

Haemovigilance of reactions associated with red blood cell transfusion: comparison across 17 Countries

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Vox Sanguinis

Background and Objectives The recent establishment of the National Healthcare Safety Network Hemovigilance Module in the United States affords an opportunity to compare results with those of other developed nations.

Materials and Methods Using data from national haemovigilance systems, reactions associated with red blood cell (RBC) transfusion and residual risks of transfusion-transmitted infectious diseases were assembled from 17 nations. Country-specific rates of adverse events were pooled using random-effects Poisson regression.

Results Febrile non-haemolytic and delayed serologic transfusion reactions were the most frequent adverse events reported after RBC transfusion, occurring in 26 patients per 100 000 RBC units and 25 patients per 100 000 RBC units administered, respectively. Rates of allergic, febrile non-haemolytic and delayed haemolytic transfusion reactions in the United States were significantly greater than the pooled rates from other countries. Frequencies of adverse events generated from the national haemovigilance programme in the United States were considerably lower than when obtained through active surveillance.

Conclusion Haemovigilance reports of adverse events in the United States are comparable to, or greater than, reports from other developed countries. Rates generated from haemovigilance programmes are lower than those obtained through active surveillance. The lack of universal leucoreduction of RBC units may be a contributing factor to the higher rate of some adverse events in the United States.

Key words: adverse reaction, haemovigilance, international, transfusion.

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Introduction

First established in France and Japan in 1993 as a response to the vulnerability of the blood supply after the emergence of HIV [1, 2], haemovigilance systems aim to improve the safety of the blood supply through systematic surveillance of transfusion-related adverse events. Such systems generate recommendations so as to encourage safety throughout the entire process, from blood donation

through monitoring of recipients. Several directives from the European Union relate to the regulation, monitoring and safety of blood products, with the haemovigilance component helping to direct member nations' reporting of serious transfusion-related adverse reactions and events [3]. Therefore, haemovigilance systems are widespread in European nations, with prime examples being the United Kingdom with its voluntary Serious Hazards of Transfusion reporting system (99.5% participation in 2013) [4], and the Netherlands with its Transfusion and Transplantation Reactions in Patients haemovigilance programme (98% participation in 2013) [5].

The USA opened its first nationwide haemovigilance system in 2010 as a voluntary module of the National

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Healthcare Safety Network [6]. Results from this new system are now available and can be compared with existing haemovigilance programmes. As more nations begin to implement haemovigilance programmes, an assessment of the abilities of national systems to report reactions and a comparative review of event rates can be informative.

Methods

Haemovigilance data on transfusion-related adverse reactions and transfusion-transmitted infections were available from the national haemovigilance systems in each of the following countries: Australia [7], Canada [8], Denmark [9], Finland [10], France [11], Germany [12], Ireland [13], Japan [14–16], the Netherlands [5], New Zealand [17], Norway [18], Portugal [19, 20], Spain [21], Sweden [22], Switzerland [23], United Kingdom [4] and the USA [6]. Data regarding adverse events after RBC transfusion were collected: allergic reactions, anaphylactic reactions, febrile non-haemolytic transfusion reactions (FNHTR), acute and delayed haemolytic transfusion reactions, hypotensive reactions, transfusion-related acute lung injury (TRALI), transfusion-associated dyspnoea, transfusion-associated circulatory overload (TACO), delayed serologic transfusion reactions, post-transfusion purpura and transfusion-transmitted bacterial sepsis. Some countries reported additional categories and these were included as well (acute transfusion-related pain, haemosiderosis). For each country, data from the most recently available report were utilized.

Risks of transfusion-transmitted viruses were available for agents with mandated testing. Reporting methods differ by country, although in the USA, data regarding residual risk of viral transmission were derived from donor testing since long-term follow-up of recipients is not feasible [24]. Because it is theoretically possible that a donor could have newly acquired a virus but is seronegative at the time of the blood donation, seroconversion rates during this infectious window period are used to predict the residual risk of viral infection [24].

Statistical analyses

Rates of non-infectious adverse events were calculated for each country using the number of events (numerator) and the number of RBC units administered (denominator). Rates were reported for each country as events per 100 000 RBC units for non-infectious adverse events and events per million RBC units for infectious adverse events. Canada and Spain were exceptions; adverse events were recorded for components combined (RBCs, platelets, plasma). In the USA, TACO was the only event in which reporting was performed for components combined (RBCs, platelets, plasma). In secondary analyses, adverse event

rates from active surveillance in the USA were compared with the rates generated from the passive haemovigilance programme; in these instances, the rates were given using several denominators (per patient, per unit and per transfusion-related hospital stay).

Following current recommendations for summarizing rates [25], random-effects Poisson regression models were generated to pool rates of transfusion-related adverse events with 95% confidence intervals. That is, the numbers of events were fit to a Poisson distribution with the number of RBC units included as an offset. Countries that reported zero events were included and, in such instances, a one-sided exact Poisson 97.5% confidence interval was used for the country-specific rate. Heterogeneity was assessed using a gamma density function (shape parameter = 2, scale = 0.5) for the variance of the random intercept (between-country variance) in the Poisson model. This Rate Index of Heterogeneity (RIH) is unit-independent, encompasses a range from 0% to 100% heterogeneity and is directly derived from the underlying random-effects Poisson model for assessment of rates. Analyses were conducted using Stata/MP 13.1 (College Station, Texas, USA).

Results

Allergic reactions after RBC transfusion occurred in 11 patients per 100 000 RBC units administered (95% CI: 6.55/100 000 to 18.08/100 000) with a RIH of 58.5% (Fig. 1). The rate of allergic reactions in the USA was significantly greater (53.61/100 000; 95% CI: 49.59/100 000–57.87/100 000) than the pooled rate of the other developed countries combined (9.7/100 000; 95% CI: 5.93/100 000–15.85/100 000). Some countries reported anaphylactic reactions separately and these occurred at a lower rate of 0.9 per 100 000 RBC units (RIH = 17.1%). In the United Kingdom, acute transfusion reactions were defined as instances of anaphylaxis or severe allergic reactions, severe febrile reactions, severe hypotensive reactions and severe mixed reactions; these occurred at a rate of nine patients per 100 000 RBC units.

There was variability in the rates of FNHTR across countries (RIH = 94.0%). Overall, the rate was 26 patients per 100 000 RBC units, although the Netherlands, New Zealand and the USA recorded rates in excess of 100 patients per 100 000 RBC units, or approximately one in one-thousand units (Fig. 2). The rate of FNHTR in the USA was significantly greater (106.32/100 000; 95% CI: 100.63/100 000–112.25/100 000) than the pooled rate of the other developed countries combined (22.85/100 000; 95% CI: 9.74/100 000–53.63/100 000). Hypotensive reactions after RBC transfusion occurred less frequently, in 2 patients per 100 000 RBC units (RIH = 34.3%). In Spain,

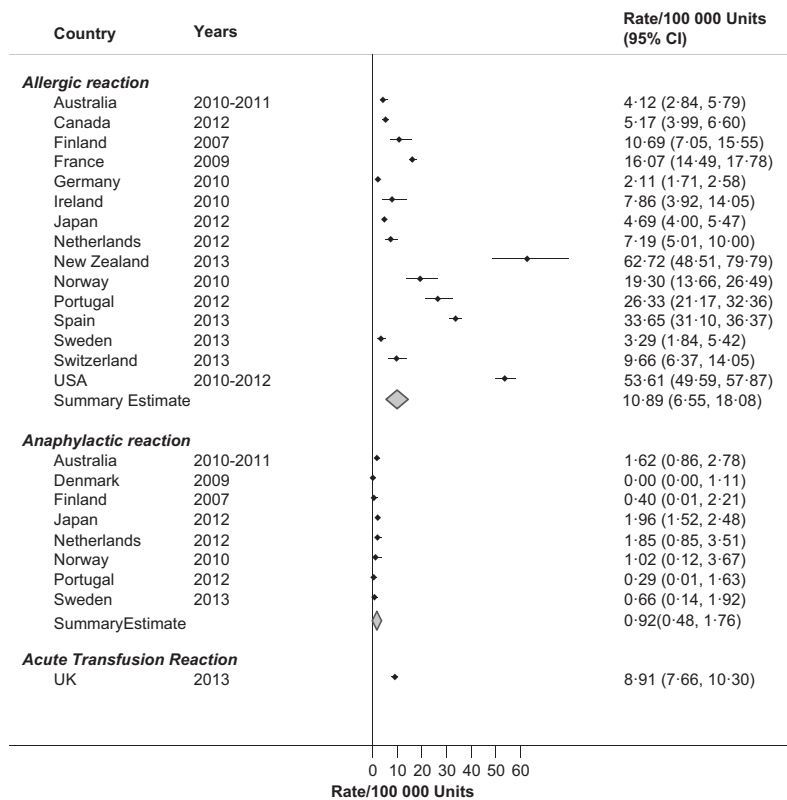


Fig. 1 Rates of allergic reactions in haemovigilance reports, by Country.

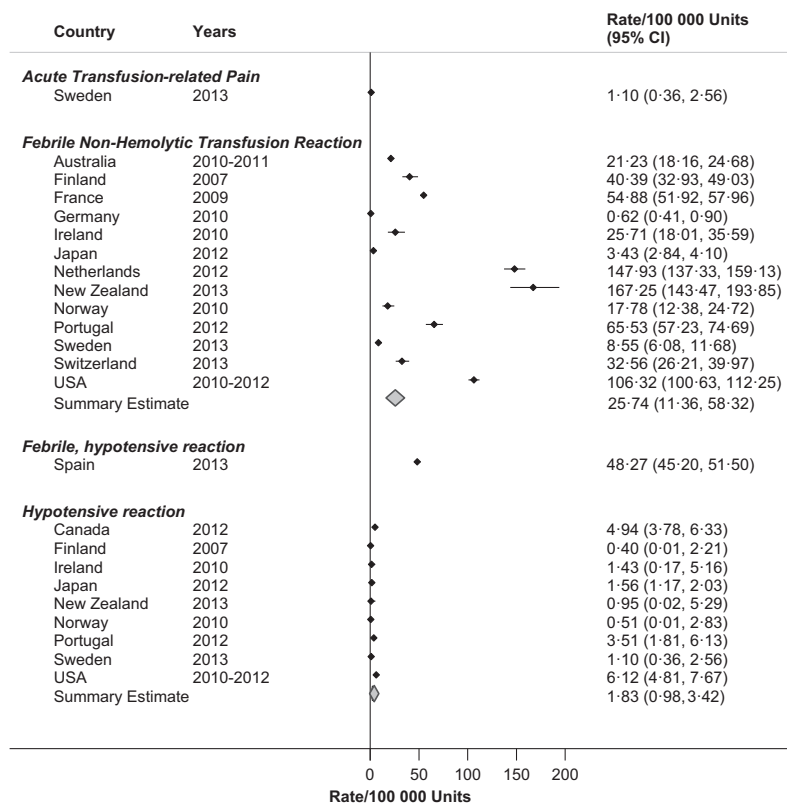


Fig. 2 Rates of acute transfusion reactions in haemovigilance reports, by Country.

hypotensive reactions were combined with FNHTR, yielding a rate of 48 patients in 100 000 RBC units.

Acute transfusion-related pain was reported separately in the Swedish haemovigilance system, occurring in one patient per 100 000 RBC units (Fig. 2).

Rates of acute and delayed haemolytic transfusion reactions are shown in Fig. 3. Acute haemolytic transfusion reactions occurred in 1 patient per 100 000 RBC units administered (RIH = 8.3%), while a delayed haemolytic transfusion reaction occurred in approximately two patients per 100 000 RBC units (RIH = 37.6%). In Germany, Spain and the United Kingdom, both acute and delayed haemolytic transfusion reactions were combined, yielding a pooled rate of 1.4/100 000 units (RIH = 57.0%). Both Ireland and the USA tended to have delayed haemolytic transfusion reactions at a greater frequency than other countries, although the confidence intervals for Ireland were wide indicating fewer RBC units due to a smaller population. The rate of delayed haemolytic transfusion reactions in the USA was significantly greater (6.94/100 000; 95% CI: 5.54/100 000–8.58/100 000) than the pooled rate of the other developed countries combined (1.6/100 000; 95% CI: 0.9/100 000–2.8/100 000).

Respiratory reactions to RBC transfusion are shown in Fig. 4. Transfusion-associated dyspnoea was reported in

two patients per 100 000 RBC units (RIH = 77.4%). New Zealand was an outlier in this category. TRALI associated with RBC units was quite low (Fig. 4), at a pooled rate of 0.35 per 100 000 RBC units (RIH = 73.2%).

TACO occurred in approximately three patients for each 100 000 RBC units transfused, although there was some variation in rates across countries (Fig. 5; RIH = 76.9%). Haemosiderosis was reported separately in France and Spain and occurred at a rate of 0.3 for every 100 000 units transfused (RIH = 99.6%).

The results for delayed serologic transfusion reactions are given in Fig. 6, showing heterogeneity across countries (RIH = 91.5%; rate = 24.6/100 000 units), with elevated rates in the Netherlands and Switzerland. Post-transfusion purpura occurred rarely, at a rate of 0.08 per 100 000 RBC units administered (Fig. 6; RIH = 0%). Other transfusion-related reactions, as shown in Fig. 6, varied by country and were not described in great detail in the country-specific annual reports.

Documented cases of transfusion-transmitted bacterial sepsis occurred rarely, approximately once in every million RBC units administered (Fig. 7; RIH = 57.8%).

Table 1 displays the estimate residual risk of viral transmission due to RBC transfusion. Rates were very low. HIV and hepatitis B and C viruses were most often monitored through haemovigilance, while data regarding

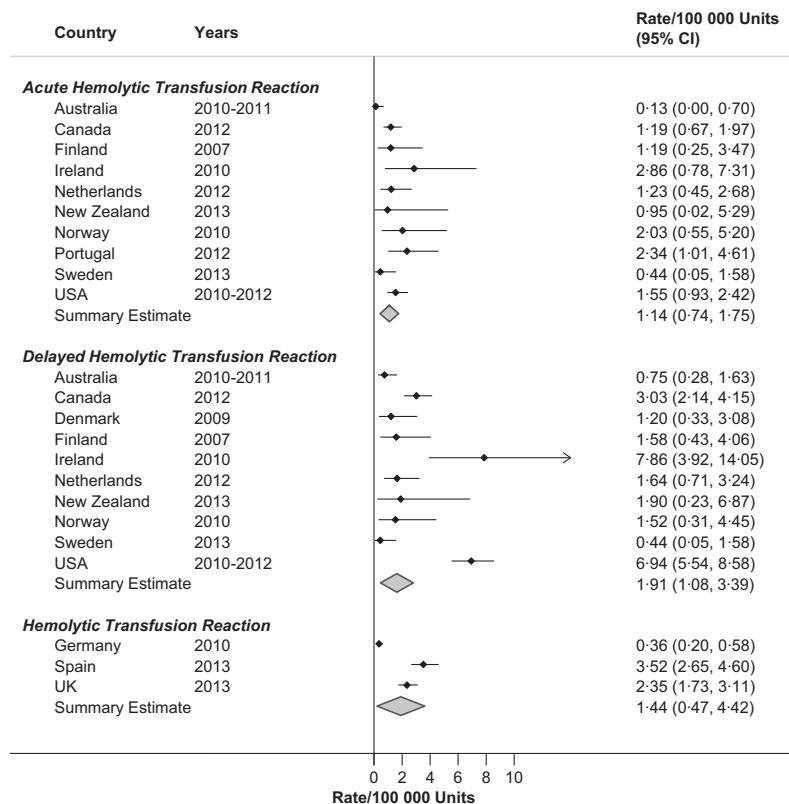


Fig. 3 Rates of haemolytic reactions in haemovigilance reports, by Country.

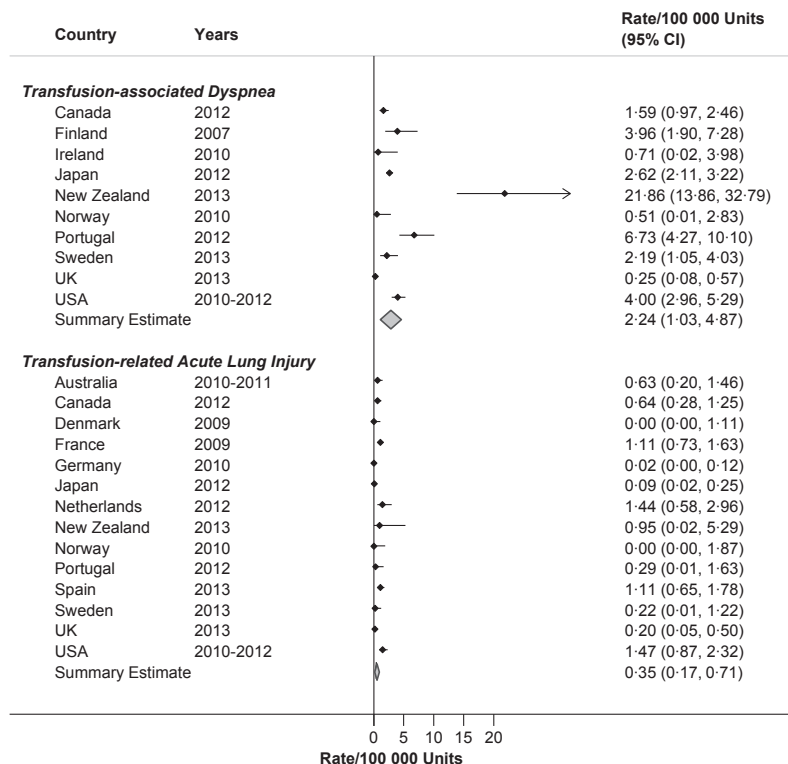


Fig. 4 Rates of respiratory transfusion reactions in haemovigilance reports, by Country.

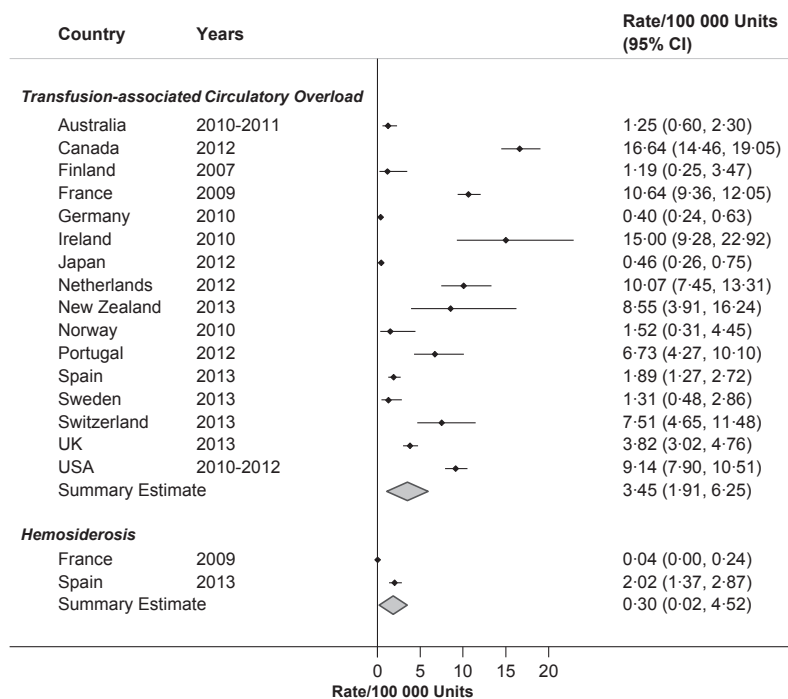


Fig. 5 Rates of circulatory overload in haemovigilance reports, by Country.

other viruses (cytomegalovirus, Epstein-Barr, etc.) were available from only a few countries.

Rates of adverse reactions in the USA, as generated through haemovigilance, were compared to documented

rates obtained through active surveillance. Published frequency rates of TACO are shown in Table 2 [26–32]. When units were used as the denominator, the pooled rate of TACO was 368 per 100 000 units or one in every 271

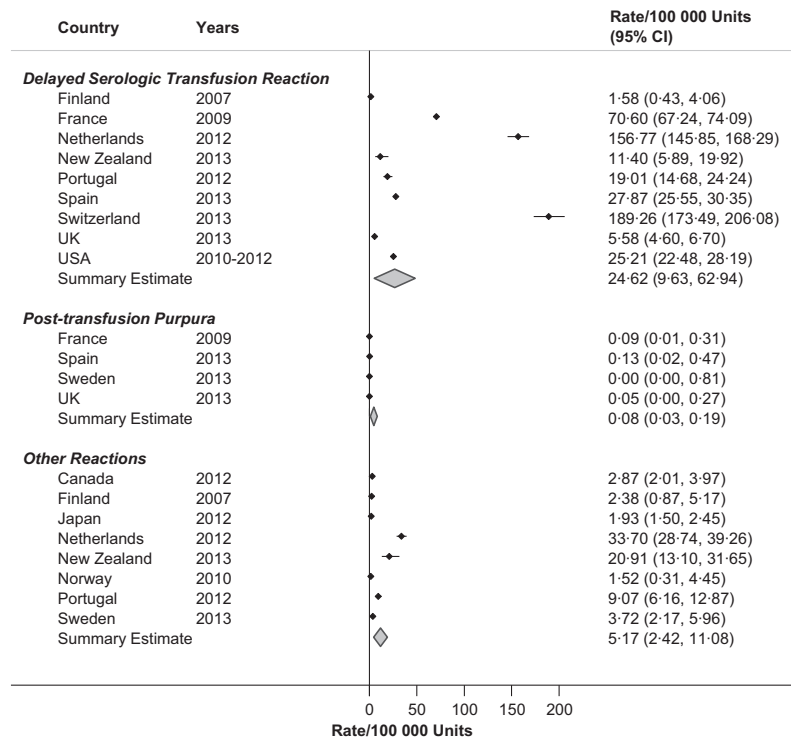


Fig. 6 Rates of other transfusion reactions in haemovigilance reports, by Country.

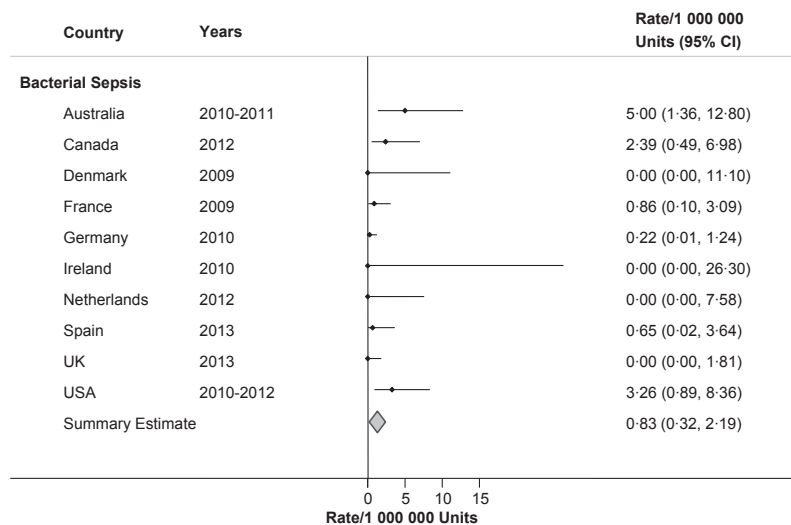


Fig. 7 Rates of transfusion-transmitted bacterial sepsis in haemovigilance reports, by Country.

units from active surveillance. This compares with one in 10942 units from passive surveillance through the haemovigilance programme in the USA.

In general, rates of FNHTR were lower in leucoreduced versus non-leucoreduced products within the same population (Table 3) [33–44]. With prospective surveillance, the pooled rate of FNHTR was 1191/100 000 units or one in every 84 units; this compares with one case in 3885 RBC units from haemovigilance. The rates tended to be

greater in children than adults; one in 20 children who received a transfusion developed FNHTR (all component types combined). FNHTR rates also appeared higher in patients with cancer.

Discussion

Haemovigilance systems in developed nations report low rates of adverse events after RBC transfusion. For

Table 1 Risk of transfusion-transmitted viruses in haemovigilance reports, by Country

Virus	Country	Years	Rate
Cytomegalovirus	France	2009	1 in 1.5 million
	The Netherlands	2012	<1 in 620 000
	Norway	2004–2010	1 in 1.4 million
Epstein–Barr Virus	The Netherlands	2012	<1 in 620 000
Hepatitis A Virus	France	2009	<1 in 3 million
	The Netherlands	2012	<1 in 620 000
Hepatitis B Virus	Norway	2004–2010	1 in 1.4 million
	Australia	2012–2013	1 in 720 000
	Canada	2006–2009	1 in 1.7 million
	Denmark	2009	1 in 270 000
	Finland	2007	<1 in 450 000
	France	2009	<1 in 3 million
	Germany	2010	1 in 6.1 million
	Ireland	2010–2011	<1 in 190 000
	Japan	2012	1 in 880 000
	The Netherlands	2012	<1 in 620 000
	New Zealand	2013	1 in 68 000
	Spain	2013	1 in 1.9 million
	Switzerland	2013	1 in 400 000
	UK	2013	1 in 2.8 million
	USA	2006–2008	1 in 300 000
Hepatitis C Virus	Australia	2012–2013	<1 in 1 million
	Canada	2006–2009	1 in 6.7 million
	Denmark	2009	<1 in 540 000
	Finland	2007	<1 in 450 000
	France	2009	<1 in 3 million
	Germany	2010	<1 in 6.1 million
	Ireland	2010–2011	<1 in 190 000
	The Netherlands	2012	<1 in 620 000
	Sweden	2013	<1 in 460 000
	Switzerland	2013	1 in 6.7 million
	UK	2013	<1 in 2.8 million
USA	2007–2008	1 in 1.1 million	
Hepatitis E Virus	France	2009	<1 in 3 million
	Japan	2012	1 in 1.3 million
	UK	2013	1 in 2.8 million
Human Immunodeficiency Virus	Australia	2012–2013	<1 in 1 million
	Canada	2006–2009	1 in 8 million
	Denmark	2009	<1 in 540 000
	Finland	2007	<1 in 450 000
	France	2009	<1 in 3 million
	Germany	2010	1 in 6.1 million
	Ireland	2010–2011	<1 in 190 000
	The Netherlands	2012	<1 in 620 000
	New Zealand	2013	<1 in 140 000
	Switzerland	2013	1 in 4.1 million
	UK	2013	<1 in 2.8 million
USA	2007–2008	1 in 1.5 million	
Human T-Lymphotropic Virus	Australia	2012–2013	<1 in 1 million
	The Netherlands	2012	<1 in 620 000
	USA	2000–2001	1 in 2.1 million
Parvovirus B19	France	2009	1 in 3 million

Table 1 (Continued)

Virus	Country	Years	Rate
Varicella Zoster Virus	The Netherlands	2012	<1 in 620 000
	Norway	2004–2010	1 in 1.4 million
	Norway	2004–2010	1 in 1.4 million

anaphylaxis, hypotension and purpura, the rates were quite consistent across countries. Rates of some reactions, however, were notably elevated in particular countries. Rates of allergic reactions were higher in the USA and New Zealand; rates of FNHTR were elevated in the USA, the Netherlands and New Zealand; and TACO was more commonly reported in Canada, France, Ireland, the Netherlands and the USA. New Zealand reported a greater rate of transfusion-associated dyspnoea in 2013. However, in a recent report, more than half of the dyspnoea cases were reclassified when additional information was retrieved (many being reclassified as TACO) [45].

Overall, TACO occurred at a rate of three cases per 100 000 units when pooled from haemovigilance reports, with the incidence of TACO in the USA alone being one in 10942 units. However, based on active surveillance studies from the USA, 0.6% to 8% of patients receiving RBC transfusions develop TACO. This disparity between active and passive surveillance rates may stem from insufficient reporting of reactions to haemovigilance systems. For example, researchers from the Mayo Clinic noted that there were 176 cases of TACO in their investigation but only three were in the transfusion database that housed adverse reactions – and even then, these three cases were not labelled as TACO [31].

Given the more comprehensive monitoring of fever after RBC transfusion, the variability of rates of FNHTR across countries may be a reflection of dissimilarities in patient populations, differential use of pretransfusion antipyretic medications or the preparation of RBC units. Of note, the USA has not adopted universal leucoreduction (70.5% RBC units leucoreduced in 2011)[46] and FNHTR has been reported more frequently in patients receiving non-leucoreduced products [33, 39, 41, 42, 47]. FNHTR rates in the USA are higher than the pooled FNHTR rates in other developed countries and the use of non-leucoreduced products could partially account for these findings.

The variability in rates of allergic reactions across nations may stem from differences in case definitions. In Australia, for example, a severe allergic reaction would be recorded if rash, allergic dyspnoea, angioedema, generalized pruritis or urticaria occurred within 24 h of the transfusion [7]. In the USA, a severe allergic reaction

Table 2 Incidence of transfusion-associated circulatory overload in the United States

Author, year	Source	Type of study	Incidence	Incidence	Components	Year
Frequency per patient						
Popovsky [26], 1996	5 Massachusetts hospitals, total hip or knee replacements	Retrospective cohort	1.0% of patients	1 in 95 patients	All	1992–1993
Bierbaum [27], 1999	235 hospitals, total hip or knee arthroplasty	Prospective cohort	8.0% of patients	1 in 12 patients	All	1996–1997
Rana [28], 2006	Mayo Clinic, intensive care units	Prospective cohort	1.85% of patients	1 in 54 patients	All	2003
Li [29], 2011	Mayo Clinic, medical intensive care unit	Prospective cohort	5.7% of patients	1 in 18 patients	All	2 years, before 2007
Andrzejewski [30], 2012	Hospital in Massachusetts, all ages	Retrospective cohort	0.6% of patients	1 in 166 patients	RBCs	2005–2008
Clifford [31], 2015	Mayo Clinic, adults, non-cardiac surgery	Retrospective cohort	5.5% of patients 3.0% of patients	1 in 18 patients 1 in 33 patients	All All	2004 2011
Frequency per unit:						
Rana [28], 2006	Mayo Clinic, intensive care units	Prospective cohort	281/100 000 units	1 in 356 units	All	2003
Andrzejewski [30], 2012	Hospital in Massachusetts, all ages	Retrospective cohort	189/100 000 units	1 in 530 units	RBCs	2005–2008
Harvey [6], 2014	National Healthcare Safety Network, 77 facilities	Voluntary haemovigilance	9/100 000 units	1 in 10942 units	All	2010–2012
Clifford [31], 2015	Mayo Clinic, adults, non-cardiac surgery	Retrospective cohort	4000/100 000 units 1087/100 000 units	1 in 25 units 1 in 92 units	RBCs RBCs	2004 2011
Frequency per hospital stay						
Menis [32], 2014	Medicare administrative database	Retrospective	0.06% of stays	1 in 1602 stays	All	2011

would be recorded if two or more symptoms (conjunctival oedema; oedema of lips, tongue and uvula; erythema and oedema of the periorbital area; generalized flushing; hypotension; localized angioedema; maculopapular rash; pruritus; respiratory distress or bronchospasm; urticaria) occurred during or within 4 h of the cessation of transfusion [48]. Moreover, in some countries such as New Zealand, both non-severe and severe allergic reactions are reported [17] (perhaps reflecting their higher rates as shown in Fig. 1) while in the USA, reporting of non-severe allergic reactions is not required [48]. Other reasons for differences in rates may be variations in hospital-specific reporting practices and the mandatory/voluntary nature of the reporting.

For events such as delayed serologic transfusion reaction and delayed haemolytic transfusion reaction, the definition hinges on laboratory testing and not symptoms. Rate differences may be a reflection of the resources afforded for testing of alloantibodies and the feasibility of longitudinal observation. Information regarding follow-up procedures or standardization of procedures would enhance the interpretability of rates. Alternatively, haemovigilance programmes may reconsider the usefulness of expending

resources to capture such data when the likelihood of consistent, meaningful information is low. Perhaps periodic systematic testing in high users of transfusion would be more appropriate such as in patients with sickle-cell disease or cancer, or in participants of cardiovascular disease registries.

Results from this investigation indicate that the residual risks from currently tested infectious agents are very low and, in many instances, could be considered negligible. However, it is the potential risks from other infectious agents (not yet tested) which are more pertinent at this time. These include vCJD, hepatitis E virus, dengue viruses, chikungunya virus, *Babesia* spp., West Nile virus and Middle East respiratory syndrome coronavirus – although the list of potential threats includes approximately 70 such agents [49]. For example, in the USA, transfusion-transmitted babesiosis has been documented in more than 200 instances and is associated with the greatest case fatality rate of transfusion-related infections [50].

Haemovigilance for transfusion-transmitted infection is meant to capture pathogen transmission from donor to recipient. The requirements include the demonstration of

Table 3 Incidence of febrile non-haemolytic transfusion reaction in the United States

Author, year	Source	Type of study	Incidence	Incidence	Components	Year
Frequency per patient Paglino [33], 2004	Yale-New Haven Hospital, Connecticut, all ages	Retrospective cohort	1-33% of patients	1 in 75 patients	25% leucoreduced RBCs	1995-1998
Sanders [34], 2005	St. Jude Children's Research Hospital	Retrospective cohort	0-79% of patients	1 in 127 patients	99% leucoreduced RBCs	2000-2002
Kennedy [35], 2008	Wake Forest University, Comprehensive Cancer Center	Prospective active surveillance	4-94% of children	1 in 20 children	All	2002
Frequency per unit			8-70% of patients	1 in 11 patients	RBCs and PLTs, leucoreduced	1993-1997
Menitove [36], 1982	33 Hospitals in South-eastern Wisconsin, all ages	Retrospective cohort	478/100 000 units	1 in 209 units	RBCs and whole blood	1980
Dziedzickowski [37], 1995	Dana-Farber Cancer Institute, Boston, Massachusetts	Prospective cohort	2147/100 000 units	1 in 47 units	RBCs, leucoreduced after storage	1993
Federowicz [38], 1996	Dana-Farber Cancer Institute, Boston, Massachusetts	Prospective cohort	1109/100 000 units	1 in 90 units	RBCs, leucoreduced before storage	Before 1995
Uhlman [39], 2001	Barnes-Jewish Hospital, St. Louis, Missouri	Retrospective cohort	124/100 000 units	1 in 809 units	Non-leucoreduced RBCs	1999
Domen [40], 2003	Cleveland Clinic, Ohio, all ages	Retrospective cohort	81/100 000 units	1 in 1238 units	Leucoreduced RBCs	2000
Paglino [33], 2004	Yale-New Haven Hospital, Connecticut, all ages	Retrospective cohort	30/100 000 units	1 in 3293 units	RBCs	1993-2001
King [41], 2004	The Johns Hopkins Hospital, all ages	Retrospective cohort	340/100 000 units	1 in 294 units	25% leucoreduced RBCs	1995-1998
Ezidiogwu [42], 2004	State University of New York, Syracuse, adults, nonsurgical	Retrospective cohort	180/100 000 units	1 in 556 units	99% leucoreduced RBCs	2000-2002
Sanders [34], 2005	St. Jude Children's Research Hospital	Retrospective cohort	369/100 000 units	1 in 271 units	4% leucoreduced RBCs	1994
Kennedy [35], 2008	Wake Forest University, Comprehensive Cancer Center	Prospective active surveillance	186/100 000 units	1 in 538 units	99-5% leucoreduced RBCs	2001
Harvey [6], 2014	National Healthcare Safety Network, 77 facilities	Voluntary haemovigilance	162/100 000 units	1 in 619 units	RBCs	1998-2000
Oakley [43], 2015	Vanderbilt University Medical Center, all ages	Retrospective cohort	79/100 000 units	1 in 1259 units	Leucoreduced RBCs	2001-2002
Frequency per hospital stay			360/100 000 units in children	1 in 278 units in children	RBCs	2002
Menis [44], 2015	Medicare administrative database	Retrospective	639/100 000 units	1 in 156 units	RBCs and PLTs, leucoreduced	1993-1997
			106/100 000 units	1 in 941 units	RBCs	2010-2012
			184/100 000 units in children	1 in 545 units in children	Leucoreduced RBCs	2011-2013
			36/100 000 units in adults	1 in 2775 units in adults	Leucoreduced RBCs	2011-2013
			0-07% of stays	1 in 1419 stays	RBCs	2011-2012

the pathogen in the transfused component, or in the donor at the time of donation, or in an additional component from the same donation, or in an additional recipient of a component from the same donation [48]. Also required is documentation that there are no other potential exposures to the pathogen that could be identified in the recipient and either evidence that the recipient was not infected with the pathogen prior to transfusion or evidence that the pathogen strains are related by molecular or extended phenotypic comparison testing [48]. This is a difficult target to reach when such in-depth testing is not usually conducted with each transfusion. Therefore, the pooled rate of transfusion-transmitted bacterial sepsis was very low (0.83/1 million RBC units). There are few published reports of prospective surveillance for comparison purposes. Barrett and colleagues [51] found a bacterial contamination rate of 3.2/100 000 RBC units, while Dzieczkowski and colleagues [37] reported this rate to be 14.1/100 000 RBC units. In a more recent report from Denmark, 35% of RBC units contained viable bacteria which were obtained from donors 50 years of age or older [52].

There are avenues for improvement in existing haemovigilance systems. The addition of active surveillance components may enhance reporting. Expansion of electronic medical records to incorporate more information regarding blood administration may augment

comprehensiveness. Adjunct programming routines could be enacted to capture pre- and post-transfusion temperatures so that detection of FNHTR could be improved. Likewise, electronic capture of pre- and post-transfusion blood pressures could assist the detection of hypotensive reactions. Some have already merged records from transfusion and apheresis medicine with the main electronic medical record [53–55]. The SCANDAT2 is a successful example of linked donor and recipient health information in Sweden and Denmark [55]. In addition, international networks (e.g. International Haemovigilance Network [56], Global Vigilance and Surveillance Database for Medical Products of Human Origin [57], World Health Organization Global Database on Blood Safety [58]) provide opportunities for surveillance and the improvement of blood safety.

National haemovigilance programmes afford an important aspect of patient safety. Such systems generally capture serious transfusion reactions but, with improvement, could generate more comprehensive information. Cross-country comparisons can provide the basis for discovery and continuous process improvement.

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