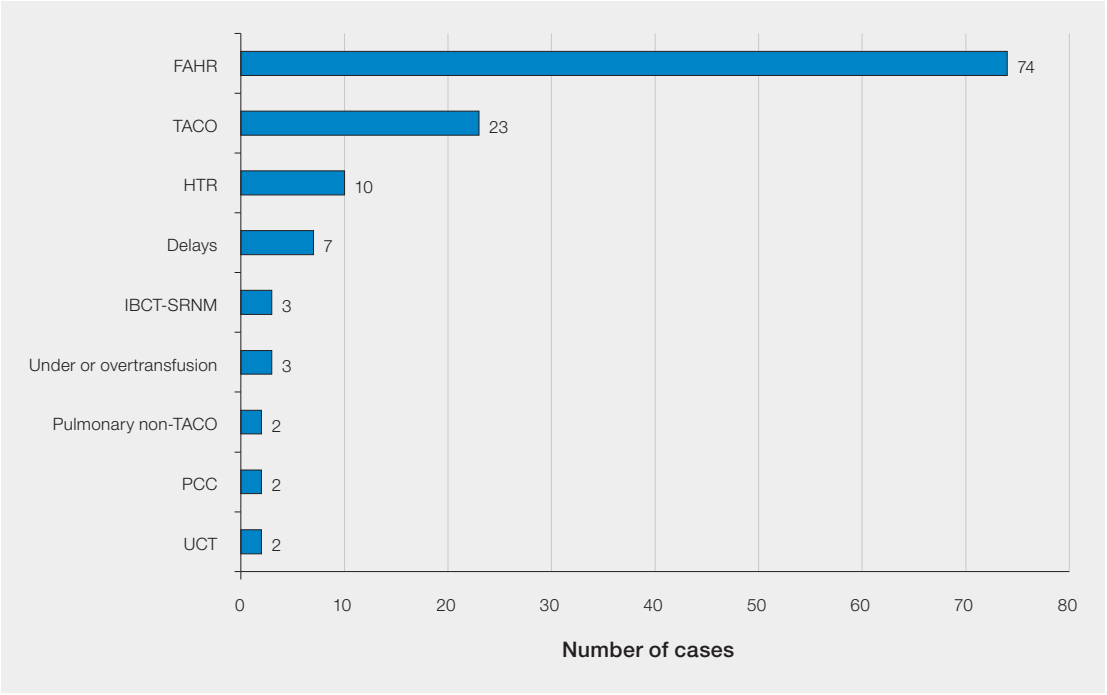


Figure 3.4: Ranking of categories to show number of serious reactions in 2021 n=126

FAHR=febrile allergic and hypotensive reactions; TACO=transfusion-associated circulatory overload; HTR=haemolytic transfusion reactions; IBCT-SRNM=incorrect blood component transfused-specific requirements not met; PCC=prothrombin complex concentrate; UCT=uncommon complications of transfusion

Most cases that resulted in major morbidity were related to FAHR (74/126, 58.7%) with 14 cases reported in paediatric patients of which 10 were related to platelet transfusions. All were allergic reactions except for 1 which was a hypotensive reaction. Minor sequelae were noted in 1 patient, but all others made a complete recovery. In the FAHR cases reported in adults that resulted in major morbidity, 24 were reactions to platelets, 15 of these noted as apheresis platelets. Fourteen patients suffered a reaction following transfusion of multiple components and 20 following a red cell transfusion. Four patients were noted to have had a transfusion that was not clinically indicated according to BSH guidelines. In 57 cases, the patients made a complete recovery, 1 minor sequalae and 2 where outcome was not known. The adult FAHR cases with major morbidity included 37 allergic reactions, 16 febrile, 1 hypotensive and 6 mixed.

In 12/23 cases of TACO that resulted in major morbidity, reporters stated the case had been reviewed but only 3 noted a change in transfusion management for the patient. No incident investigation was carried out in 12/23 cases.

Delays accounted for 7 of the cases with major morbidity and in only 3 cases, reporters stated that an incident investigation had been completed.

Summary data and risks associated with transfusion

Data collected in 2021 are shown in Figure 3.5. Near miss reports are again the largest reporting category, 1155/3161 (36.5%). Reporting and investigating near misses helps identify and control risks before actual harm results, providing valuable opportunities to improve transfusion safety.

Cumulative data for 25 years are shown in Figure 3.6.

Cumulative risk data from SHOT

Figure 3.7 shows the number of reactions reported per 10,000 components issued in the UK between 2010-2021. Although red cells are the most common blood component transfused, platelets overall account for the highest number of reactions reported per 10,000 components. Platelet transfusions are associated with a high frequency of febrile and anaphylactoid reactions (Kiefel 2008). The same pattern is seen in the cases reported to SHOT and these are further elaborated in Chapter 16, Febrile, Allergic and Hypotensive Reactions (FAHR). The incidence of allergic reactions is lower with pooled platelets (suspended in PAS) than apheresis platelets and could most likely be associated with the reduction in plasma content. Reactions to platelets are at least in part caused by release of substances from the platelets themselves and therefore cannot be completely eliminated (Garraud et al. 2016, Maurer-Spurej et al. 2016).

It is also important to note that following the SaBTO recommendations (2019) that there is a reduction in the use of MB-FFP as it is no longer necessary for UK Blood Services to import plasma as a vCJD risk-reduction measure removing the selection of plasma components based on whether the patient was born before/after 1st January 1996. This reduction in use must be taken into account when interpreting the risk of reactions. A review of 7 years data from the ISTARE database had shown that pathogen-inactivated plasma was associated with fewer transfusion reactions than untreated plasma (Saadah et al. 2018).

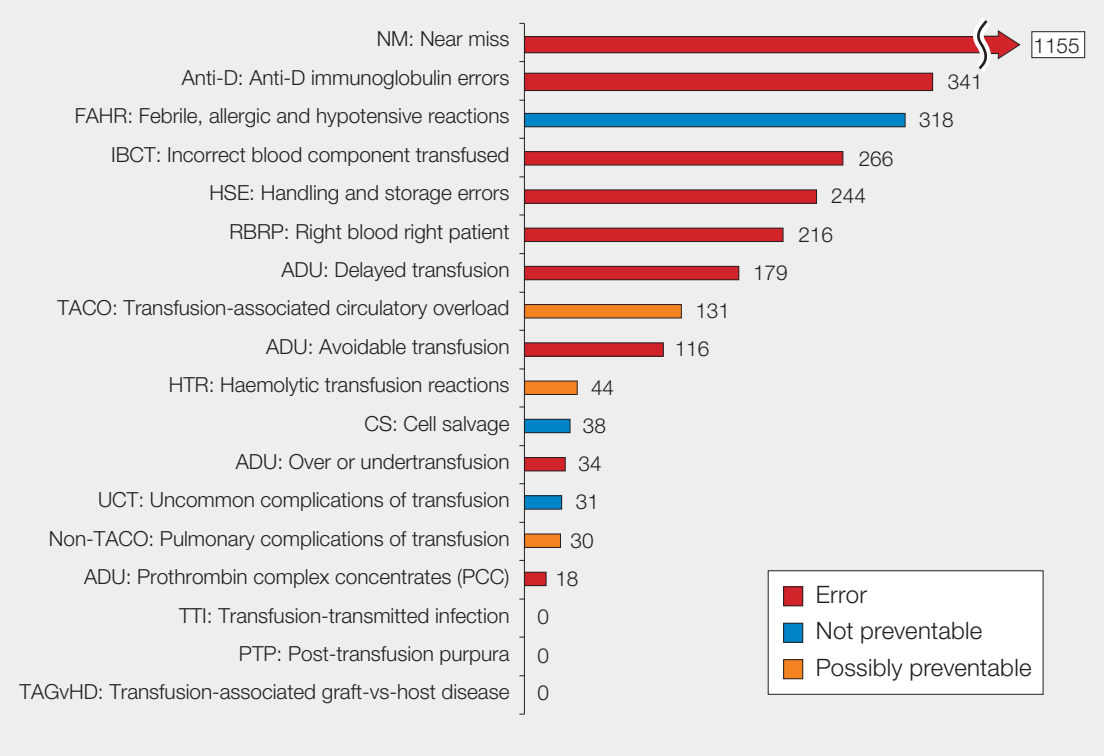


Figure 3.5: Summary data for 2021, all categories (includes RBRP and NM) n=3161

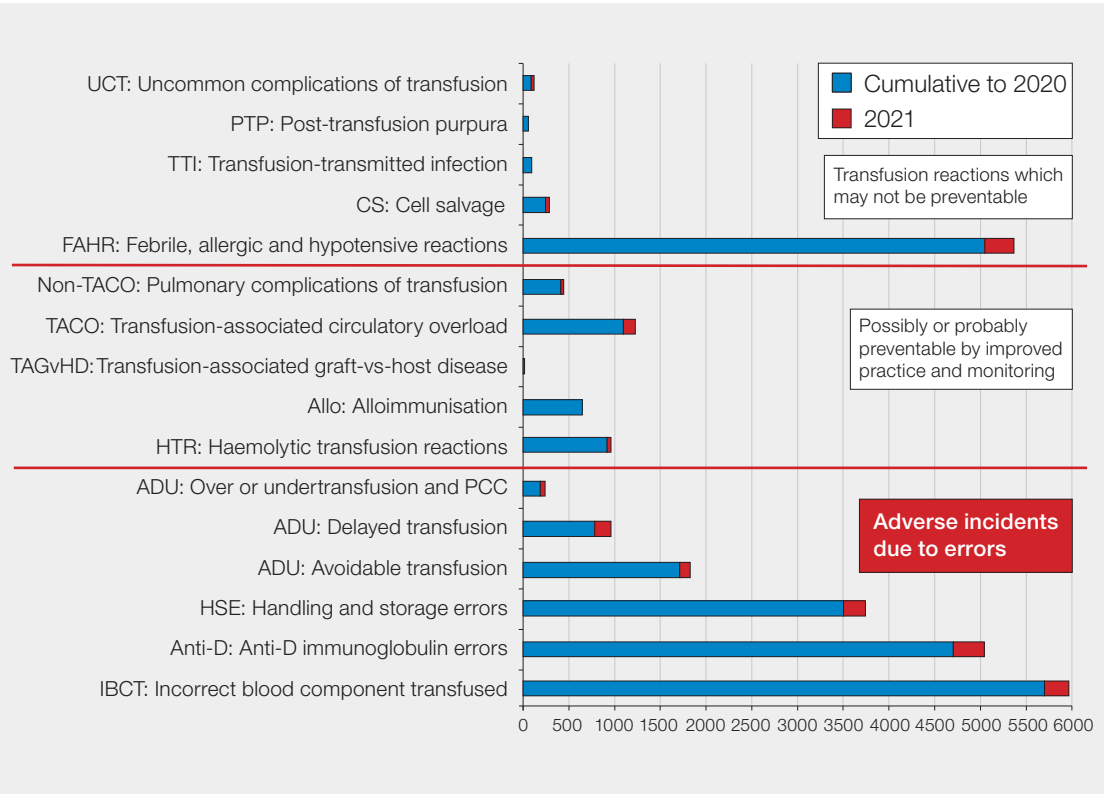
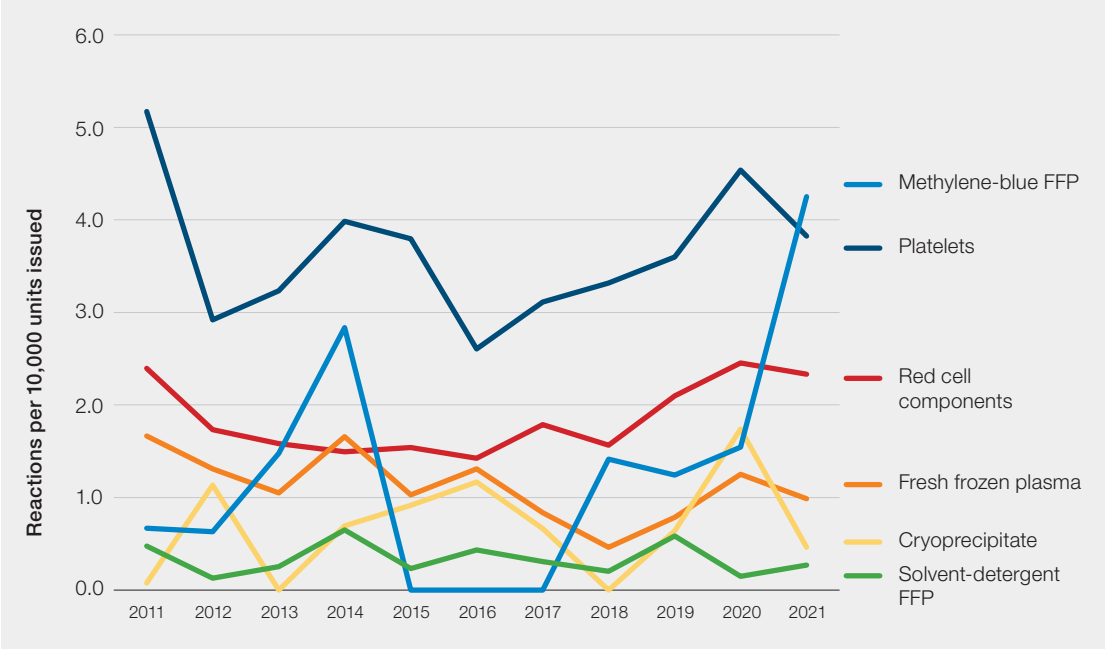


Figure 3.6: Cumulative data for SHOT categories 1996-2021 n=27008

**Data on alloimmunisation is no longer collected by SHOT since 2015*

Figure 3.7: Reactions per 10,000 components, by component type 2011-2021



**Not including COVID-19 convalescent plasma*

The following table shows the risk of transfusion reactions based on SHOT data 2012-2021. It should be noted that these are based on the number of blood components issued as accurate data regarding actual number of transfusions is lacking. Variations in reporting especially in certain categories over the years, changes in definitions, validation, and variation in practices should be considered when interpreting these data. Despite these limitations, the data are useful and provide valuable information about the risks for some of the common transfusion reactions reported to SHOT.

Table 3.2: Risk of transfusion reaction by reaction type 2012-2021

Transfusion reaction	Risk of transfusion reaction based on SHOT data 2012-2021
Febrile, allergic or hypotensive reactions	1 in 8,138
Transfusion-associated circulatory overload	1 in 23,175
Haemolytic transfusion reactions	1 in 55,216
Pulmonary non-TACO	1 in 117,530
Post-transfusion purpura	1 in 3,085,171
Transfusion-associated graft vs host disease	1 in 24,681,368

ABO-incompatible (ABOi) transfusions n=3

Transfusion safety involves a series of complex events from appropriate specimen collection, compatibility testing, and component issue from the blood bank to administration of the blood component at the patient's bedside. Transfusion of blood to the wrong patient is one of the most serious hazards of transfusion which can potentially result in patient death. The chain of events may be initiated by a WBIT leading to transfusion of a wrong component and are the result of procedural errors that are generally preventable with missed opportunities to pick up these errors. Inadvertent ABOi transfusions represent failure of the hospital transfusion process, which needs to be identified and subsequently corrected to prevent similar events happening in the future. Effective investigation of these process failures will help identify measures that need to be taken to improve safety.

In 2021, there were no ABOi red cell transfusions reported and all the 3 ABOi reports were in adult patients involving plasma components; 1 each involving CCP, FFP and cryoprecipitate. Figure 3.8 shows the number of ABOi red cell transfusions reported to SHOT between 1996 and 2021 and Figure 3.9 shows the number of ABOi plasma transfusions reported from 2003 onwards. Figure 3.10 shows the outcome of ABOi red cell transfusions in the 25 years of SHOT reporting. ABOi red cell transfusions can be fatal. Compatibility issues and potential impact on patients in case of plasma components is different. Plasma components such as FFP, cryoprecipitate and CCP should be compatible with the ABO group

of the recipient to avoid potential haemolysis caused by donor anti-A or anti-B. ABO group identical FFP should be given whenever possible; if not possible, FFP of a different ABO group may be acceptable as per BSH guidelines (BSH Green et al. 2018). Haemolysis after the transfusion of ABOi plasma is rare but is of particular risk to infants (Handbook of Transfusion Medicine, 2013).

All 3 cases reported in 2021 were due to a component selection error in the transfusion laboratory with group O plasma component being transfused to non-group O recipient. These occurred despite alerts and/or manual notes on LIMS with staff overriding the alerts. While there was no clinical reaction in 2 cases, 1 patient had complained of loin pain approximately 20 minutes into the transfusion when the error was detected, and the transfusion was stopped. The patient recovered uneventfully. Two of these transfusions occurred during core working hours while 1 was out-of-hours. Pre-administration safety checks were said to have been carried out in all 3 cases. Contributory factors identified in these incidents included staffing issues, high workload, knowledge gaps, suboptimal and unclear handovers, decision fatigue and assumption bias. These are explored in more detail in Chapter 9, Incorrect Blood Component Transfused (IBCT) and Chapter 14, Laboratory Errors in this Annual SHOT Report.

ABO-compatibility for plasma components is different to that of red cells and group O FFP/cryoprecipitate must only be given to group O recipients. One of the key SHOT recommendations in the 2017 Annual SHOT Report was that training in ABO and D blood group principles is essential for all laboratory and clinical staff with any responsibility for the transfusion process and should form part of the competency-assessments (Bolton Maggs et al. 2018). This continues to be pertinent, and a compatibility check is an essential part of the pre-administration process. LIMS should be set up to prevent release of group O FFP to any patients other than group O; but as was evident in the cases reported in 2021, staff were overriding these alerts and not heeding the safety messages. Unjustified overriding of these safety alerts threaten patient safety. A safe alerting system has high specificity and sensitivity, presents clear information, does not unnecessarily disrupt workflow, and facilitates safe and efficient handling. It is recommended that LIMS block release of group O plasma components to non-group O patients. Reducing the number of inappropriate alerts would help in addressing alert fatigue.

In the SCRIPT UK LIMS suppliers survey conducted, all 10 LIMS providers state that ABO/D incompatibilities are controlled for issue of red cells and plasma, with 50% stating override is configurable, and 50% stating ABOi is a ‘hard stop’. ABO/D compatibility rules for haemopoietic stem cell transplant recipient transfusions were configurable in 8/10 LIMS yet reports where incorrect blood components were transfused in transplant recipients continue to be reported. Appropriately configured LIMS can reduce patient harm by preventing ABOi transfusions.

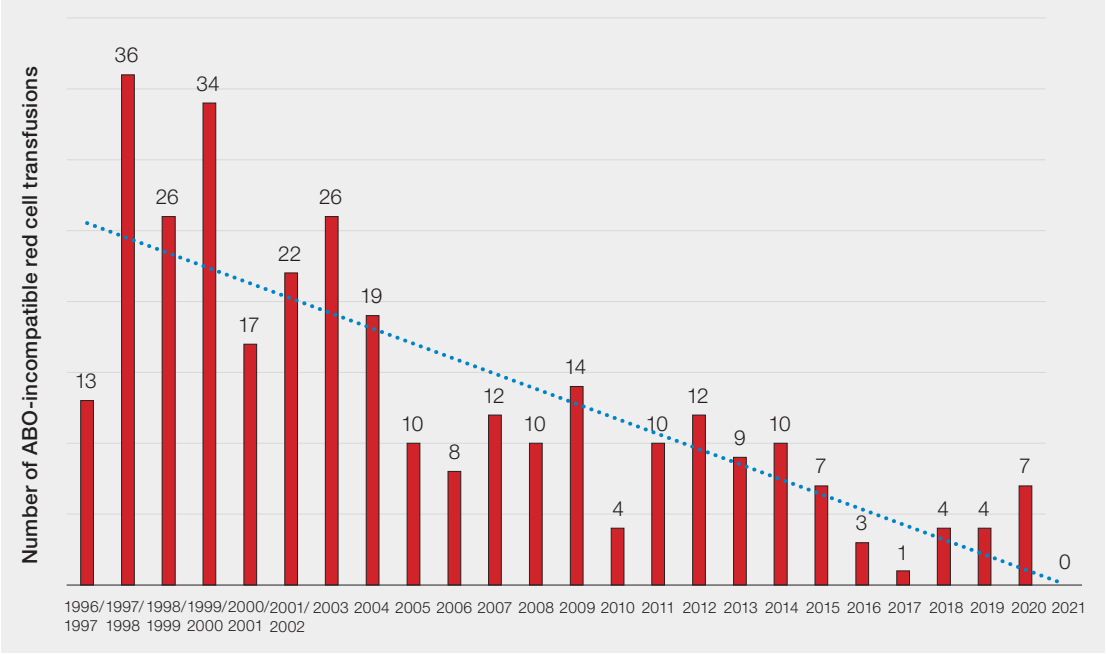
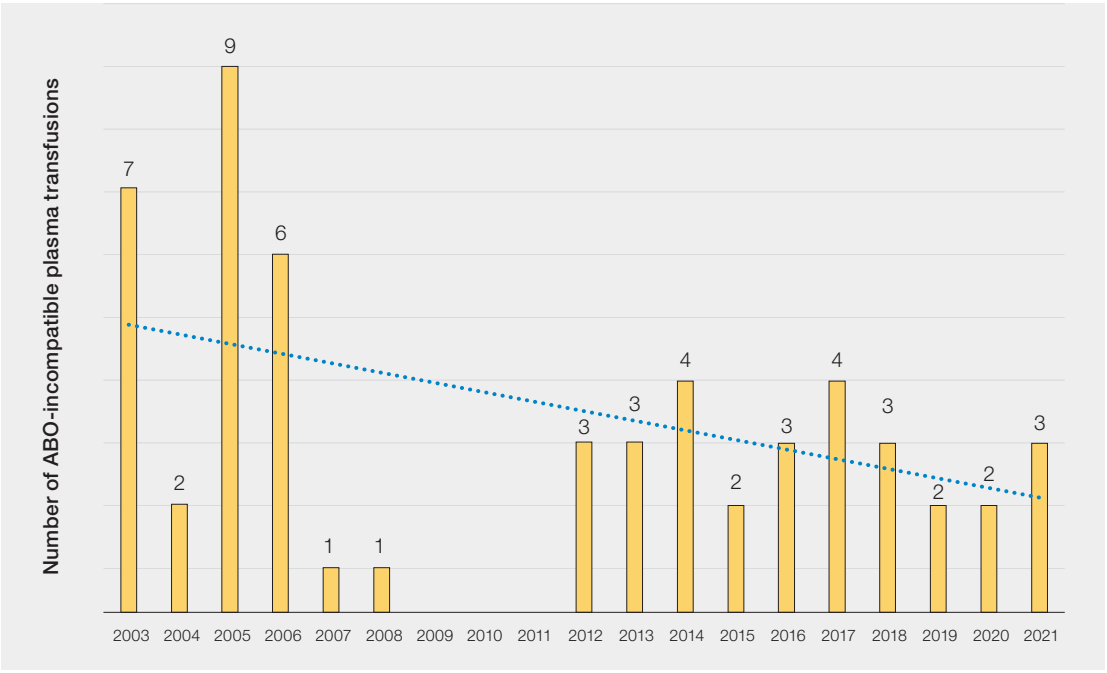


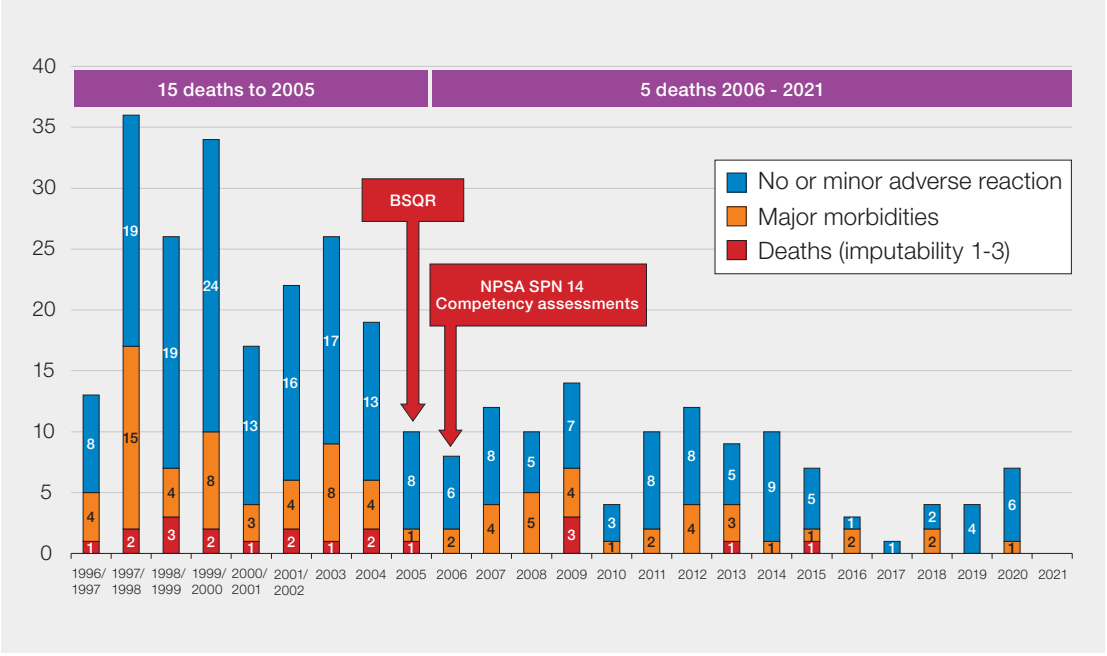
Figure 3.8: Number of ABO-incompatible red cell transfusions 1996-2021

Figure 3.9: Number of ABO-incompatible plasma transfusions 2003-2021



Cryoprecipitate ABOi reports in 2018 and 2021 (n=1); COVID-19 convalescent plasma ABOi in 2020 and 2021 (n=1)

Figure 3.10: Outcome of ABO-incompatible red cell transfusions in 25 years of SHOT reporting



BSQR=Blood Safety and Quality Regulations; NPSA=National Patient Safety Agency; SPN=safer practice notice

Laboratory transfusion staff can get overwhelmed by multiple alerts resulting in 'alert fatigue' i.e., tendency to ignore notifications when they become too frequent and hence potential for errors and impact on transfusion safety. Staff can overcome alert fatigue, identify, and respond to critical issues in real time, and reduce risk continuously over time if these alerts can be transformed into relevant and actionable intelligence.

A structured, proactive approach is suggested to address this by using the following practices:

1. Regularly review and reduce redundant alerts
2. Make all alerts contextual and actionable
3. Ensure appropriate escalation of alerts

4. Apply human factors principles when designing alerts (e.g., format, content, legibility, and colour of alerts). Consider having tiered alerts according to severity, consistently throughout laboratories, so that attention is drawn to those more clinically consequential thus allowing staff to maintain situational awareness and responsiveness

5. Improve the culture of safety in transfusion by creating a shared sense of responsibility between users and suppliers, paying careful attention to safe IT implementation, and engaging leadership in IT planning, implementation, and evaluation.

Data from 2016-2021 show that although there were 19 ABOi red cell transfusions, there were 1778 near misses where an ABOi transfusion could have resulted, the majority of these were WBIT incidents. WBIT constitute the largest subset of near miss cases reported to SHOT in 2021, 734/1155 (63.5%) of all NM events, and these are discussed separately. These may not be detected routinely unless there is a historical record in the transfusion laboratory and demonstrate the importance of the group-check policy (BSH Milkins et al. 2013). These errors, which could have lethal outcomes, demonstrate the importance of positive patient identification at the time of collecting and labelling pre-transfusion samples. As with all NM, WBIT incidents provide valuable opportunities to learn and improve systems. As is evident from the iceberg representation below (Figure 3.11), these occur much more frequently and afford more opportunities to learn than the rarer serious adverse events. When they are not identified or investigated, they are missed opportunities that can contribute to future risks of potentially lethal ABOi.

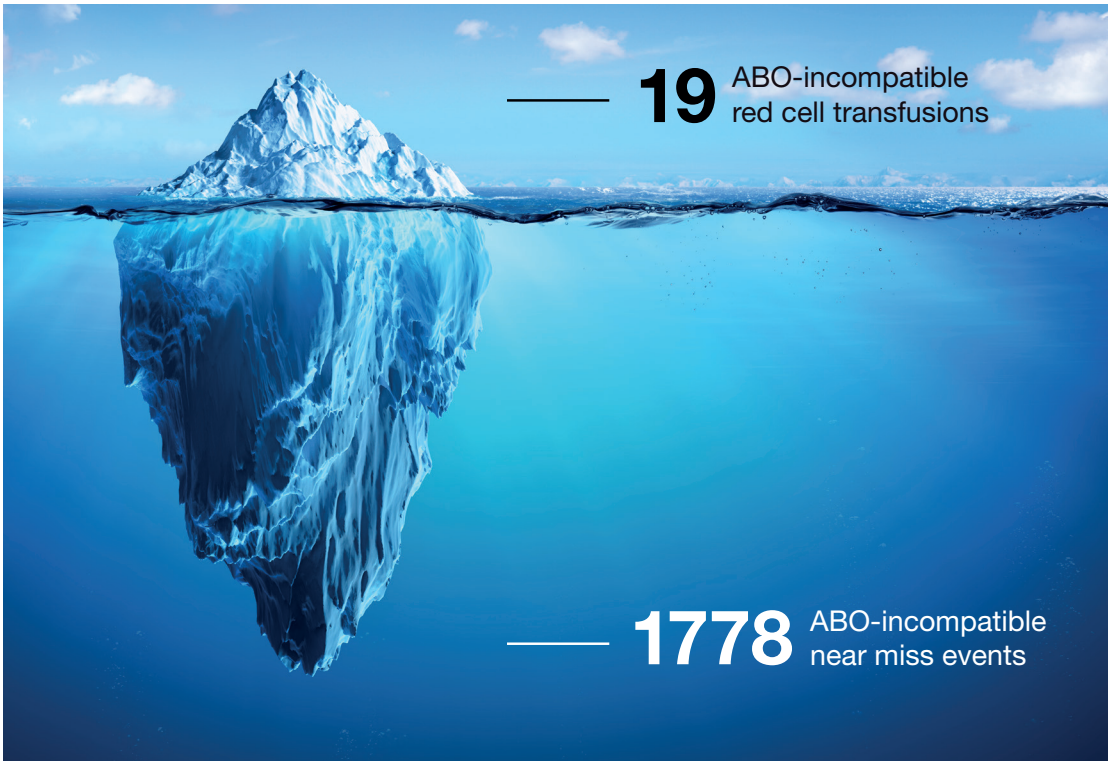


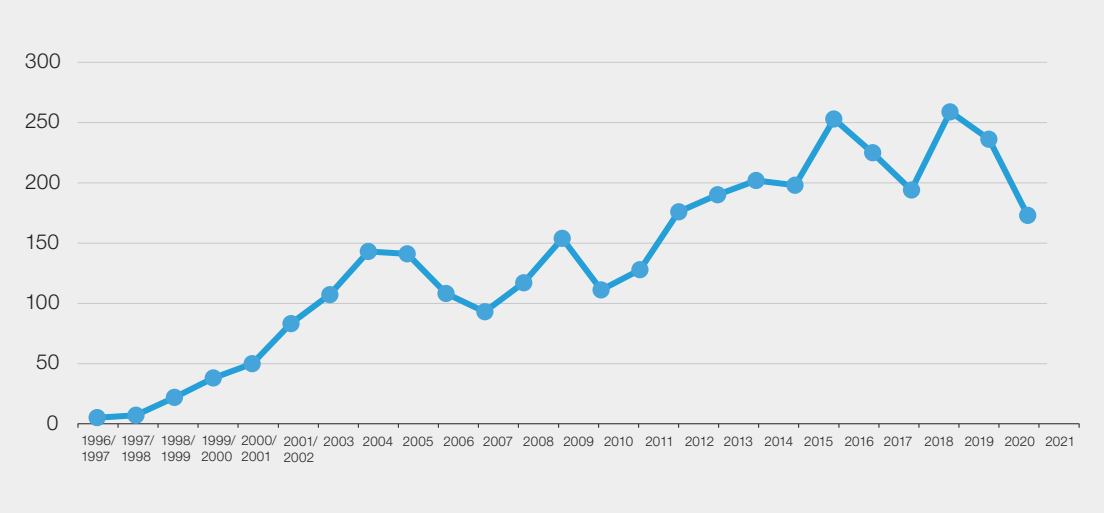
Figure 3.11: ABO-incompatible transfusions 2016-2021: few events (n=19) but many near misses (n=1778)

Investigating these incidents, including WBIT, using human factors principles will help identify the causal and contributory factors; and will inform the corrective and preventative actions to improve patient safety.

Transfusion errors where specific transfusion requirements were not met

Reports related to IBCT-SRNM have been increasing since SHOT reporting began in 1996 (Figure 3.12).

Figure 3.12: IBCT-SRNM errors by year of Annual SHOT Report 1996-2021



Between 2016-2021, IBCT-SRNM errors accounted for 1340/16402 (8.2%) of errors analysed and included in the Annual SHOT Reports. Of these, 135/1340 (10.1%) cases involved paediatric patients. No deaths occurred due to IBCT-SRNM during this period, but 15 cases of major morbidity resulted due to these errors. Errors have been reported from both clinical and transfusion laboratory settings. Most clinical errors are failure to request irradiated or CMV-screened components, and most laboratory errors are failure to complete testing prior to issue, inappropriate use of electronic issue or providing the incorrect phenotype. These are detailed further in Chapter 9, Incorrect Blood Components Transfused (IBCT).

Staff involved in blood transfusions must have basic knowledge of blood components, indications for use, rationale for specific transfusion requirements and an understanding of the availability of alternative options. Staff authorising, prescribing, and ordering blood should be aware of the risks and benefits of transfusions including risks of not meeting specific transfusion requirements for patients and must be able to identify and manage and possible reactions and their management.

Conclusion

Transfusion remains very safe with few serious incidents or deaths related to pathological events. However, patients continue to be at risk from potentially preventable causes, particularly TACO and avoidable transfusion delays. Error-related transfusion incidents continue to be the largest group reported to SHOT, and it is essential that the learning from incidents reported to SHOT inform healthcare improvements. Errors made at any point in the transfusion pathway can have a serious patient impact and interventions introduced to address/prevent these must be system oriented and sustainable.

Near misses present valuable learning opportunities and should be investigated thoroughly. As emphasised in recent Annual SHOT Reports, system level changes are needed for safer transfusions. With the transfusion process being multidisciplinary, staff training should ensure that each participant is aware how important their individual role is as part of the whole process to ensure patient safety. Ensuring transfusion process safety is as important as blood component safety and quality. Potential for error exists at each step in the process of transfusion and learning from incidents should drive improvements in healthcare.

Recommended resources

SHOT Bite No. 1a and 1b: Incident Investigation
SHOT Bite No. 17: Near Miss
SHOT Bite No. 20: IBCT-SRNM
https://www.shotuk.org/resources/current-resources/shot-bites/

Safe transfusions in transplants document
https://www.shotuk.org/resources/current-resources/

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